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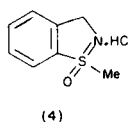
5-Hexyl-7-(*S*-methylsulfonylimidoyl)xanthone-2-carboxylic acid **1a**, when heated above its melting point gives a number of products including the corresponding methyl ester **1b**, which arises by a novel methyl group transfer. A similar methyl transfer reaction is observed when the sulfoximide and carboxylic acid groups are present in different molecules.

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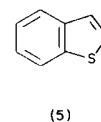
The electron-impact mass spectrum of the anti-allergic compound, 5-hexyl-7-(*S*-methylsulfonylimidoyl)xanthone-2-carboxylic acid **1a** (1,2) exhibits a peak at *m/e* 415, 14 mass units higher than the expected parent. The peak first increases and then decreases in intensity depending upon the time the sample has been in the source. When a sample of **1a** was heated at 230° for 2 minutes in an open tube, a complex mixture of products resulted, one of which was identified as the corresponding methyl ester **1b** which is evidently responsible for the *m/e* 415 peak in the mass spectrum. The products were separated by hplc using adsorption chromatography on silica gel for the less polar compounds, and reverse phase ion-pair partition chromatography on "Spherisorb-ODS" for the more polar constituents. In addition to the ester **1b** (6%), the sulfoxide **2a** (12%) and corresponding ester **2b** (4%), the sulfonamide **3a** (8%) and ester **3b** and starting material **1a** (13%), have so far been identified. The occurrence of the three esters **1b**, **2b** and **3b** gives ample evidence of an esterification reaction, and the subsequent isolation of a small amount of the amide **1c** (2%) is indicative of a similar, but less significant amination process. The identification of the sulfonamides **3a** and **3b** suggested that the source of the ester methyl group was the sulfoximide group, presumably acting in an intermolecular fashion. Further evidence was obtained from the mass spectrum of the S-CD₃ labelled analogue **1d**, prepared by base-catalysed equilibration of **1a** with deuterium oxide. Whilst the results were complicated by scrambling of the label, the difference between the major peak due to labelled acid (*d*₃) **1d** at *m/e* 404 and the major peak due to labelled ester (*d*₅) at *m/e* 420 was clear evidence that the source of the methyl group was the

sulfoximide group and that it was possibly being transferred as a CD₂ moiety.

The cleavage of the C-S bond of sulfoximides is known to occur under strongly basic conditions (3-5) when the thus formed carbanion reacts with, for example, a carbonyl group in a three-centre reaction intermediate from which a sulfinamide is expelled, yielding an epoxide. Demethylation of an *S*-methyl sulfoximide, namely the conversion of methyl *p*-tolyl-*N*-methylsulfoximide to *N*-methyl-*N*-tosyl-*p*-toluenesulfonamide using tosyl chloride in pyridine has been reported (6). Also since the completion of our work, the thermal demethylation of 1-methyl-1*H*,3*H*-1,2-benzisothiazole 1-oxide hydrochloride **4** to give 1,2-benzisothiazole **5** with loss of methyl chloride, has been described (7). There appears to be no precedent for the thermal decomposition of a sulfoximide with the concomitant methylation of the carboxylic acid group as described in this paper, however.

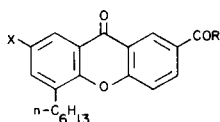


(4)



(5)

In an attempt to probe the reaction further we have examined the behaviour of the simple sulfoximide, the *S*-methyl-*S*-phenyl compound **6a**. Heated on its own to 240°, no decomposition was observed, but on heating in the presence of benzoic acid at 230° for a short time reaction occurred. The reaction product was chromatographed on silica when methyl benzoate (11%), methyl phenyl sulfoxide **7** (15%) and benzene sulfonamide **8** (12%), all products which would have been anticipated, were identified. In addition, the benzoyl derivative **6b** (9%) of the sulfoximide **6a** and a mixture of thiophenol **9** and diphenyl disulphide **10** (51%) were identified.



