Synthesis of Sulfonamides and 1,3-Oxazine-2,4-diones from Arylsulfonyl Isocyanates and Diketene

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Abstract: An effective route to functionalized N^1-[(2,6-dimethyl-4-oxo-4*H*-pyran-3-yl)carbonyl]-1-arylsulfonamide and 3-(arylsulfonyl)-6-methyl-2*H*-1,3-oxazine-2,4(3*H*)-dione derivatives is described. This involves the reaction of arylsulfonyl isocyanates and diketene in the presence of N-heteroaromatic compounds such as 1,3,5-triazine, 1-methyl-1*H*-imidazole, or pyridine as catalyst. The reactive 1:1 zwitterions obtained from the addition of N-heteroaromatic compound to arylsulfonyl isocyanates were trapped by diketene to produce functionalized sulfonamide and 1,3-oxazine-2,4(3*H*)-dione derivatives.

Key words: arylsulfonyl isocyanate, catalytic reaction, diketene, N-heteroaromatic compounds, sulfonamides, zwitterions

The importance of the sulfonamide unit in medicinal chemistry cannot be overstated.[1,2] They have been found to possess a large number of different biological activities, including antibacterial, antiviral, antidiabetic, diuretic, and antithyroid activities.[3–6] Recently, sulfonamides have been found to be potent cysteine protease inhibitors, which could possibly extend their therapeutic applications to include conditions such as Alzheimer's disease, arthritis, and cancer.[7] Using cell-based and microarray-based screening strategies, sulfonamide-focused compound libraries have also been evaluated for their antitumor potential.[8] Compound **1** is a precursor for the synthesis of Celecoxib analgesic (Figure 1).[9]

4*H*-Pyran-4-ones (γ-pyrones) and their benzologues (chromones and flavones), play different roles in plant physiology and exhibit a diverse spectrum of biological functions.[10] They are interesting as pharmacological agents since they stimulate or inhibit a wide variety of enzyme systems and have potential as antibacterial, anticancer, and anti-allergic agents.[11] Maltol (**2**) is a natural compound, which is used widespread in food industry as additive due to its flavor and antioxidant properties[12] and also in coordination chemistry (Figure 2).[13]

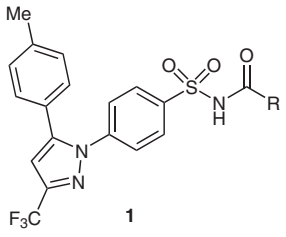

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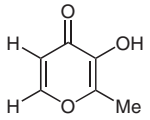
Figure 1 Precursor sulfonamide **1** for the synthesis of Celecoxib analgesic



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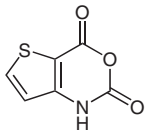

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Figure 2 Structure of maltol (**2**) and thiaisatoic anhydride (**3**)

Due to the broad spectrum of biological activities of 1,3-oxazine-2,4-diones, including analgesic, antipyretic, bacteriostatic, fungistatic, and monoaminoxidase inhibitory activity, they are an interesting class of compounds for studying their chemistry.[14] 1*H*-Thieno[3,2-*d*][1,3]oxazine-2,4-dione (**3**, thiaisatoic anhydride) is a useful building block for the synthesis of numerous heterocycles with therapeutic interest (Figure 2).[15]

Although a variety of sulfonamide[16] and pyrane[17] syntheses are known, despite the biological importance of them, there currently exists no efficient procedure for preparing compounds that have both *N*-acylsulfonamide and γ-pyrone units in their structure in one synthetic step. On the other hand, surprisingly, only few synthetic methods for 1,3-oxazin-2,4-dione moiety have been reported in the literature so far. Most of them are multistep reactions using expensive reagents and give low total yields[18] and thus, there is a clear need for generally useful, mild, and novel method for their synthesis.

