Polarized Ketene Dithioacetals. Part 26. Studies on Base-catalysed Rearrangements of 3,3-Bis(alkylthio)-2-methyl-1-arylprop-2-en-1-ones and 3,3-Bis(methylthio)-2-benzyl-1-phenylprop-2-en-1-one

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3,3-Bis(alkylthio)-2-methyl-1-arylprop-2-en-1-ones (1a–e) undergo facile rearrangement in the presence of sodium hydride in dimethylformamide to give the corresponding 3-alkylthio-2-alkylthioalkylmethylacrylophenones (2a–e), respectively. Similarly, 3,3-bis(methylthio)-2-benzyl-1-phenylprop-2-en-1-one (13) under similar conditions yielded the rearranged product, the chalcone (14) and the acrylophenone (15), in addition to two more products, β-methylthiochalcone (16) and the propenone (17). The mechanisms governing these transformations have been studied and it has been shown that the 1,3-RS shift in the dithioacetal intermediate (19) involves intermolecular participation of thiolate anion rather than a concerted process. A probable mechanism involving the solvent equilibrated enolate anion (27) formed by Michael addition of thiolate anion to (19) or the phenyl derivative (26) has been suggested for the rearrangement of (19) to the products (2) and of (26) to either compound (14) or (15). Also, the formation of products (16) and (17) is explained through oxidative cleavage of the carbanions (28) and (31) respectively.

Results and Discussion
When the dimethyl dithioacetal (1a) was treated with sodium hydride in dry dimethylformamide at 50–60 °C for 3 h and then worked up, the rearranged product (2a) was isolated in 35% yield (55% on the basis of recovered starting material). The other acetals (1b–e) similarly yielded, under identical conditions, the corresponding products (2b–e) in 35–45% overall yield (Scheme 1). The products (2a–e) thus obtained were assigned E-geometry on the basis of recovered starting materials. These values are found to be similar to those observed for 2-isomers of compounds (3a–d). 3

In one of the experiments, when the p-chlorophenyl derivative (4), derived from p-chloropropiophenone, was subjected to a similar rearrangement, the expected rearranged product (6) was accompanied by two additional products, p-methylthiochalcone (16) and the propenone (17). The formation of a mixture of several compounds, (13) (5%), (14) (35%), (15) (15%), (16) (5%), and (17) (20%), respectively, which were characterized on the basis of their spectral and analytical data (Scheme 4). The product (14), which was found to be mixture of the E and Z isomers, showed the molecular ion peak in its mass spectrum at m/z 314 (M+). It exhibited i.r. bands at 1650 and 1655 cm⁻¹, which were assigned to the carbonyl groups of the Z and E isomers, respectively. The n.m.r. spectrum (Figure) showed two singlets at δ 1.60 and 1.80 (total 3 H), which were assigned to the methylene SMe protons of the Z and E isomers.
Mechanistic Studies.—A plausible mechanism involving the unstable, mobile ketoallyl intermediate (19), which spontaneously rearranges to the product (2), has already been reported (Scheme 6). Efforts to isolate (19) were unsuccessful, although its formation appears to be a definite step in the production of the thermodynamically more stable rearranged compound (2). Our earlier experiments on the reactions of the dithioacetals (1) with guanidine and cyanoacetamide to yield the corresponding unexpected pyrimidines (20) and pyridones (21) respectively further support the intermediacy of (19). It is therefore apparent that compound (19) spontaneously undergoes subsequently a facile 1,3-RS shift to give the more stable structure (2). We had thought that the rearrangement of (19) to (2) probably involves a sulphur assisted polar concerted mechanism via an antipolar transient complex (A), although we did not rule out the alternative possible mechanisms. However our results from rearrangement studies on the ketene dithioacetal (4) (Scheme 2) show...
the presence of free alkylthiolate anions which rules out both the intermediacy of (A) and any other concerted process. Further, the precursors (19) of the proposed intermediate (A) are structurally different from those of Kwart in that the latter carry an electron-rich terminal olefinic function whereas the former carry an electron-withdrawing benzoyl group conjugated to the double bond, reverting the nucleophility of the β-carbon. An alternative possibility, that the sulphur lone pair stabilised thietanium ion (B) * is formed from (19) and collapses to form (2), is ruled out since: (a) the cation (B) does not permit the existence of the free alkylthiolate anions observed in the displacement reaction of (4); and (b) the 4-endo-trig process involving strained (B) is unlikely to occur since the rearrangement is found to be more facile.†

An alternative mechanism involving a radical dissociation and combination process for the conversion of the intermediate (19) into (2), as proposed by Warren and co-workers for a thermal and photochemical 1,3-PhS shift, was also ruled out since the yield of (2a) was unaffected when (1a) was rearranged in the presence of radical inhibitors [diphenylpicrylhydrazyl (DPPH) and hydroquinone]. Besides, when (1b) was treated with sodium hydride, either in the presence or absence of nitrogen, the formation of dimeric products such as diethyl disulphide was not observed, despite the fact that alkylthiolate anions are known to undergo fast oxidation to alkylthienyl radicals in polar aprotic solvents. It therefore

*A similar dipolar four-membered cyclic intermediate has been proposed by Cromwell and co-workers for the amine unassisted aminotropic allylic rearrangement of mobile β-ketoallylamines.† We are grateful to one of the referees who made this observation.
appears that the alkylthiolate anion attacks the substrate faster than it is oxidised to radicals which would lead to dimeric products.

