The Alkylation of Amine Sulfides[1]

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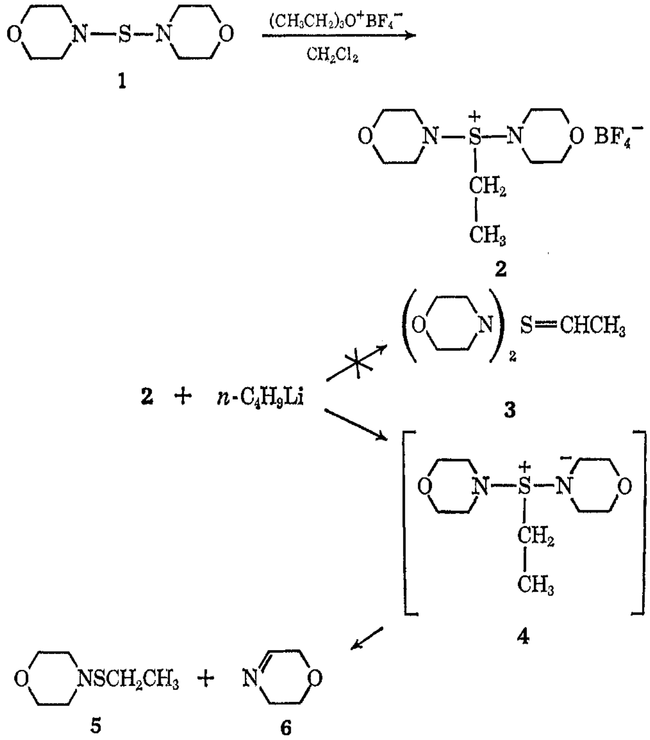
It has been shown that trialkyloxonium salts alkylate several types of organic sulfur compounds,[2] and that treatment of dithiocarbamates with trialkyloxonium salts or with less reactive alkylating agents yields the S-alkylated symmetrical products[3] instead of other possible unsymmetrical structures.

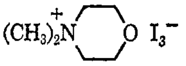
This note demonstrates a successful alkylation of an amine sulfide **1** by triethyloxonium fluoroborate to give the novel resonance-stabilized sulfonium salt **2**. Numerous other alkylation reactions on amine sulfides with a variety of alkylating agents did not lead to isolatable products analogous to **2**.



The structure of **2** (obtained in 30–40% yield) was assigned on the basis of the elementary analysis and the very characteristic nmr spectrum; the latter showed the characteristic sharp complex triplets of the methylene protons of the morpholine rings, which were shown by morpholine sulfide itself. The methylene triplets at 3.80 and 3.52 ppm were present in a 1:1 ratio, as in morpholine sulfide. This rules out structures for the alkylation product in which the ethyl group is on nitrogen or oxygen of the morpholine rings, because such onium compounds would show a shift to lower field of two pairs of methylene protons, and the symmetrical arrangement of the methylene protons in morpholine sulfide would disappear. Furthermore, the nmr spectrum of **2** showed a sharp triplet at 1.39 ppm, due to the CH_3 protons of the ethyl group; portions of the expected quartet for the CH_2 protons of the ethyl attached to sulfur were distinguishable at the base of the morpholine proton absorption. The integration of the nmr spectrum agreed completely with structure **2**.

Treatment of the sulfonium salt **2** with *n*-butyllithium, with later addition of benzophenone, yielded 37% of the sulfenamide **5** (which was identified by synthesis), with 90% recovery of the benzophenone. The sulfenamide was probably formed by abstraction of an α proton from the morpholino methylene group, to give **4** which then formed the sulfenamide **5** and the morpholine derivative **6** or products derived from **6**. No evidence was obtained for the formation of the ylide **3**.

