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Diastereoselective synthesis of strained spiro-cyclopropanooxindoles from cyclic diazoamides

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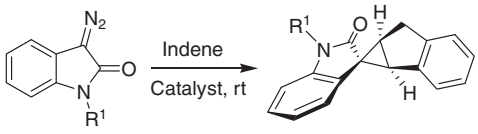
ABSTRACT

Reaction of cyclic diazoamides and cyclic olefins or heteroaromatic systems using copper(I) triflate as a catalyst furnished a variety of strained spiro-cyclopropanooxindoles in a diastereoselective manner under mild reaction conditions. The effect of copper(I) triflate and rhodium(II) acetate catalysts on the cyclopropanation was also studied.

Spiro[cyclopropan-1,3′-oxindoles] are known to have inotropic[1] and herbicidal[2] properties and their novel ring-expansion reaction[3] with a range of imines furnished spiro[pyrrolidin-3,3′-oxindoles],[4] which are well-known indole-based natural products. α-Diazocarbonyl compounds have found extensive applications in organic synthesis due to their versatile reactivities.[5] Research in this area has been mostly concentrated on the transition metal complex-catalysed diazo decomposition, which generates metallo-carbenoid intermediates. Transition metal complexes catalysed a large number of organic reactions which led to a variety of C–C bond formations that are important for creation of the basic skeleton of the organic structure. Particularly, copper- or rhodium-catalysed reaction of α-diazocarbonyl compound with alkene is an efficient method for the preparation of cyclopropane derivatives.[6] The intermolecular[7] cyclopropanation reactions are limited only to simple precursors like acyclic diazo ketones or diazo esters. The cyclic diazo ketones and amides always have a tendency to furnish cycloadducts[8] via 1,3-dipolar cycloaddition reactions in the presence of olefins. We have reported many stereo- and regioselective reactions of diazocarbonyl compounds based on ylide formation,[9] carbenoid insertion,[10] N–H insertion,[11] O–H insertion[12] and nucleophilic trapping of ylide.[13] There is only scarcity of reports[14] available on the cyclic diazocarbonyl compounds used for the cyclopropanation process. Our earlier work[15] on the rhodium(II) acetate catalyzed cyclopropanation of diazomides led to a mixture of products. To the best of our knowledge, there is no report dealt on cyclic diazoamides for the stereoselective cyclopropanation process with cyclic olefins. In this Letter, we describe a mild method for the construction of strained spiro-cyclopropanooxindole systems utilizing cyclic diazoamides and cyclic olefins or heteroaromatic systems in the presence of copper(I) triflate or rhodium(II) acetate catalyst in a diastereoselective manner.

Initially, the rhodium(II)-catalysed reaction of cyclic diazoamides **1** with cyclic olefins such as indene, dihydronapthalene and cyclooctadiene was planned. Towards this, reaction[16] of cyclic diazoamide **1a** and indene with 2 mol % of rhodium(II) acetate dimer catalyst for 4 h at room temperature afforded the spiro-cyclopropane **2a** in 90% yield (Scheme 1) as a single isomer based on the crude NMR analysis. Further, the product was confirmed by the characteristic C–H protons in proton NMR and two C–H carbons in carbon NMR. Mass spectrum shows the required mass value of 284 $(M+Na)^+$. Subsequently, the rhodium(II)-catalysed reaction of cyclic diazoamides **1b–d** with indene was carried out for 4 h at



1a: R^1 = methyl
1b: R^1 = benzyl
1c: R^1 = allyl
1d: R^1 = propargyl

2a-d

Scheme 1.

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Table 1
Synthesis of spiro-cyclopropanooxindoles **2**

Entry	Cyclopropanooxindoles **2**	Yield of **2**[a] (%) and time (h)	
		Rhodium catalyst	Copper catalyst
1	**2a**	90 (4)	94 (0.5)
2	**2b**	92 (4)	90 (0.5)
3	**2c**	86 (4)	88 (0.5)
4	**2d**	81 (4)	92 (0.5)

[a] Yields are unoptimized and refer to isolated yields.

room temperature and the chromatographic purification of the reaction mixture gave the respective spiro-cyclopropanes **2b–d** in very good yields with diastereoselectivity (Table 1).