Therefore, to reach the mentioned purposes, we report here the one-pot catalytic reaction between arylsulfonyl isocyanates **4** and diketene in the presence of N-heteroaromatic compounds. The reaction between arylsulfonyl isocyanate **4** and diketene in the presence of *N*-methylimidazole (NMI) or 1,3,5-triazine as N-heteroaromatic catalyst proceeds in dichloromethane at ambient temperature to produce exclusively N^1-[(2,6-dimethyl-4-oxo-4*H*-pyran-3-yl)carbonyl]-1-arylsulfonamides **5** in high yields. But in the presence of pyridine, this reaction affords 3-(arylsulfonyl)-6-methyl-2*H*-1,3-oxazine-2,4(3*H*)-diones **6**

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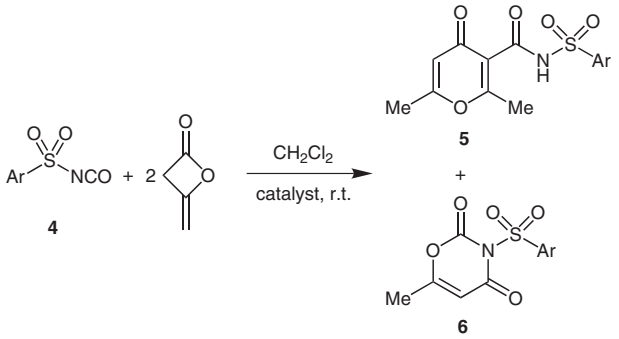
Table 1 Reaction of Arylsulfonyl Isocyanates **4** with Diketene



Entry	**4**, Ar	Catalyst (20 mol%)	Yield (%)	Ratio of **5**:**6**
1	Tol	*N*-methylimidazole	85	100:0
2	Ph	*N*-methylimidazole	88	100:0
3	Tol	1,3,5-triazine	90	100:0
4	Ph	1,3,5-triazine	90	100:0
5	Tol	pyridine	80	20:80
6	Ph	pyridine	83	18:82

in addition to **5** as the main product with a ratio of 80:20 (Table 1).

The structures of compounds **5a**,**b** and **6a**,**b** were deduced from their elemental analyses, IR, and high-field ^{1}H and ^{13}C NMR spectra. The IR spectrum of **5a** showed absorption bands due to the two carbonyl groups at 1695 and 1652 cm^{-1} and a NH group at 3425 cm^{-1}. The ^{1}H NMR spectrum of **5a** exhibited five sharp singlet signals readily recognized as arising from three methyl groups (δ = 2.31, 2.42, and 2.72), vinylic hydrogen (δ = 6.29) along with NH at δ = 13.06. The phenyl moiety gave rise to characteristic signals in the aromatic region of the spectrum.

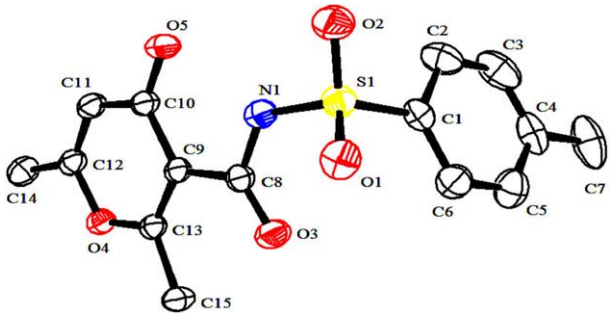
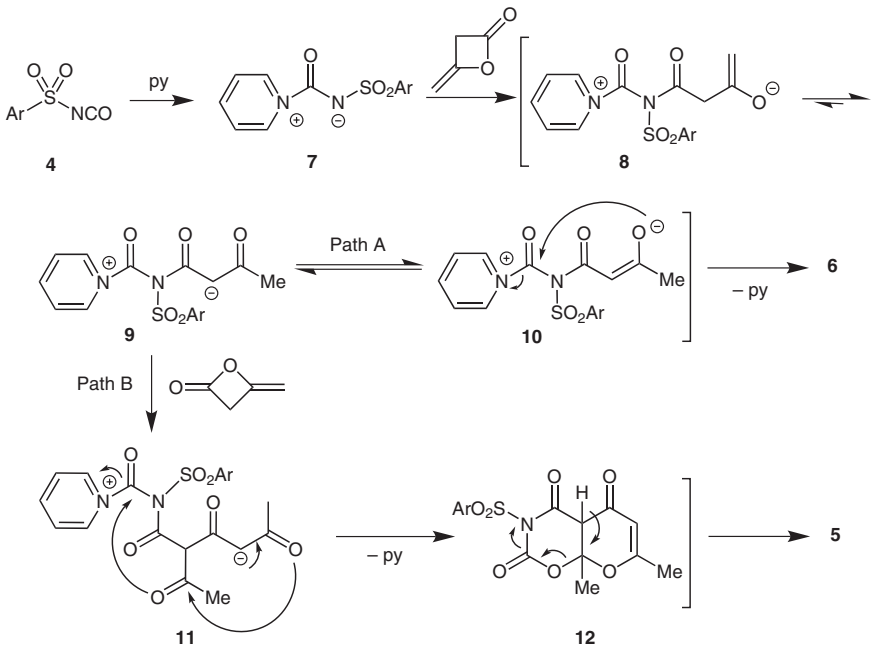