The intermolecularity of the rearrangement was further confirmed from 'cross-over' experiments carried out with the following systems. When a 1:1 mixture of compounds (1b) and (1c) (Scheme 7) was treated with sodium hydride in dimethylformamide under identical conditions, two spots other than the starting materials were observed (t.l.c.). After work-up and chromatographic separation the products corresponding to the two spots were each found to be a mixture of four compounds. Thus the n.m.r. spectrum of the first spot, with higher $R_F$ value, showed it to be a mixture of four compounds, (2a), (2b), (22), and (23), respectively. Similarly the n.m.r. spectrum of the second spot, with lower $R_F$ value, showed it to be a mixture of four rearranged compounds (2c), (2d), (24), and (25) (Scheme 7). The mass spectra of these mixtures further confirmed the presence of four compounds in each fraction. Thus the product mixture with higher $R_F$ value showed molecular ion peaks at $m/z$ 266, 252, and 238 corresponding to (2b), (22) and/or (23), and (2a), respectively. Similarly, the mass spectrum of the second mixture of products with lower $R_F$ value showed the molecular ion peaks at $m/z$ 296, 282, and 268 corresponding to (2d), (24) and/or (25), and (2c), respectively (Scheme 7). In another experiment the rearranged product (2c) was treated with sodium hydride in the presence of ethanethiol under a nitrogen blanket and a mixture of four products (2c), (24), (25), and (2d) (Scheme 7) was formed. These experiments, therefore, suggest that the rearrangement is intermolecular.

The rearrangement was found to be unsatisfactory in less polar solvents. Unchanged (1a) was recovered in the presence of sodium hydride in refluxing benzene, while in refluxing tetrahydrofuran it gave only 5% of the product (2a) in 3 h. In the latter case the yield could be improved to 30%, but only after 12 h of refluxing and with considerable formation of polymeric material. These facts suggest that the reactive intermediates in the conversion of (1) into (2) are polar. Also, on changing the base from sodium hydride to sodium ethoxide in ethanol, no product (2a) was obtained at room temperature, and only the polymeric mixture was produced in refluxing ethanol, possibly owing to the nucleophilic behaviour of the ethoxide ion. Therefore the sodium hydride-dimethylformamide combination was found to give the optimum yield of product (2). This yield, however, could not be further improved under different conditions; thus, while the reaction did not proceed satisfactorily at room temperature, polymerization began to occur beyond 60 °C. In order to assess the time required for the optimum formation of (2a) the rearrangement was carried out at 55 °C at different time intervals (Table). It was found that the optimum yield of (2a) was obtained between 2-3 h, as the yield started dropping after 4 h. After 12 h the yield of (2a) had decreased to 10%, the starting material (1a) had completely disappeared, and quantities of tarry polymeric material had been formed. Also, when the rearrangement of (1b) to give (2b) was carried out in the presence of ethanethiol (with added alkylthiolate anion), no improvement in the yield of (2b) was observed. Therefore, it appears that the limiting factor for the yield of (2) is the

![Scheme 6](image1)

![Scheme 7](image2)

Scheme 7. Reagents: i, NaH, DMF; ii, EtSH, N₂, NaH, DMF
Table. Rearrangement of (1a) to (2a) under varying conditions

<table>
<thead>
<tr>
<th>Experiment no.</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>10</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reaction time (h)</td>
<td>0.25</td>
<td>0.5</td>
<td>0.75</td>
<td>1.0</td>
<td>1.5</td>
<td>2.0</td>
<td>3.0</td>
<td>4.0</td>
<td>6.0</td>
<td>12.0</td>
</tr>
<tr>
<td>Yield of (2a) (%)</td>
<td>7</td>
<td>20</td>
<td>25</td>
<td>30</td>
<td>32</td>
<td>35</td>
<td>38</td>
<td>30</td>
<td>20</td>
<td>10</td>
</tr>
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</table>

equilibrium concentration of the intermediate (19) which is optimum between 0.5–3 h.