Of the many other alkylation processes tried on several amine sulfides, treatment of **1** with methyl iodide was the only one giving an identifiable product; a violet solid, N,N-dimethylmorpholinium triiodide **7** was obtained, as well as a small amount of N,N-dimethylmorpholinium iodide. The formation of the triiodide may be explained by a scheme analogous to that worked out by Heimer and Field[4] for the action of methyl iodide on sulfenamides.



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Experimental Section[5]

Alkylation of Morpholine Sulfide with Triethyloxonium Fluoroborate to Yield 2.—Morpholine sulfide[6] (2.37 g) and triethyloxonium fluoroborate[7] (2.20 g) were refluxed for 1.5 hr in methylene chloride. The dark red solution was cooled, 25 ml of anhydrous ether was added dropwise with stirring, and the ether was decanted from the red oil which separated. After two similar treatments with 10 ml of ether, the partially solidified oil was dissolved in 15 ml of hot methanol, and the solution was cooled in a refrigerator. The resulting tan ethyldimorpholinosulfonium fluoroborate (**2**) was collected and washed with 5 ml of cold methanol; it melted at 171.5–172.5° (dec) and weighed 1.22 g (32%). The nmr spectrum, taken in D_2O with 1% of DDS (sodium 2,2-dimethyl-2-silapentane-5-sulfonate) has been discussed above. An analytical sample of **2**, mp 181–182°, was prepared by repeated recrystallizations from anhydrous methanol followed by drying at 56° (0.5 mm).

Anal. Calcd for $C_{10}H_{21}BF_4N_2O_2S$: C, 37.51; H, 6.61; S, 10.02. Found: C, 36.99; 38.20; H, 6.79, 6.56; S, 10.28.

In other runs, the methylene chloride solution and the ether washes from **2** were shown to contain a mixture of morpholine sulfide **1** and the corresponding disulfide, by nmr studies, by elemental sulfur analysis, and by isolation of crystalline disulfide in one case, mp 122–124°; the reported[6] value is 124–125°.

The OCH_2 protons of the disulfide and monosulfide were coincident from 3.50 to 3.80. The NCH_2 protons of the sulfide were from 3.13 to 3.38 with the same protons in the disulfide from 2.70 to 2.95. These values were shown by the mixture and also by authentic samples taken separately.

Formation of the Sulfenamide 5 by Butyllithium and the Sulfonium Salt 2.—A slurry of 1.00 g (0.0031 mol) of **2** in 100 ml of tetrahydrofuran (predistilled from lithium aluminum

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[1] Aided by Grant 2252-C from the Petroleum Research Fund of the American Chemical Society.

[2] Cf. G. K. Helmkamp, H. N. Cassey, B. A. Olsen, and D. J. Pettitt, *J. Org. Chem.*, **30**, 933 (1965). D. J. Pettitt and G. K. Helmkamp, *ibid.*, **28**, 2932 (1963); **29**, 2702 (1964).

[3] J. L. Richards, D. S. Tarbell, and E. H. Hoffmeister, *Tetrahedron*, **24**, 6485 (1968).

[4] N. Heimer and L. Field, *J. Org. Chem.*, in press.

[5] Microanalyses were by Galbraith Laboratories; ir spectra were taken on a Beckman IR-10 spectrometer and nmr spectra on a Varian A-60. TMS was used as an internal standard unless otherwise specified, and chemical shifts are reported in parts per million.

[6] E. S. Blake, *J. Amer. Chem. Soc.*, **65**, 1267 (1943).

[7] H. Meerwein, *Org. Syn.*, **46**, 113 (1966).

hydride) in a nitrogen atmosphere was stirred in an ice bath. To this, a solution of 1.4 ml of a 22% *n*-butyllithium–hexane mixture (0.0031 mol of *n*-butyllithium) in 15 ml of tetrahydrofuran was added dropwise. The colorless slurry turned yellow and, after 0.15 hr, the reaction was warmed and heated at reflux for 0.15 hr. The reaction was cooled, a solution of 0.547 g (0.003 mol) of benzophenone in 15 ml of tetrahydrofuran was added dropwise, and, after the mixture stirred for 1 hr at room temperature, 700 ml of water was added, which precipitated a solid. Extraction with two portions of ether yielded 0.96 g of a mixture of a liquid and an oily solid. The nmr spectrum in chloroform indicated that the mixture consisted of benzophenone and morpholine or derivative thereof.

