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A New Synthesis of N-Sulfinylamines via β-Elimination of Chloroform from Trichloromethanesulfinamides

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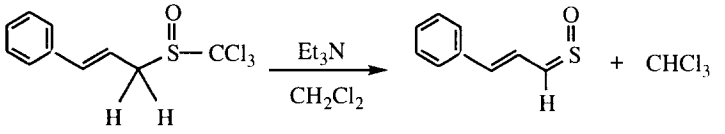
Abstract: The synthesis of various N-monosubstituted trichloromethanesulfinamides by two alternative and novel procedures is described. All these compounds have been found to undergo base-induced elimination of chloroform with formation of the corresponding N-sulfinylamines. Reaction proceeds smoothly under mild conditions. Copyright © 1996 Published by Elsevier Science Ltd

In view of the α-elimination of chloroform which has been thoroughly studied and extensively used for the generation of dichlorocarbene in the past[1], and in view of the good leaving group ability of trihalomethyl anions which is well demonstrated by the old haloform reaction[2], the apparent lack of previously documented examples of β-elimination of chloroform in the literature is rather surprising.

Recently, we have reported that allylic and benzylic trichloromethyl sulfoxides undergo a facile and unexpected base-induced β-elimination of chloroform and afford monosubstituted sulfines[3] (eq.1). In continuation we have decided to explore the application of chloroform elimination for the synthesis of various other heterocumulenes, including N-sulfinylamines.



(1)

In order to investigate the application of chloroform elimination for the synthesis of N-sulfinylamines the preparation of appropriate trichloromethanesulfinamides **1** was required. The most direct method for preparation of sulfinamides involves reaction of amines with the corresponding sulfinyl chlorides[4a]. However, because of the high cost of trichloromethanesulfinyl chloride, we prepared the required trichloromethanesulfinamides by the two alternative methods described below.

The first method involves reaction of the appropriate amines with trichloromethanesulfenyl chloride[4b] followed by oxidation of obtained sulfenamides to sulfinamides with MCPBA.[5] Trichloromethanesulfinamides **1a-d** were prepared by this method as nice crystalline compounds (eq.2)[6].

Compounds **1e-g**[7] were prepared by a novel method, which involved reaction of the appropriate amine with Cl_3CSO_2Cl in the presence of trimethyl phosphite and triethylamine at low temperature (eq.3). Thus N-

$$ArNH_2 \xrightarrow[0^oC,\ 70\text{-}78\%]{Cl_3CSCl,\ Et_2O} ArNHSCCl_3 \xrightarrow[0^oC,\ 80\text{-}85\%]{MCPBA\ ,\ CH_2Cl_2} ArNH\text{—}\overset{\overset{O}{\|}}{S}\text{—}CCl_3$$

1a-d

a: Ar=Ph; **b**: Ar=*p*-Tol; **c**: Ar=*o*-Cl-Ph; **d:** Ar=*p*-Cl-Ph; **(2)**

α-phenylethyl trichloromethanesulfinamide **1f** was obtained as a mixture of two diastereomeres in the ratio of 1:2. Starting with optically active S(-)-1-phenylethylamine the product shows $[\alpha]_D$ -24° (c=1, $CHCl_3$). This method is analogous to the recently described synthesis of various sulfinate esters by Klunder and Sharpless[8].

$$RNH_2 + Cl_3CSO_2Cl + (MeO)_3P \xrightarrow[0^0C]{Et_3N,\ CH_2Cl_2} RNH\text{—}\overset{\overset{O}{\|}}{S}\text{—}CCl_3$$

1e-g

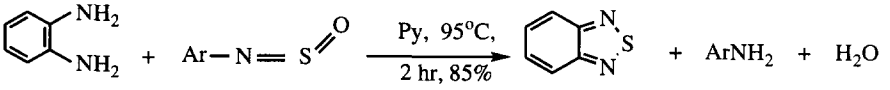
e: R=t-Bu; **f**: R=PhCH(CH_3); **g**: R=$PhCH_2$ **(3)**

We have found that trichloromethanesulfinamides **1** undergo practically instantaneous base-induced β-elimination of chloroform and formation of the corresponding N-sulfinylamines **2** (eq.4). The formation of sulfinylamine and chloroform were easily detected by carrying out the reaction in the NMR-tube. As expected[9a] throughout the series of compounds **2** a consistent lowfield shift in the proton spectra of sulfinylamines as compared to corresponding sulfinamides **1** and parent amines was observed. Interestingly, while DBU, pyrrolidine, triethylamine, and even diisopropylamine were effective at room temperature for several minutes, the use of DABCO in certain solvents such as chloroform or acetone requires heating to 50°C for 5 hours.

$$RNH\text{—}\overset{\overset{O}{\|}}{S}\text{—}CCl_3 \xrightarrow{base} R\text{—}N{=}S{=}O + CHCl_3$$