On the basis of the foregoing results it appears that the rearrangement of either (1) to (2), or (13) to (14) and (15), takes place as shown in Scheme 8. It appears that some nucleophilic species present in the reaction mixture initiates the displacement of thiolate anion either in (19), or in (26). The thiolate anion thus released in turn attacks (19), or (26), Michael-wise to give the corresponding solvent equilibrated enolate anions (27) which eliminate one of the thiolate anions to give either (2), or (15).* The product (15) undergoes a base-catalysed 1,3-proton shift to yield the thermodynamically more stable product (14). The whole process is reversible and should, in principle, give a mixture of all the possible geometrical isomers of (2), (14), and (15). However, when \( R' = \text{Ph} \), the corresponding, more stable \( E,E-(C) \) and \( Z,E-(D) \) anions appear to exist in equilibrium in a 3:1 ratio and on protonation yield either \( E-(15) \) or \( Z-(14) \), and \( E-(14) \), in a 1:3 ratio. When (14) was treated with sodium hydride under identical conditions in the presence of nitrogen, an equilibrium mixture containing products (14) (55%), (15) (25%), and (13) (5%) was obtained, further supporting the reversible nature of the rearrangement.

The most plausible mechanism for the formation of (17), which was the major product when (13) was treated with sodium hydride in the absence of nitrogen, is shown in Scheme 10. The carbanion (28) derived from (13) reacts with molecular oxygen to give the hydroperoxide intermediate (29) which cleaves further to give (30), and is then debenzoylated in the presence of sodium hydride or hydroxide ion (during work-up) to give (17) and benzoic acid.† The intermediacy of (30) was confirmed by its independent synthesis; the authentic sample thus obtained underwent debenzoylation.

Similar observations have been reported in the base-catalysed oxygenation of 3-hydroxyflavones.‡

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* We thank one of the referees for his comments on the mechanism.

† The oxygen incorporation in (28) could be either through a radical intermediate or a direct ionic process, which is not yet clear.

‡ Similar observations have been reported in the base-catalysed oxygenation of 3-hydroxyflavones.
under identical conditions to give (17) (80%) and benzoin acid (40%) (Scheme 10).

Similarly the mechanism of the formation of (16) from (13) which is obtained as a minor product can be explained by the hydroperoxide intermediate (32), formed via (14) which then undergoes sequential base-assisted cleavage and fragmentation (Scheme 11).

**Experimental**

M.p.s were determined on a 'Boetius' apparatus (Germany) and are uncorrected. I.r. spectra were recorded on a Perkin-Elmer 297 spectrophotometer, while the 1H n.m.r. spectra were obtained on a Varian EM-390 90 MHz n.m.r. spectrometer using SiMe$_3$ as the internal reference. In all the reactions a 50% suspension of sodium hydride was used. T.l.c. was carried out on a silica gel plate using EtOAc-benzene as solvent. Ether refers to diethyl ether.

Starting Materials.—Ketene dithioacetals (1a–e), (4), and (8) were prepared according to the method reported earlier.8 α-Benzylacetophenone, m.p. 69–70 °C (lit.,9 m.p. 70–71 °C) was prepared by hydrogenation of chalcone using Raney Ni as catalyst instead of Pt as reported.19

3,3-Bis(methylthio)-2-benzoyl-1-phenylprop-2-en-1-one (30), m.p. 67–68 °C (lit.,10 68–69 °C) was prepared according to the standard procedure used for analogous compounds.28

3,3-Bis(methylthio)-2-benzyl-1-phenylprop-2-en-1-one (13).—This compound was prepared by the standard procedure by condensation of α-benzylacetophenone (10.5 g, 0.05 mol) with carbon disulphide (0.05 mol) in the presence of sodium t-butoxide (2 equiv.) followed by treatment with methyl iodide (14.2 g, 0.5 mol). Work-up and column chromatography [hexane–EtOAc (9:1), silica gel] of the reaction mixture gave compound (13) (9.2 g, 57%) as light yellow prisms, m.p. 66 °C (CHCl$_3$–hexane), $v_{max}$ (Nujol) 1 660 cm$^{-1}$; δ (CCl$_3$) 2.35 (s, 3 H, SMe), 2.70 (s, 3 H, SMe), 4.35 (s, 2 H, CH$_2$), and 7.10—7.75 (m, 10 H, arom.); $m/z$ 314 (M$^+$) [Found: C, 68.3; H, 5.4. Calc. for C$_{13}$H$_{16}$O$_2$S$_2$ (M 314): C, 68.79; H, 5.73%].

