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**Enantioselective copper catalysed intramolecular C–H insertion reactions of α-diazo-β-keto sulfones, α-diazo-β-keto phosphine oxides and 2-diazo-1,3-diketones; the influence of the carbene substituent.**

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## Abstract:

Enantioselectivities in C–H insertion reactions, employing the copper-bis(oxazoline)-NaBARF catalyst system, leading to cyclopentanones are highest with sulfonyl substituents on the carbene carbon, and furthermore, the impact is enhanced by increased steric demand on the sulfonyl substituent (up to 91%ee). Enantioselective intramolecular C–H insertion reactions of α-diazo-β-keto phosphine oxides and 2-diazo-1,3-diketones are reported for the first time.

## Introduction:

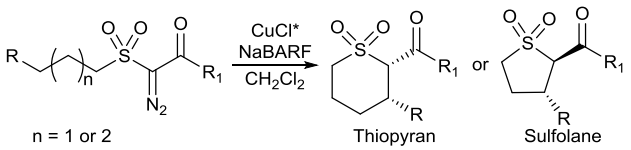
Intramolecular carbenoid insertion into a previously unactivated C–H bond is a powerful method for new C–C bond formation. The generation and subsequent reactions of carbenoids from an α-diazocarbonyl precursor *via* transition-metal catalysis have been extensively explored due to the diverse range of synthetically powerful reaction pathways observed, including Wolff rearrangement, aromatic addition, cyclopropanation, ylide formation and X–H insertion.[1-5]

Rhodium and copper are among the most utilised transition metals for catalysing intramolecular C–H insertion reactions. Initial research in the area began with copper, although poor reaction efficiencies were observed.[6] The turning point in C–H insertion chemistry came with the introduction of the rhodium carboxylate catalysts *e.g.* $Rh_2(OAc)_4$ which made the reaction more generally applicable.[7] The tendency for $Rh_2(OAc)_4$ catalysed C–H insertion to form five membered rings initially reported by Wenkert[8] has been extensively explored by Taber and developed to a useful methodology for the synthesis of cyclopentanones.[9-11]

In most instances of the reports of C–H insertion, the "carbenoids" are acceptor-acceptor type, and usually both of the electron withdrawing groups are carbonyls with a couple of exceptions including nitro, cyano, phosphoryl and sulfonyl groups.[4, 12-14]

Focusing specifically on the effect of substitution on the carbene substituent, early work by Hashimoto on α-diazo-β-keto esters found that increasing the size of the alkoxy group of the ester moiety led to an increased level of asymmetric induction, going from a methyl to a CH(*i*-Pr)$_2$ group resulted in an increase in enantiocontrol of 46 %ee to 76 %ee.[15] Interestingly, Taber observed the opposite effect in the cyclisation of β-ketoesters, when increasing the steric bulk of the ester from a methyl group to a dimethylpentyl group, this resulted in a decrease in diastereomeric excess, 58 %de to 34 %de.[16] Other electron withdrawing substituents on the carbene carbon have been explored, albeit to a lesser extent than the esters. Corbel and co-workers conducted investigations into the intramolecular C–H insertion of α-phosphorylated cyclopentanones. They observed low yields of cyclopentanones due to the occurrence of the Wolff rearrangement which competed with the C–H insertion reaction.[13] Monteiro synthesised 2-phenylsulfonyl cyclopentanones from α-diazo-β-keto sulfones *via* C–H insertion in good yields of up to 75%, which was comparable to their ester equivalents.[12]

For the first twenty years of research in this area the vast majority of carbocyclic rings formed were five membered, with some exceptions,[17-19] when the insertion occurs into the sulfonyl group rather than the carbonyl containing chain the presence of the sulfone alters the geometry of the C–H insertion transition state enabling access to six membered thiopyrans, and, where the six membered ring is not accessible, five membered sulfolanes (Scheme 1).[17, 20-22]

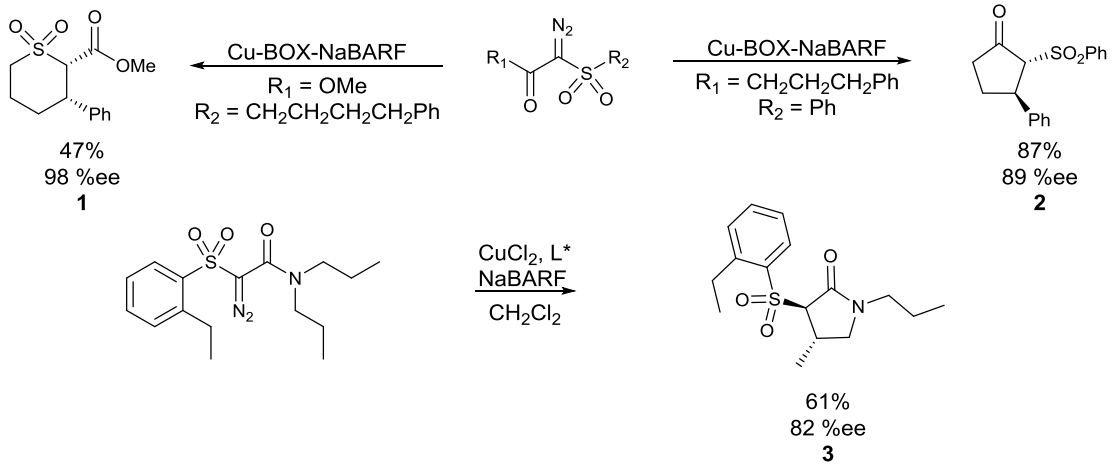



**Scheme 1** Copper catalysed C–H insertion reactions of α-diazo-β-oxo-sulfones.[22]

The first catalytic asymmetric C–H insertion reaction was carried out in 1990 in which a cyclopentanone was generated in up to 12 %ee using a rhodium catalyst.[23] Since this

pioneering work, insertion reactions have been further developed to achieve high levels of enantiocontrol with a diverse range of chiral rhodium catalysts.[1, 2]

Previous studies from our laboratory have shown that the use of a copper catalyst system comprised of copper-bis(oxazoline)-NaBARF is very effective in inducing high levels of enantiocontrol in C–H insertions of α-diazocarbonyl compounds bearing arylsulfonyl substituents. Thiopyrans **1**, cyclopentanones **2** and γ-lactams **3** have been synthesised in excellent enantioselectivities of up to 98 %ee,[22] 89 %ee[24] and 78 %ee[25] respectively (Scheme 2). The presence of the additive NaBARF was found to be essential for achieving high levels of asymmetric induction,[24, 26] through abstraction of chloride by the sodium cation of NaBARF, thereby altering the catalyst geometry as Fraile has previously discussed.[27, 28]



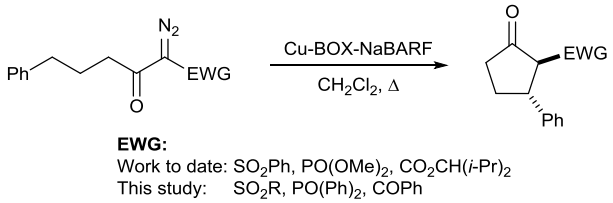

**Scheme 2** Copper catalysed C–H insertion reactions of α-diazo-β-keto sulfones, α-diazo-β-oxo sulfones and α-diazoacetamides.[22, 25]

The enantioselectivities described above are the highest reported for copper catalysed C–H insertion reactions[29] and, indeed, are comparable with the enantioselectivities reported for the rhodium mediated C–H insertions.[2]

Our studies into enantioselective intramolecular C–H insertion reactions of α-diazo-β-keto sulfones have predominately focused on the steric and electronic effects of the substituent adjacent to the C–H insertion site using phenyl sulfones. Specifically, we have observed that

more sterically demanding groups at the site of insertion lead to higher levels of enantiocontrol.[26] The presence of both electron withdrawing and electron donating substituents on the phenyl moiety, lead to a slight decrease in enantioselectivity relative to the unsubstituted compound, in line with observations by Hashimoto.[30] Interestingly, the presence of an electron donating substituent leads to a less efficient C–H insertion reaction.[31]

Focusing on the substituent on the carbene, our work to date has been predominantly conducted with phenyl sulfone derivatives. We briefly explored C–H insertion with α-diazo-β-ketophosphonates and α-diazo-β-ketoester substrates; however, these proceeded with lower enantioselectivities when compared to the sulfone containing compounds.[32]



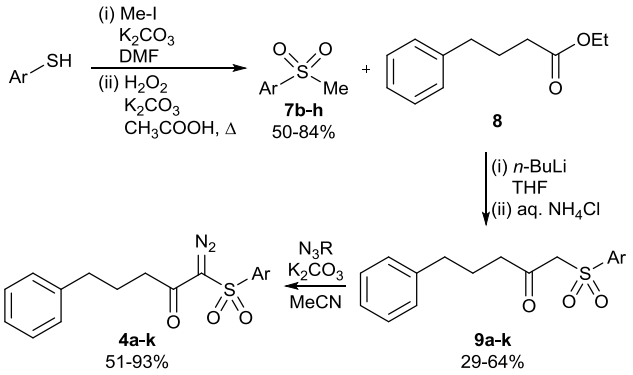

**Scheme 3** Enantioselective copper catalysed C–H insertion of various α-diazocarbonyl compounds.

We report herein our recent investigations into the effect of a wider range of electron withdrawing groups present on the carbene carbon (Scheme 3), firstly, by exploring the importance of the substituent on the sulfone moiety and secondly, by expanding the substrate scope to include phosphine oxides and diketones, both of which are the first reports of asymmetric intramolecular C–H insertion for these types of compounds.

## Results and Discussion:

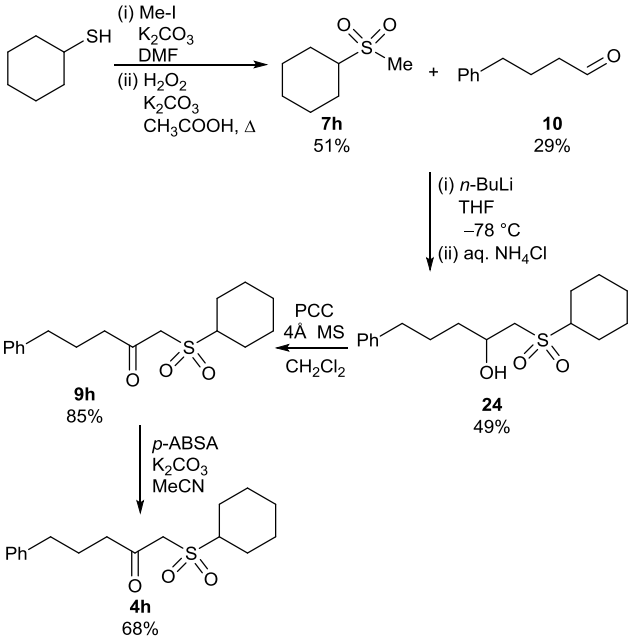
Thirteen α-diazocarbonyl substrates were selected for investigation including eleven α-diazo-β-keto sulfones (**4a**-**4k**), an α-diazo-β-keto phosphine oxide (**5**) and a 2-diazo-1,3-diketone (**6**) all of which were novel other than **4a**.[26] These compounds were chosen to enable exploration of the impact of alteration of the substituent, including variation of the electronic and steric properties of the sulfonyl substituents, in addition to the replacement of the sulfone by phosphine oxides and ketones. To permit comparability across the series this investigation was conducted with a phenyl substituent at the site of insertion, which, in our earlier studies, had led to the optimum outcome.[26]

The substrates were synthesised following standard diazo transfer to the requisite sulfone, phosphine oxide and diketone precursors (Scheme 4), (Scheme 6) and (Scheme 7) respectively. The precursor sulfones **4b–h** were synthesised from the corresponding thiols by methylation using iodomethane, followed by oxidation of the crude sulfide using hydrogen peroxide to form methyl sulfones **7b** to **7h**, which were then treated with butyllithium in the presence of ethyl 4-phenylbutanoate **8** to form β-ketosulfones **9a–g** and **9i–k** (Scheme 5). A slightly modified sequence was required for the synthesis of the cyclohexyl sulfone **9h**; as condensation of methyl cyclohexylsulfone **7h** with ethyl 4-phenylbutanoate **8** proved unsuccessful, reaction with the aldehyde **10** followed by oxidation was employed to provide the β-ketosulfone **9h** (Scheme 5). A similar approach was used for the synthesis of the phosphine oxide, methyldiphenylphosphine oxide was lithiated and condensed with ethyl 4-phenylbutanoate **8** to lead to the β-keto phosphine oxide **11** (Scheme 6). To generate the diketone precursor acetophenone was condensed with the acylbenzotriazole **12** (Scheme 7).

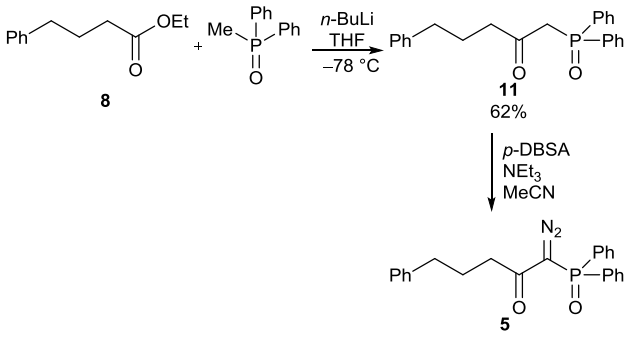



**Scheme 4** General procedure for α-diazo-β-keto sulfone synthesis **4a-k**.

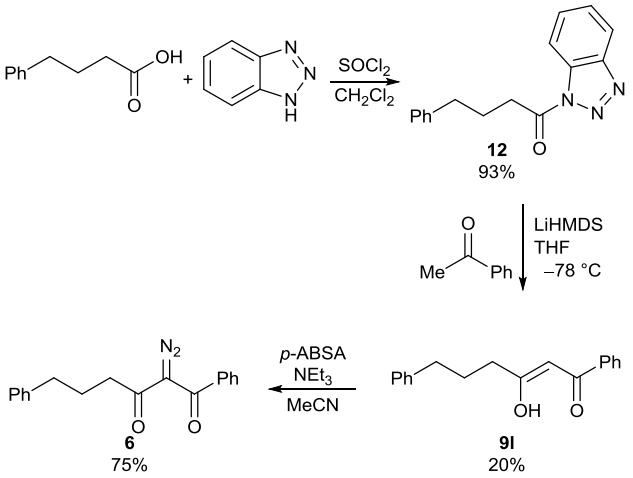
**a** = phenyl, **b =** 4-fluorophenyl, **c =** 2-naphthalene, **d** = 1-naphthalene, **e** = mesityl, **f** 2-ethylphenyl, **g** = 4-methoxyphenyl, **h** = cyclohexyl, **i** = 4-methylphenyl, **j** = 4-bromophenyl, **k** = methyl




**Scheme 5** Synthetic route to α-diazo-β-keto cyclohexyl sulfone **4h.**




**Scheme 6** Synthetic route to α-diazo-β-keto phosphine oxide **5.**



**Scheme 7** Synthetic route to α-diazo diketone **6.**

Focusing initially on the sulfones, cyclisations were conducted with $Rh_2(OAc)_4$ to afford racemic samples of cyclopentanones **13a–k**; the reactions proceeded efficiently with reaction times of ~30 min which were comparable to similar substrates.[26] For enantioselective intramolecular C–H insertion reactions, in all cases the catalyst was prepared by pre-mixing the constituents, which we have previously reported. This involved refluxing the constituents: copper(II) chloride (5 mol%), bis(oxazoline) ligand **14–18** (Fig. 1) (6 mol%) and NaBARF [sodium tetrakis[(3,5-trifluoromethyl)phenyl]borate] (6 mol%) for 1.5 h in dry dichloromethane under an atmosphere of nitrogen, upon which a homogenous mixture was obtained. A solution of α-diazocarbonyl substrate in dry dichloromethane was added dropwise to this mixture.

Within the α-diazo-β-keto sulfone substrate screen (Table 1 **4a–4k** and Fig. 2) we found that the bis(oxazoline) ligands **15** and **18** led to the highest levels of enantioselectivity in cyclopentanone formation across a wide range of compounds. The indane ligand **18,** was the most effective ligand yielding the highest levels of asymmetric induction of up to 91 %ee (**13i**). Interestingly, use of the benzyl ligand **15** was the most consistent with enantioselectivities of approximately 70 %ee across the substrate range. Use of ligands **14**, **16** and **17** led to lower levels of enantiocontrol. This is consistent with results previously obtained with α-diazo-β-keto sulfones.[26]

Focusing first on the steric effect, it is clear that the steric demand of the sulfone substituent has a significant impact on the enantioselectivity achieved. In general, replacing the phenyl sulfone with the methyl sulfone resulted in significantly decreased enantioselectivities (other than the benzyl ligand **15**) while the increased steric demand in the 1-naphthyl sulfone leads to enhanced enantioselectivity across the ligand series although still not matching the optimum achieved for **13i** with ligand **18**.

In contrast, electronic effects on the aryl substituent on the sulfone are less evident. While there is some evidence of a slight increase in enantioselectivity with the *p*-tolyl substituent **13i** and a slight decrease with the *p*-halo substituents **13b** and **13j**, the extent of this is minor**.** Interestingly, the cyclohexyl sulfone **13h** revealed similar ligand trends but with an overall decrease in enantioselectivity relative to the aryl substituent.

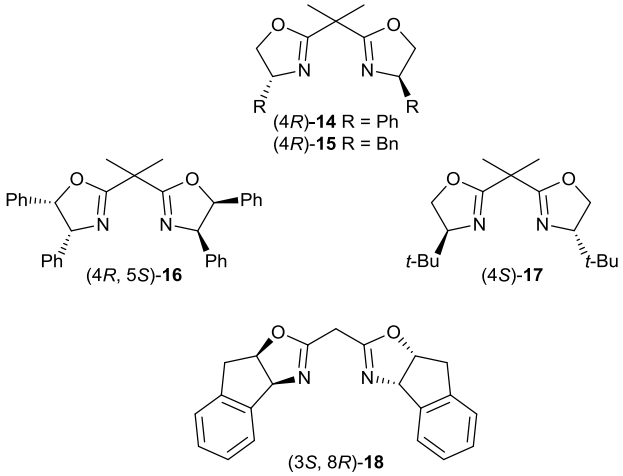
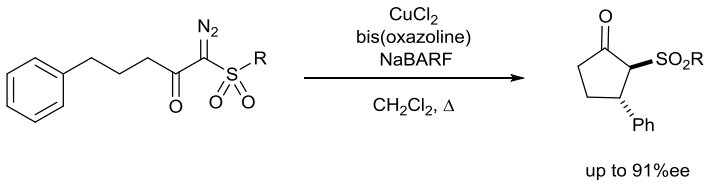
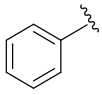
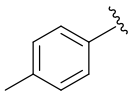
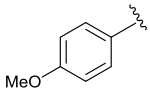
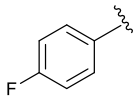
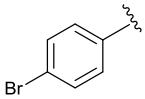
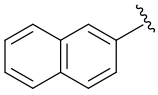
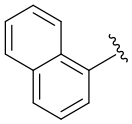
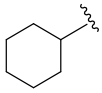
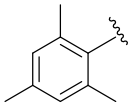
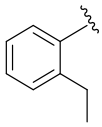



**Fig. 1** Bis(oxazoline) ligands **14**-**18**.

Table 1 **Enantioselective transition metal catalysed C–H insertion reactions of α-diazo-β-keto sulfones,** 4




**4a-k** **13a-k**

| **Diazo** | **R** | $Rh_2(OAc)_4$ | $CuCl_2$ + NaBARF + ligand **14–18** | | | | |
|---|---|---|---|---|---|---|---|
| | | | (4*R*)-Ph | (4*R*)-Bn | (4*R*, 5*S*)-diPh | (4*S*)-*t*-Bu | (3*S*, 8*R*)-Ind |
| | | | Ligand **14** | Ligand **15** | Ligand **16** | Ligand **17** | Ligand **18** |
| | | % Yield[a] (%ee)[b] | % Yield[a] (%ee)[b] | % Yield[a] (%ee)[b] | % Yield[a] (%ee)[b] | % Yield[a] (%ee)[b] | % Yield[a] (%ee)[b] |
| | | | (2*S*, 3*S*)-**13** | | | (2*R*, 3*R*)-**13** | |
| **4a**[c26] |  | 89(0) | 69(50) | 58(81) | 54(52) | 55(64) | 53(89) |
| **4i** |  | 69(0) | 56(52) | 66(78) | 23(56) | 64(55) | 64(91) |
| **4g** |  | 29(0) | 44(45) | 73(77) | 43(52) | 26(61) | 62(87) |
| **4b** |  | 74(0) | 61(37) | 66(78) | 55(47) | 64(58) | 70(86) |
| **4j** |  | 75(0) | 59(37) | 60(72) | 54(41) | 57(57) | 52(89) |
| **4k** |  | 82(0) | 49(8)[f] | 74(72) | 23(2) | 73(34) | 70(52) |
| **4c** |  | 14(0) | 59(50) | 60(76) | 54(47) | 57(46) | 52(78) |
| **4d** |  | 60(0) | 54(81) | 72(71) | 51(76) | 62(66) | 67(81) |
| **4h** |  | 88(0) | 10(33) | 92(68) | 25(45) | 51(47) | 62(78) |
| **4e**[d] |  | 30[e](0) | (-)[g] | 47(66) | (-)[g] | 4(72) | 31(82) |
| **4f**[d] |  | 27[e](0) | (-)[g] | 34(78) | (-)[g] | 4(67) | 53(87) |

[a] Total yield of cyclised products after chromatography. [b] The enantiomeric excess measured by chiral HPLC analysis (for full details see ESI). [c] Data for **13a** included for comparison.[26] [d] Calculated yields of cyclopentanone **13** from ratios of **13:19** (for

full details see Table 2). [e] Cyclisation's were carried out with $Cu(OTf)_2$ in order to obtain racemic samples of cyclopentanones **13e** and **13f** (for full details see Table 2). [f] Opposite stereochemistry observed (2*R*, 3*R*). [g] Not formed.