Figure 3 X-ray crystal structure of **5a**

The ^{1}H decoupled ^{13}C NMR spectrum of **5a** showed 13 distinct resonances in agreement with the sulfonamide structure. Finally, the structure of **5a** was further confirmed by a single crystal X-ray diffraction analysis (Figure 3).

The ^{1}H NMR spectrum of **6a** exhibited three sharp singlet signals due to the two methyl groups and a vinylic hydrogen (δ = 2.15, 2.45 and 5.66, respectively). The ^{1}H decoupled ^{13}C NMR spectrum of **6a** showed 10 distinct resonances in agreement with the sulfonamide structure.

Although the mechanism of the reaction between arylsulfonyl isocyanates **4** and diketene in the presence of N-heteroaromatic catalyst has not yet been established in an experimental manner, a possible explanation for pyridine catalyst that produces both **5** and **6** is proposed in Scheme 1. Based on the well-established chemistry of isocyanates with various nucleophiles,[19–22] it is reasonable to assume that **7** results from initial addition of pyridine (or other catalysts) to arylsulfonyl isocyanates **4**. Intermediate **7** is a stable zwitterion, but in the presence of diketene



Scheme 1

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is converted into intermediate **8** which is in equilibrium with **9** and **10**.[23–29] In path A, intermediate **10** cyclizes by losing pyridine to give the corresponding 1,3-oxazine-2,4(3*H*)-dione **6** derivatives. In path B, due to the result of attack of intermediate **9** to a second molecule of diketene, zwitterion **11** is formed, which loses pyridine to give pyranooxazine tricarbonyl intermediate **12**. Intermediate **12** is unstable and with loss of CO_2 is converted into the corresponding N^1-[(2,6-dimethyl-4-oxo-4*H*-pyran-3-yl)carbonyl]-1-arylsulfonamide derivatives **5**.

In conclusion, the present method has the following advantages: (i) the reaction is performed under neutral conditions and (ii) the substances can be mixed without any activation or modification. The simplicity of the present procedure makes it an interesting alternative to the complex multistep approaches.

Arylsulfonyl isocyanates **4** and diketene were obtained from Merck (Germany) and Fluka (Switzerland) and were used without further purification. Melting points were measured on an Electrothermal 9100 apparatus. Elemental analyses for C, H and N were performed using a Heraeus CHN–O–Rapid analyzer. Mass spectra were recorded on a Finnigan-Matt 8430 mass spectrometer operating at an ionization potential of 20 eV. ^{1}H and ^{13}C NMR spectra were measured ($CDCl_3$ solution) with a Bruker DRX-500 Avance spectrometer at 500.1 and 125.8 MHz, respectively. IR spectra were recorded on a Shimadzu IR-460 spectrometer. Chromatographic columns were prepared from Merck silica gel (230–240 mesh).