1a X = -SO(=NH)Me; R = -OH

2a X = -SOMe; R = -OH

1b X = -SO(=NH)Me; R = -OMe

2b X = -SOMe; R = -OMe

1c X = -SO(=NH)Me; R = -NH₂3a X = -SO₂NH₂; R = -OH1d X = -SO(=NH)CD₃; R = -OH3b X = -SO₂NH₂; R = -OMe

6a PhSO(=NH)Me

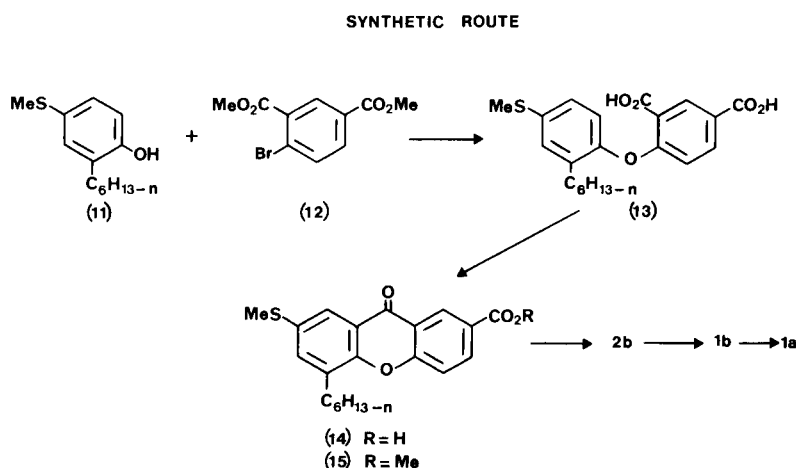
6b PhSO(=NCOPh)Me

7 PhSOMe

8 PhSO₂NH₂

9 PhSH

10 PhSSPh



The benzoyl compound **6b** is a possible reaction intermediate, and consequently its behaviour at the reaction temperature was investigated. However, it proved to be quite stable under these conditions. It is worthy of note that diphenyl disulfide **10** was a major product resulting from the pyrolysis of a closely related sulfilimide, *S*-methyl-*S*-phenyl-*N*-*p*-toluenesulfonylsulfilimide (**8**).

These results and the observation that **1a** when heated to 230° in a non-protic solvent, Dowtherm A, does not undergo reaction, have clearly demonstrated the intermolecular nature of the reaction.

EXPERIMENTAL

Melting points were determined on a Kofler Hotstage Apparatus, and are uncorrected. Infrared spectra were measured on a Pye-Unicam SP 1000 instrument as potassium bromide discs. Nmr spectra were obtained on solutions in either deuteriochloroform or DMSO-*d*₆ using a Perkin-Elmer R 12 A instrument. Infrared and nmr spectra were run on all compounds and are consistent with the assigned structure in each case. Mass spectra were obtained on a Varian MAT 311A mass spectrometer at St. Bartholomew's Hospital, London. Satisfactory elemental analyses were obtained for all new compounds.

4-[2-Hexyl-4-(methylthio)phenoxy]isophthalic Acid (**13**).

To a solution of dimethyl 4-bromoisophthalate (**12**) (5.5 g., 0.02 mole) and 2-hexyl-4-(methylthio)phenol (**11**) 4.5 g., 0.02 mole) in nitrobenzene (40 ml.), were added copper powder (0.4 g.) and potassium carbonate (5.5 g., 0.04 mole). The mixture was then heated at 140° in an atmosphere of nitrogen for 3 hours. After cooling, a solution of sodium hydroxide (3.2 g., 0.08 mole) in ethanol:water (3:1) (60 ml.) was added, and the resulting mixture was refluxed for one hour, then cooled and poured into ice-water. Extraction with dichloromethane (3 x 50 ml.) removed the nitrobenzene and then the aqueous solution was acidified with dilute hydrochloric acid. The solid was filtered off and recrystallised from methanol to give 4-[2-hexyl-4-(methylthio)phenoxy]isophthalic acid (**13**) (5.8 g., 74%) melting at 135-140°.

Anal. Calcd. for C₂₁H₂₄O₅S: C, 64.93; H, 6.23; S, 8.25. Found: C, 64.88; H, 6.29; S, 8.22.

5-Hexyl-7-(methylthio)xanthone-2-carboxylic Acid (**14**).

4-[2-Hexyl-4-(methylthio)phenoxy]isophthalic acid (**13**) (3.9 g., 0.01 mole) was dissolved in sulfolane (40 ml.) and heated to 80°. Polyphosphoric acid (40 ml.) was added and the solution stirred for 1 hour before being cooled and poured into water. The crude product was filtered off and washed thoroughly with water. It was then recrystallised from ethanol to give 5-hexyl-7-(methylthio)xanthone-2-carboxylic acid (**14**) (2.8 g., 75%) melting at 164-170°.