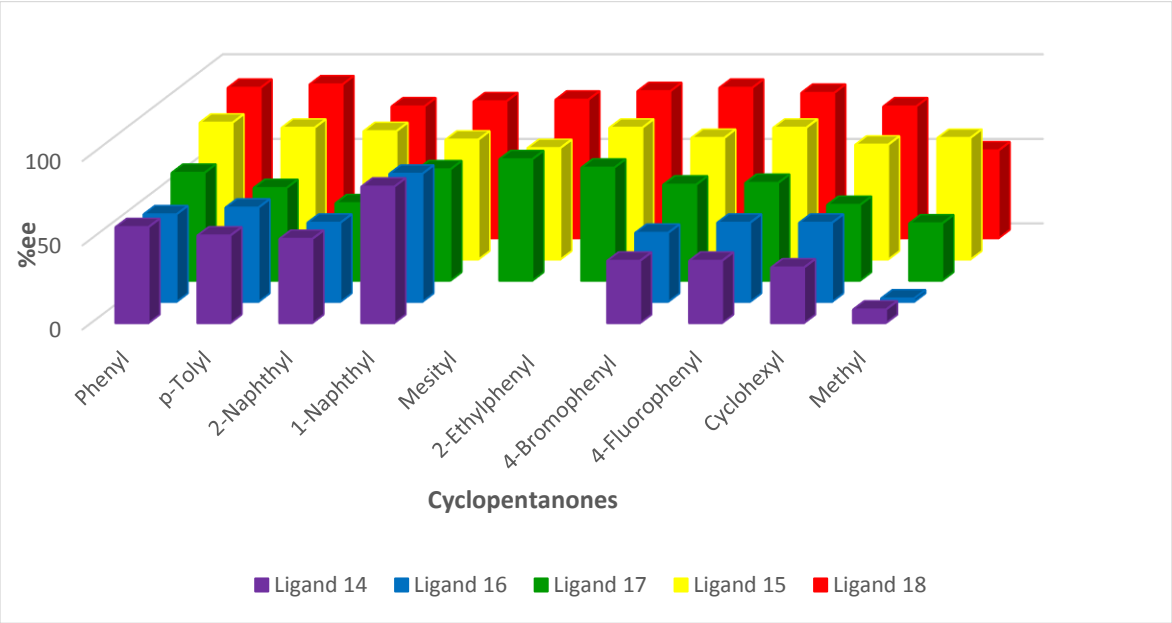


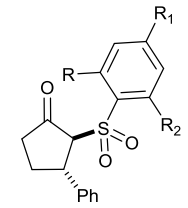

**Fig. 2** Impact of variation of the sulfone on enantioselectivity with the ligands **14–18**.

In most cases the sulfonyl cyclopentanones **13** were formed very efficiently with only minor byproducts evident in the $^1$H NMR spectra of the crude products (Table 1). However, for compounds **4e** and **4f** a competing C–H insertion pathway leading to the sulfolane through insertion into the aryl methyl (**19e**) and methylene (**19f**) group was observed. By X-Ray crystallography the absolute stereochemistry of **13a** has been previously determined[33] indicating that when the (4*R*)-**14**, (4*R*)-**15** and (4*R*, 5*S*)-**16** ligands are used the (2*S*, 3*S*) cyclopentanone is selectively formed, while using the (4*S*)-**17** and (3*S*, 8*R*)-**18** ligands selectively leads to the (2*R*, 3*R*) cyclopentanone. The absolute stereochemistry of samples **13j** and **13k** -derived from reactions using ligands (4*R*)-**15**, (3*S*, 8*R*)-**18** and (4*R*)-**15** respectively, were also determined (for full details see ESI) and it was found that the sense of enantioselectivity agrees with our earlier report of phenylsulfonyl cyclopentanones.[26, 33]

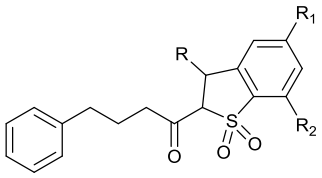
By analogy (using HPLC data and specific rotations) the absolute stereochemistry of the remaining cyclopentanone derivatives **13b–i** is similarly assigned. Thus, when using (4*S*)-**17** and (3*S*, 8*R*)-**18** the (2*R*, 3*R*) cylopentanone is formed while using (4*R*)-**14**, (4*R*)-**15** and (4*R*, 5*S*)-**16**, in general, the (2*S*, 3*S*) enantiomer of the cyclopentanone is formed. Interestingly, there is just one exception with (2*R*, 3*R*) **13k,** formed with the opposite sense selectively with

ligand (4*R*)-**14** albeit with a low %ee**.** This can be rationalised as replacement of the phenyl sulfone with the methyl sulfone alters the ligand substrate interactions substantially.

**Table 2** Enantioselective transition metal catalysed C–H insertion reactions of α-diazo-β-keto sulfones **4e** and **4f**.




**13e** R = $R_1$ = $R_2$ = Me
**13f** R = Et, $R_1$ = $R_2$ = H



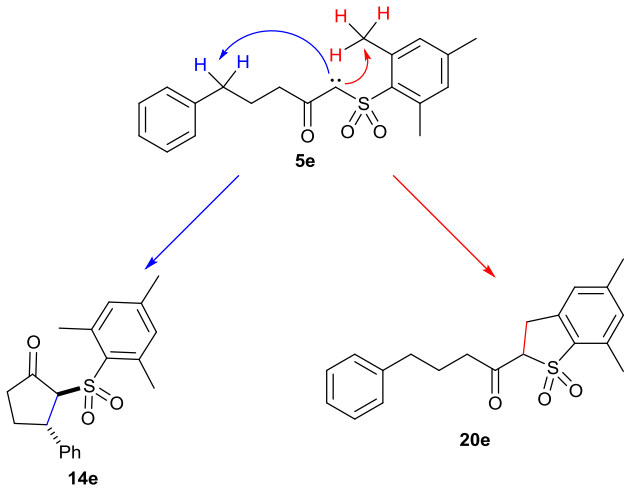

**19e** R = H, $R_1$ = $R_2$ = Me
**19f** R = Me, $R_1$ = $R_2$ = H

| **Ligand** | Diazo | Time (h) | Yield[a] % | Crude Ratio[b] (Purified Ratio)[b] **13:19** | **13** | %ee[c] | **19** | %ee[c] |
|---|---|---|---|---|---|---|---|---|
| **$Rh_2(OAc)_4$** | 4e | 24 | 78 | 0:100 (0:100) | 13e | - | 19e | 0 |
| **$Cu(OTf)_2$** | 4e | 8 | 70 | 27:73 (38:62) | 13e | 0 | 19e | 0 |
| **14** | 4e | 2.5 | 74 | 0:100 (0:100) | 13e | - | 19e | 0 |
| **15** | 4e | 4 | 71 | 70:30 (66:34) | 13e | 66 | 19e | 0 |
| **16** | 4e | 2.5 | 60 | 0:100 (0:100) | 13e | - | 19e | 0 |
| **17** | 4e | 24 | 43 | 16:84 (10:90) | 13e | 72 | 19e | 0 |
| **18** | 4e | 4.5 | 62 | 46:54 (50:50) | 13e | 82 | 19e | 0 |
| **$Rh_2(OAc)_4$** | 4f | 1.5 | 74 | 0:100 (0:100) | 13f | - | 19f | 0 |
| **$Cu(OTf)_2$** | 4f | 22 | 68 | 37:63 (37:63) | 13f | 0 | 19f | 0 |
| **14** | 4f | 6.5 | 75 | 0:100 (0:100) | 13f | - | 19f | 60 |
| **15** | 4f | 22 | 47 | 72:28 | 13f | 78 | 19f | 0 |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | | (72:28) | | | | |
| **16** | 4f | 1.5 | 73 | 0:100 (0:100) | 13f | - | 19f | 74 |
| **17** | 4f | 22 | 56 | 17:83 (7:93) | 13f | 67 | 19f | 5 |
| **18** | 4f | 21 | 83 | 61:39 (64:36) | 13f | 87 | 19f | 0 |

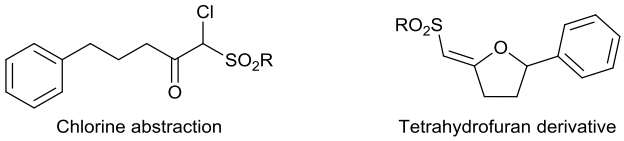
[a] Combined yield of cyclopentanone and sulfolane. [b] Ratios of isomers were calculated from signals in the crude/purified $^1$H NMR spectra: $\delta_H$ 3.92 [1H, d, *J* 7.6, C(2)*H*] for cyclopentanone **13e**; $\delta_H$ 4.45 (1H, dd, X of ABX, $J_{BX}$ 8.5, $J_{AX}$ 5.7, C*H*) for sulfolane **19e** and $\delta_H$ 1.13 (3H, t, *J* 7.4, $CH_2CH_3$) for cyclopentanone **13f**; $\delta_H$ 1.44 (3H, d, *J* 6.9, $CH_3$) for sulfolane **19f**. [c] The enantiomeric excess measured by chiral HPLC analysis (for full details see ESI).

Previous studies had demonstrated that the preference for C–H insertion is methine>methylene>methyl,[9] however, in investigating the copper mediated reactions of **4e** and **4f**, competition between C–H insertion into methylene and methyl C–H bonds was observed leading to the formation of cyclopentanone (**13e** and **f**) and fused sulfolane (**19e** and **f**) (Scheme 8). As summarised in Table 2, the regioselectivity of the C–H insertion displayed sensitivity to the variation of the metal from rhodium to copper and, even more remarkably, to the variation of the bis(oxazoline) ligand. When $Rh_2(OAc)_4$ was used as the catalyst with **4e** and **4f**, the fused sulfolanes **19e** and **f** were the sole product obtained while use of $Cu(OTf)_2$ led to racemic samples of **13e** and **f**. Sulfolane **19f** was predominantly obtained as a single diastereomer, presumably *trans*, although, with $Rh_2(OAc)_4$, minor signals in the crude $^1$H NMR spectrum were ascribed to the *cis* isomer. Interestingly, with the copper catalysts significant formation of the cyclopentanone was only seen with the complexes from the ligands **15** and **18**. As these are the ligands which provide the highest enantioselectivities in the cyclopentanones (Table 1), it is highly likely that specific substrate interactions favouring C–H insertion to form the cyclopentanones are enabled with ligands **15** and **18**. [26] All samples of sulfolane **19e** recovered were racemic; this was as expected due to the single, easily racemised, stereocentre. The samples of **19f** obtained using ligands (4*R*)-**14**, and (4*R*, 5*S*)-**16** displayed moderate enantioselectivity (60 and 74 %ee respectively) with a very low enantiomeric excess obtained using ligand (4*S*)-**17** (5 %ee) with the opposite sense of enantioselection, as anticipated.




**Scheme 8** Possible C–H insertion pathways for mesityl substrate **4e**.

Interesting patterns in terms of chemoselectivity and efficiency of the C–H insertions across the substrate and ligand series were evident from comparison of the $^{1}$H NMR spectra of the crude mixtures. In general use of $Rh_2(OAc)_4$ led to the cleanest insertions to provide the cyclopentanone with little or no byproducts. In contrast, use of copper catalysts can lead to minor competing reaction pathways including chlorine abstraction from the solvent and hydride abstraction at the site of insertion leading to a tetrahydrofuran derivative (Scheme 9).[31] Notably C–H insertion to form cyclopentanone was most efficient with the benzyl or indane ligand **15** and **18**; use of phenyl or *t*-butyl ligands **14** and **17** in general led to more of the tetrahydrofuran product, while use of the diphenyl ligand **16** tended to lead to a more complex mix of unidentified products.



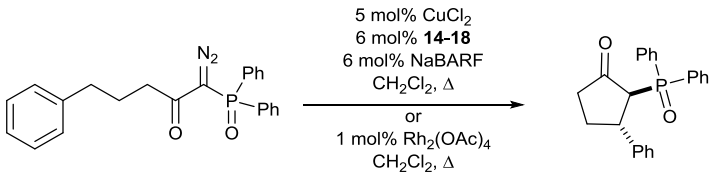

**Scheme 9** Possible byproducts formed in the copper catalysed C–H insertion reactions of **4a–k**

As optimum enantioselectivities in the copper mediated C–H insertion were achieved with the aryl sulfones, exploration of the substituent on the carbene was undertaken to explore the effect of other electron withdrawing groups on the outcome of the insertion process. Accordingly, extending our work with the phosphonates and esters,[32] C–H insertions with α-

diazo-β-keto phosphine oxide (**5**) and 2-diazo-1,3-diketone (**6**) were investigated. Interestingly, these are the first reports of asymmetric intramolecular C–H insertion in these types of compounds. Intramolecular C–H insertion reactions of **5** with the copper catalyst system led to α-phosphine oxide-substituted cyclopentanone **20** in poor to moderate enantioselectivities (Table 3); reaction times, were also significantly longer and yields poorer than their sulfone counterparts. The longer reaction times may be due to the inferior electron-withdrawing abilities of the diphenyl phosphine oxide group ($\sigma_p$0.53),[34] compared to the phenylsulfonyl moiety ($\sigma_p$0.68),[34] which results in a less electrophilic carbene in the phosphine oxide series. In an effort to reduce reaction times two higher boiling point solvents, chloroform and 1,2-dichloroethane, were used. With chloroform, comparable times and enantioselectivities were obtained to those seen in the reactions conducted in dichloromethane. When 1,2-dichloroethane was used the reaction time was reduced from 162 h to 22 h and the yield was increased by ~50%; predictably however, the higher temperature led to a dramatic decrease in asymmetric induction.

While the absolute stereochemistry of **20** has not been determined, as anticipated ligands (4*R*)-**14**, (4*R*)-**15** and (4*R*, 5*S*)-**16** lead to the same major enantiomer of **20**, while (4*S*)-**17** and (3*S*, 8*R*)-**18** lead to the opposite. It is reasonable to assume that this has the same stereochemical preference as seen with the sulfonyl cyclopentanones **13** *i.e.* (4*R*)-**14**, (4*R*)-**15** and (4*R*, 5*S*)-**16** lead to the (2*S*, 3*S*) cyclopentanone and (4*S*)-**17** and (3*S*, 8*R*)-**18** lead to the (2*R*, 3*R*) cyclopentanone.

**Table 3** Enantioselective transition metal catalysed C–H insertion reactions of α-diazo-β-keto phosphine oxide, **5**




**5** **20**

| **Ligand** | Solvent | Time (h) | Yield (%)[a] | Rotation | %ee[b,] |
|---|---|---|---|---|---|
| **$Rh_2(OAc)_4$** | $CH_2Cl_2$ | 67 | 64 | | 0 |
| **14** | $CH_2Cl_2$ | 19 | 26 | (+) | 29 |
| **15** | $CH_2Cl_2$ | 124 | 5 | (+) | 30 |

| | | | | | |
|---|---|---|---|---|---|
| **16** | $CH_2Cl_2$ | 19 | 24 | (+) | 31 |
| **17** | $CH_2Cl_2$ | 49 | 44 | (−) | 2 |
| **18** | $CH_2Cl_2$ | 124 | 8 | (−) | 53 |
| **18** | $C_2H_4Cl_2$ | 22 | 60 | (−) | 9 |
| **18** | $CHCl_3$ | 124 | 6 | (−) | 11 |

[a] Total yield of cyclised products after chromatography. [b] The enantiomeric excess measured by chiral HPLC analysis (for full details see ESI).

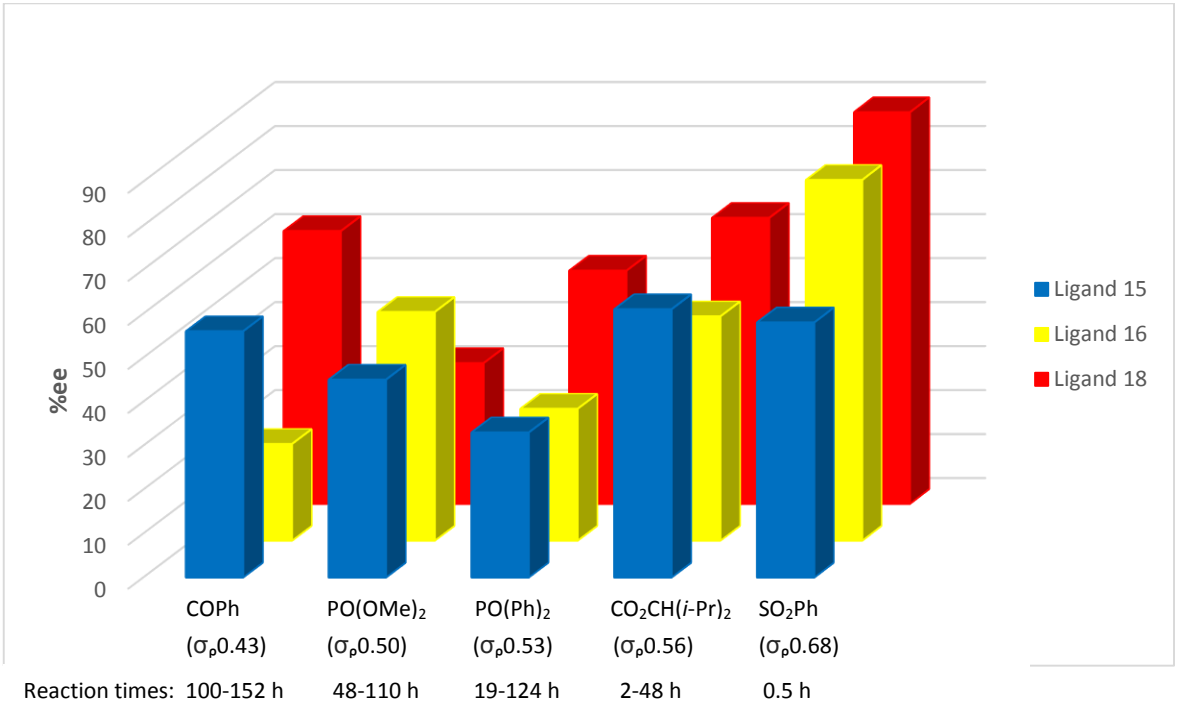
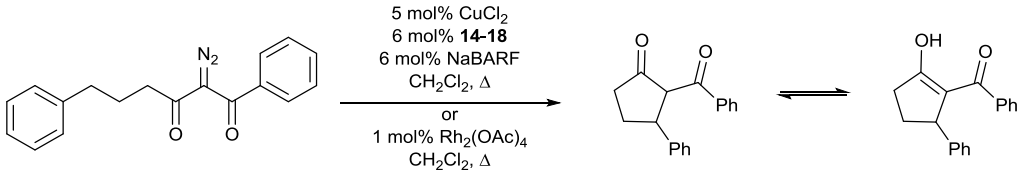



**Fig. 3** Impact of variation of the electron withdrawing group on the enantioselectivity with ligands **15, 16** and **18**.