N^1-[(2,6-Dimethyl-4-oxo-4*H*-pyran-3-yl)carbonyl]-4-methyl-1-benzenesulfonamide (5a); Typical Procedure

To a magnetically stirred solution of *p*-toluenesulfonyl isocyanate [**4** (Ar = 4-MeC_6H_4); 0.2 g, 1 mmol] and the respective N-heterocyclic catalyst (20 mol%) in anhyd CH_2Cl_2 (5 mL) was added dropwise a solution of diketene (0.17 g, 2 mmol) in anhyd CH_2Cl_2 (3 mL) at 25 °C over 2 h. The mixture was stirred for 24 h. The solvent was removed under reduced pressure, and the residue was separated by silica gel column chromatography (hexane–EtOAc, 3:1). The product was recrystallized in a mixture of toluene, *n*-hexane and EtOAc. **5a** was obtained as colorless crystals; mp 191–193 °C (Table 1).

IR (KBr): 3425 (NH), 1695 (C=O), 1652 (NC=O), 1584 (C=C), 1538 and 1407 (Ar), 1343 and 1134 (SO_2), 1163 and 1076 cm^{-1} (C–O).

^{1}H NMR (500.13 MHz, $CDCl_3$): δ = 2.31 (s, CH_3, 3 H), 2.42 (s, CH_3, 3 H), 2.72 (s, CH_3, 3 H), 6.29 (s, C=CH, 1 H), 7.31 (d, *J* = 8.2 Hz, 2 H_{arom}), 7.98 (d, *J* = 8.2 Hz, 2 H_{arom}), 13.06 (s, NH, 1 H).

^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 19.51 (CH_3), 21.48 (CH_3), 21.65 (CH_3 of Ar), 114.66 (C=*C*H), 114.79 (C-3 of pyran), 128.43 (2 CH_{arom}), 129.43 (2 CH_{arom}), 136.53 (C_{ipso}-ArSO$_2$), 144.51 (C_{ipso}-ArMe), 161.72 (NCO), 165.80 (C-2 of pyran), 176.46 (C-6 of pyran), 178.82 (C=O).

MS: *m*/*z* (%) = 151 (23), 150 (70), 109 (28), 108 (46), 91 (50), 77 (18), 65 (38), 67 (50), 43 (100), 41 (30).

Anal. Calcd for $C_{15}H_{15}NO_5S$ (321.34): C, 56.07; H, 4.70; N, 4.36. Found: C, 56.10; H, 4.80; N, 4.46.

Crystal Data[30]

$C_{15}H_{15}NO_5S$; M_W = 321.34, triclinic, space group *P*–1, *a* = 7.3885(9) Å, *b* = 8.1143(10) Å, *c* = 14.1248(18) Å, *α* = 76.866(1)°, *β* = 79.723(1)°, *γ* = 69.187(1)°, *V* = 766.40(16) Å^3, *Z* = 2, D_{calcd} = 1.392 mg/m^3, *F* (000) = 336, crystal dimension 0.43 × 0.32 × 0.25 mm, MoKα radiation (λ = 0.71073 Å), 2.73 ≤ 2*θ* ≤ 26.0, intensity data were collected at 295(2) K with a Bruker APEX area-detector diffractometer employing *w*/2*θ* scanning technique in the range of –9 ≤ *h* ≤ 9, –10 ≤ *k* ≤ 5, –17 ≤ *l* ≤ 17. The structure was solved by a direct method, all nonhydrogen atoms were positioned and anisotropic thermal parameters refined from 2457 observed reflections with *R* (int) = 0.0119 by a full-matrix least-squares technique converged to *R*1 = 0.0476 and *wR*2 = 0.1467 [*I* > 2σ(*I*)].

N^1-[(2,6-Dimethyl-4-oxo-4*H*-pyran-3-yl)carbonyl]-1-benzenesulfonamide (5b)

Colorless crystals; mp 135–137 °C.