Next, we studied the cyclopropanation reactions in the presence of CuOTf. Thus, reaction of **1a–d** with indene was performed with 20 mol % of CuOTf as catalyst. The reaction was completed within 30 min at room temperature to afford the corresponding strained cyclopropanes **2a–d** in very good yields (Table 1). All the products were characterized based on the spectral data. The stereochemistry of the representative product[17] **2d** was unequivocally supported[18] by single-crystal X-ray (Fig. 1) analysis.

The reaction was completed in less duration and improves the yield up to 10% when compared to rhodium(II) catalyst. The facile diastereoselective synthesis of substituted strained cyclopropanes **2** in good yield was demonstrated evidently from the above examples. Representatively, the formation of product **2a** was studied with other catalysts (Table 2) such as Cu(bis-oxazoline), Cu(II), Co(I), Rh(I) and Rh(III). Only Cu(bis-oxazoline) catalyst afforded the cyclopropane **2a** in 86% yield after stirring at room temperature for 24 h whereas other catalysts failed to provide cyclopropane.

Subsequently, we investigated the copper-catalysed reaction of cyclic diazoamide **1a** with dihydronapthalene. Thus, the reaction was performed in the presence of 20 mol % of CuOTf catalyst at room temperature to furnish the spiro-cyclopropane **3a** in 94% yield (Scheme 2) as a single isomer based on the crude NMR analysis. 3-Diazooxindoles **1b–d** were subjected in the presence of CuOTf to afford the corresponding cyclopropanes[17] **3b–d** in very good yield with diastereoselectivity (Table 3). No formation of

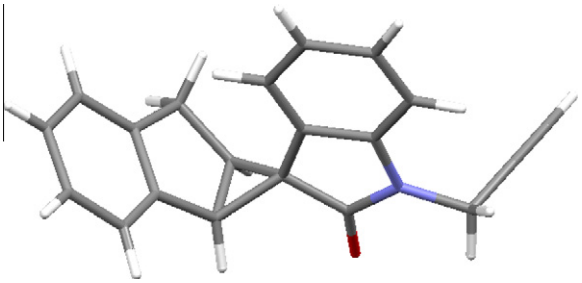
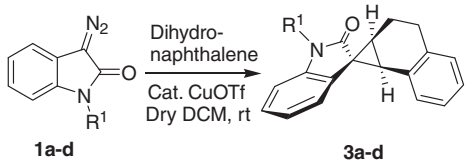


Figure 1. X-ray structure of compound **2d**.

Table 2
Effect of catalyst for spiro-cyclopropanooxindole **2a**

Entry	Catalyst	Yield of **2a**[a] (%) and time (h)
1	$Rh_2(OAc)_4$	92 (4)
2	CuOTf	90 (0.5)
3	CuOTf and bis-oxazoline ligand	86 (24)
4	$Cu(OTf)_2$	—
5	Cyanocobalamine	—
6	Wilkinson catalyst [Rhodium(I)]	—
7	$RhCl_3$ [Rhodium(III)]	—

[a] Yields are unoptimized and refer to isolated yields.



Scheme 2.

Table 3
Synthesis of spiro-cyclopropanooxindoles **3**

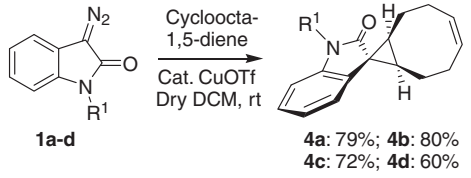
Entry	Cyclopropanooxindoles **3**	Catalyst	Yield of **3**[a] (%) and time (h)
1	**3a**	CuOTf	94 (0.5)
2	**3b**	CuOTf	94 (0.5)
3	**3c**	CuOTf	89 (0.5)
4	**3d**	CuOTf	86 (0.5)
5	**3a**	$Rh_2(OAc)_4$	—

[a] Yields are unoptimized and refer to isolated yields.

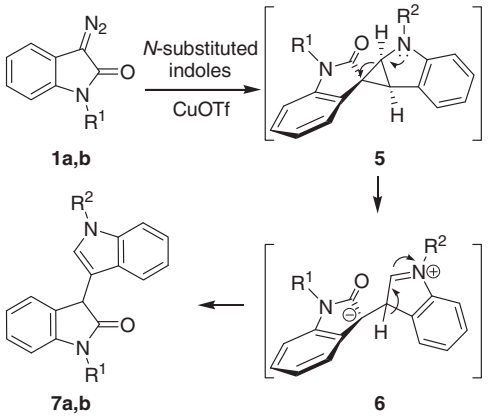
the cyclopropane product **3a** was observed when the reaction was carried out with rhodium(II) acetate catalyst.