With diazodiketone **6**, reaction times were significantly longer than for the sulfonyl counterparts and yields of the cyclopentanone **21** were poor (Table 4). Across the series altering the substituent on the carbene from the phenyl sulfone ($\sigma_p$0.68),[34] to the ester ($\sigma_p$0.56),[34] phosphine oxide ($\sigma_p$0.53),[34] phosphonate ($\sigma_p$0.50),[34] and ketone ($\sigma_p$0.43),[34] resulted in a decrease in the electrophilicity of the carbene and a substantial increase in the reaction times for the C–H insertion reactions (Fig. 3). The products of reduction and Wolff

rearrangement were evident as significant competing reaction pathways as the efficiency for C–H insertion decreased. Interestingly, moderate enantioselectivities were achieved across the ligand screen indicating that the ligand sensitivity in terms of enantioselectivity in this insertion is much less than in the other systems studied to date. Furthermore, the low enantioselectivity obtained with the benzyl ligand **15** contrasts with other results. Once again ligands (4*R*)-**14**, (4*R*)-**15** and (4*R*, 5*S*)-**16** lead selectively to one enantiomer of **21** while (4*S*)-**17** and (3*S*, 8*R*)-**18** lead selectively to the opposite enantiomer and while it is reasonable to assume that the sense of enantioselection follows that seen in the sulfonyl derivatives the absolute stereochemistry has not been determined. The cyclopentanone **21** was initially recovered as a mixture of keto and enol tautomers, however, over time the keto tautomer was observed to predominate.

**Table 4** Enantioselective transition metal catalysed C–H insertion reactions of α-diazo-diketone, **6**




**6** **21**

| Ligand | Solvent | Time (hr) | Yield (%)[a] | %ee[b,] |
|---|---|---|---|---|
| **$Rh_2(OAc)_4$** | $CH_2Cl_2$ | 1.5 | 38 | - |
| **14** | $CH_2Cl_2$ | 126 | 27 | 68 |
| **15** | $CH_2Cl_2$ | 142 | 10 | 22 |
| **16** | $CH_2Cl_2$ | 100 | 33 | 56 |
| **17** | $CH_2Cl_2$ | 142 | 27 | 54 |
| **18** | $CH_2Cl_2$ | 152 | 19 | 62 |

[a] Total yield of cyclised products after chromatography. [b] The enantiomeric excess measured by chiral HPLC analysis (for full details see ESI).

## Conclusions:

We have found that the copper-bis(oxazoline)-NaBARF catalytic system is efficient in achieving high levels of enantiocontrol across a broad range of substrates. From our studies to date, it is clear that the sulfonyl moiety leads to the highest levels of enantioselectivity in intramolecular C–H insertion reactions of α-diazocarbonyl compounds resulting in

cyclopentanone formation. The indane bis(oxazoline) ligand **18** has consistently led to the highest levels of enantiocontol across a wide variety of substrates. Within the α-diazo-β-keto sulfone series increasing the steric demand of the substituents attached to the sulfone moiety leads to higher levels of asymmetric induction across the bis(oxazoline) ligand screen, while electronic effects have little impact. In addition to impacting on the enantioselectivity, changing from the sulfonyl group to a phosphine oxide or ketone with decreased electron withdrawing character, decreased the efficiency of the C–H insertion.

**Experimental:**

All solvents were distilled prior to use by the following methods: dichloromethane (DCM) was distilled from phosphorus pentoxide and when used for α-diazocarbonyl cyclisations, was further distilled from calcium hydride; ethyl acetate was distilled from potassium carbonate; hexane was distilled prior to use. Organic phases were dried using anhydrous magnesium sulfate. All reactions were carried out under a nitrogen atmosphere unless otherwise stated.

Infrared (IR) spectra were recorded as thin films on sodium chloride plates for oils or as potassium bromide (KBr) discs for solids on a Perkin Elmer Paragon 1000 FT-IR spectrometer. NMR spectra were run on Bruker Avance 300 MHz, 400 MHz, 500 MHz and 600 MHz NMR machines. $^{1}$H spectra were run at 300 MHz, 400 MHz, 500 MHz and 600 MHz and $^{13}$C spectra were run at 75 MHz, 100 MHz, 125 MHz and 150 MHz. All spectra were recorded at room temperature (~20 °C) in deuterated chloroform ($CDCl_3$), unless otherwise stated, using tetramethylsilane (TMS) as an internal standard. Chemical shifts ($\delta_H$ and $\delta_C$) are reported in parts per million (ppm) relative to TMS and coupling constants (*J*) are expressed in Hertz (Hz). $^{13}$C NMR spectra were calibrated using the solvent signals, *i.e.* $CDCl_3$: $\delta_C$ 77.0 ppm and were assigned with the aid of DEPT experiments.

Flash column chromatography was carried out using Kieselgel silica gel 60, 0.040–0.063 mm (Merck). Thin layer chromatography (TLC) was carried out on precoated silica gel plates (Merck 60 PF254). Visualisation was achieved by UV (254 nm) detection, vanillin staining and potassium permanganate staining.

Enantiopurity of the chiral compounds was determined by chiral stationary phase high performance liquid chromatography (HPLC) performed on a Phenomenex® LUX Cellulose-4, Phenomenex® LUX Cellulose-2, Phenomenex® LUX Amylose-1, Chiralpak OJ-H or Chiralcel OD-H column. HPLC analysis was performed on a Waters alliance 2690 separations module.

Optical rotations were measured on a Perkin-Elmer 141 polarimeter at 589 nm in a 10 cm cell; concentrations (*c*) are expressed in g/100 mL. $[\alpha]_D^T$ is the specific rotation of a compound and is expressed in units of $10^{-1}$ deg cm$^2$ g$^{-1}$. The Microanalysis Laboratory, National University of Ireland, Cork, performed elemental analysis using a Perkin-Elmer 240 and Exeter Analytical CE440 elemental analysers. Low resolution mass spectra (LRMS) were recorded on a Waters Quattro Micro triple quadrupole instrument in electrospray ionization (ESI) mode using 50% acetonitrile-water containing 0.1% formic acid as eluent; samples were made up in acetonitrile. High resolution mass spectra (HRMS) were recorded on a Waters LCT Premier Tof LC-MS instrument in electrospray ionization (ESI) mode using 50% acetonitrile-water containing 0.1% formic acid as eluent; samples were prepared in acetonitrile. Single crystal X-ray analysis was conducted using a Bruker APEX II DUO diffractometer at temperature 100 K using graphite monochromatic Mo Kα (λ = 0.7107 Å) radiation fitted with an Oxford Cryosystems Cobra low-temperature device or a Bruker SMART X2S diffractometer. All calculations and refinement were made using the APEX software. The structures were solved using direct methods and refined on F2 using SHELXL-97.17 Analysis was undertaken with the SHELX suite of programs and diagrams prepared with Mercury 3.0.18 All non-hydrogen atoms were located and refined with anisotropic thermal parameters. Hydrogen atoms were included in calculated positions or they were located and refined with isotropic thermal parameters. $^1$H NMR spectra, IR spectra and melting point (mp) analysis were recorded for all previously prepared compounds. For novel compounds, $^{13}$C NMR, LRMS and microanalysis and/or HRMS were also obtained. HETCOR/HSQC, HMBC and COSY experiments were carried out to aid the NMR assignment of novel chemical structures.

**1-(1*H*-Benzo[*d*][1,2,3]triazol-1-yl)-4-phenylbutan-1-one 12.** Thionyl chloride (0.88 mL, 0.0122 mol) was added in one portion to a solution of benzotriazole (5.80 g, 0.0487 mol) in dichloromethane (50 mL), the reaction mixture was stirred at room temperature for 30 min. 4-Phenylbutyric acid (2.00 g, 0.0122 mol) was added in one portion and a colour change from yellow to cloudy white was observed. The reaction mixture was stirred for 2 h at room temperature. The white precipitate was removed by filtration and extracted with dichloromethane (2 x 50 mL). The combined organic extracts were washed with aqueous sodium hydroxide (1.0 M, 3 x 60 mL), dried with magnesium sulfate and concentrated under reduced pressure to yield the acylbenzotriazole **12** as a white sticky oil; $\nu_{max}$(neat)/cm$^{-1}$ 1704

(C=O), 1210, 743, 698; $\delta_H$ (400 MHz) 2.26 [2H, apparent qu, *J* 7.5, C(3)$H_2$], 2.82 [2H, t, *J* 7.6, C(4)$H_2$], 3.45 (2H, t, *J* 7.4, C(2)$H_2$), 7.15–7.32 (5H, m, aromatic *H* of phenyl group), 7.47–7.53 (1H, m, aromatic *H* of benzotriazole group), 7.61–7.68 (1H, m, aromatic *H* of benzotriazole group), 8.11 (1H, d, *J* 8.3, aromatic *H* of benzotriazole group), 8.28 (1H, d, *J* 8.3, aromatic *H* of benzotriazole group); $\delta_C$ (106.6 MHz) 26.3 [$CH_2$, *C*(3)$H_2$], 33.4 [$CH_2$, *C*(4)$H_2$], 35.0 [$CH_2$, *C*(2)$H_2$], 115.5 (CH, aromatic *C*H), 126.1 (CH, aromatic *C*H), 126.3 (CH, aromatic *C*H), 128.45 (CH, aromatic *C*H), 128.51 (CH, aromatic *C*H), 138.8 (C, *C*), 141.3 (C, *C*), 179.2 (C, *C*O); HRMS (ESI+): Exact mass calculated for $C_{16}H_{16}N_3O$ $[M+H]^+$, 266.1293 Found 266.1286. m/z (ESI+): 266.1 $[M+H]^+$.

*Note: The crude products were sufficiently pure to use for diazo transfer but contained some unreacted methyl sulfone* ***7b***-***7h****. Purification by careful column chromatography was necessary to separate the closely eluting products in order to obtain an analytically clean sample.*

**1-Phenylsulfonyl-5-phenylpentan-2-one 9a.** *n*-Butyllithium (1.6 M solution in hexanes; 46.0mL, 0.0740 mol), was added dropwise to a solution of methyl phenyl sulfone (5.62 g, 0.0360 mol) in THF (230 ml) while stirring at 0 °C. The resulting cloudy yellow solution was stirred for 1.5 h at 0 °C then a solution of ethyl 4-phenylbutanoate **8** (7.00 g, 0.0360 mol) in THF (20 mL) was added dropwise over 15 min producing a light orange solution. The reaction mixture was stirred overnight and then was quenched with saturated ammonium chloride solution (75 mL). The organic layer was isolated and the aqueous layer washed with diethyl ether (3 × 50 mL). The organic layers were combined and washed with brine (50 mL), dried with magnesium sulfate, filtered and concentrated under reduced pressure to give the crude β-keto sulfone **9a** as a sticky yellow solid. Purification by careful column chromatography, employing 20% ethyl acetate in hexane as eluent, gave the pure β-keto sulfone **9a** (4.46 g, 41%) as a white solid, Rf = 0.39 (40:60 ethyl acetate/hexane); mp 80–81 °C (lit.,[35] 79–80 °C); $\nu_{max}$(KBr)/$cm^{-1}$ 1718 (C=O), 1319, 1150 ($SO_2$); $\delta_H$ (300 MHz) 1.90 [2H, apparent qu, *J* 7.4,

C(4)$H_2$], 2.61 [2H, t, *J* 7.5, C(5)$H_2$], 2.71 [2H, t, *J* 7.2, C(3)$H_2$], 4.11 [1H, s, C(1)$H_2$], 7.13–7.32 (5H, m, aromatic *H* of phenyl group), 7.54–7.60 (2H, m, aromatic *H* of phenylsulfonyl group), 7.65–7.71 (1H, m, aromatic *H* of phenylsulfonyl group), 7.85–7.88 (2H, m, aromatic *H* of phenylsulfonyl group); $\delta_C$ (75.5 MHz) 24.6 ($CH_2$, *C*(4)$H_2$), 34.6 ($CH_2$, *C*(5)$H_2$), 43.5 ($CH_2$, *C*(3)$H_2$), 66.0 ($CH_2$, *C*(1)$H_2$), 126.0 (CH, aromatic *C*), 127.2 (CH, aromatic *C*H), 128.2 (CH, aromatic *C*H), 128.4 (CH, aromatic *C*H), 129.3 (CH, aromatic *C*H), 134.2 (CH, aromatic *C*H), 138.9 (C, aromatic *C*), 141.2 (C, aromatic *C*), 197.9 (C, *C*O). Spectral characteristics were consistent with previously reported data.[35]

**1-[(4-Fluorophenyl)sulfonyl]-5-phenylpentan-2-one 9b.** 1-Fluoro-4-(methylsulfonyl)benzene **7b** (2.28 g, 0.0131 mol), *n*-butyllithium (2.5 M solution in hexanes; 10.47mL, 0.0262 mol), ethyl 4-phenylbutanoate **8** (2.52 g, 0.0131 mol) and THF (185 mL) were used following the procedure described for **9a** to give the crude β- keto sulfone **9b** as a red oil. Purification by careful column chromatography, employing 20% ethyl acetate in hexane as eluent, gave the pure β-keto sulfone **9b** (1.83 g, 44%) as a white solid, Rf = 0.20 (20:80 ethyl acetate/hexane); mp 98–100 °C; $\nu_{max}$(neat)/$cm^{-1}$ 1716 (C=O), 1321, 1145 ($SO_2$); $\delta_H$ (400 MHz) 1.91 [2H, apparent qu, *J* 7.4, C(4)$H_2$], 2.62 [2H, t, *J* 7.5, C(5)$H_2$], 2.70 [2H, t, *J* 7.2, C(3)$H_2$], 4.10 [1H, s, C(1)$H_2$], 7.11–7.33 (7H, m, aromatic *H* 5 x phenyl and 2 x 4-fluorophenyl group), 7.86–7.92 (2H, m, aromatic *H* of 4-fluorophenyl group); $\delta_F$ (376.5 MHz) -102.2 (1F, s, *p-F*); $\delta_C$ (100.6 MHz) 24.6 [$CH_2$, *C*(4)$H_2$], 34.7 [$CH_2$, *C*(5)$H_2$], 43.6 [$CH_2$, *C*(3)$H_2$], 66.8 [$CH_2$, *C*(1)$H_2$], 116.7 (CH, d, $^2J_{CF}$, 22.8, aromatic *C*H), 126.2 (CH, aromatic *C*H), 128.46 (CH, aromatic *C*H), 128.49 (CH, aromatic *C*H), 131.4 (CH, d, $^3J_{CF}$ 9.7, aromatic *C*H), 134.7 (C, d, $^4J_{CF}$, 3.1, aromatic *C*), 141.1 (C, aromatic *C*), 166.2 (C, $^1J_{CF}$ 257.5, aromatic *C*F), 197.9 (C, *C*O); HRMS (ESI): Exact mass calculated for $C_{17}H_{16}FO_3S$ $[M-H]^-$, 319.0804. Found 319.0803. m/z (ESI-): 319.1 $[M-H]^-$.

**1-(Naphthalen-2-ylsulfonyl)-5-phenylpentan-2-one 9c.** *n*-Butyllithium (2.5 M solution in hexanes; 11.64 mL, 0.0291 mol) was added dropwise to a stirring solution of freshly distilled diisopropylamine (4.28 mL, 0.0305 mol) in THF (25 mL) at 0 °C. 2-(Methylsulfonyl)naphthalene **7c** (3.00 g, 0.0146 mol) in THF (85 mL) was added dropwise to this solution over 5 min and the resulting cloudy orange solution was stirred for 1.5 h at 0 °C. To this solution ethyl 4-phenylbutanoate **8** (2.80 g, 0.0146mol) in THF (15 mL) was added dropwise over 15 min producing a light orange solution. The reaction mixture was stirred overnight and then was quenched with saturated ammonium chloride solution (75 mL). The organic layer was isolated and the aqueous layer washed with diethyl ether (3 x 50 mL). The organic layers were combined and washed with brine (50 mL), dried with magnesium sulfate, filtered and concentrated under reduced pressure to give the crude β-keto sulfone **9c** as an orange solid. Purification by careful column chromatography, employing 20% ethyl acetate in hexane as eluent, gave the pure β-keto sulfone **9c** (2.72 g, 53%) as a white solid, Rf = 0.14 (20:80 ethyl acetate/hexane); mp 121–123 °C; (Found C, 71.54; H, 5.73. $C_{21}H_{20}O_3S$ requires C, 71.57; H, 5.72%); $\nu_{max}$(neat)/$cm^{-1}$ 1720 (C=O), 1301, 1149 ($SO_2$); $\delta_H$ (300 MHz) 1.89 [2H, apparent qu, *J* 7.4, C(4)$H_2$], 2.59 [2H, t, *J* 7.6, C(5)$H_2$], 2.72 [2H, t, *J* 7.2, C(3)$H_2$], 4.18 [2H, s, C(1)$H_2$], 7.08–7.31 (5H, m, 5 x aromatic *H* of phenyl group), 7.57–7.75 (2H, m, 2 x aromatic *H* of 2-naphthyl group), 7.82 (1H, dd, *J* 8.7, 1.9, aromatic *H* of 2-naphthyl group), 7.89–8.04 (3H, m, 3 x aromatic *H* of 2-naphthyl group), 8.45 (1H, d, *J* 1.5, aromatic *H* of 2-naphthyl group); $\delta_C$ (100.6 MHz) 24.7 [$CH_2$, *C*(4)$H_2$], 34.7 [$CH_2$, *C*(5)$H_2$], 43.7 [$CH_2$, *C*(3)$H_2$], 67.0 [$CH_2$, *C*(1)$H_2$], 122.6 (CH, aromatic *C*H), 126.1 (CH, aromatic *C*H), 127.9 (CH, aromatic *C*H), 128.1 (CH, aromatic *C*H), 128.4 (CH, aromatic *C*H), 129.59 (CH, aromatic *C*H), 129.62 (CH, aromatic *C*H), 129.7 (CH, aromatic *C*H), 130.3 (CH, aromatic *C*H), 132.1 (C, aromatic *C*), 135.6 (C, aromatic *C*), 135.7 (C,

aromatic *C*), 141.2 (C, aromatic *C*), 197.9 (C, *C*O); HRMS (ESI+): Exact mass calculated for $C_{21}H_{21}O_3S$ $[M+H]^+$, 353.1211. Found 353.1227. m/z (ESI+): 353.1 $[M+H]^+$.

**1-(Naphthalen-1-ylsulfonyl)-5-phenylpentan-2-one 9d.** 1-(Methylsulfonyl)naphthalene **7d** (2.25 g, 0.0109 mol), *n*-butyllithium (2.5 M solution in hexanes; 8.75 mL, 0.0219mol), ethyl 4-phenylbutanoate **8** (2.10 g, 0.0109 mol) and THF (185 mL) were used following the procedure described for **9a** to give the crude β-keto sulfone **9d** as a brown oil. Purification by careful column chromatography, employing 20% ethyl acetate in hexane as eluent, gave the pure β-keto sulfone **9d** (2.15 g, 56%) as a white solid, Rf = 0.21 (20:80 ethyl acetate/hexane); mp 93–95 °C; (Found C, 71.41; H, 5.65. $C_{21}H_{20}O_3S$ requires C, 71.57; H, 5.72%); $\nu_{max}$(neat)/$cm^{-1}$ 1718 (C=O), 1309, 1124 ($SO_2$); $\delta_H$ (400 MHz) 1.87 [2H, apparent qu, *J* 7.4, C(4)$H_2$], 2.57 [2H, t, *J* 7.6, C(5)$H_2$], 2.70 [2H, t, *J* 7.1, C(3)$H_2$], 4.28 [2H, s, C(1)$H_2$], 7.04–7.31 (5H, m, 5 x aromatic *H* of phenyl group), 7.54–7.77 (3H, m, 3 x aromatic *H* of 1-naphthyl group), 7.99 (1H, d, *J* 8.0, aromatic *H* of 1-naphthyl group), 8.16 (1H, d, *J* 8.1, aromatic *H* of 1-naphthyl group), 8.25 (1H, d, *J* 7.3, aromatic *H* of 1-naphthyl group), 8.68 (1H, d, *J* 8.6, aromatic *H* of 1-naphthyl group); $\delta_C$ (100.6 MHz) 24.6[$CH_2$, *C*(4)$H_2$], 34.7 [$CH_2$, *C*(5)$H_2$], 43.9 [$CH_2$, *C*(3)$H_2$], 66.4 [$CH_2$, *C*(1)$H_2$], 123.6 (CH, aromatic *C*H), 124.4 (CH, aromatic *C*H) 126.1(CH, aromatic *C*H), 127.2 (CH, aromatic *C*H), 128.4 (CH, aromatic *C*H), 128.6 (C, aromatic *C*), 129.2 (CH, aromatic *C*H), 129.6 (CH, aromatic *C*H), 131.1 (CH, aromatic *C*H), 133.7 (C, aromatic *C*), 134.2 (C, aromatic *C*), 135.9 (CH, aromatic *C*H), 141.2 (C, aromatic *C*), 197.6 (C, *C*O); HRMS (ESI+): Exact mass calculated for $C_{21}H_{21}O_3S$ $[M+H]^+$, 353.1211. Found 353.1202. m/z (ESI+): 353.1 $[M+H]^+$.