IR (KBr): 3410 (NH), 1696 (C=O), 1649 (NC=O), 1577 (C=C), 1537 and 1419 (Ar), 1346 and 1137 (SO_2), 1170 and 1079 cm^{-1} (C–O).

^{1}H NMR (500.13 MHz, $CDCl_3$): δ = 2.32 (s, 3 H), 2.72 (s, 3 H), 6.30 (s, 1 H), 7.53 (t, *J* = 7.9 Hz, 2 H), 7.61 (t, *J* = 7.4 Hz, 1 H), 8.12 (d, *J* = 7.6 Hz, 2 H), 13.07 (s, 1 H).

^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 19.52, 21.52, 114.69, 114.76, 128.40, 128.81, 133.51, 139.46, 161.72, 165.77, 176.54, 178.83.

GC-MS (EI 70 eV): *m*/*z* (%) = 308 (1, M$^+$), 243 (9), 226 (21), 151 (22), 150 (100), 124 (11), 109 (17), 77 (22), 67 (19), 43 (17).

Anal. Calcd for $C_{14}H_{13}NO_5S$ (307.32): C, 54.72; H, 4.26; N, 4.56. Found: C, 54.30; H, 4.60; N, 4.70.

6-Methyl-3-[(4-methylphenyl)sulfonyl]-2*H*-1,3-oxazine-2,4(3*H*)-dione (6a)

White powder; mp 140–142 °C.

IR (KBr): 1769 (OC=ON), 1717 (NC=O), 1670 (C=C), 1635 and 1586 (Ar), 1382 and 1191 (SO_2), 1111 and 1077 cm^{-1} (C–O).

^{1}H NMR (500.13 MHz, $CDCl_3$): δ = 2.15 (s, 3 H), 2.45 (s, 3 H), 5.66 (s, 1 H), 7.39 (d, *J* = 8.2 Hz, 2 H), 8.14 (d, *J* = 8.2 Hz, 2 H).

^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 19.03, 21.85, 101.92, 129.40, 129.81, 134.49, 144.39, 146.72, 158.42, 165.11.

GC-MS (EI 70 eV): *m*/*z* (%) = 217 (1), 197 (2), 155 (40), 133 (41), 91 (100), 65 (29), 43 (18).

Anal. Calcd for $C_{12}H_{11}NO_5S$ (281.28): C, 51.24; H, 3.94; N, 4.98. Found: C, 51.36; H, 3.90; N, 4.90.

6-Methyl-3-(phenylsulfonyl)-2*H*-1,3-oxazine-2,4(3*H*)-dione (6b)

White powder; mp 144–146 °C.

IR (KBr): 1763 (OC=ON), 1714 (NC=O), 1665 (C=C), 1617 and 1571 (Ar), 1380 and 1175 (SO_2), 1117 and 1076 cm^{-1} (C–O).

^{1}H NMR (500.13 MHz, $CDCl_3$): δ = 2.17 (s, 3 H), 5.71 (s, 1 H), 7.61 (t, *J* = 7.5 Hz, 2 H), 7.75 (t, *J* = 7.5 Hz, 1 H), 8.28 (d, *J* = 8.5 Hz, 2 H).

^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 19.08, 101.89, 129.21, 129.31, 135.29, 137.34, 144.35, 158.35, 165.24.

GC-MS (EI 70 eV): *m*/*z* (%) = 267 (1, M$^+$), 203 (1), 183 (1), 141 (28), 119 (32), 100 (5), 77 (100), 51 (34), 43 (29).

Anal. Calcd for $C_{11}H_9NO_5S$ (267.25): C, 49.44; H, 3.39; N, 5.24. Found: C, 49.32; H, 3.45; N, 5.28.

References

(1) Navia, M. A. *Science* **2000**, *288*, 2132.
(2) Mohamed, S. K. *Afinidad* **2000**, *57*, 451; *Chem. Abstr.* **2000**, *133*, 73818x.
(3) Maren, T. H.; Conroy, C. W. *J. Biol. Chem.* **1993**, *268*, 26233.