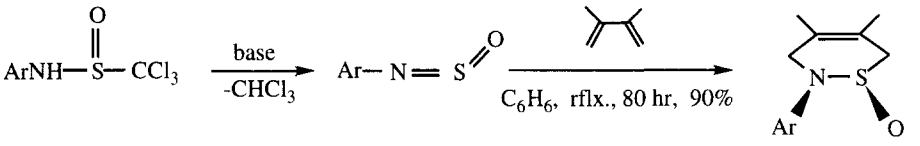
1a-g **2a-g** **(4)**

It is worthwhile noting that due to the excessive sensitivity of sulfinylamines to moisture and their base catalyzed hydrolysis in general,[10] isolation is rather difficult and results in loss of sulfur dioxide and formation of the corresponding amines. To overcome this problem, we have found that by reducing the amount of base to just a few mole percent, or alternatively by the use of anhydrous potassium carbonate the isolation is greatly improved. We have thus succeeded to obtain the expected products in good to excellent yields (71-97%). In the case of compounds **2f** and **2g**, owing to a known secondary redox reaction[10a] acetophenone and benzaldehyde, respectively, were isolated, instead. The formation of N-sulfinylamines **2** has been confirmed by the trapping of the latter with *o*-phenylenediamine[11] which affords benzothiadiazole and the corresponding amines (eq.5).



(5)

N-Sulfinylamines **2** generated from trichloromethanesulfinamides **1** in the presence of a catalytic amount of base were used *in situ* without separation of base for the formation of Diels-Alder adducts with 2,3-dimethylbuta-1,3-diene[9] with the yields more than 90% (eq.6).



(6)

In conclusion, the results described above demonstrate that trichloromethanesulfinamides are conveniently prepared from readily available starting materials and undergo a facile and unprecedented β-elimination of chloroform affording the corresponding N-sulfinylamine derivatives. An obvious advantage of our method, besides its mechanistic significance, is the mild reaction conditions. Another advantage is the avoidance of the use of thionyl chloride which may affect other functional groups as well. The later feature is also common to several other methods for the preparation of N-sulfinylamines, such as the trans-sulfinylation reaction, particularly by means of N-sulfinylsulfonamides[10b,c], sulfinylation of lithiated amines[10c,12a] or N-trimethylsilylamines[12b] using sulfur dioxide, and treatment of amines with N,N-sulfinylbisimidazole[12c] or with dialkyl[10c] and di-2-pyridyl[12d] sulfites.

Preparation of N-Sulfinylamines. A general procedure for the preparation of the aromatic compounds is as follows. To a solution of 0.8 mmole of the appropriate trichloromethanesulfinamide **1a-d** in 4 mL of dry acetonitrile under nitrogen, was added with stirring anhydrous potassium carbonate powder (0.15 g) at ambient temperature. Stirring of the suspension, which turns bright yellow, is continued for about half an hour. Filtration of the potassium carbonate and removal of the solvent under reduced pressure afforded the expected product **2a - 2d**. Due to the relative volatility of *t*-butyl N-sulfinylamine **2e**, the above procedure was modified as follows: A solution of 2 g (8.4 mmoles) of sulfinamide **1e** in 1mL of dry DMSO was treated with 0.94 g (8.4 mmoles) of DABCO with stirring under a nitrogen atmosphere. After 30 min of further stirring, the product was separated by distillation from the reaction mixture under reduced pressure. B.p. 22^0/20 mm Hg[12c]. NMR data for N-sulfinylamines: **2a** : ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 7.30 (m, 3H), 7.81 (m, 2H); ^{13}C NMR ($CDCl_3$, 300 MHz) δ: 127.17 (C-2), 129.26 (C-3), 130.59 (C-4), 142.67 (C-1); Yield 97.2%. **2b**: ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 2.38 (s, 3H), 7.22 (d, 2H, J=8Hz), 7.77 (d, 2H, J=8Hz); ^{13}C NMR ($CDCl_3$, 300 MHz) δ: 21.72 (**C**H_3), 127.28 (C-2), 129.83 (C-3), 140.80 (C-1), 141.49 (C-4); Yield 71%. **2c**: ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 7.30 (m, 2H), 7.49 (m, 1H), 8.32 (m, 1H); ^{13}C NMR ($CDCl_3$, 300 MHz) δ: 127.51 (C-5), 128.42 (C-6), 129.90 (C-2), 130.36 (C-3), 130.86 (C-4), 139.47 (C-1); Yield 75%. **2d** : ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 7.39 (d, 2H, J=8.5Hz), 7.82 (d, 2H, J=8.5Hz); ^{13}C NMR ($CDCl_3$, 300 MHz) δ: 126.44 (C-2), 129.50 (C-3), 136.17 (C-4), 141.10 (C-1); Yield 71%. **2e**: ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 1.53 (s, 9H). ^{13}C NMR (DMSO-d_6, 300 MHz) δ: 30.58 (**C**H_3), 79.97 (C_q); Yield 90.7%.