**1-(Mesitylsulfonyl)-5-phenylpentan-2-one 9e.** *n*-Butyllithium (2.5 M solution in hexanes; 8.05 mL, 0.0201 mol), freshly distilled diisopropylamine (2.96 mL, 0.0211 mol), mesityl methyl sulfone **7e** (2.00 g, 0.0101 mol), ethyl 4-phenylbutanoate **8** (1.93 g, 0.0101mol) and THF (135

mL) were added following the procedure described for **9c** to give the crude β-keto sulfone **9e** as an orange solid. Purification by careful column chromatography, employing 20% ethyl acetate in hexane as eluent, gave the pure β-keto sulfone **9e** (1.65 g, 48%) as a white solid, Rf = 0.40 (20:80 ethyl acetate/hexane); mp 78–80 °C; (Found C, 70.06; H, 7.07. $C_{20}H_{24}O_3S$ requires C, 69.74; H, 7.02%); $\nu_{max}$(neat)/cm$^{-1}$ 1717 (C=O), 1311, 1133 ($SO_2$); $\delta_H$ (300 MHz) 1.90 [2H, apparent qu, *J* 7.4, C(4)$H_2$], 2.31 (3H, s, C$H_3$), 2.57–2.65 [8H, m, C(5)$H_2$ contains s at δ2.16 for 2 x C$H_3$], 2.73 [2H, t, *J* 7.2, C(3)$H_2$], 4.09 [2H, s, C(1)$H_2$], 6.97 (2H, s, aromatic *H* of mesityl group), 7.11–7.23 (3H, m, aromatic *H* of phenyl group), 7.23–7.32 (2H, m, aromatic *H* of phenyl group); $\delta_C$ (100.6 MHz) 21.1 ($CH_3$, *p*-*C*$H_3$), 22.8 ($CH_3$, 2 x *o*-*C*$H_3$), 24.7 [$CH_2$, *C*(4)$H_2$], 34.7 [$CH_2$, *C*(5)$H_2$], 44.0 [$CH_2$, *C*(3)$H_2$], 66.9 [$CH_2$, *C*(1)$H_2$], 126.1 (CH, aromatic *C*H of phenyl group), 128.5 (CH, aromatic *C*H of phenyl group), 132.4 (CH, aromatic *C*H of mesityl group), 140.1 (C, aromatic *C*), 141.3 (C, aromatic *C*), 144.0 (C, aromatic *C*), 198.2 (C, *C*O); HRMS (ESI+): Exact mass calculated for $C_{20}H_{25}O_3S$ $[M+H]^+$, 345.1520. Found 345.1524. m/z (ESI+): 345.2 $[M+H]^+$.

**1-[(2-Ethylphenyl)sulfonyl]-5-phenylpentan-2-one 9f.** 1-Ethyl-2-(methylsulfonyl)benzene **7f** (2.16 g, 0.0117 mol), *n*-butyllithium (2.5 M solution in hexanes; 4.68 mL, 0.0234 mol), ethyl 4-phenylbutanoate **8** (2.25 g, 0.0117 mol) and THF (115 mL) were used following the procedure described for **9a** to give the crude β-keto sulfone **9f** as a brown oil. Purification by careful column chromatography, employing 20% ethyl acetate in hexane as eluent, gave the pure β-keto sulfone **9f** (1.48 g, 38%) as a white solid, Rf = 0.14 (20:80 ethyl acetate/hexane); mp 59–62 °C; (Found C, 69.17; H, 6.71. $C_{19}H_{22}O_3S$ requires C, 69.06; H, 6.71%); $\nu_{max}$(neat)/cm$^{-1}$ 1716 (C=O), 1303, 1148 ($SO_2$); $\delta_H$ (300 MHz) 1.33 (3H, t, *J* 7.5, $CH_2C$*H*$_3$), 1.88 [2H, qu, *J* 7.5, C(4)$H_2$], 2.60 [2H, t, *J* 7.6, C(5)$H_2$], 2.72 [2H, t, *J* 7.2, C(3)$H_2$], 3.04 (2H, q, *J* 7.5, C$H_2$CH$_3$), 4.13 [2H, s, C(1)$H_2$], 7.11–7.23 (3H, m, aromatic *H* of phenyl group), 7.24–7.46 (4H, m, aromatic *H* of 2 x phenyl group and 2 x 2-ethylphenyl group), 7.59 (1H, dt, *J* 7.6, 1.4, aromatic *H* of 2-ethylphenyl

group), 7.91 (1H, dd, *J* 8.0, 1.3, aromatic *H* of 2-ethylphenyl group); $\delta_C$ (75.5 MHz) 15.9 (*C*$H_3$), 24.7 [$CH_2$, *C*(4)$H_2$], 26.1 ($CH_2$, *C*$H_2CH_3$), 34.7 [$CH_2$, *C*(5)$H_2$], 43.7 [$CH_2$, *C*(3)$H_2$], 67.1 [$CH_2$, *C*(1)$H_2$], 126.1 (CH, aromatic *C*H), 126.6 (CH, aromatic *C*H), 128.5 (CH, aromatic *C*H), 130.3 (CH, aromatic *C*H), 131.2 (CH, aromatic *C*H), 134.4 (CH, aromatic *C*H), 136.6 (C, aromatic *C*), 141.2 (C, aromatic *C*), 144.5 (C, aromatic *C*), 197.8 (C, *C*O); HRMS (ESI+): Exact mass calculated for $C_{19}H_{23}O_3S$ $[M+H]^+$, 331.1368. Found 331.1366. m/z (ESI+): 331.1 $[M+H]^+$.

**1-[(4-Methoxyphenyl)sulfonyl]-5-phenylpentan-2-one 9g.** 1-Methoxy-4-(methylsulfonyl)benzene **9g** (4.00 g, 0.0215 mol), *n*-butyllithium (1.75 M solution in hexanes; 24.55 mL, 0.0430 mol), ethyl 4-phenylbutanoate **8** (4.13 g, 0.0215 mol) and THF (115 mL) were used following the procedure described for **9a** to give the crude β-keto sulfone **9g** as an orange oil. Purification by careful column chromatography, employing 20% ethyl acetate in hexane as eluent, gave the pure β-keto sulfone **9g** (2.10 g, 29%) as a white solid, Rf = 0.09 (20:80 ethyl acetate/hexane); mp 65–67 °C; $\nu_{max}$(neat)/$cm^{-1}$ 1714 (C=O), 1299, 1148 ($SO_2$); $\delta_H$ (300 MHz) 1.90 [2H, apparent qu, *J* 7.4, C(4)$H_2$], 2.61 [2H, t, *J* 7.6, C(5)$H_2$], 2.71 [2H, t, *J* 7.2, C(3)$H_2$], 3.88 (3H, s, OC$H_3$), 4.08 [2H, s, C(1)$H_2$], 6.97–7.04 (2H, m, aromatic *H* of 4-methoxyphenyl group), 7.12–7.33 (5H, m, aromatic *H* of phenyl group), 7.73–7.81 (2H, m, aromatic *H* of 4-methoxyphenyl group); $\delta_C$ (75.5 MHz) 24.7 [$CH_2$, *C*(4)$H_2$], 34.7 [$CH_2$, *C*(5)$H_2$], 43.6 [$CH_2$, *C*(3)$H_2$], 55.7 ($CH_3$, O*C*$H_3$), 67.2 [$CH_2$, *C*(1)$H_2$], 114.5 (CH, aromatic *C*H), 126.1 (CH, aromatic *C*H), 128.5 (CH, aromatic *C*H), 130.2 (C, aromatic *C*), 130.6 (CH, aromatic *C*H), 141.2 (C, aromatic *C*), 164.2 (C, aromatic *C*O$CH_3$), 198.3 (C, *C*O); HRMS (ESI+): Exact mass calculated for $C_{18}H_{21}O_4S$ $[M+H]^+$, 333.1161. Found 333.1157. m/z (ESI+): 333.1 $[M+H]^+$.

**1-(Cyclohexylsulfonyl)-5-phenylpentan-2-ol 24.** *n*-Butyllithium (2.5 M solution in hexanes; 0.25 mL, 0.63 mmol) was added to a solution of (methylsulfonyl)cyclohexane **7h** (0.10 g, 0.62 mmol) in dry tetrahydrofuran (10 mL) while stirring at −78 °C. The resultant mixture was stirred for 20 min at −78 °C followed by the addition of 4-phenylbutanal **8** (0.14 g, 0.93 mmol) in dry tetrahydrofuran (2 mL) dropwise over 1 h while stirring at −78 °C. Stirring was continued for 4 h while the solution was warmed to room temperature, then the reaction mixture was diluted with ether (10 mL) and quenched with saturated ammonium chloride solution (15 mL). The organic layer was washed with brine (20 mL), dried over magnesium sulfate, filtered and concentrated to give the crude β-hydroxysulfone **24** as an oil. Purification by column chromatography, employing 20% ethyl acetate in hexane as eluent, gave the pure β-hydroxysulfone **24** (0.03 g, 27%) as a white solid, Rf = 0.16 (20:80 ethyl acetate/hexane); mp 74–76 °C; (Found C, 65.80; H, 8.20 $C_{17}H_{26}O_3S$ requires C, 65.77; H, 8.44%); $\nu_{max}$(neat)/cm$^{-1}$ 3493 (OH), 2930, 2850 (CH), 1299, 1124 ($SO_2$); $\delta_H$ (400 MHz) 1.10–2.25 [14H, m, C(3)*H*$_2$, C(4)*H*$_2$ and 5 x cyclohexyl C*H*$_2$], 2.65 [2H, t, *J* 7.4, C(5)*H*$_2$], 2.86–2.98 [2H, m, cyclohexyl C*H* and 1 x C(1)*H*$_2$], 3.00–3.10 [1H, m, 1 x C(1)*H*$_2$], 3.27 (1H, bs, O*H*), 4.25–4.42 [1H, m, C(2)*H*], 7.12–7.22 (3H, m, 3 x aromatic *H*), 7.24–7.32 (2H, m, 2 x aromatic *H*); $\delta_C$ (100.6 MHz) 24.6 ($CH_2$, *C*$H_2$), 25.00 ($CH_2$, *C*$H_2$), 25.04 ($CH_2$, *C*$H_2$), 25.2 ($CH_2$, *C*$H_2$), 26.9 ($CH_2$, *C*$H_2$), 35.5 [$CH_2$, *C*(5)$H_2$], 36.2 ($CH_2$, *C*$H_2$), 55.4 [$CH_2$, *C*(1)$H_2$], 62.3 (CH, cylcohexyl *C*H), 65.6 [CH, *C*(2)H], 125.9 (CH, aromatic *C*H), 128.41 (CH, aromatic *C*H), 128.43 (CH, aromatic *C*H), 141.8 (C, *C*O); HRMS (ESI+): Exact mass calculated for $C_{17}H_{27}O_3S$ $[M+H]^+$, 311.1681. Found 311.1671. m/z (ESI+): 311.2 $[M+H]^+$.

**1-(Cyclohexylsulfonyl)-5-phenylpentan-2-one 9h.** 1-(Cyclohexylsulfonyl)-5-phenylpentan-2-ol **24** (0.47 g, 0.0015 mol), pyridinium chlorochromate (PCC) (0.59 g, 0.0027 mol) and 4Å molecular sieves (2.00 g) in dichloromethane (20 mL) were stirred at room temperature for 24 h. The reaction mixture was diluted with ether (60 mL) and filtered through a short plug of

silica gel and the filtrate was concentrated under reduced pressure to give the crude β-keto sulfone **9h** as a light brown solid. Purification by column chromatography, employing 10% ethyl acetate in hexane as eluent, gave the pure β-keto sulfone **9h** (0.39 g, 85%) as a white solid, Rf = 0.20 (20:80 ethyl acetate/hexane); mp 55–57 °C; (Found C, 66.44; H, 7.74. $C_{17}H_{24}O_3S$ requires C, 66.20; H, 7.84%); $\nu_{max}$(neat)/cm$^{-1}$ 1714 (C=O), 1305, 1121 ($SO_2$); $\delta_H$ (400 MHz) 1.13–1.40 (3H, m, 3 x cyclohexyl C*H*), 1.46–1.61 (2H, m, 2 x cyclohexyl C*H*), 1.67–1.78 (1H, m, 1 x cyclohexyl C*H*), 1.87–2.00 [4H, m, 2 x C(4)$H_2$ and 2 x cyclohexyl C*H*], 2.15 (2H, bd, *J* 12.6, 2 x cyclohexyl C*H*), 2.64 [2H, t, *J* 7.6, C(5)$H_2$], 2.74 [2H, t, *J* 7.6, C(3)$H_2$], 3.03–3.15 (1H, m, cyclohexyl C*H*), 3.93 [2H, s, C(1)$H_2$], 7.13–7.22 (3H, m, 3 x aromatic *H* of phenyl group), 7.23–7.32 (2H, m, 2 x aromatic *H* of phenyl group); $\delta_C$ (100.6 MHz) 24.6 ($CH_2$, cyclohexyl *C*$H_2$), 24.8 ($CH_2$, cyclohexyl *C*$H_2$), 24.9 ($CH_2$, cyclohexyl *C*$H_2$), 25.0 ($CH_2$, cyclohexyl *C*$H_2$), 34.7 [$CH_2$, *C*(5)$H_2$], 44.1 [$CH_2$, *C*(3)$H_2$], 60.3 [$CH_2$, *C*(1)$H_2$], 61.4 (CH, cyclohexyl *C*H), 126.1 (CH, aromatic *C*H), 128.5 (CH, aromatic *C*H), 141.2 (C, aromatic *C*), 199.5 (C, *C*O); HRMS (ESI+): Exact mass calculated for $C_{17}H_{25}O_3S$ $[M+H]^+$, 309.1524. Found 309.1518. m/z (ESI+): 309.2 $[M+H]^+$.

**1-[(4-Methylphenyl)sulfonyl]-5-phenylpentan-2-one 9i.** *n*-Butyllithium (2.5 M solution in hexanes; 14.08 mL, 0.0352 mol), freshly distilled diisopropylamine (5.22 mL, 0.0369 mol), 4-(methylsulfonyl)toluene (3.00 g, 0.0176 mol), ethyl 4-phenylbutanoate **8** (3.38 g, 0.0176mol) and THF (135 mL) were added following the procedure described for **9c** to give the crude β-keto sulfone **9i** as an orange solid. Purification by careful column chromatography, employing 20% ethyl acetate in hexane as eluent, gave the pure β-keto sulfone **9i** (3.21 g, 58%) as a white solid, Rf = 0.62 (40:60 ethyl acetate/hexane); mp 96–98 °C; (Found C, 68.17; H, 6.32. $C_{18}H_{20}O_3S$ requires C, 68.33; H, 6.37%); $\nu_{max}$(neat)/cm$^{-1}$ 1715 (C=O), 1319, 1146 ($SO_2$); $\delta_H$ (300 MHz) 1.89 [2H, qu, *J* 7.3, C(4)$H_2$], 2.44 (3H, s, C$H_3$), 2.61 [2H, t, *J* 7.3, C(5)$H_2$], 2.71 [2H, t, *J* 7.2, C(3)$H_2$], 4.08 [2H, s, C(1)$H_2$], 7.10–7.22 (3H, m, 3 x aromatic *H* of phenyl group), 7.23–7.31 (2H, m, 2 x

aromatic *H* of phenyl group), 7.35 (2H, d, *J* 7.4, aromatic *H* of 4-methylphenyl group), 7.73 (2H, d, *J* 8.2, aromatic *H* of 4-methylphenyl group); $\delta_C$ (100.6 MHz) 21.7 (*C*$H_3$), 24.7 [$CH_2$, *C*(4)$H_2$], 34.7 [$CH_2$, *C*(5)$H_2$], 43.6 [$CH_2$, *C*(3)$H_2$], 67.1 [$CH_2$, *C*(1)$H_2$], 126.1 (CH, aromatic *C*H), 128.3 (CH, aromatic *C*H) 128.5 (CH, aromatic *C*H), 130.0 (CH, aromatic *C*H), 135.8 (C, aromatic *C*), 141.2 (C, aromatic *C*), 145.4 (C, aromatic *C*), 198.1 (C, *C*O); HRMS (ESI+): Exact mass calculated for $C_{18}H_{21}O_3S$ $[M+H]^+$, 317.1211. Found 317.1227. m/z (ESI+): 317.1 $[M+H]^+$.

**1-[(4-Bromophenyl)sulfonyl]-5-phenylpentan-2-one 9j.** *n*-Butyllithium (1.6 M solution in hexanes; 14.8 mL, 0.023 mol), freshly distilled diisopropylamine (3.5 mL, 0.025 mol), 1-Bromo-4-(methylsulfonyl) benzene (2.78 g, 0.0118 mol), ethyl 4-phenylbutanoate **8** (2.27 g, 0.0360 mol) in THF (95 mL) were then added following the procedure described for **9a** to give the crude β-keto sulfone **9j** as an orange sticky solid. Purification by careful column chromatography, employing 20% ethyl acetate in hexane as eluent, gave the pure β-keto sulfone **9j** (1.37 g, 30%) as a light yellow solid, Rf = 0.32 (20:80 ethyl acetate : hexane); mp 95–99 °C, (Found C, 53.89; H, 4.55. $C_{17}H_{17}BrO_3S$ requires C, 53.55; H, 4.49%); $\nu_{max}$(KBr)/$cm^{-1}$ 1715 (C=O), 1323, 1149 ($SO_2$); $\delta_H$(300 MHz) 1.91 [2H, apparent qu, *J* 7.4, C(4)*H*$_2$], 2.62 [2H, t, *J* 7.6, C(5)*H*$_2$], 2.70 [2H, t, *J* 7.2, C(3)*H*$_2$], 4.10 [2H, s, C(1)*H*$_2$], 7.14–7.33 (5H, m, aromatic H of phenyl group), 7.72 (4H, s, aromatic H of *p*-bromophenylsulfonyl group); $\delta_C$ (75.5 MHz) 24.6 [$CH_2$, *C*(4)$H_2$], 34.6 [$CH_2$, *C*(5)$H_2$], 43.7 [$CH_2$, *C*(3)$H_2$], 66.6 [$CH_2$, *C*(1)$H_2$], 126.2 (CH, aromatic *C*H), 128.47 (CH, aromatic *C*H), 128.50 (CH, aromatic *C*H), 129.8 (C, aromatic *C*Br), 129.9 (CH, aromatic *C*H), 132.7 (CH, aromatic *C*H), 137.5 (C, aromatic *C*), 141.9 (C, aromatic *C*), 197.9 (C, *C*O); m/z (ES–) 379.1/381.1 $[(M–H)^–$, ($^{79}$Br : $^{81}$Br, 1 : 1)].