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(4) Scozzafava, A.; Owa, T.; Mastrolorenzo, A.; Supuran, C. T. *Curr. Med. Chem.* **2003**, *10*, 925.
(5) Owa, T.; Yoshino, H.; Okauchi, T.; Yoshimatsu, K.; Ozawa, Y.; Sugi, N. H.; Nagasu, T.; Koyanagi, N.; Kitoh, K. *J. Med. Chem.* **1999**, *42*, 3789.
(6) Koyanagi, N.; Nagasu, T.; Fujita, F.; Watanabe, T.; Tsukahara, K.; Funahashi, Y.; Fujita, M.; Taguchi, T.; Yoshino, H.; Kitoh, K. *Cancer Res.* **1994**, *54*, 1702.
(7) (a) Roush, W. R.; Gwaltney, S. L.; Cheng, J.; Scheidt, K. A.; McKerrow, J. H.; Hansell, E. *J. Am. Chem. Soc.* **1998**, *120*, 10994. (b) Roush, W. R.; Cheng, J.; Knapp-Reed, B.; Alvarez-Hernandez, A.; McKerrow, J. H.; Hansell, E.; Engel, J. C. *Bioorg. Med. Chem. Lett.* **2001**, *11*, 2759. (c) Maren, T. H. *Annu. Rev. Pharmacol. Toxicol.* **1976**, *16*, 309. (d) Supuran, C. T.; Briganti, F.; Tilli, S.; Chegwidden, W. R.; Scozzafava, A. *Bioorg. Med. Chem.* **2001**, *9*, 703. (e) Scozzafava, A.; Menabuoni, L.; Mincione, F.; Briganti, F.; Mincione, G.; Supuran, C. T. *J. Med. Chem.* **2000**, *43*, 4542.
(8) (a) Yokoi, A.; Kuromitsu, J.; Kawai, T.; Nagasu, T.; Sugi, N. H.; Yoshimatsu, K.; Yoshino, H.; Owa, T. *Mol. Cancer Ther.* **2002**, *1*, 275. (b) Oda, Y.; Owa, T.; Sato, T.; Boucher, B.; Daniels, S.; Yamanaka, H.; Shinohara, Y.; Yokoi, A.; Kuromitsu, J.; Nagasu, T. *Anal. Chem.* **2003**, *75*, 2159. (c) Owa, T.; Yokoi, A.; Yamazaki, K.; Yoshimatsu, K.; Yamori, T.; Nagasu, T. *J. Med. Chem.* **2002**, *45*, 4913. (d) Owa, T.; Okauchi, T.; Yoshimatsu, K.; Sugi, N. H.; Ozawa, Y.; Nagasu, T.; Koyanagi, N.; Okabe, T.; Kitoh, K.; Yoshino, H. *Bioorg. Med. Chem. Lett.* **2000**, *10*, 1223.
(9) Huang, S.; Connolly, P. J.; Lin, R.; Emanuel, S.; Middleton, S. A. *Bioorg. Med. Chem. Lett.* **2006**, *16*, 3639.
(10) (a) Staunton, J. In *Comprehensive Organic Chemistry*, Vol. 4; Barton, D. H. R.; Ollis, W. D., Eds.; Pergamon Press: Oxford, **1979**, 679. (b) See also: Staunton, J. In *Comprehensive Organic Chemistry*, Vol. 4; Barton, D. H. R.; Ollis, W. D., Eds.; Pergamon Press: Oxford, **1979**, 688.
(11) (a) See also: Ellis, G. P. In *The Chemistry of Heterocyclic Compounds Chromenes, Chromanones and Chromones*, Vol. 31; Weissberger, A.; Taylor, E. C., Eds.; Wiley: New York, **1977**, 912. (b) Ellis, G. P. In *The Chemistry of Heterocyclic Compounds Chromenes, Chromanones and Chromones*, Vol. 31; Weissberger, A.; Taylor, E. C., Eds.; Wiley: New York, **1977**, 985. (c) Ellis, G. P. In *The Chemistry of Heterocyclic Compounds Chromenes, Chromanones and Chromones*, Vol. 31; Weissberger, A.; Taylor, E. C., Eds.; Wiley: New York, **1977**, 1063.