Encouraged by the above results with CuOTf, we then performed the cyclopropanation reaction with cyclooctadiene. To this end, diazoamide **1a** was reacted with cyclooctadiene in the presence of 20 mol % of CuOTf for 30 min to yield the corresponding cyclopropane **4a** in 79% yield (Scheme 3). The above reaction in the presence of rhodium(II) acetate did not furnish the product **4a** and the starting material might be dimerized. Reaction of other cyclic diazoamides **1b–d** with cyclooctadiene in the presence of CuOTf afforded the respective products[16] **4b–d** in good yield.

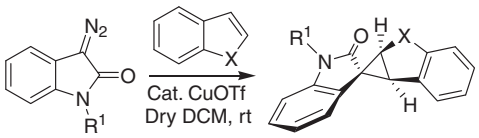
In order to extend the study of cyclopropanation, the reaction was then anticipated with heteroaromatic systems instead of cyclic olefins. Thus, the reaction of cyclic diazoamide **1a** with *N*-benzylindole in the presence of CuOTf afforded the corresponding 3-alkylated product[10a] **7a** in 98% yield (Scheme 4). Similarly, the product **7b** was also obtained from **1b**. This indicates that the formation of product **7** may be produced via the corresponding spiro-cyclopropane



Scheme 3.



Scheme 4.



1a-d **8a-d** and **9a-c**

Scheme 5.

Table 4
Synthesis of spiro-cyclopropanooxindoles **8** and **9**

Entry	Cyclopropanooxindoles **8**	X	Time (min)	Yield of **8**,**9**[a] (%)
1	**8a**	O	30	86
2	**8b**	O	30	92
3	**8c**	O	30	90
4	**8d**	O	30	91
5	**9a**	S	120	83
6	**9b**	S	120	86
7	**9c**	S	120	85

[a] Yields are unoptimized and refer to isolated yields.

5 and followed by ring opening to zwitterion **6** as intermediates in the presence of copper catalyst as observed in our previous study[10a] using rhodium catalyst. Hence, the reactions of diazoamides with indoles did not provide the corresponding spiro-cyclopropanooxindoles.

Further, we explored the cyclopropanation with other heteroaromatic systems such as benzofuran and benzothiophene. Thus, the reaction of diazoamide **1a** and benzofuran was carried out in the presence of 20 mol % of CuOTf to yield the respective spiro-cyclopropane[17] **8a** in 86% yield with diastereoselectivity (Scheme 5, entry 1, Table 3). The above reaction was repeated in presence of rhodium(II) acetate to afford the product **8a** in 80% yield. The reaction with benzofuran was generalized in the presence of CuOTf to afford the products **8b**–**d** in good yield (Table 4). It may be noted that the reaction of cyclic diazoketone with benzofuran furnished[8c] a mixture of cycloadducts.

Next, the cyclopropanation with benzothiophene was carried out. Reaction of diazoamide **1a** and benzothiophene was performed in the presence of 20 mol % of CuOTf to furnish the respective spiro-cyclopropane[17] **9a** in 83% yield (Scheme 5). The reaction with benzothiophene was also generalized in the presence of CuOTf to afford the products **9b**,**c** in good yield (Table 4). The reaction was repeated in the presence of rhodium(II) acetate to afford the product **9b** in 81% yield. It is noteworthy that benzofuran and benzothiophene furnished the respective spiro-cyclopropanooxindole in a diastereoselective manner whereas indole facilitates C-alkylation. No other isomers were detected by ^{1}H NMR analysis of the crude reaction mixture involved in the above study. Based on the crystal structure of **2d**, the stereochemistry of other products is tentatively assigned.

In conclusion, we have demonstrated that the diastereoselective synthesis of strained spiro-cyclopropanooxindoles from diazoamides using copper(I) triflate as a catalyst. A variety of spiro-cyclopropanooxindoles were achieved using symmetrical as well as asymmetrical cyclic olefins and heteroaromatic systems such as benzofuran and benzothiophene under mild reaction conditions. The effect of catalysts on the cyclopropanation was also studied and it was found that copper(I) triflate is better than rhodium(II) acetate.