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References and Notes

1. Hine. J. *Physical Organic Chemistry*, 2nd ed.; McGrow Hill: New York, 1982; pp.484-488.
2. March, J. *Advanced Organic Chemistry*, 3rd ed.; Wiley: New York, 1985; p.567.
3. Braverman, S.; Grinstein, D.; Gottlieb, H.E. *Tetrahedron Lett.* **1994**, *35*, 953.
4. (a) Andersen, K.K.; Malver, O. *J. Org. Chem.* **1983**, *48*, 4803.(b) Glass, R.S.; Swedo, R.J. *Synthesis* **1977**, 798.
5. Davis, F.A.; Friedman, A.J.; Klunger, E.W. *J. Amer. Chem. Soc.* **1974**, *96*, 5000.
6. Satisfactory spectral data were obtained for all new compounds. Selected data are as follows: **1a**: mp 110-112°C (dec) (from hexane). ^{1}H NMR ($CDCl_3$, 200 MHz) δ: 6.25 (br s, 1H); 7.25 (m, 5H). IR (KBr): 2959, 1498, 1048, 800 cm^{-1}. MS m/e: 258 (M^+), 140, 92, 77. **1b**: mp 110-111°C (dec) (from hexane). ^{1}H NMR ($CDCl_3$, 200 MHz) δ: 2.32 (s, 3H); 6.07 (br s, 1H); 7.01 (d, 2H, J=8 Hz); 7.12 (d, 2H, J=8Hz). IR (KBr): 3173, 1509, 1103, 811 cm^{-1}. MS m/e: 272 (M^+), 154, 138, 106, 91, 77. **1d**: mp 153-154°C (dec) (from *i*-PrOH). ^{1}H NMR ($CDCl_3$, 200 MHz) δ: 6.15 (br s, 1H); 7.05 (d, 2H, J=8.5Hz); 7.29 (d, 2H, J=8.5Hz). IR (KBr): 3162, 1593, 1489, 1105, 822 cm^{-1}. MS m/e: 294 (M^+), 174, 126, 99.
7. Satisfactory spectral data are as follow: **1e**: mp 77-78°C (from Et_2O/hexane). Yield 71%. ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 1.41 (s, 9H); 3.94 (s, 1H). IR (KBr): 3209, 2977, 1413, 1112, 993, 809 cm^{-1}. MS m/e: 238 (M^+), 183, 120, 105, 82, 69. **1f**: Yield 64 %. ^{1}H NMR ($CDCl_3$, 200 MHz), δ (major diastereomer): 1.60 (d, 3H, J=7 Hz); 4.36 (br d, 1H); 4.75 (quintet, 1H, J=7 Hz); 7.36 (m, 5H). δ (minor diastereomer): 1.67 (d, 3H, J=7 Hz); 4.29 (br d, 1H); 4.75 (quintet, 1H, J=5 Hz); 7.36 (m, 5H). IR (KBr): 3228, 1495, 1454, 1120, 809 cm^{-1}. MS m/e: 288 (M^+), 119, 105, 77.
8. Klunder, J.M.; Sharpless, J.B. *J.Org. Chem.* **1987**, *52*, 2598.
9. (a) Butler, R.N.; O'Halloran, G.A.O.; Burke, L.A. *J. Chem. Soc., Perkin Trans.* 2, **1989**, 1855. (b) Boan, Ch.; Skattebol, L. *J. Chem. Soc., Perkin Trans.* 1, **1978**, 1568.
10. Reviews: (a) Kresze, G.; Maschke, A.; Albrecht, R.; Bederke, K.; Patzschke, H.P.; Small, H.; Treede, A. *Angew. Chem., Int. Ed. Engl.***1962**, *1*, 89. (b) Johnson, C.R. in *Comprehensive Organic Chemistry*, Barton, D.H.R.; Ollis, W.D. Eds., Vol.3, Pergamon, Oxford, 1979, p. 241. (c) Beckert, R.; Mayer, R. in *Houben-Weyl Methoden der Organische Chemie*, Klamann, D. Ed., G. Thieme Verlag, Stuttgart, Vol. E11/1, **1985**, pp. 558-579.
11. Cava, M.P.; Schlessinger, R.H. *Tetrahedron Lett.* **1964**, 3815.
12. (a) Sakai, S.; Fujinami, T.; Komizo, K. *J. Org. Chem.* **1975**, *40*, 3291. (b) Porksamp, P.A.T.W.; Zwanenburg, B. *Synthesis*, **1981**, 368. (c) Kim, Y.H.; Shin, J.M. *Tetrahedron Lett.* **1985**, *26*, 3821. (d) Kim, S.; Yi, K.Y. *ibid.*, **1986**, *27*, 1925.

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