(12) (a) Kato, Y. *Food Sci. Technol. Res.* **2003**, *9*, 264. (b) Yanagimoto, K.; Ochi, H.; Lee, K. G.; Shibamoto, T. *J. Agric. Food Chem.* **2004**, *52*, 592.
(13) (a) Caravan, P.; Gelmini, L.; Glover, N.; Herring, F. G.; McNeill, H.; Li, J. H.; Rettig, S. J.; Setyawati, I. A.; Shuter, E.; Sun, Y.; Tracey, A. S.; Yuen, V. G.; Orvig, C. *J. Am. Chem. Soc.* **1995**, *117*, 12759. (b) Reffitt, D. M.; Burden, T. J.; Seed, P. T.; Wood, J.; Thompson, R. P. H.; Powell, J. J. *Ann. Clin. Biochem.* **2000**, *37*, 457. (c) Johnson, V. J.; Sharma, R. P. *Neurotoxicology* **2003**, *24*, 261. (d) Hinds, F. E.; Aldrich-Wright, J. R.; Leverett, P.; Hazell, S. L. *J. Inorg. Biochem.* **2003**, *96*, 144. (e) Ellis, B. L.; Duhme, A. K.; Hider, R. C.; Hossian, M. B.; Rizvi, S.; van der Helm, D. *J. Med. Chem.* **1996**, *39*, 3659.
(14) (a) Clauson-Kaas, N.; Denss, R.; Ostermayer, F.; Renk, E. J. R. Geigy A.G., Swiss Appl. 1339175, **1961**; *Chem. Abstr.* **1964**, *60*, 4158d. (b) Clauson-Kaas, N.; Denss, R.; Ostermayer, F.; Renk, E. J. R. Geigy A.G. Swiss Appl. 419160, **1967**; *Chem. Abstr.* **1967**, *66*, 115718v.
(15) (a) Coppola, G. M. *Synthesis* **1980**, 503. (b) Coppola, G. M.; Marsden, C. M. *Heterocycl. Commun.* **1996**, *2*, 301.
(16) (a) Kawai, M.; BaMaung, N. Y.; Fidanze, S. D.; Erickson, S. A.; Tedrow, J. S.; Sanders, W. J.; Vasudevan, A.; Park, C.; Hutchins, C.; Comess, K. M.; Kalvin, D.; Wang, J.; Zhang, Q.; Lou, P.; Tucker-Garcia, L.; Bouska, J.; Bell, R. L.; Lesniewski, R.; Henkin, J.; Sheppard, G. S. *Bioorg. Med. Chem. Lett.* **2006**, *16*, 3574. (b) Siddiqui, N.; Pandeya, S. N. *Bioorg. Med. Chem. Lett.* **2007**, *17*, 255. (c) Johnson, D. C.; Widlanski, T. S. *Tetrahedron Lett.* **2001**, *42*, 3677. (d) Vogel, A. *Textbook of Practical Organic Chemistry*; Longman: London, **1978**, 4th ed., 647. (e) Cremlyn, R. *Organosulfur Chemistry: An Introduction*; Wiley: New York, **1996**. (f) Anderson, K. K. *Sulfonic Acids and Their Derivatives,* In *Comprehensive Organic Chemistry*, Vol. 3; Barton, D. H. R.; Ollis, W. D.; Jones, D. N., Eds.; Pergamon Press: Oxford, **1979**. (g) Domínguez, J. N.; León, C.; Rodrigues, J.; Domínguez, N.; Gut, J.; Rosenthal, P. *Farmaco* **2005**, *60*, 307. (h) Murakami, Y.; Kondo, K.; Sekimoto, E.; Nakao, J. *Tetrahedron* **2000**, *56*, 5843. (i) Ito, Y.; Manabe, S.; Sugioka, T. *Tetrahedron Lett.* **2007**, *48*, 787. (j) Alizadeh, A.; Rostamnia, S.; Esmaili, A. *Synthesis* **2007**, 709.