**1-(Methylsulfonyl)-5-phenylpentan-2-one 9k.** Dimethyl sulfone (1.94 g, 0.0206 mol), *n*-butyllithium (2.0 M solution in hexanes; 20.6 mL, 0.041 mol), ethyl 4-phenylbutanoate **8** (3.96

g, 0.0206 mol) in THF (200 mL) were used following the procedure described for **9a** to give, following purification by column chromatography employing 10% ethyl acetate in hexane as eluent, the sulfone **9k** (2.09 g, 42%) as a white solid, Rf = 0.54 (20:80 ethyl acetate/hexane); mp 72–75 °C; (Found C, 60.37; H, 6.77. $C_{12}H_{16}O_3S$ requires C, 59.97; H, 6.71%); $\nu_{max}$(KBr)/$cm^{-1}$ 1709 (C=O), 1312, 1144 ($SO_2$); $\delta_H$(400 MHz) 1.96 [2H, apparent qu, *J* 7.4, C(4)$H_2$], 2.65 [2H, t, *J* 7.6, C(5)H2], 2.71 [2H, t, *J* 7.2, C(3)$H_2$], 3.03 (3H, s, C$H_3SO_2$), 3.97 [2H, s, C(1)$H_2$], 7.14– 7.23 (3H, m, aromatic *H*), 7.25–7.32 (2H, m, aromatic *H*); $\delta_C$(75.5 MHz) 24.5 [$CH_2$, *C*(4)$H_2$], 34.6 [$CH_2$, *C*(5)$H_2$], 41.5 ($CH_3$, *C*$H_3SO_2$), 44.1 [$CH_2$, *C*(3)$H_2$], 64.58 [$CH_2$, *C*(1)$H_2$], 126.2 (CH, aromatic *C*H), 128.5 (CH, aromatic *C*H), 141.0 (C, aromatic *C*), 199.4 (C, *C*O); m/z (ES+) 281.0 [$(M+MeCN)^+$, 10%], 354.4 [$(M+H+TFA)^+$, 36%].

**1-Hydroxy-1,6-diphenylhex-1-en-3-one 9l.** Lithium bis(trimethylsilyl)amide [(LiHMDS), 1.0 M in THF, 2.0 mL, 2.00 mmol] was diluted in freshly distilled tetrahydrofuran (6 mL) and cooled to −78 °C. A solution of acetophenone (0.22 mL, 1.88 mmol) in tetrahydrofuran (2 mL) was added dropwise over 4 min. The reaction mixture was stirred at −78 °C for 1 h, then a solution containing 1-(1*H*-benzo[*d*][1,2,3]triazol-1-yl)-4-phenylbutan-1-one **12** (0.5 g, 1.88 mmol) in tetrahydrofuran (2mL) was added in one portion. The reaction mixture was allowed to slowly warm to room temperature and stirred overnight. The reaction mixture was diluted with aqueous hydrochloric acid (2.0 M, 20 mL) and stirred for 10 min. The layers were separated and the aqueous layer was extracted with ether (2 x 50 mL). The combined organic extracts were washed with brine (20 mL), dried with magnesium sulfate and concentrated to yield a yellow oil. The resulting oil was redissolved in ether (100 mL), washed with aqueous hydrochloric acid (2.0 M, 3 x 20 mL), brine (20 mL) and concentrated under reduced pressure to yield the crude diketone **9l** as light yellow oil. Purification by column chromatography employing 20% ethyl acetate in hexane as the eluent gave the purified diketone **9l** (1.61 g,

32%) as a cloudy oil that solidifies upon storage to a white solid. $^1$H NMR indicates this exists predominately as the enol form in $CDCl_3$ ~4% keto at 4.05ppm [s, C(2)$H_2$]. Rf = 0.54 (20:80 ethyl acetate/hexane); mp 25–27 °C; $\nu_{max}$(neat)/cm$^{-1}$ 2946 (OH), 1598, 1571 (C=O), 737, 752, 688; $\delta_H$ (400 MHz) 2.02 [2H, apparent qu, *J* 7.6, C(5)$H_2$], 2.45 [2H, t, *J* 7.6, C(6)$H_2$], 2.70 [2H, t, *J* 7.6, C(4)$H_2$], 6.15 [1H, s, C(2)*H*], 7.12–7.34 (5H, m, aromatic *H*), 7.38–7.58 (3H, m, aromatic *H*), 7.84–7.90 (2H, m, aromatic *H*), 16.19 (1H, s, O*H*); $\delta_C$ (106.6 MHz) 27.3 [$CH_2$, *C*(5)$H_2$], 35.3 [$CH_2$, *C*(6)$H_2$], 38.6 [$CH_2$, *C*(3)$H_2$], 96.2 [CH, *C*(2)$H_2$], 126.1 (CH, aromatic *C*H), 127.0 (CH, aromatic *C*H), 128.45 (CH, aromatic *C*H), 128.54 (CH, aromatic *C*H), 128.6 (CH, aromatic *C*H), 132.3 (CH, aromatic *C*H), 135.0 (C, aromatic *C*), 141.5 (C, aromatic *C*), 183.4 (C, *C*OH), 196.9 (C, *C*O); HRMS (ESI+): Exact mass calculated for $C_{18}H_{19}O_2$ $[M+H]^+$, 267.1373. Found 267.1385. m/z (ESI+): 267.1 $[M+H]^+$. Keto peaks seen at $\delta_H$ (400 MHz) 4.05 [2H, s, C(2)$H_2$]; $\delta_C$ (106.6 MHz) 25.0 (*C*$H_2$), 34.9 (*C*$H_2$), 42.6 (*C*$H_2$), 54.0 (*C*$H_2$), 128.4(CH, aromatic *C*H), 128.5(CH, aromatic *C*H), 128.6(CH, aromatic *C*H), 128.7(CH, aromatic *C*H), 128.8(CH, aromatic *C*H), 133.2(CH, aromatic *C*H), 133.8 (CH, aromatic *C*H), 136.3 (C, aromatic *C*), 137.2 (C, aromatic *C*), 194.0 (C, *C*O), 204.2 (C, *C*O).

**1-(Diphenylphosphoryl)-5-phenylpentan-2-one 11.** *n*-Butyllithium (2.5 M solution in hexanes; 8.07 mL, 0.0210 mol) was added dropwise to a solution of methyl(diphenyl)phosphine oxide (4.50 g, 0.0210 mol) in THF (90 mL) while stirring at −78 °C. The resulting translucent yellow solution was stirred for 1 h at −78 °C. A solution of ethyl 4-phenylbutanoate **8** (3.00 g, 0.0155 mol) in THF (10 mL) was added dropwise over 15 min producing a light yellow solution. The reaction mixture was stirred for an hour at −78 °C followed by a quench with saturated ammonium chloride solution (75 mL). The organic layer was isolated and the aqueous layer washed with diethyl ether (3 × 50 mL). The organic layers were combined and washed with brine (50 mL), dried with magnesium sulfate, filtered and

concentrated under reduced pressure to give the crude β- keto phosphine oxide **11** as a white solid. Purification by column chromatography, employing 60% ethyl acetate in hexane as eluent, gave the pure β- keto phosphine oxide **11** (6.70 g, 89%) as a white solid, Rf = 0.19 (50:50 ethyl acetate/hexane); mp 143–145 °C; $\nu_{max}$(neat)/cm$^{-1}$ 1704 (C=O), 1176 (P=O); $\delta_H$ (400 MHz) 1.81 [2H, apparent qu, *J* 7.5, C(4)*H*$_2$], 2.51 [2H, t, *J* 7.7, C(5)*H*$_2$], 2.67 [2H, t, *J* 7.2, C(3)*H*$_2$], 3.57 [2H, d, $^2J_{PH}$ 14.9, C(1)*H*$_2$], 7.07–7.20 (3H, m, aromatic *H*), 7.21–7.29 (2H, m, aromatic *H*), 7.43–7.59 (6H, m, aromatic *H*), 7.70–7.81 (4H, m, aromatic *H*); $\delta_P$ (162 MHz) 26.51 (1P, s, *P*O); $\delta_C$ (100.6 MHz) 24.9[CH$_2$, *C*(4)H$_2$], 34.8 [CH$_2$, *C*(5)H$_2$], 44.7 [CH$_2$, *C*(3)H$_2$], 47.14 [CH$_2$, d, $^1J_{CP}$ 56.7, *C*(1)H$_2$], 125.9 (CH, aromatic *C*H), 128.3 (CH, aromatic *C*H), 128.5 (CH, aromatic *C*H), 128.8 (CH, d, $^2J_{CP}$ 12.3, aromatic *C*H), 130.9 (CH, d, $^3J_{CP}$ 9.9, aromatic *C*H), 132.3 (CH, d, $^4J_{CP}$ 2.8, aromatic *C*H), 132.0 (C, d, $^1J_{CP}$ 103.0, aromatic *C*), 141.6 (C, aromatic *C*), 202.8 (C, d, $^2J_{CP}$ 5.3*, C*O); HRMS (ESI+): Exact mass calculated for $C_{23}H_{24}O_2P$ $[M+H]^+$, 363.1514. Found 363.1530. m/z (ESI+): 363.2 $[M+H]^+$.

**1-Diazo-1-phenylsulfonyl-5-phenylpentan-2-one 4a.** Anhydrous potassium carbonate (2.25 g, 16.3 mmol) was added to a solution of 1-phenylsulfonyl-5-phenylpentan-2-one **9a** (3.80 g, 12.6 mmol) in acetonitrile (75 mL). The mixture was stirred at room temperature and a solution of *p*-toluenesulfonyl azide (0.50 g, 2.10 mmol) in acetonitrile (10 mL) was added over 2 min. The reaction mixture was stirred for 4 h then diethyl ether (10 mL) and hexane (20 mL) were added to precipitate the amide salts. The resultant mixture was filtered through a short pad of Celite® and the filtrate concentrated under reduced pressure. Purification by column chromatography, employing 10% ethyl acetate in hexane as eluent, gave the α-diazo-β-keto sulfone **9a** (3.19 g, 77%) as a yellow solid, Rf = 0.53 (40:60 ethyl acetate/hexane) mp 80–82 °C; (lit., 78–81 °C); $\nu_{max}$(KBr)/cm$^{-1}$ 2122 ($CN_2$), 1677 (C=O), 1336, 1154 ($SO_2$); $\delta_H$ (300 MHz) 1.90 [2H, qu, *J* 7.4, C(4)*H*$_2$], 2.54, 2.59 [4H, 2 x overlapping t, *J* 7.5 x 2, C(5)*H*$_2$ and C(3)*H*$_2$], 7.07–

7.13 (2H, m, aromatic *H* of phenyl group), 7.17–7.31 (3H, m, aromatic *H* of phenyl group), 7.51–7.58 (2H, m, aromatic *H* of phenylsulfonyl group), 7.62–7.69 (1H, m, aromatic *H* of phenylsulfonyl group), 7.87–7.92 (2H. m, aromatic *H* of phenylsulfonyl group); $\delta_C$ (75.5 MHz) 25.1 [$CH_2$, *C*(4)$H_2$], 34.8 [$CH_2$, *C*(5)$H_2$], 38.3 [$CH_2$, *C*(3)$H_2$], 125.9 (CH, aromatic *C*H), 127.6 (CH, aromatic *C*H), 128.8 (CH, aromatic *C*H), 129.8 (CH, aromatic *C*H), 134.3 (CH, aromatic *C*H), 141.0 (C, aromatic *C*), 142.1 (C, aromatic *C*), 188.2 (C, *C*O), *C*$N_2$ signal not observed. Spectral characteristics were consistent with previously reported data.[35]

**1-Diazo-1-[(4-fluorophenyl)sulfonyl]-5-phenylpentan-2-one 4b.** Anhydrous potassium carbonate (0.80 g. 5.80 mmol), 1-[(4-fluorophenyl)sulfonyl]-5-phenylpentan-2-one **9b** (1.42 g, 4.40 mmol), *p*-acetamidobenzenesulfonyl azide (*p*-ABSA) (1.07 g, 4.40 mmol) and acetonitrile (50 mL) were used following the procedure described for **4a** to yield, following column chromatography employing 20% ethyl acetate in hexane as eluent, the α-diazo-β-keto sulfone **4b** (1.20 g, 66%) as a yellow solid, Rf = 0.40 (20:80 ethyl acetate/hexane); mp 73–75 °C; (Found C, 58.95; H, 4.40; N, 7.95, $C_{17}H_{15}FN_2O_3S$ requires C, 58.95; H, 4.37; N, 8.09%); $\nu_{max}$(neat)/$cm^{-1}$ 2125 ($CN_2$), 1667 (C=O), 1337, 1166 ($SO_2$); $\delta_H$ (400 MHz) 1.92 [2H, qu, *J* 7.3, C(4)$H_2$], 2.50 [2H, t, *J* 7.3, C(5)$H_2$], 2.61 [2H, t, *J* 7.3, C(3)$H_2$], 7.22 (2H, d, *J* 7.4, aromatic *H* of *p*-fluorophenylsulfonyl group), 7.15–7.31 (5H, m, aromatic *H* of phenyl group), 7.86–7.97 (2H, m, aromatic *H* of *p*-fluorophenylsulfonyl group); $\delta_F$ (376.5 MHz) -102.1 (1F, s, *p-F*); $\delta_C$ (100.6 MHz) 24.9 [$CH_2$, *C*(4)$H_2$], 34.7 [$CH_2$, *C*(5)$H_2$], 38.2 [$CH_2$, *C*(3)$H_2$], 85.0 (C, *C*$N_2$), 116.8 (CH, d, $^2J_{CF}$ 22.8, aromatic *C*H), 126.2 (CH, aromatic *C*H), 128.5 (CH, aromatic *C*H), 128.5 (CH, aromatic *C*H), 130.5 (CH, d, $^3J_{CF}$ 9.7, aromatic *C*H), 137.9 (C, d, $^4J_{CF}$ 3.2, aromatic *C*), 140.8 (C, aromatic *C*), 165.9 (C, $^1J_{CF}$ 257.7, aromatic *C*F), 187.8 (C, *C*O); HRMS (ESI+): Exact mass calculated for $C_{17}H_{16}FN_2O_3S$ $[M+H]^+$, 347.0862. Found 347.0866. m/z (ESI+): 347.1 $[M+H]^+$.

**1-Diazo-1-(naphthalen-2-ylsulfonyl)-5-phenylpentan-2-one 4c.** Anhydrous potassium carbonate (0.47 g. 3.40 mmol), 1-naphthalen-2-ylsulfonyl)-5-phenylpentan-2-one **9c** (0.91 g, 2.60 mmol), *p*-ABSA (0.62 g, 2.60 mmol) and acetonitrile (35 mL) were used following the procedure described for **4a** to yield, following column chromatography employing 20% ethyl acetate in hexane as eluent, the α-diazo-β-keto sulfone **4c** (0.63 g, 64%) as a yellow solid, Rf = 0.43 (20:80 ethyl acetate/hexane); mp 67–70 °C; (Found: C, 66.32; H, 5.09; N, 7.46, $C_{21}H_{18}N_2O_3S$ requires C, 66.65; H, 4.79; N, 7.40%); $\nu_{max}$ (neat)/$cm^{-1}$ 2122 ($CN_2$), 1669 (C=O), 1336, 1174 ($SO_2$); $\delta_H$ (300 MHz) 1.87 [2H, qu, *J* 7.4, C(4)$H_2$], 2.55 [4H, t, *J* 7.4, C(5)$H_2$ and C(3)$H_2$], 6.98–7.06 (2H, m, aromatic *H* of phenyl group), 7.07–7.23 (3H, m, aromatic *H* of phenyl group), 7.68 (2H, qud, *J* 7.0, 1.4, aromatic *H* of 2-naphthyl group), 7.84 (1H, dd, *J* 8.8, 1.9, aromatic *H* of 2-naphthyl group), 7.90–8.04 (3H, m, aromatic *H* of 2-naphthyl group), 8.50 (1H, d, *J* 1.4, aromatic *H* of 2-naphthyl group); $\delta_C$ (75.5 MHz) 25.1 [$CH_2$, *C*(4)$H_2$], 34.7 [$CH_2$, *C*(5)$H_2$], 38.3 [$CH_2$, *C*(3)$H_2$], 121.8 (CH, aromatic *C*H), 126.1 (CH, aromatic *C*H), 128.0 (CH, aromatic *C*H), 128.1 (CH, aromatic *C*H), 128.4 (CH, aromatic *C*H), 129.3 (CH, aromatic *C*H), 129.67 (CH, aromatic *C*H), 129.71 (CH, aromatic *C*H), 130.0 (CH, aromatic *C*H), 132.0 (C, aromatic *C*), 135.4 (C, aromatic *C*), 138.8 (C, aromatic *C*), 140.9 (C, aromatic *C*), 188.2 (C, *C*O), *C*$N_2$ signal not observed; HRMS (ESI+): Exact mass calculated for $C_{21}H_{19}N_2O_3S$ $[M+H]^+$, 379.1111. Found 379.1116. m/z (ESI +): 379.1 $[M+H]^+$.

**1-Diazo-1-(naphthalen-1-ylsulfonyl)-5-phenylpentan-2-one 4d**. Anhydrous potassium carbonate (0.26 g. 1.90 mmol), 1-naphthalen-1-ylsulfonyl)-5-phenylpentan-2-one **9d** (0.51 g, 1.40 mmol), *p*-ABSA (0.35 g, 1.40 mmol) and acetonitrile (25 mL) were used following the procedure described for **4a** to yield, following column chromatography employing 20% ethyl acetate in hexane as eluent, the α-diazo-β-keto sulfone **4d** (0.28 g, 52%) as a yellow solid, Rf = 0.38 (20:80 ethyl acetate/hexane); mp 88–91 °C; (Found: C, 66.59; H, 4.50, $C_{21}H_{18}N_2O_3S$

requires C, 66.65; H, 4.79%); $\nu_{max}$ (neat)/$cm^{-1}$ 2114 ($CN_2$), 1664 (C=O), 1332, 1154 ($SO_2$); $\delta_H$ (300 MHz) 1.79 [2H, apparent qu, *J* 7.4, C(4)$H_2$], 2.42, 2.48 [4H, 2 x overlapping t, *J* 7.4 x 2, C(3)$H_2$ and C(5)$H_2$], 6.96–7.07 (2H, m, aromatic *H* of phenyl group), 7.13–7.30 (3H, m, aromatic *H* of phenyl group), 7.56 (1H, t, *J* 7.8, aromatic *H* of 1-naphthyl group), 7.61–7.66 (1H, m aromatic *H* of 1-naphthyl group), 7.72 (1H, td, *J* 8.5, 1.3, aromatic *H* of 1-naphthyl group), 7.99 (1H, d, *J* 7.9, aromatic *H* of 1-naphthyl group), 8.13 (1H, d, *J* 8.2, aromatic *H* of 1-naphthyl group), 8.31 (1H, d, *J* 7.4, aromatic *H* of 1-naphthyl group), 8.42 (1H, d, *J* 8.6, aromatic *H* of 1-naphthyl group); $\delta_C$ (100.6 MHz) 24.9 [$CH_2$, *C*(4)$H_2$], 34.7 [$CH_2$, *C*(5)$H_2$], 38.2 [$CH_2$, *C*(3)$H_2$], 123.3 (CH, aromatic *C*H), 124.3 (CH, aromatic *C*H), 126.1 (CH, aromatic *C*H), 127.3 (CH, aromatic *C*H), 127.9 (C, aromatic *C*), 128.4 (CH, aromatic *C*H), 129.3 (CH, aromatic *C*H), 129.7 (CH, aromatic *C*H), 131.5 (CH, aromatic *C*H), 134.4 (C, aromatic *C*), 135.8 (CH, aromatic *C*H), 136.3 (C, aromatic *C*), 140.9 (C, aromatic *C*), 188.4 (C, *C*O), *C*$N_2$ signal not observed; HRMS (ESI+): Exact mass calculated for $C_{21}H_{19}N_2O_3S$ $[M+H]^+$, 379.1107. Found 379.1116. m/z (ESI+): 379.1 $[M+H]^+$.