Acknowledgements

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References and notes

1. Robertson, D. W.; Krushinski, J. H.; Pollock, G. D.; Wilson, H.; Kauffman, R. F.; Hayes, J. S. *J. Med. Chem.* **1987**, *30*, 824.
2. (a) Cordon, M. E.; Karp, G. M.; Birk, J. H. European Patent 459,133, 1991; *Chem. Abstr.* **1992**, *117*, 48332; (b) Condon, M. E.; Karp, G. M. European Patent 549,892, 1993; *Chem. Abstr.* **1993**, *119*, 225817.
3. Alper, P. B.; Meyers, C.; Lerchner, A.; Siegel, D. R.; Carreira, E. M. *Angew. Chem., Int. Ed.* **1999**, *38*, 3186.
4. (a) Cui, C. B.; Kakeya, H.; Okada, G.; Onose, R.; Ubukata, M.; Takahashi, I.; Isono, K.; Osada, H. *J. Antibiot.* **1995**, *48*, 1382; (b) Cui, C. B.; Kakeya, H.; Osada, H. *Tetrahedron* **1996**, *52*, 12651; (c) Chan, K. C.; Morsingh, F.; Yeoh, G. B. *J. Chem. Soc. C: Org.* **1966**, 2245; (d) Sebahar, P. R.; Williams, R. M. *J. Am. Chem. Soc.* **2000**, *122*, 5666.
5. Doyle, M. P.; McKervey, M. A.; Ye, T. *Modern Catalytic Methods for Organic Syntheis with Diazo Compounds. From Cyclopropanes to Ylides*; Wiley-Interscience: New York, 1998.
6. (a) Davies, H. M. L.. In *Comprehensive Organic Chemistry*; Trost, B. M., Fleming, I., Eds.; Pergamon Press: New York, 1991; Vol. 4, pp 1031–1067; (b) Davies, H. M. L.; Antoulinakis, E. G. *Organic Reactions*; John Wiley and Sons: New York, 2001; (c) Doyle, M. P. *Chem. Rev.* **1986**, *86*, 919; (d) Ye, T.; McKervey, M. A. *Chem. Rev.* **1994**, *94*, 1091; (e) Reissig, H.-U.; Zimmer, R. *Chem. Rev.* **2003**, *103*, 1151.
7. (a) Doyle, M. P.; Forbes, D. C. *Chem. Rev.* **1998**, *98*, 911. and references cited therein; (b) Miller, J. A.; Jin, W.; Nguyen, S. T. *Angew. Chem., Int. Ed.* **2002**, *41*, 2953; (c) Davies, H. M. L.; Townsend, R. J. *J. Org. Chem.* **2001**, *66*, 6595; (d) Davies, H. M. L.; Panaro, S. A. *Tetrahedron* **2000**, *56*, 4781; (e) Doyle, M. P.; Davies, S. B.; Hu, W. *J. Chem. Soc., Chem. Commun.* **2000**, 867.
8. (a) Pirrung, M. C.; Lee, Y. R. *J. Am. Chem. Soc.* **1995**, *117*, 4814; (b) Pirrung, M. C.; Lee, Y. R. *J. Chem. Soc., Chem. Commun.* **1995**, 673; (c) Pirrung, M. C.; Lackey, K.; Zhang, J.; Sternbach, D. D.; Brown, F. *J. Org. Chem.* **1995**, *60*, 2112; (d) Pirrung, M. C.; Zhang, J.; McPhail, A. T. *J. Org. Chem.* **1991**, *56*, 6269; (e) Pirrung, M. C.; Blume, F. *J. Org. Chem.* **1999**, *64*, 3642.
9. (a) Muthusamy, S.; Babu, S. A.; Gunanathan, C.; Ganguly, B.; Suresh, E.; Dastidar, P. *J. Org. Chem.* **2002**, *67*, 8019; (b) Muthusamy, S.; Babu, S. A.; Gunanathan, C.; Suresh, E.; Dastidar, P. *Bull. Chem. Soc. Jpn.* **2002**, *75*, 801; (c) Muthusamy, S.; Krishnamurthi, J.; Babu, S. A.; Suresh, E. *J. Org. Chem.* **2007**, *72*, 1252; (d) Muthusamy, S.; Krishnamurthi, J.; Nethaji, M. *Chem. Commun.* **2005**, 3862; (e) Muthusamy, S.; Gnanaprakasam, B. *Tetrahedron* **2007**, *63*, 3355.
10. (a) Muthusamy, S.; Gunanathan, C.; Babu, S. A.; Suresh, E.; Dastidar, P. *J. Chem. Soc., Chem. Commun.* **2002**, 824; (b) Muthusamy, S.; Gunanathan, C. *Synlett* **2002**, 1783.
11. Muthusamy, S.; Srinivasan, P. *Tetrahedron Lett.* **2005**, *46*, 1063.
12. Muthusamy, S.; Srinivasan, P. *Tetrahedron Lett.* **2009**, *50*, 3794.