(17) (a) Bartol, G.; Bosco, M.; Cimarreli, C.; Dalpozo, R.; Guereio, G.; Palmieri, G. *J. Chem. Soc., Perkin Trans. 1* **1993**, 2081. (b) Yamamoto, Y.; Morita, Y. *Chem. Pharm. Bull.* **1984**, *32*, 2957. (c) Majetich, G.; Zhanj, Y.; Dreger, G. *Tetrahedron Lett.* **1993**, *34*, 449. (d) Ficini, J.; Pouliquen, J. *Tetrahedron Lett.* **1972**, 1135. (e) Sano, T.; Saitoh, T. *Heterocycles* **1993**, *36*, 2139. (f) Kim, H. S.; Yoon, Y. H. *Bull. Korean Chem. Soc.* **1993**, *14*, 159. (g) Andrey Chicov, Y. S.; Vinokurova, O. V.; Gein, V. L. *Chem. Heterocycl. Compd. (English Trans.)* **1989**, 126. (h) Weeks, P. D.; Brennan, T. M.; Brannegan, T. D.; Kuhla, D. E.; Elliott, M. L.; Watson, H. A. *J. Org. Chem.* **1980**, *45*, 1109. (i) Grrige, R.; Jachson, G. L. *J. Chem. Soc. C* **1970**, 552. (j) Harris, T. M.; Wachter, M. P. *Tetrahedron* **1970**, *26*, 5255.
(18) (a) Clauson-Kaas, N.; Denss, R.; Ostermayer, F.; Renk, E. J. R. Geigy A.G., Swiss Appl. 436323, **1968**; *Chem. Abstr.* **1968**, *69*, 27435g. (b) Clauson-Kaas, N.; Denss, R.; Ostermayer, F.; Renk, E. J. R. Geigy A.G., Swiss Appl. 412 602, **1967**; *Chem. Abstr.* **1967**, *67*: 11492w.
(19) Huisgen, R.; Herbig, K.; Morikawa, M. *Chem. Ber.* **1967**, *100*, 1107.
(20) Ulrich, H. *Chem. Rev.* **1962**, *2*, 186.
(21) Adib, M.; Yavari, H.; Mollahosseini, M. *Tetrahedron Lett.* **2004**, *45*, 1803.
(22) Ozaki, S. h. *Chem. Rev.* **1972**, *72*, 457.
(23) Alizadeh, A.; Zohreh, N.; Rostamnia, S. *Tetrahedron* **2007**, *63*, 8083.
(24) Mansson, M.; Nakase, Y.; Sunner, S. *Acta Chem. Scand.* **1968**, *22*, 171.
(25) Briody, J. M.; Satchell, D. P. N. *J. Chem. Soc.* **1965**, 3778.
(26) Briody, J. M.; Satchell, D. P. N. *Chem. Ind. (London)* **1964**, 893.
(27) Eck, H. Wacker Chemie GmbH, Br. Patent 1346701, **1974**; *Chem. Abstr.* **1973**, *79*, 18109.
(28) Marcus, E.; Chan, J. K.; Strow, C. B. *J. Org. Chem.* **1966**, *31*, 1369.
(29) (a) Pochan, M. Lonza Ltd., Swiss Patent 523223, **1972**; *Chem. Abstr.* **1972**, *77*, 100857. (b) Stocker, A. Lonza, US Patent 3778474, **1973**; *Chem. Abstr.* **1974**, *80*, 59503. (c) Kunstle, G.; Spes, H.; Siegl, H. Wacker-Chemie GmbH, U.S. Patent 4129596, **1978**; *Chem. Abstr.* **1978**, *89*, 42479f.
(30) Crystallographic data for **5a** have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication number CCDC 642465. Copies of the data may be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge, CB2 1EZ, UK (fax: +44 1223 33603 or e-mail: deposit@ccdc.cam.ac.uk).

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