A short-path vacuum distillation of 0.70 g of the mixture gave 0.48 g of distillate (the distillation was not continued to dryness), collected at 0.50 mm (pot temperature 100–140°). Tlc of the distillate showed only one spot—a streak, R_f 0.55–0.75. A sample of reactant benzophenone showed a similar R_f value and the ir spectrum of the distillate (liquid film) showed a strong band at 1660 cm^{-1}, which is characteristic of benzophenone.[8] The nmr spectrum of the distillate showed a triplet at 1.22, a quartet at 2.73 and overlapping into the NCH$_2$ absorption of morpholine centered at 2.95, the OCH$_2$ absorption at 3.65, and aromatic protons from 7.24 to 7.92. The integration was 19 (triplet): 36 (total of quartet and NCH$_2$):24:158. These data suggested that the distillate was a mixture of benzophenone and either N-ethylmorpholine or the sulfenamide **5** [N-(ethylthio)morpholine].

Vpc of the distillate (10 ft × $^1/_4$ in. 10% SE-30 on 80–100S, column temperature 180°, flow rate 24 ml of He/min) showed seven peaks, with those at 4.3 and 27 min accounting for 95% of the material. The 4.3-min peak corresponded with the retention time of an authentic sample of the sulfenamide **5** (prepared as below), and coinjection enhanced this peak without showing additional peaks. Furthermore, the chemical shifts observed for the ethyl and morpholine protons in the mixture were identical with those for the sulfenamide **5**. The broad peak at 27 min was identical in shape and retention time with that obtained from injection of an acetone solution of benzophenone. An injection of the benzophenone solution and the mixture increased the 27-min peak with the only additional peak observed due to acetone at 1 min.

Based on the nmr integrations, the minimum yields were 36% sulfenamide and 90% recovery of benzophenone.

N-(Ethylthio)morpholine. The Sulfenamide 5.—Chlorine (0.5 ml, 0.11 mol, trapped in a Dry Ice–acetone bath) was allowed to evaporate and the vapors were passed over a stirred solution of 12.3 ml (0.1 mol) of ethyl disulfide (Aldrich) in 50 ml of petroleum ether at −20°. The reaction was stirred for an additional 0.25 hr after complete evaporation of the chlorine. The yellow solution was added in portions to a stirred solution of 53 ml (0.6 mol) of morpholine in 200 ml of petroleum ether in an ice bath. The white slurry that resulted was extracted with three portions of water to remove morpholine hydrochloride. The petroleum ether solution was dried and concentrated. Distillation of the residue gave 20.75 g (72%) of colorless sulfenamide, bp 76–77° (14 mm). Its nmr spectrum showed a triplet at 1.22 (3 H) and a quartet centered at 2.72 (SCH$_2$) which overlapped into a complex triplet at 2.93 for the NCH$_2$ (total of 6 H) and with the OCH$_2$ at 3.62 integrating for 4 H.

Anal. Calcd for $C_6H_{13}NOS$: C, 48.94; H, 8.90. Found: C, 48.69; H, 8.63.