**1-Diazo-1-(mesitylsulfonyl)-5-phenylpentan-2-one 4e.** Anhydrous potassium carbonate (0.89 g. 6.40 mmol), 1-(mesitylsulfonyl)-5-phenylpentan-2-one **9e** (1.70 g, 4.90 mmol), *p*-ABSA (1.19 g, 4.90 mmol) and acetonitrile (60 mL) were used following the procedure described for **4a** to yield, following column chromatography employing 20% ethyl acetate in hexane as eluent, the α-diazo-β-keto sulfone **4e** (1.20 g, 66%) as a yellow solid, Rf = 0.57 (20:80 ethyl acetate/hexane); mp 111–114 °C; (Found: C, 65.07; H, 5.98, $C_{20}H_{22}N_2O_3S$ requires C, 64.84; H, 5.99%); $\nu_{max}$ (neat)/$cm^{-1}$ 2101 ($CN_2$), 1674 (C=O), 1322, 1147 ($SO_2$); $\delta_H$ (300 MHz) 1.82 [2H, apparent qu, *J* 7.5, C(4)$H_2$], 2.31 (3H, s, C$H_3$), 2.38 [2H, t, *J* 7.5, C(5)$H_2$], 2.51 [2H, t, *J* 7.5, C(3)$H_2$], 2.61 (6H, s, 2 x C$H_3$), 6.97 (2H, s, aromatic *H* of mesityl group), 7.04 (2H, d, *J* 7.1, aromatic *H* of phenyl group), 7.12–7.29 (3H, m, aromatic *H* of phenyl group); $\delta_C$ (75.5 MHz)

21.1 ($CH_3$, $CH_3$), 22.5 ($CH_3$, 2 x $CH_3$), 24.9 [$CH_2$, $C(4)H_2$], 34.7 [$CH_2$, $C(5)H_2$], 38.1 [$CH_2$, $C(3)H_2$], 126.1 (CH, aromatic *C*H)*, 128.3 (CH, aromatic *C*H), 128.4 (CH, aromatic *C*H), 132.6 (CH, aromatic *C*H), 135.1 (C, aromatic *C*), 140.1 (C, aromatic *C*), 141.0 (C, aromatic *C*), 144.1 (C, aromatic *C*), 188.7 (C, *C*O), *C*$N_2$ signal not observed; HRMS (ESI+): Exact mass calculated for $C_{20}H_{23}N_2O_3S$ $[M+H]^+$, 371.1423. Found 371.1429. m/z (ESI+): 371.1 $[M+H]^+$.

**1-Diazo-1-[(2-ethylphenyl)sulfonyl]-5-phenylpentan-2-one 4f.** Anhydrous potassium carbonate (0.48 g. 3.40 mmol), 1-[(2-ethylphenyl)sulfonyl]-5-phenylpentan-2-one **9f** (0.88 g, 2.70 mmol), *p*-ABSA (0.64 g, 2.70 mmol) and acetonitrile (35 mL) were used following the procedure described for **4a** to yield, following column chromatography employing 20% ethyl acetate in hexane as eluent, the α-diazo-β-keto sulfone **4f** (0.55 g, 58%) as a yellow oil, Rf = 0.76 (40:60 ethyl acetate/hexane); $\nu_{max}$ (neat)/$cm^{-1}$ 2104 ($CN_2$), 1662 (C=O), 1330, 1152 ($SO_2$); $\delta_H$ (300 MHz) 1.29 (3H, t, *J* 7.5, $CH_2CH_3$), 1.83 [2H, qu, *J* 7.5, $C(4)H_2$], 2.44 [2H, t, *J* 7.4, $C(5)H_2$], 2.52 [2H, t, *J* 7.5, $C(3)H_2$], 2.94 (2H, q, *J* 7.5, $CH_2CH_3$), 7.01–7.12 (2H, m, aromatic *H* of phenyl group), 7.13–7.29 (3H, m, aromatic *H* of phenyl group), 7.32–7.46 (2H, m, aromatic *H* of 2-ethylphenyl group), 7.58 (1H, td, *J* 7.6, 1.2, aromatic *H* of 2-ethylphenyl group), 8.00 (1H, dd, *J* 8.0, 1.1, aromatic *H* of 2-ethylphenyl group); $\delta_C$ (75.5 MHz) 15.0 ($CH_3$, $CH_2CH_3$), 25.1 [$CH_2$, $C(4)H_2$], 25.7 ($CH_2$, $CH_2CH_3$), 34.8 [$CH_2$, $C(5)H_2$], 38.3 [$CH_2$, $C(3)H_2$], 126.1 (CH, aromatic *C*H), 126.5 (CH, aromatic *C*H), 128.4 (CH, aromatic *C*H), 130.2 (CH, aromatic *C*H), 131.1 (CH, aromatic *C*H), 134.3 (CH, aromatic *C*H), 139.3 (C, aromatic *C*), 141.0 (C, aromatic *C*), 143.6 (C, aromatic *C*), 188.6 (C, *C*O), *C*$N_2$ signal not observed; HRMS (ESI +): Exact mass calculated for $C_{19}H_{21}N_2O_3S$ $[M+H]^+$, 357.1259. Found 357.1273. m/z (ESI +): 357.1 $[M+H]^+$.

**1-Diazo-1-[(4-methoxyphenyl)sulfonyl]-5-phenylpentan-2-one 4g.** Anhydrous potassium carbonate (0.32 g. 2.35 mmol), 1-[(4-methoxyphenyl)sulfonyl]-5-phenylpentan-2-one **9g**

(0.60 g, 1.81 mmol), *p*-ABSA (0.43 g, 1.81 mmol) and acetonitrile (35 mL) were used following the procedure described for **4a** to yield, following column chromatography employing 10% ethyl acetate in hexane as eluent, the α-diazo-β-keto sulfone **4g** (0.47 g, 72%) as a yellow oil, Rf = 0.23 (20:80 ethyl acetate/hexane); $\nu_{max}$(neat)/cm$^{-1}$ 2105 ($CN_2$), 1661 (C=O), 1334, 1144 ($SO_2$); $\delta_H$ (300 MHz) 1.90 [2H, qu, *J* 7.4, C(4)$H_2$], 2.52 [2H, t, *J* 7.4 C(5)$H_2$], 2.59 [2H, t, *J* 7.4, C(3)$H_2$], 3.88 (3H, s, OC$H_3$), 6.93–7.01 (2H, m, aromatic *H* of 4-methoxyphenyl group), 7.06–7.14 (2H, m, aromatic *H* of phenyl group), 7.15–7.32 (3H, m, aromatic *H* of phenyl group), 7.79–7.87 (2H, m, aromatic *H* of 4-methoxyphenyl group); $\delta_C$ (75.5 MHz) 25.0 [$CH_2$, *C*(4)$H_2$], 34.8 [$CH_2$, *C*(5)$H_2$], 38.2 [$CH_2$, *C*(3)$H_2$], 55.8 ($CH_3$, O*C*$H_3$), 114.6 (CH, aromatic *C*H), 126.1 (CH, aromatic *C*H), 128.44 (CH, aromatic *C*H), 128.45 (CH, aromatic *C*H), 129.7 (CH, aromatic *C*H), 133.6 (C, aromatic *C*), 141.0 (C, aromatic *C*), 164.0 (C, aromatic *C*OC$H_3$), 188.4 (C, *C*O), *C*$N_2$ signal not observed; HRMS (ESI+): Exact mass calculated for $C_{18}H_{19}N_2O_4S$ $[M+H]^+$, 359.1066. Found 359.1073. m/z (ESI+): 359.1 $[M+H]^+$.

**1-(Cyclohexylsulfonyl)-1-diazo-5-phenylpentan-2-one 4h.** Anhydrous potassium carbonate (0.67 g. 4.80 mmol), 1-(cyclohexylsulfonyl)-5-phenylpentan-2-one **9h** (1.15 g, 3.70 mmol), *p*-ABSA (0.90 g, 3.70 mmol) and acetonitrile (50 mL) were used following the procedure described for **4a** to yield, following column chromatography employing 20% ethyl acetate in hexane as eluent, the α-diazo-β-keto sulfone **4h** (1.16 g, 93%) as a yellow oil which solidifies upon storage at a low temperature, Rf = 0.40 (20:80 ethyl acetate/hexane); mp 48–50 °C; $\nu_{max}$(neat)/cm$^{-1}$ 2107 ($CN_2$), 1660 (C=O), 1324, 1138 ($SO_2$); $\delta_H$ (400 MHz) 1.11–1.37 (3H, m, 3 x cyclohexyl C$H_2$), 1.45–1.60 (2H, m, 2 x cyclohexyl C$H_2$), 1.67–1.78 (1H, m, 1 x cyclohexyl C$H_2$), 1.87–2.06 (4H, m, 2 x C(4)$H_2$ and 2 x cyclohexyl C$H_2$), 2.12 (2H, d, *J* 11.5, 2 x cyclohexyl C$H_2$), 2.64, 2.66 [4H, 2 x overlapping t, *J* 7.5, 7.4, C(5)$H_2$ and C(3)$H_2$], 3.17 (1H, tt, *J* 3.3, 12.0, cyclohexyl C*H*), 7.14–7.23 (3H, m, aromatic *H*), 7.24–7.33 (2H, m, aromatic *H*); $\delta_C$ (100.6 MHz)

25.0 ($CH_2$, 3 x *C*$H_2$), 25.4 ($CH_2$, 3 x *C*$H_2$), 34.8 [$CH_2$, *C*(5)$H_2$], 38.3 [$CH_2$, *C*(3)$H_2$], 66.0 (C, cyclohexyl *C*H), 80.3 (C, *C*$N_2$), 126.2 (CH, aromatic *C*H), 128.47 (CH, aromatic *C*H), 128.49 (CH, aromatic *C*H), 141.02 (C, aromatic *C*), 189.1 (C, *C*O); HRMS (ESI+): Exact mass calculated for $C_{17}H_{23}N_2O_3S$ $[M+H]^+$, 335.1429. Found 347.0866. m/z (ESI+): 335.1 $[M+H]^+$.

**1-Diazo-1-[(4-methylphenyl)sulfonyl]-5-phenylpentan-2-one 4i.** Anhydrous potassium carbonate (0.38 g, 2.70 mmol), 1-[(4-methylphenyl)sulfonyl]-5-phenylpentan-2-one **9i** (0.66g, 2.10 mmol), *p*-ABSA (0.50 g, 2.10 mmol) and acetonitrile (30 mL) were used following the procedure described for **4a** to yield, following column chromatography employing 20% ethyl acetate in hexane as eluent, the α-diazo-β-keto sulfone **4i** (0.66 g, 93%) as a yellow solid, Rf = 0.42 (20:80 ethyl acetate/hexane); mp 100–102 °C; (Found: C, 63.05; H, 5.37; N, 7.91, $C_{18}H_{18}N_2O_3S$ requires C, 63.14; H, 5.30; N, 8.18%); $\nu_{max}$ (neat)/$cm^{-1}$ 2126 ($CN_2$), 1671 (C=O), 1330, 1156 ($SO_2$); $\delta_H$ (400 MHz) 1.89 [2H, apparent qu, *J* 7.4, C(4)*H*$_2$], 2.45 (1H, s, C*H*$_3$), 2.52 [2H, t, *J* 7.4, C(5)*H*$_2$], 2.58 [2H, t, *J* 7.5 C(3)*H*$_2$], 7.07–7.13 (2H, m, aromatic *H* of 4-methylphenyl group), 7.16–7.22 (1H, m, aromatic *H* of phenyl group), 7.23–7.29 (2H, m, aromatic *H* of phenyl group), 7.30–7.36 (2H, m, aromatic *H* of phenyl group), 7.78 (2H, d, *J* 8.3, aromatic *H* of 4-methylphenyl group); $\delta_C$ (100.6 MHz) 21.7 ($CH_3$, 4-methylphenyl *C*$H_3$), 25.1 [$CH_2$, *C*(4)$H_2$], 34.8 [$CH_2$, *C*(5)$H_2$], 38.3 [$CH_2$, *C*(3)$H_2$], 126.1 (CH, aromatic *C*H), 127.4 (CH, aromatic *C*H), 128.45 (CH, aromatic *C*H), 128.46 (CH, aromatic *C*H), 130.1 (CH, aromatic *C*H), 139.1 (C, aromatic *C*), 141.0 (C, aromatic *C*), 145.4 (C, aromatic *C*), 188.4 (C, *C*O), *C*$N_2$ signal not observed; HRMS (ESI +): Exact mass calculated for $C_{18}H_{19}N_2O_3S$ $[M+H]^+$, 343.1110. Found 343.1116. m/z (ESI +): 343.1 $[M+H]^+$.

**1-Diazo-1-[(4-bromophenyl)sulfonyl]-5-phenylpentan-2-one 4j.** Anhydrous potassium carbonate (0.50 g, 0.0036 mol), 1-[(4-bromophenyl) sulfonyl]-5-phenylpentan-2-one **9j** (1.07

g, 0.0028 mol), *p*-toluenesulfonyl azide (0.55 g, 0.0028 mol) and acetonitrile (45 mL) were used following the procedure described for **4a** to yield, following column chromatography employing 20% ethyl acetate in hexane as eluent, the α-diazo-β-keto sulfone **4j** (0.72 g, 63%) as a yellow solid, Rf = 0.43 (20:80 ethyl acetate/hexane); mp 87–89 °C, (Found C, 50.13; H, 4.09; N, 7.09; $C_{17}H_{15}BrN_2O_3S$ requires C, 50.13; H, 3.71; N, 6.88%); $\nu_{max}$(KBr)/cm$^{-1}$ 2128 ($CN_2$), 1672 (C=O), 1337, 1158 ($SO_2$); $\delta_H$(300 MHz) 1.92 [2H, apparent qu, *J* 7.4, C(4)$H_2$], 2.49 [2H, t, *J* 7.4, C(3)$H_2$], 2.61 [2H, t, *J* 7.3, C(5)$H_2$], 7.08–7.12 (2H, m, aromatic *H* of phenyl group), 7.20–7.32 (3H, m, aromatic *H* of phenyl group), 7.64–7.70 (2H, m, aromatic *H* of *p*-bromophenylsulfonyl group), 7.73–7.79 (2H, m, aromatic *H* of *p*-bromophenylsulfonyl group); $\delta_C$ (75.5 MHz) 24.8 [$CH_2$, *C*(4)$H_2$], 34.6 [$CH_2$, *C*(5)$H_2$], 38.3 [$CH_2$, *C*(3)$H_2$], 126.2 (CH, aromatic *C*H), 128.4 (CH, aromatic *C*H), 128.5 (CH, aromatic *C*H), 128.9 (CH, aromatic *C*H), 129.5 (C, aromatic *C*Br), 132.8 (CH, aromatic *C*H), 140.7 (C, aromatic *C*), 140.8 (C, aromatic *C*), 187.8 (C, *C*O), *C*$N_2$ signal not observed; HRMS (ESI+): Exact mass calculated for $C_{17}H_{16}BrN_2O_3S$ $[M+H]^+$, 407.0065. Found 407.0059. m/z (ESI+): 407.0 $[M+H]^+$.

**1-Diazo-1-(methylsulfonyl)-5-phenylpentan-2-one 4k.** Anhydrous potassium carbonate (1.49 g, 0.0108 mol), 1-(methylsulfonyl)-5-phenylpentan-2-one **9k** (2.00 g, 0.0083 mol), *p*-toluenesulfonyl azide (1.64 g, 0.0083 mol) and acetonitrile (100 mL) were used following the procedure described for **4a** to give, following purification by column chromatography employing 20% ethyl acetate in hexane as eluent, the pure α-diazo-β-keto sulfone **4k** (1.68 g, 76%) as a yellow solid, Rf = 0.20 (20:80 ethyl acetate/hexane); mp 72–74 °C; (Found C, 54.18; H, 5.41; N, 10.45. $C_{12}H_{14}N_2O_3S$ requires C, 54.12; H, 5.30; N, 10.52%); $\nu_{max}$(KBr)/cm$^{-1}$ 2112 ($CN_2$), 1664 (C=O), 1332, 1144 ($SO_2$); $\delta_H$ (400 MHz) 2.04 [2H, apparent qu, *J* 7.3, C(4)$H_2$], 2.60 [2H, t, *J* 7.4, C(3)$H_2$], 2.69 [2H, t, *J* 7.4, C(5)$H_2$], 3.23 (3H, s, $SO_2CH_3$), 7.14–7.24 (3H, m, aromatic *H*), 7.26–7.32 (2H, m, aromatic *H*); $\delta_C$ (75.5 MHz) 25.1 [$CH_2$, *C*(4)$H_2$], 34.7 [$CH_2$, *C*(5)$H_2$], 38.3

[$CH_2$, *C*(3)$H_2$], 45.47 ($CH_3$, *C*$H_3SO_2$), 126.3 (CH, aromatic *C*H), 128.5 (CH, aromatic *C*H), 128.6 (CH, aromatic *C*H), 140.8 (C, aromatic *C*), 188.4 (C, *C*O), *C*$N_2$ signal not observed; HRMS (ESI+): Exact mass calculated for $C_{12}H_{15}N_2O_3S$ $[M+H]^+$, 267.0803. Found 267.0794. m/z (ESI+): 267.1 $[M+H]^+$.

**2-Diazo-1,6-diphenylhexane-1,3-dione 6.** Triethylamine (0.68 mL, 4.88 mmol) was added to a solution of 1,6-diphenylhexane-1,3-dione **9l** (1.00 g, 3.76 mmol) in acetonitrile (20 mL). The mixture was stirred at room temperature and a solution of *p*-ABSA (0.90 g, 3.76 mmol) in acetonitrile (10 mL) was added over 2 min. The reaction mixture was stirred for 4 h then diethyl ether (10 mL) and hexane (20 mL) were added to precipitate the amide salts. The resultant mixture was filtered through a short pad of Celite® and the filtrate concentrated under reduced pressure. Purification by column chromatography, employing 20% ethyl acetate in hexane as eluent, gave the 2-diazo-1,3-diketone **6** (0.92 g, 84%) as a yellow solid, Rf = 0.63 (20:80 ethyl acetate/hexane); mp 65–68 °C; (Found C, 73.82; H, 5.54; N, 9.78 $C_{18}H_{16}N_2O_2$ requires C, 73.95; H, 5.52; N, 9.58%); $\nu_{max}$(neat)/$cm^{-1}$ 2128 ($CN_2$), 1654, 1628 (C=O), 1320, 1187 ($SO_2$); $\delta_H$ (300 MHz) 2.03 [2H, apparent qu, *J* 7.5, C(4)$H_2$], 2.70 [2H, apparent t, *J* 7.7, C(5)$H_2$], 2.98 [2H, t, *J* 7.4, C(3)$H_2$], 7.14–7.23 (3H, m, aromatic *H*), 7.24–7.32 (2H, m, aromatic *H*), 7.43–7.52 (2H, m, aromatic *H*), 7.53–7.65 (3H, m, aromatic *H*); $\delta_C$ (75.5 MHz) 25.9 [$CH_2$, *C*(4)$H_2$], 35.3 [$CH_2$, *C*(5)$H_2$], 40.8 [$CH_2$, *C*(3)$H_2$], 83.3 (C, *C*$N_2$), 125.9 (CH, aromatic *C*H), 127.3 (CH, aromatic *C*H), 128.4 (CH, aromatic *C*H), 128.5 (CH, aromatic *C*H), 128.9 (CH, aromatic *C*H), 132.6 (CH, aromatic *C*H), 137.5 (C, aromatic *C*), 141.6 (C, aromatic *C*), 185.1 (C, *C*O), 193.2 (C, *C*O); HRMS (ESI+): Exact mass calculated for $C_{18}H_{17}N_2O_2$ $[M+H]^+$, 293.1290. Found 293.1288. m/z (ESI+): 293.1 $[M+H]^+$.

**1-Diazo-1-(diphenylphosphoryl)-5-phenylpentan-2-one 5.** Anhydrous potassium carbonate (0.61 g. 4.42 mmol) was added to a solution of 1-(diphenylphosphoryl)-5-phenylpentan-2-one **11** (0.80 g, 2.21 mmol) in acetonitrile (30 mL). The mixture was stirred at room temperature and a solution of *p*-dodecylbenzenesulfonyl azide (1.09 mL, 3.31 mmol) in acetonitrile (10 mL) was added over 2min. The reaction was stirred for 3 h followed by a quench with 10% potassium hydroxide (10 mL). The reaction mixture was washed with ethyl acetate (2 x 30 mL). The organic layers were combined and washed with brine (50 mL), dried with magnesium sulfate, filtered and concentrated under reduced pressure to give the crude diazo **5** as a light yellow oil. Purification by column chromatography 50% ethyl acetate in hexane as eluent gave the α-diazo-β-keto sulfone **5** (0.52 g, 60%) as a yellow solid, Rf = 0.31 (50:50 ethyl acetate/hexane); mp 126–129 °C; $\nu_{max}$(neat)/cm$^{-1}$ 2114 ($CN_2$), 1651 (C=O), 1194 (P=O); $\delta_H$ (300 MHz) 1.88 [2H, apparent qu, *J* 7.5, C(4)$H_2$], 2.52 [4H, t, *J* 7.3, C(5)$H_2$ and C(3)$H_2$], 7.02–7.09 (2H, m, aromatic *H*), 7.10–7.28 (3H, m, aromatic *H*), 7.46–7.65 (6H, m, aromatic *H*), 7.75–7.87 (4H, m, aromatic *H*); $\delta_P$ (162 MHz) 22.55 (1P, s, *P*O); $\delta_C$ (100.6 MHz) 25.6 [$CH_2$, *C*(4)$H_2$], 34.9 [$CH_2$, *C*(5)$H_2$], 39.4 [$CH_2$, *C*(3)$H_2$], 126.0 (CH, aromatic *C*H), 128.37 (CH, aromatic *C*H), 128.39 (CH, aromatic *C*H), 128.9 (CH, d, $^2J_{CP}$ 13.2, aromatic *C*H), 130.6 (C, d, $^1J_{CP}$ 114.5, aromatic *C*), 131.7 (CH, d, $^3J_{CP}$ 10.7, aromatic *C*H), 133.0 (CH, d, $^4J_{CP}$ 2.9, aromatic *C*H), 141.3 (C, aromatic *C*), 193.2 (C, d, $^2J_{CP}$ 8.7, *C*O), *C*$N_2$ signal not observed; HRMS (ESI+): Exact mass calculated for $C_{23}H_{22}N_2O_2P$ $[M+H]^+$, 389.1419. Found 389.1418. m/z (ESI+): 389.1 $[M+H]^+$.