Methyl 5-Hexyl-7-(methylthio)xanthone-2-carboxylate (**15**).

5-Hexyl-7-(methylthio)xanthone-2-carboxylic acid (**14**) (2.0 g., 0.0054 mole) was added to a solution of concentrated sulfuric acid (2 ml.) in methanol (40 ml.). The solution was refluxed for 3 hours before being poured into water. The product was isolated in chloroform, the chloroform solution then being washed with sodium bicarbonate solution and water, before being dried (magnesium sulfate) and evaporated to leave a gummy solid (2.0 g.) which was recrystallised from petroleum ether (40-60°) giving pale yellow crystals of methyl 5-hexyl-7-(methylthio)xanthone-2-carboxylate (**15**) (1.64 g., 79%) melting at 63-64°.

Anal. Calcd. for C₂₂H₂₄O₄S: C, 68.74; H, 6.29; S, 8.32. Found: C, 68.51; H, 6.42; S, 8.37.

Methyl 5-Hexyl-7-(methylsulfinyl)xanthone-2-carboxylate (**2b**).

A solution of sulfuryl chloride (10.57 g., 4.2 mmoles) in dichloromethane (5 ml.) was added dropwise at room temperature to a stirred mixture of wet silica [prepared by shaking silica (Kieselgel 60; 70-230 mesh) (1.2 g.) with water (1.2 g.) such that the water is totally absorbed] and methyl 5-hexyl-7-(methylthio)xanthone-2-carboxylate (**15**) (1.54 g., 4.0 mmoles) in dichloromethane (25 ml.). Stirring was continued for 2 hours after the addition was complete. After being filtered, the reaction mixture was washed with sodium bicarbonate solution, then with water and then dried (magnesium sulfate) before being evaporated to dryness. The crude product (1.62 g.) was recrystallised from methanol giving methyl 5-hexyl-7-(methylsulfinyl)xanthone-2-carboxylate (**2b**) (1.52 g., 95%) melting at 130-132°.

Anal. Calcd. for C₂₂H₂₄O₅S: C, 65.99; H, 6.04; S, 7.99. Found: C, 65.72; H, 6.12; S, 7.84.

Methyl 5-Hexyl-7-(*S*-methylsulfonylimidoyl)xanthone-2-carboxylate (**1b**).

A solution of methyl 5-hexyl-7-(methylsulfinyl)xanthone-2-carboxylate (**2b**) (1.2 g., 3 mmoles) dissolved in polyphosphoric acid (100 ml.) was stirred at 45-50° while sodium azide (0.24 g., 3.7 mmoles) was added in small portions. Stirring was continued for a further hour before the mixture was poured onto ice. The resulting mixture was neutralised by the addition of 30% ammonia solution and then extracted with ethyl acetate. The organic layer was washed with water, then dried (magnesium sulfate) and evaporated to a yellow solid (1.12 g.) which was recrystallised from ethyl acetate giving methyl 5-hexyl-7-(S-methylsulfonimidoyl)xanthone-2-carboxylate (**1b**) (0.85 g., 68%) as white crystals melting at 145-146°.

Anal. Calcd. for $C_{22}H_{25}NO_5S$: C, 63.60; H, 6.06; N, 3.38. S, 7.72. Found: C, 63.47; H, 5.91; N, 3.40; S, 7.75.

5-Hexyl-7-(S-methylsulfonimidoyl)xanthone-2-carboxylic Acid (**1a**).

Methyl 5-hexyl-7-(S-methylsulfonimidoyl)xanthone-2-carboxylate (**1b**) (0.42 g., 1.0 mmole) was dissolved in ethanol (10 ml.) and 0.1N sodium hydroxide solution (12 ml.) added. The resulting solution was refluxed for 1 hour and then poured onto ice. Acidification with dilute hydrochloric acid produced a solid which was filtered off, washed well with water and dried. Recrystallisation from ethanol gave 5-hexyl-7-(S-methylsulfon-

imidoyl)xanthone-2-carboxylic acid (**1a**) (0.36 g., 89%) melting at 194-196°.

Anal. Calcd. for $C_{21}H_{23}NO_5S \cdot H_2O$: C, 60.12; H, 6.01; N, 3.34; S, 7.64. Found: C, 60.45; H, 6.02; N, 3.29; S, 7.78.

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