13. Muthusamy, S.; Gnanaprakasam, B.; Suresh, E. *Org. Lett.* **2005**, *7*, 4577.
14. (a) Lund, E. A.; Kennedy, I. A.; Fallis, A. G. *Tetrahedron Lett.* **1993**, *34*, 6841; (b) Padwa, A.; Coats, S. J.; Hadjiarapoglou, L. *Heterocycles* **1995**, *41*, 1631.
15. Muthusamy, S.; Gunanathan, C. *Synlett* **2003**, 1559.
16. *General procedure for the synthesis of spiro-cyclopropanooxindoles* **2**–**4**, **8** *and* **9**: To an oven-dried flask, a solution containing cyclic diazoamide **1** (1 mmol) and cyclic olefin (1.1 mmol) in dry dichloromethane (50 mL) under inert atmosphere was added 20 mol % of CuOTf or 2.0 mol % of rhodium(II) acetate dimer and stirred for appropriate duration at room temperature. The reaction was monitored by TLC and IR. After the decomposition of all diazoamide, the reaction mixture was evaporated and subjected to 100–200 mesh silica-gel column chromatography (EtOAc/hexane) to afford the respective spiro-cyclopropanooxindoles **2**–**4**, **8** and **9**.
17. *Selected spectral data*. Product **2d**: Brown colour solid; mp 141–143 °C; IR (neat) ν 3047, 2918, 1696, 1466, 1382, 1280, 736 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 2.24 (s,1H, ≡C*H*), 2.92–2.98 (t, 1H, C*H*), 3.20–3.59 (m, 2H, CH_2), 4.58 (d, 2H, NCH_2), 5.65–5.69 (d, 1H, C*H*), 6.63–7.32 (m, 8H, =C*H*); ^{13}C NMR (50 MHz, $CDCl_3$) δ 29.2 (NCH_2), 32.3 (CH), 34.9 (CH_2), 35.5 (*quat-C*), 42.6 (CH), 72.0 (CH), 76.9 (*quat-C*), 108.8 (=CH), 120.9 (=CH), 121.9 (=CH), 124.1 (=CH), 125.4 (*quat-C*), 125.9 (=CH), 126.5 (=CH), 126.9 (=CH), 127.4 (=CH), 139.1 (*quat-C*), 142.5 (*quat-C*), 144.3 (*quat-C*). 174.4 (C=O); HRMS (ESI) calcd for $C_{20}H_{15}NONa$ (M+Na)$^+$: 308.1051, found 308.1039. Product **3b**: Brown colour solid; mp 178–180 °C; IR (neat) ν 3046, 2918, 1698, 1470, 1382, 1280, 736 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.21–3.27 (m, 5H, C*H* and CH_2), 4.87–5.11 (q, 2H, NCH_2), 5.72 (d, 1H, C*H*, *J* = 8 Hz), 6.58–7.32 (m, 13H, Arom-*H*); ^{13}C NMR (50 MHz, $CDCl_3$), δ 18.5 (CH_2), 28.3 (CH_2), 29.1 (CH), 30.7 (CH), 38.9 (*quat-C*), 44.0 (NCH_2), 108.7 (=CH), 121.1 (=CH), 122.0 (=CH), 125.8 (*quat-C*), 126.2 (=CH), 126.8 (=CH), 127.3 (=CH), 128.7 (=CH), 131.0 (=CH), 136.3 (=CH), 136.3 (*quat-C*), 138.9 (*quat-C*), 143.6 (*quat-C*), 144.5 (*quat-C*), 176.0 (C=O); HRMS (ESI) calcd for $C_{25}H_{21}NONa$ (M+Na)$^+$: 374.1521, found 374.1534. Product **4b**: Brown colour solid; mp 87–89 °C; IR (neat) ν 3046, 2918, 1696, 1466, 1382, 1280, 736 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.75–2.43 (m, 10H, C*H* and CH_2), 4.82–4.92 (m, 2H, NCH_2), 5.63–5.64 (m, 2H, =C*H*), 6.62 (d, 1H, Arom-*H*, *J* = 8 Hz), 6.75 (d, 1H, Arom-*H*, *J* = 8 Hz), 6.90–7.21 (m, 7H, Arom-*H*); ^{13}C NMR (50 MHz, $CDCl_3$), δ 23.0 (CH_2), 26.7 (CH_2), 34.5 (CH), 43.6 (CH), 44.1 (NCH_2), 108.9 (=CH), 121.3 (=CH), 122.4 (=CH), 126.1 (=CH), 127.3 (=CH), 128.7 (=CH), 129.5 (=CH), 133.1 (*quat-C*), 136.5 (*quat-C*), 143.1 (*quat-C*), 177.4 (C=O); HRMS (ESI) calcd for $C_{23}H_{23}NONa$ (M+Na)$^+$: 352.1677, found 352.1664. Product **8a**: Brown colour solid; m.p 127–129 °C; IR (neat) ν 3043, 2914, 1698,