**2-Phenylsulfonyl-cyclopentanone synthesis**

**General procedure for rhodium-catalysed C–H insertion reactions:**

A solution of α-diazo-β-keto sulfone (100 mg, 1 equiv.) in DCM (10 mL) was added dropwise over ~15 min to a solution of rhodium(II) catalyst (1 mol%) in DCM (10 mL) heated under

reflux. The mixture was heated under reflux while stirring until reaction completion was indicated by IR analysis. The reaction mixture was then cooled to room temperature and concentrated under reduced pressure to give the crude product. Purification by column chromatography employing ethyl acetate in hexane as eluent gave the pure cyclopentanone product.

*Note: this general procedure was employed for all rhodium-catalysed C–H insertion reactions and reactions took 0.5 h unless otherwise stated.*

**General procedure for copper-catalysed C–H insertion reactions:**

A solution of $CuCl_2$ (5 mol%), bis(oxazoline) ligand (6 mol%) and NaBARF (6 mol%) in DCM (10 mL) was heated under reflux while stirring for 1.5 h then a solution of α-diazo- β-keto sulfone (100 mg, 1 equiv.) in DCM (10 mL) was added dropwise to this solution under reflux over ~15 min. The mixture was heated under reflux while stirring until reaction completion was indicated by TLC and/or IR analysis. The reaction mixture was then cooled to room temperature and concentrated under reduced pressure to give the crude product. Purification by column chromatography employing ethyl acetate in hexane as eluent gave the pure cyclopentanone product.

*Note: this general procedure was employed for all copper-catalysed C–H insertion reactions and reactions took 0.5 h unless otherwise unless otherwise stated.*

**(±)-*trans*-2-Phenylsulfonyl-3-phenylcyclopentanone 13a**. 1-Diazo-1-phenylsulfonyl-5-phenylpentan-2-one **4a** (50 mg, 0.15 mmol), rhodium(II) acetate (0.7 mg, 1 mol%) and DCM (2 x 5 mL) were used following the general procedure described for rhodium-catalysed C–H

insertion to give the crude cyclopentanone **13a** as the *trans* isomer only. Following purification by column chromatography employing 10% ethyl acetate in hexane as eluent, to give the *trans*-cyclopentanone **13a** (45 mg, 99%) was obtained as a white solid, Rf = 0.17 (20:80 ethyl acetate/hexane); mp 96–99 °C (lit.,[33] 96–98 °C); $\nu_{max}$(KBr)/cm$^{-1}$ 1749 (C=O), 1306, 1151 ($SO_2$); $\delta_H$ (400 MHz) 1.92–2.07 [1H, m, 1 x C(4)$H_2$], 2.49–2.70 [3H, m, C(5)$H_2$ and 1 x C(4)$H_2$], 3.91 [1H, d, *J* 7.5, C(2)*H*], 4.05–4.14 [1H, m, C(3)H], 7.12–7.16 (2H, m, aromatic *H* of phenyl group), 7.20–7.32 (3H, m, aromatic *H* of phenyl group), 7.47–7.53 (2H, m, aromatic *H* of phenylsulfonyl group), 7.59–7.65 (1H, m, aromatic *H* of phenylsulfonyl group), 7.77–7.83 (2H, m, aromatic *H* of phenylsulfonyl group). Spectral characteristics were consistent with previously reported data.[33]

**(±)-*trans*-2-[(4-Fluorophenyl)sulfonyl]-3-phenylcyclopentan-1-one 13b**. 1-Diazo-1-[(4-fluorophenyl)sulfonyl]-5-phenylpentan-2-one **4b** (100 mg, 0.29 mmol), rhodium(II) acetate (1.3 mg, 1 mol%) and DCM (2 x 10 mL) were used following the general procedure described for rhodium-catalysed C–H insertion to give the crude cyclopentanone **13b** as the *trans* isomer only. The crude product was purified by column chromatography, employing 10% ethyl acetate in hexane as eluent, to give the *trans*-cyclopentanone **13b** (68 mg, 74%) as a white solid, Rf = 0.17 (20:80 ethyl acetate/hexane); mp 85–88 °C; $\nu_{max}$(neat)/cm$^{-1}$ 1750 (C=O), 1323, 1147 ($SO_2$); $\delta_H$ (400 MHz) 1.89–2.08 [1H, m, 1 x C(4)$H_2$], 2.43–2.70 [3H, m, C(5)$H_2$ and 1 x C(4)$H_2$], 3.93 [1H, d, *J* 7.8, C(2)*H*], 4.00–4.11 [1H, m, C(3)H], 7.06–7.38 (7H, m, 7 x aromatic *H*), 7.79 (2H, dd, *J* 8.7, 5.1, 2 x aromatic *H* of 4-fluorophenyl group); $\delta_F$ (376.5 MHz) -102.7 (1F, s, *p-F*); $\delta_C$ (100.6 MHz) 29.7 [$CH_2$, *C*(4)$H_2$], 39.3 [$CH_2$, *C*(5)$H_2$], 43.8 [CH, *C*(3)H], 75.5 [CH, *C*(2)H], 116.4 (CH, d, $^2J_{CF}$ 22.7, aromatic *C*H), 126.9 (CH, aromatic *C*H), 127.4 (CH, aromatic *C*H), 129.0 (CH, aromatic *C*H), 132.0 (CH, d, $^3J_{CF}$ 9.8, aromatic *C*H), 134.0 (C, d, $^4J_{CF}$ 3.1, aromatic *C*), 141.5

(C, aromatic *C*), 166.1 (C, d, $^{1}J_{CF}$ 257.1, aromatic *C*), 206.2 (C, *C*O); HRMS (ESI +): Exact mass calculated for $C_{17}H_{16}O_3FS$ $[M+H]^+$, 319.0804. Found 319.0797. m/z (ESI +): 319.1 $[M+H]^+$.

**(±)-*trans*-2-(Naphthalen-2-ylsulfonyl)-3-phenylcyclopentan-1-one 13c**. 1-Diazo-1-(naphthalen-2-ylsulfonyl]-5-phenylpentan-2-one **4c** (100 mg, 0.26 mmol), rhodium(II) acetate (1.2 mg, 1 mol%) and DCM (2 x 10 mL) were used following the general procedure described for rhodium-catalysed C–H insertion to give the crude cyclopentanone **13c** as the *trans* isomer only. The crude product was purified by column chromatography, employing 10% ethyl acetate in hexane as eluent, to give the *trans*-cyclopentanone **13c** (55 mg, 59%), as a white solid, recrystallisation from MeOH gave an analytically pure sample of **13c** (13 mg, 14%), Rf = 0.18 (20:80 ethyl acetate/hexane); mp 153–156 °C; $\nu_{max}$(neat)/$cm^{-1}$ 1749 (C=O), 1316, 1149 ($SO_2$); $\delta_H$ (300 MHz) 1.90–2.10 [1H, m, 1 x C(4)$H_2$], 2.45–2.74 [3H, m, C(5)$H_2$ and 1x C(4)$H_2$], 3.99 [1H, d, *J* 7.6, C(2)*H*], 4.06–4.20 [1H, m, C(3)H], 7.07–7.24 (5H, m, 5 x aromatic *H* of phenyl group), 7.54–7.79 (3H, m, 3 x aromatic *H* of 2-naphthyl group), 7.84–8.01 (3H, m, 3 x aromatic *H* of naphthyl group), 8.43 (1H, bs, aromatic *H* of 2-naphthyl group); $\delta_C$ (100.6 MHz) 29.6 [$CH_2$, *C*(4)$H_2$], 39.2 [$CH_2$, *C*(5)$H_2$], 43.8 [CH, *C*(3)H], 75.6 [CH, *C*(2)H], 123.3 (CH, aromatic *C*H), 126.9 (CH, aromatic *C*H), 127.2 (CH, aromatic *C*H), 127.6 (CH, aromatic *C*H), 127.9 (CH, aromatic *C*H), 128.8 (CH, aromatic *C*H), 129.3 (CH, aromatic *C*H), 129.5 (CH, aromatic *C*H), 129.6 (CH, aromatic *C*H), 131.1 (CH, aromatic *C*H), 132.0 (C, aromatic *C*), 134.8 (C, aromatic *C*), 135.5 (C, aromatic *C*), 141.6 (C, aromatic *C*), 206.2 (C, *C*O); HRMS (ESI +): Exact mass calculated for $C_{21}H_{19}O_3S$ $[M+H]^+$, 351.1055. Found 351.1050. m/z (ESI +): 351.1 $[M+H]^+$.

**(±)-*trans*-2-(Naphthalen-1-ylsulfonyl)-3-phenylcyclopentan-1-one 13d.** 1-Diazo-1-(naphthalen-1-ylsulfonyl)-5-phenylpentan-2-one **4d** (100 mg, 0.26 mmol), rhodium(II) acetate (1.2 mg, 1 mol%) and DCM (2 x 10 mL) were used following the general procedure described

for rhodium-catalysed C–H insertion to give the crude cyclopentanone **13d** as the *trans* isomer only. The crude product was purified by column chromatography , employing 10% ethyl acetate in hexane as eluent, to give the *trans*-cyclopentanone **13d** (55 mg, 60%) as a white solid, Rf = 0.15 (20:80 ethyl acetate/hexane); mp 137–140 °C; $\nu_{max}$(neat)/cm$^{-1}$ 1749 (C=O), 1314, 1122 ($SO_2$); $\delta_H$ (400 MHz) 1.82–1.98 [1H, m, 1 x C(4)$H_2$], 2.48–2.61 [2H, m, 1 x C(4)$H_2$ and 1 x C(5)$H_2$], 2.62–2.75 [1H, m, 1 x C(5)$H_2$], 3.98–4.10 [1H, m, C(3)*H*], 4.21 [1H, d, *J* 8.4, C(2)H], 6.90–6.98 (2H, m, 2 x aromatic *H* of phenyl group), 7.04–7.15 (3H, m, 3 x aromatic *H* of phenyl group), 7.48–7.60 (3H, m, 3 x aromatic *H* of 1-naphthyl group), 7.80–7.88 (1H, m, 1 x aromatic *H* of 1-naphthyl group), 8.04 (1H, d, *J* 8.2, 1 x aromatic *H* of 1-naphthyl group), 8.23 (1H, dd, *J* 7.3, 1.2, 1 x aromatic *H* of 1-naphthyl group), 8.33–8.41 (1H, m, 1 x aromatic *H* of 1-naphthyl group); $\delta_C$ (100.6 MHz) 30.0 [$CH_2$, *C*(4)$H_2$], 39.7 [$CH_2$, *C*(5)$H_2$], 44.2 [CH, *C*(3)H], 74.4 [CH, *C*(2)H], 123.4 (CH, aromatic *C*H), 124.2 (CH, aromatic *C*H), 126.6 (CH, aromatic *C*H), 126.8 (CH, aromatic *C*H), 127.1 (CH, aromatic *C*H), 128.6 (CH, aromatic *C*H), 128.8 (CH, aromatic *C*H), 129.3 (CH, aromatic *C*H), 131.6 (CH, aromatic *C*H), 132.6 (C, aromatic *C*), 134.1 (C, aromatic *C*), 135.7 (CH, aromatic *C*H), 140.9 (C, aromatic *C*), 206.0 (C, *C*O); HRMS (ESI +): Exact mass calculated for $C_{21}H_{19}O_3S$ $[M+H]^+$, 351.1055. Found 351.1048. m/z (ESI +): 351.1 $[M+H]^+$.

**1-(5,7-Dimethyl-1,1-dioxido-2,3-dihydrobenzo[*b*]thiophen-2-yl)-4-phenylbutan-1-one 19e.** 1-Diazo-1-(mesitylsulfonyl)-5-phenylpentan-2-one **4e** (100 mg, 0.27 mmol), rhodium(II) acetate (1.2 mg, 1 mol%) and DCM (2 x 8 mL) were used following the general procedure described for rhodium-catalysed C–H insertion, with a reaction time of 24 h, to give the crude sulfolane **19e**. The crude product was purified by column chromatography, employing 5% ethyl acetate in hexane as eluent, to give the pure sulfolane **19e** (72 mg, 78%) as a clear oil, Rf = 0.76 (50:50 ethyl acetate/hexane); $\nu_{max}$(neat)/cm$^{-1}$ 1722 (C=O), 1297, 1133 ($SO_2$); $\delta_H$ (300

MHz) 1.93–2.12 [2H, m, C(4)$H_2$], 2.36 (3H, s, C$H_3$), 2.53 (3H, s, C$H_3$), 2.56–2.80 [3H, m, C(5)$H_2$ and 1 x C(3)$H_2$], 2.94–3.12 [1H, m, 1 x C(3)$H_2$], 3.17 (1H, dd, A of ABX, $J_{AB}$ 16.7, $J_{AX}$ 8.3, 1 x sulfolane C$H_2$), 3.65 (1H, dd, B of ABX, $J_{AB}$ 16.3, $J_{AX}$ 5.7, 1 x sulfolane C$H_2$), 4.45 (1H, dd, X of ABX, $J_{BX}$ 8.5, $J_{AX}$ 5.7, C*H*), 6.94–7.02 (2H, m, 2 x aromatic *H* of mesityl group), 7.13–7.22 (2H, m, 2 x aromatic *H* of phenyl group), 7.23–7.33 (3H, m, 3 x aromatic *H* of phenyl group); $\delta_C$ (75.5 MHz) 16.7 ($CH_3$, *C*$H_3$), 21.5 ($CH_3$, *C*$H_3$), 24.9 [$CH_2$, *C*(4)$H_2$], 26.9 ($CH_2$, sulfolane *C*$H_2$), 34.9 [$CH_2$, *C*(5)$H_2$], 43.5 [$CH_2$, *C*(3)$H_2$], 70.6 (CH, sulfolane *C*H) 124.9 (CH, aromatic *C*H), 126.9 (CH, aromatic *C*H), 128.4 (CH, aromatic *C*H), 128.5 (CH, aromatic *C*H), 131.6 (CH, aromatic *C*H), 133.0 (C, aromatic *C*), 134.8 (C, aromatic *C*), 136.7 (C, aromatic *C*), 141.4 (C, aromatic *C*), 144.7 (C, aromatic *C*), 198.8 (C, *C*O); HRMS (ESI +): Exact mass calculated for $C_{20}H_{23}O_3S$ $[M+H]^+$, 343.1368. Found 343.1375. m/z (ESI +): 343.1 $[M+H]^+$.

**(±)-*trans*-2-(Mesitylsulfonyl)-3-phenylcyclopentan-1-one 13e.** 1-Diazo-1-(mesitylsulfonyl)-5-phenylpentan-2-one **4e** (100 mg, 0.29 mmol), copper(II) chloride (1.8 mg, 5 mol%), sodium tetrakis[3,5-bis(trifluoromethyl)phenyl]borate (14.4 mg, 6 mol%), ligand-**18** (5.4 mg, 6 mol%) and DCM (2 x 10 mL) were used following the general procedure described for copper-catalysed C–H insertion to give the crude cyclopentanone and fused sulfolane in a 46:54 mix. The crude product was purified by column chromatography, employing 5% ethyl acetate in hexane as eluent, to give a 50:50 mix of *trans*-cyclopentanone **13e** and fused sulfolane **19e** (62 mg, 62%) as a clear oil, Rf = 0.76 (50:50 ethyl acetate/hexane). Signals for the *trans*-cyclopentanone **13e** were seen at: $\nu_{max}$(neat)/$cm^{-1}$ 1751 (C=O), 1300, 1141 ($SO_2$); $\delta_H$ (300 MHz) 1.93–2.11 [1H, m, C(4)$H_2$], 2.46 (6H, s, 2 x C$H_3$), 2.54 (3H, s, C$H_3$), 2.57–2.80 [3H, m, C(5)$H_2$ and 1 x C(4)$H_2$], 3.92 [1H, d, *J* 7.6, C(2)*H*], 4.03–4.16 [1H, m, C(3)*H*], 6.99 (2H, bs, aromatic *H* of mesityl group), 7.10–7.34 (5H, m, aromatic *H*); $\delta_C$ (100.6 MHz) 21.1 ($CH_3$, *C*$H_3$), 22.7 ($CH_3$, 2 x *C*$H_3$), 29.6 [$CH_2$, *C*(4)$H_2$], 39.6 [$CH_2$, *C*(5)$H_2$], 43.1 [CH, *C*(3)H], 70.5 [CH. *C*(2)H],

127.0 (CH, aromatic *C*H), 127.2 (CH, aromatic *C*H), 128.9 (CH, aromatic *C*H), 132.3 (CH, aromatic *C*H), 140.3 (C, aromatic *C*), 141.8 (C, aromatic *C*), 143.8 (C, aromatic *C*), 207.0 (C, *C*O); HRMS (ESI +): Exact mass calculated for $C_{20}H_{23}O_3S$ $[M+H]^+$, 343.1368. Found 343.1363. m/z (ESI +): 343.1 $[M+H]^+$. Signals for the sulfolane were the same as **19e**.

**1-(3-Methyl-1,1-dioxido-2,3-dihydrobenzo[*b*]thiophen-2-yl)-4-phenylbutan-1-one 19f.** 1-Diazo-1-[(2-ethylphenyl)sulfonyl]-5-phenylpentan-2-one **4f** (100 mg, 0.28 mmol), rhodium(II) acetate (1.2 mg, 1 mol%) and DCM (2 x 8 mL) were used following the general procedure described for rhodium-catalysed C–H insertion, with a reaction time of 24 h, to give the crude sulfolane **19f** as a 17:83 mixture of *cis* : *trans* isomer; [Signals for the tentatively assigned *cis* isomer of **19f** were observed at $\delta_H$ 4.36 [1H, d, *J* 6.3, C(1)*H*] and $\delta_H$ 3.71–3.81 [1H, m, C*H*$CH_3$]. The crude product was purified by column chromatography, employing 5% ethyl acetate in hexane as eluent, to give the pure sulfolane **19f** (68 mg, 74%) as a clear oil, Rf = 0.56 (40:60 ethyl acetate/hexane); $\nu_{max}$(neat)/$cm^{-1}$ 1721 (C=O), 1307, 1156 ($SO_2$); $\delta_H$ (300 MHz) 1.44 (3H, d, *J* 6.9, C$H_3$), 1.96–2.12 [2H, m, C(4)$H_2$], 2.57–2.80 [3H, m, C(5)$H_2$ and 1 x C(3)$H_2$], 3.01 (1H, ddd, *J* 18.1, 7.7, 6.7, 1 x C(3)$H_2$), 3.96–4.09 (1H, m, C*H*$CH_3$), 4.12 [1H, d, *J* 6.8, C(1)$H_2$], 7.15–7.23 (3H, m, 3 x aromatic *H*), 7.24–7.33 (2H, m, 2 x aromatic *H*), 7.41–7.51 (2H, m, 2 x aromatic *H*), 7.57–7.71 (2H, m, 2 x aromatic *H*); $\delta_C$ (106.6 MHz) 18.8 ($CH_3$, *C*$H_3$), 24.8 [$CH_2$, *C*(4)$H_2$], 34.4 (CH, *C*H$CH_3$), 34.8 [$CH_2$, *C*(5)$H_2$], 43.6 [$CH_2$, *C*(3)$H_2$], 77.8 [CH, *C*(1)H], 121.5 (CH, aromatic *C*H), 125.5 (CH, aromatic *C*H), 126.1 (CH, aromatic *C*H), 128.5 (CH, aromatic *C*H), 128.9 (CH, aromatic *C*H), 129.0 (CH, aromatic *C*H), 134.2 (CH, aromatic *C*H), 137.0 (C, aromatic *C*), 141.0 (C, aromatic *C*), 141.4 (C, aromatic *C*), 198.1 (C, *C*O); HRMS (ESI +): Exact mass calculated for $C_{19}H_{21}O_3S$ $[M+H]^+$, 329.1211. Found 329.1200. m/z (ESI +): 329.1 $[M+H]^+$.