N,N-Dimethylmorpholinium Triiodide (7) from Sulfide and Methyl Iodide.—A solution of 2.50 g (0.012 mol) of morpholine sulfide and excess methyl iodide (7.5 ml, 0.12 mol) in 15 ml of methylene chloride was stirred for 16 hr at room temperature. The resulting solid was collected and washed with 15 ml of cold methylene chloride; the product was 2.00 g of dark violet solid, mp 118–122° dec. The nmr spectrum of the crude product (in acetonitrile) showed only the absorptions expected for N,N-dimethylmorpholinium iodide. Recrystallization of the product from 25 ml of methanol gave 0.841 g of violet solid, mp 118–119°. Repeated recrystallizations from methanol gave a violet solid, mp 125–126° (apparently with decomposition). Although the solid had the same melting point as morpholine sulfide, its color, the depression of a mixture melting point, and its nmr spectrum showed it to be a different compound. The nmr spectrum (in acetonitrile, TMS as reference) showed the characteristic complex triplets of the morpholine ring from 3.70 to 4.10 (OCH$_2$) and 3.22 to 3.57 (NCH$_2$) with a singlet at 3.18. The integration was 4:4:6 respectively. The elemental analysis was correct for N,N-dimethylmorpholinium triiodide.

Anal. Calcd for $C_6H_{14}I_3NO$: C, 14.50; H, 2.84; I, 76.62; N, 2.82. Found: C, 14.52; H, 2.86; I, 76.60; N, 2.83.

Evaporation of the red filtrate from the first recrystallization gave 0.65 g of pale violet solid, mp 188–205°, which, after crystallization from 2 ml of hot methanol, yielded a small amount of the violet triiodide. Further concentration of the filtrate gave a small amount of white crystals, mp 245.5–247° dec; the melting point and nmr spectrum of the crude solid indicated that it was N,N-dimethylmorpholinium iodide, reported[9] to melt at 246°.

Registry No.—**2**, 24407-43-0; **5**, 24378-12-9; **7**, 24378-13-0.

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[8] H. W. Thompson and P. Torkington, *J. Chem. Soc.*, 640 (1945).

[9] L. Knorr, *Ann.*, **301**, 1 (1898).

Triphasiaxanthin, a New Carotenone[1]

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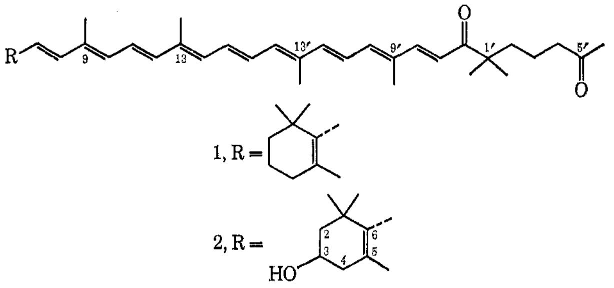
Semi-β-carotenone (1) occurs as the principal carotenoid constituent in the fruit of the *Citrus* relative *Triphasia trifolia*.[3] A new, more polar carotenone, triphasiaxanthin, was isolated.



The visible absorption spectrum of triphasiaxanthin was very similar to that of the semi-β-carotenone. Its infrared spectrum indicated the presence of two carbonyl groups: saturated, 1715 cm^{-1}; and conjugated, 1660 cm^{-1}. Reduction with LiAlH$_4$ caused a hypsochromic shift (*ca.* 25 nm) in the visible absorption maxima. Taken together these evidences indicated a decaenone chromophore in the isolated pigment.

The infrared spectrum also indicated the presence of a secondary hydroxyl group (3450 and 1025 cm^{-1}). Tlc[4] tests indicated the facile quantitative formation of the trimethylsilyl derivative on silylation of the new carotenone. On allylic oxidation with nickel peroxide[5] or on treatment with acid chloroform, no bathochromic shift in the visible absorption maxima

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[1] Part X in the series Citrus Carotenoids.

[2] A laboratory of the Western Utilization Research and Development Division, Agricultural Research Service, U. S. Department of Agriculture.

[3] H. Yokoyama and M. J. White, *Phytochemistry*, **7**, 1031 (1968).

[4] A. McCormick and S. L. Jensen, *Acta Chem. Scand.*, **20**, 1989 (1966).

[5] K. Nakagawa, R. Konaka, and T. Nakata, *J. Org. Chem.*, **27**, 1597 (1962).