1610, 1492, 1468, 1378, 1346, 1124, 751, 726, cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) 3.20, (s, 3H, NC*H*$_3$), 3.75–3.76 (d, 1H, C*H*), 5.33 (d, 1H, C*H*, *J* = 8 Hz), 6.60–7.33 (m, 8H, Arom-*H*); ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.5 (N*C*H$_3$), 28.51 (*quat-C*), 38.3 (*C*H), 74.21 (*C*H), 108.0 (=*C*H), 110.0 (=*C*H), 121.1 (=*C*H), 121.9 (=*C*H), 122.0 (=*C*H), 123.3 (*quat-C*), 124.4 (*quat-C*) 126.4 (=*C*H), 126.9 (=*C*H), 129.0 (=*C*H), 144.6 (*quat-C*), 161.7 (*quat-C*), 175.0 (*C*=O); HRMS (ESI) calcd for $C_{17}H_{13}NO_2Na$ $(M+Na)^+$: 286.0844, found 286.0859. Product **9b**: Brown colour solid; m.p 161–163 °C; IR (neat) *v* 3049, 3024, 2926, 1695, 1611, 1464, 1361, 1345, 1279, 1187, 731, 702, 679 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 3.83–3.84 (d, 1H, C*H*), 4.90 (s, 2H, NC*H*$_2$), 5.53–5.60 (d, 1H, C*H*, *J* = 8 Hz), 6.53–6.57 (t, 1H, Arom-*H*), 6.69–6.70 (d, 1H, Arom-*H*), 7.00–7.31 (m, 11H, Arom-*H*); ^{13}C NMR (100 MHz, $CDCl_3$) δ 30.45 (*quat-C*), 38.54 (N*C*H$_2$), 42.12 (*C*H), 54.40 (=*C*H), 109.0 (=*C*H), 110.0 (=*C*H), 121.2 (=*C*H), 121.9 (=*C*H), 122.1 (=*C*H), 123.4 (*quat-C*), 124.3 (*quat-C*), 126.5 (=*C*H), 127.3 (=*C*H), 127.6 (=*C*H), 127.8 (=*C*H), 128.7 (=*C*H), 129.0 (=*C*H), 135.9 (*quat-C*), 143.7 (*quat-C*), 145.78 (*quat-C*), 175.2 (*C*=O); HRMS (ESI) calcd for $C_{23}H_{17}NOS$ Na $(M+Na)^+$: 378.0929, found 378.0921.

18. Crystallographic data for **2d** have been deposited (CCDC 647633) with the Cambridge Crystallographic Data Centre. Copy of the data can be obtained free of charge on application to 12, Union Road, Cambridge CB21EZ, UK (fax: +44 1223 336 033; e-mail: deposit@ccdc.cam.ac.uk).