**(±)-*trans*-2-[(2-Ethylphenyl)sulfonyl)-3-phenylcyclopentan-1-one 13f.** 1-Diazo-1-[(2-ethylphenyl)sulfonyl]-5-phenylpentan-2-one **4f** (100 mg, 0.28 mmol), copper(II) chloride (1.9 mg, 5 mol%), sodium tetrakis[3,5-bis(trifluoromethyl)phenyl]borate (14.9 mg, 6 mol%), ligand-**15** (6.1 mg, 6 mol%) and DCM (2 x 10 mL) were used following the general procedure described for copper-catalysed C–H insertion to give the crude cyclopentanone and fused sulfolane in a 71:29 mix. The crude product was purified by column chromatography, employing 5% ethyl acetate in hexane as eluent, to give a 72:28 mix of *trans*-cyclopentanone **13f** and fused sulfolane **19f** (43 mg, 47%) as a clear oil, Rf = 0.56 (40:60 ethyl acetate/hexane). Signals for the *trans*-cyclopentanone **13f** were seen at: $\nu_{max}$(neat)/cm$^{-1}$ 1750 (C=O), 1305, 1149 ($SO_2$); $\delta_H$ (400 MHz) 1.13 (3H, t, *J* 7.4, $CH_2CH_3$), 1.89–2.12 (1H, m, 1 x C(4)$H_2$), 2.48–2.91 [5H, m, C(5)$H_2$ and 1 x C(4)$H_2$ and $CH_2CH_3$], 3.91–4.14 [2H, m, C(2)*H* and C(3)*H*], 7.01 (2H, d, *J* 6.5, 2 x aromatic *H*), 7.13–7.40 (5H, m, 5 x aromatic *H*), 7.41–7.55 (1H, m, aromatic *H*), 7.93 (1H, d, *J* 7.8, aromatic *H*); $\delta_C$ (106.6 MHz) 15.5 ($CH_3$, $CH_3$), 25.9 ($CH_2$, $CH_2CH_3$), 29.8 [$CH_2$, *C*(4)$H_2$], 39.5 [$CH_2$, *C*(5)$H_2$], 43.9 [CH, *C*(3)H], 75.3 [CH, *C*(2)H], 126.2 (CH, aromatic *C*H), 126.8 (CH, aromatic *C*H), 127.2 (CH, aromatic *C*H), 128.9 (CH, aromatic *C*H), 130.9 (CH, aromatic *C*H), 131.0 (CH, aromatic *C*H), 134.2 (CH, aromatic *C*H), 135.6 (C, aromatic *C*), 141.5 (C, aromatic *C*), 144.7 (C, aromatic *C*), 206.1 (C, *C*O); HRMS (ESI +): Exact mass calculated for $C_{19}H_{21}O_3S$ $[M+H]^+$, 329.1211. Found 329.1215. m/z (ESI +): 329.1 $[M+H]^+$. Signals for the sulfolane were the same as **19f**.

**(±)-*trans*-2-[(4-Methoxyphenyl)sulfonyl]-3-phenylcyclopentan-1-one 13g.** 1-Diazo-1-[(4-methoxyphenyl)sulfonyl]-5-phenylpl)entan-2-one **4g** (100 mg, 0.28 mmol), rhodium(II) acetate (1.2 mg, 1 mol%) and DCM (2 x 10 mL) were used following the general procedure described for rhodium-catalysed C–H insertion to give the crude cyclopentanone **13g** as the *trans* isomer only. The crude product was purified by column chromatography, employing

30% ethyl acetate in hexane as eluent, to give the *trans*-cyclopentanone **13g** (45 mg, 48%), as a white solid, Rf = 0.06 (20:80 ethyl acetate/hexane); mp 129–132 °C; $\nu_{max}$(neat)/cm$^{-1}$ 1749 (C=O), 1262, 1144 ($SO_2$); $\delta_H$ (300 MHz) 1.82–2.10 [1H, m, 1 x C(4)$H_2$], 2.40–2.72 [3H, m, C(5)$H_2$ and 1 x C(4)$H_2$], 3.80–3.92 [4H, m, C(2)*H* contains s at δ3.86 for OC$H_3$], 4.00–4.14 [1H, m, C(3)*H*], 6.90–6.97 (2H, m, aromatic *H* of 4-methoxyphenyl group), 7.09–7.34 (5H, m, aromatic *H* of phenyl group), 7.67–7.75 (2H, m, aromatic *H* of 4-methoxyphenyl group); $\delta_C$ (75.5 MHz) 29.5 [$CH_2$, *C*(4)$H_2$], 39.1 [$CH_2$, *C*(5)$H_2$], 43.7 [CH, *C*(3)H], 55.7 ($CH_3$, O*C*$H_3$), 75.9 [CH, *C*(2)H], 114.3 (CH, aromatic *C*H), 126.9 (CH, aromatic *C*H), 127.2 (CH, aromatic *C*H), 128.9 (CH, aromatic *C*H), 129.4 (C, aromatic *C*), 131.3 (CH, aromatic *C*H), 141.9 (C, aromatic *C*), 164.1 (C, aromatic *C*O$CH_3$), 206.6 (C, *C*O); HRMS (ESI +): Exact mass calculated for $C_{18}H_{19}O_4S$ $[M+H]^+$, 331.1004. Found 331.1002. m/z (ESI +): 331.1 $[M+H]^+$.

**(±)-*trans*-2-(Cyclohexylsulfonyl)-3-phenylcyclopentan-1-one 13h.** 1-(Cyclohexylsulfonyl)-1-diazo-5-phenylpentan-2-one **4h** (50 mg, 0.15 mmol), rhodium(II) acetate (0.7 mg, 1 mol%) and DCM (2 x 5 mL) were used following the general procedure described for rhodium-catalysed C–H insertion to give the crude cyclopentanone **13h** as the *trans* isomer only. The crude product was purified by column chromatography, employing 10% ethyl acetate in hexane as eluent, to give the *trans*-cyclopentanone **13h** (40 mg, 88%) as a white solid, Rf = 0.43 (20:80 ethyl acetate/hexane); mp 122–125 °C; $\nu_{max}$(neat)/cm$^{-1}$ 1750 (C=O), 1299, 1118 ($SO_2$); $\delta_H$ (400 MHz) 1.08–2.14 (11H, m, 10 x cyclohexyl *H* and 1 x C(4)$H_2$), 2.51–2.73 [3H, m, C(5)$H_2$ and 1 x C(4)$H_2$], 3.33 (1H, tt, *J* 12.1, 3.5, cyclohexyl C*H*), 3.88 [1H, d, *J* 7.6, C(2)*H*], 4.11–4.21 [1H, m, C(3)*H*], 7.24–7.31 (3H, m, 3 x aromatic *H*), 7.32–7.40 (2H, m, 2 x aromatic *H*); $\delta_C$ (100.6 MHz) 22.9 (*C*$H_2$ of cyclohexyl group), 24.8 (*C*$H_2$ of cyclohexyl group), 24.9 (*C*$H_2$ of cyclohexyl group), 25.1 (*C*$H_2$ of cyclohexyl group), 26.2 (*C*$H_2$ of cyclohexyl group), 29.5 [$CH_2$, *C*(4)$H_2$], 39.3 [$CH_2$, *C*(5)$H_2$], 41.8 [CH, *C*(3)H], 59.7 (*C*H of cyclohexyl group), 69.4 [CH, *C*(2)H], 127.1 (CH, aromatic

*C*H), 127.4 (CH, aromatic *C*H), 129.0 (CH, aromatic *C*H), 142.0 (C, aromatic *C*), 208.1 (C, *C*O); HRMS (ESI +): Exact mass calculated for $C_{17}H_{23}O_3S$ $[M+H]^+$, 307.1368. Found 307.1366. m/z (ESI +): 307.1 $[M+H]^+$.

**(±)-*trans*-2-[(4-Methylphenyl)sulfonyl]-3-phenylcyclopentan-1-one 13i.** 1-Diazo-1-[(4-methylphenyl)sulfonyl]-5-phenylpentan-2-one **4i** (100 mg, 0.29 mmol), rhodium(II) acetate (1.3 mg, 1 mol%) and DCM (2 x 10 mL) were used following the general procedure described for rhodium-catalysed C–H insertion to give the crude cyclopentanone **13i** as the *trans* isomer only. The crude product was purified by column chromatography , employing 10% ethyl acetate in hexane as eluent, to give the *trans*-cyclopentanone **13i** (63 mg, 69%) as a white solid, Rf = 0.20 (20:80 ethyl acetate/hexane); mp 134–136 °C; $\nu_{max}$(neat)/$cm^{-1}$ 1749 (C=O), 1320, 1150 ($SO_2$); $\delta_H$ (300 MHz) 1.88–2.08 [1H, m, 1 x C(4)$H_2$], 2.42 (3H, s, C$H_3$), 2.47–2.71 [3H, m, C(5)$H_2$ and 1 x C(4)$H_2$], 3.88 [1H, d, *J* 7.4, C(2)*H*], 4.09 [1H, m, C(3)H], 7.09–7.17 (2H, m, 2 x aromatic *H* of 4-methylphenyl group), 7.18–7.35 (5H, m, 5 x aromatic *H* of phenyl group), 7.67 (2H, d, *J* 8.2, 2 x aromatic *H* of 4-methylphenyl group); $\delta_C$ (100.6 MHz) 21.7 (*C*$H_3$), 29.5 [$CH_2$, *C*(4)$H_2$], 39.1 [$CH_2$, *C*(5)$H_2$], 43.6 [CH, *C*(3)H], 75.7 [CH, *C*(2)H], 126.9 (CH, aromatic *C*H), 127.2 (CH, aromatic *C*H), 128.9 (CH, aromatic *C*H), 129.0 (CH, aromatic *C*H), 129.7 (CH, aromatic *C*H), 135.0 (C, aromatic *C*), 141.8 (C, aromatic *C*), 145.2 (C, aromatic *C*), 206.4 (C, *C*O); HRMS (ESI +): Exact mass calculated for $C_{18}H_{19}O_3S$ $[M+H]^+$, 315.1055. Found 315.1061. m/z (ESI +): 315.1 $[M+H]^+$.

**(±)-*trans*-2-[(4-Bromophenyl)sulfonyl]-3-phenylcyclopentan-1-one 13j**. 1-Diazo-1-[(4-bromophenyl)sulfonyl]-5-phenylpentan-2-one **4j** (100 mg, 0.25 mmol), rhodium(II) acetate (1.1 mg, 1 mol%) and DCM (2 x 10 mL) were used following the general procedure described for rhodium-catalysed C–H insertion to give the crude cyclopentanone **13j** as the *trans* isomer

only. The crude product was purified by column chromatography, employing 10% ethyl acetate in hexane as eluent, to give the *trans*-cyclopentanone **13j** (70 mg, 75%) as a white solid, Rf = 0.27 (20:80 ethyl acetate/hexane); mp 117–120 °C; (Found C, 54.00; H, 4.05. $C_{17}H_{15}BrO_3S$ requires C, 53.84; H 3.99%); $\nu_{max}$(KBr)/cm$^{-1}$ 1750 (C=O), 1308, 1148 ($SO_2$); $\delta_H$ (300 MHz) 1.92–2.09 [1H, m, 1 x C(4)$H_2$], 2.49–2.72 [3H, m, C(5)$H_2$ and 1 x C(4)$H_2$], 3.90 [1H, d, *J*8.1, C(2)*H*] 4.02–4.12 [1H, m, C(3)*H*], 7.10–7.18 (2H, m, aromatic *H* of phenyl group), 7.22–7.34 (3H, m, aromatic *H* of phenyl group), 7.58–7.67 (4H, m, aromatic *H* of *p*-bromophenylsulfonyl group); $\delta_C$ (75.5 MHz) 29.7 [$CH_2$, *C*(4)$H_2$], 39.3 [$CH_2$, *C*(5)$H_2$], 43.7 [CH, *C*(3)H], 75.5 [CH, *C*(2)H], 126.9 (CH, aromatic *C*H), 127.4 (CH, aromatic *C*H), 129.0 (CH, aromatic *C*H), 129.7 (C, aromatic *C*Br), 130.5 (CH, aromatic *C*H), 132.4 (CH, aromatic *C*H), 136.8 (C, aromatic *C*), 141.4 (C, aromatic *C*), 206.1 (C, *C*O); HRMS (ESI +): Exact mass calculated for $C_{17}H_{16}O_3BrS$ $[M+H]^+$, 378.0004. Found 378.9999. m/z (ESI +): 379.0 $[M+H]^+$.

**(±)-*trans*-2-(Methylsulfonyl)-3-phenylcyclopentan-1-one 13h**. 1-Diazo-1-(methylsulfonyl)-5-phenylpentan-2-one **4h** (100 mg, 0.38 mmol), rhodium(II) acetate (1.2 mg, 1 mol%) and DCM (2 x 10 mL) were used following the general procedure described for rhodium-catalysed C–H insertion to give the crude cyclopentanone **13h** as the *trans* isomer only. The crude product was purified by column chromatography, employing 10% ethyl acetate in hexane as eluent, to give the *trans*-cyclopentanone **13h** (73 mg, 82%), as a white solid, Rf = 0.16 (20:80 ethyl acetate/hexane); mp 120–122 °C; (Found C, 60.62; H, 5.98. $C_{12}H_{14}O_3S$ requires C, 60.48; H, 5.92%); $\nu_{max}$(KBr)/cm$^{-1}$ 1750 (C=O), 1302, 1143 ($SO_2$); $\delta_H$ (300 MHz) 2.01–2.18 [1H, m, 1 x C(4)$H_2$], 2.53–2.69 [3H, m, 1 x C(4)$H_2$ and C(5)$H_2$], 3.08 (3H, s, $SO_2CH_3$), 3.76 [1H, d, *J* 7.8, C(2)*H*], 4.08–4.19 [1H, m, C(3)*H*], 7.26–7.41 (5H, m, aromatic *H* of phenyl group); $\delta_C$ (75.5 MHz) 29.4 [$CH_2$, *C*(4)$H_2$], 39.2 [$CH_2$, *C*(5)$H_2$], 40.7 ($CH_3$, $CH_3SO_2$), 41.8 [CH, *C*(3)H], 74.3 [CH, *C*(2)H], 127.1 (CH, aromatic *C*H), 127.6 (CH, aromatic *C*H), 129.1 (CH, aromatic *C*H), 141.5 (C,

aromatic *C*), 207.7 (C, *C*O); HRMS (ESI +): Exact mass calculated for $C_{12}H_{14}O_3S$ $[M+H]^+$, 239.0742. Found 239.0739. m/z (ESI +): 239.1 $[M+H]^+$.

**(±)-*trans*-2-Benzoyl-3-phenylcyclopentan-1-one 21.** 2-Diazo-1,6-diphenylhexane-1,3-dione **6** (100 mg, 0.34 mmol), rhodium(II) acetate 1.5 mg, 1 mol%) and DCM (2 x 10 mL) were used following the general procedure described for rhodium-catalysed C–H insertion to give the crude cyclopentanone **21** as the *trans* isomer only, in 1.5 h. The crude product was purified by column chromatography, employing 10% ethyl acetate in hexane as eluent, to give the *trans*-cyclopentanone **21** (34 mg, 38%) as a clear oil, Rf = 0.34 (20:80 ethyl acetate/hexane); $\nu_{max}$(neat)/$cm^{-1}$ 1742, 1674 (C=O); $\delta_H$ (400 MHz) 2.05–2.25 [1H, m, 1 x C(4)$H_2$], 2.42–2.72 [3H, m, C(5)$H_2$ and 1 x C(4)$H_2$], 4.15–4.26 [1H, m, C(3)*H*], 4.42 [1H, d, *J* 10.8, C(2)*H*], 7.10–7.34 (5H, m, aromatic *H*), 7.40–7.49 (2H, m, aromatic *H*), 7.51–7.60 (1H, m, aromatic *H*), 7.92 (2H, bd, *J* 7.8, aromatic *H*), integration on occasion was impacted by the presence of enol in the aromatic region; $\delta_C$ (100.6 MHz) 28.7 [$CH_2$, *C*(4)$H_2$], 39.3 [$CH_2$, *C*(5)$H_2$], 45.4 [CH, *C*(3)H], 64.9 [CH, *C*(2)H], 127.0 (CH, aromatic *C*H), 127.1 (CH, aromatic *C*H), 128.6 (CH, aromatic *C*H), 128.8 (CH, aromatic *C*H), 129.4 (CH, aromatic *C*H), 133.5 (CH, aromatic *C*H), 136.9 (C, aromatic *C*), 141.9 (C, aromatic *C*), 195.1 (C, *C*O), 211.8 (C, *C*O); HRMS (ESI +): Exact mass calculated for $C_{18}H_{17}O_2$ $[M+H]^+$, 265.1229. Found 265.1224. m/z (ESI +): 265.1 $[M+H]^+$.

**(±)-trans-2-(Diphenylphosphoryl)-3-phenylcyclopentan-1-one 20.** 1-Diazo-1-(diphenylhexane)-1,3-dione **5** (100 mg, 0.26 mmol), copper(II) chloride 1.7 mg, 5 mol%), sodium tetrakis[3,5-bis(trifluoromethyl)phenyl]borate (13.7 mg, 6 mol%), ligand-**18** (5.1 mg, 6 mol%) and DCM (2 x 10 mL) were used following the general procedure described for copper-catalysed C–H insertion to give the crude cyclopentanone **20** as the *trans* isomer only in 124 h. The crude product was purified by column chromatography, employing 50% ethyl

acetate in hexane as eluent, to give the *trans*-cyclopentanone **20** (7.5 mg, 8%) as a clear oil, Rf = 0.14 (50:50 ethyl acetate/hexane); $\nu_{max}$(neat)/cm$^{-1}$ 1738 (C=O), 1118 (P=O); $\delta_H$ (400 MHz) 1.91–2.22 [1H, m, C(4)$H_2$], 2.44–2.60 [3H, m, 1 x C(4)$H_2$ and 2 x C(5)$H_2$], 3.49 [1H, dd, *J* 11.7, 7.0, C(2)*H*], 3.85–4.01 [1H, m, C(3)*H*], 6.65–8.10 (15H, m, 15 x aromatic *H*); $\delta_P$ (162 MHz) 30.55 (1P, s, *P*O); $\delta_C$ (75.5 MHz) 31.3 [$CH_2$, d, $J_{CP}$ 6.7, *C*(4)$H_2$], 40.1 [$CH_2$, *C*(5)$H_2$], 43.4 [CH, *C*(3)H], 56.5 [CH, d, $J_{CP}$ 61.2, *C*(2)H], 126.6 (CH, aromatic *C*H), 126.8 (CH, aromatic *C*H), 128.3 (CH, d, $J_{CP}$ 3.9, aromatic *C*H), 128.5 (CH, d, $J_{CP}$ 4.1, aromatic *C*H), 128.7 (CH, aromatic *C*H), 131.1 (CH, d, $J_{CP}$ 9.5, aromatic *C*H), 131.4 (CH, d, $J_{CP}$ 9.5, aromatic *C*H), 131.8 (CH, d, $J_{CP}$ 2.7, aromatic *C*H), 132.0 (CH, d, $J_{CP}$ 2.8, aromatic *C*H), 143.9 (C, aromatic *C*), 212.0 (C, d, $J_{CP}$ 3.5, *C*O); HRMS (ESI +): Exact mass calculated for $C_{23}H_{22}O_2P$ $[M+H]^+$, 361.1357. Found 361.1359. m/z (ESI +): 361.1 $[M+H]^+$.

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