**Scheme 10. Reagents:** i, NaH; ii, O$_2$; iii, NaH, DMF

Rearrangement of the 3,3-Bis(alkylthio)-2-methyl-1-arylprop-2-en-1-ones (1a–e) to the 2-Alkylthiomethyl-3-alkylthioacrylophenones (2a–e). General Procedure.—A solution of ketene dithioacetal (1) (0.01 mol) in dry dimethylformamide (20 ml) was added dropwise (30 min) to a well stirred suspension of sodium hydride (1.5 g, 0.03 mol) and dry dimethylformamide (20 ml) and the reaction mixture was stirred at 50–60 °C for 3–4 h. It was then quenched over crushed ice (100 g), neutralised with dilute acetic acid, extracted with chloroform (3 x 50 ml) and the combined extract was washed with water (4 x 150 ml), dried (Na$_2$SO$_4$), and the solvent removed to give the crude residue, which was purified by column chromatography over silica gel. Elution with hexane–EtOAc (9:1) gave first the unchanged starting materials (1a–e) and further elution with hexane–EtOAc (4:1) yielded the pure rearranged acrylophenones (2a–e). The physical, analytical, and spectral data of the products (2a–e) were reported in our earlier communication.2

**Scheme 11.**
(8) (1.95 g, 0.005 mol) was treated with sodium hydride (1 g, 0.02 mol) in dry dimethylformamide (25 ml) under standard reaction conditions for 6 h, till the starting material disappeared completely. The reaction mixture, after usual work-up followed by column chromatography over silica gel using hexane–EtOAc (95:5) as eluant, yielded the product (12) (0.05 g, 50%) as white needles (hexane), m.p. 91–92 °C, up followed by column chromatography over silica gel using vmx.

Extracted with chloroform (3 extracts washed with water (4

suspension) in dry dimethylformamide (30 ml) was stirred at 35–40 °C for 2 h. The reaction mixture was then poured over crushed ice (150 g), neutralised with dilute acetic acid, extracted with chloroform (3×50 ml), and the combined extracts washed with water (4×150 ml), dried (Na₂SO₄), and evaporated to give a crude residue which showed five spots on column chromatography and elution with hexane–ethyl ether. Evaporation of the ether gave benzoic acid (0.12 g, 0.005 mol) and sodium hydride (0.75 g, 0.015 mol) in dry dimethylformamide (1 ml) was stirred at 50-55 °C and the reaction mixture displayed the following prominent peaks, m/z 296, 282, and 268 are the molecular ion peaks of compounds (2b), (22) and/or (23), and (2a), thus showing the presence of the cross-over products [particularly RF(22) or RF(23)] in the mixture. The n.m.r. spectrum of the mixture showed the following signals: δ (CDCl₃) 1.10-1.45 (2 t, SCH₂CH₃, 22 squares), 2.05 (s, SMe, 22 squares), 2.28 (s, SMe, 22 squares), 2.40-3.30 (m, 17 squares), 6.85-6.95 (m, Hvinylic, 17 squares), and 7.60 (d, Ha,,,., 17 squares). From the above data, it is clear that all four components of the mixture are present in nearly equal concentrations. The mass spectrum of this mixture gave the following significant peaks, m/z (%) 266 (95), 252 (100), 238 (98), 223 (85), 205 (90), 191 (95), 175 (90), 105 (97) etc. The peaks at m/z 266, 252, and 238 are the molecular ion peaks of compounds (2b), (22) and/or (23), and (2a), thus showing the presence of the cross-over products [particularly (22) and/or (23)] in the mixture.

Further elution with hexane–EtOAc (4:1) gave an orange oil (t.i.c. single spot, RF ca. 0.45), which was also found to be a mixture of compounds (2c) and (2d), 2-ethyliothioethyl-1-(p-methoxyphenyl)-prop-2-en-1-one (24) and 3-ethyliothio-2-ethyliothioethyl-1-(p-methoxyphenyl)-prop-2-en-1-one (25). The n.m.r. spectrum of the mixture showed the following signals: δ (CDCl₃) 1.28 (2 t, SCH₂CH₃, 21 squares), 2.05 (s, SMe, 22 squares), 2.28 (s, SMe, 22 squares), 2.40-2.75 (m, SMe, CH₂, 33 squares), 3.45 (d, CH₂, 24 squares), 6.85–6.95 (m, Hvinylic 17 squares), and 7.05–7.90 (m, Hvinylic, 82 squares). From the above data, it is clear that all four components of the mixture are present in nearly equal concentrations. The mass spectrum of this mixture gave the following significant peaks, m/z (%) 266 (95), 252 (100), 238 (98), 223 (85), 205 (90), 191 (95), 175 (90), 105 (97) etc. The peaks at m/z 266, 252, and 238 are the molecular ion peaks of compounds (2b), (22) and/or (23), and (2a), thus showing the presence of the cross-over products [particularly (22) and/or (23)] in the mixture.

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Rearrangement of the Dimethyl Dithioacetal (1a) in the Presence of Diphenyliodicrylhydrazyl or Hydroquinone.—A mixture of diphenyliodicrylhydrazyl (0.2 g) and compound (1a) (1.2 g, 0.005 mol) in dry dimethylformamide (10 ml) was slowly added to a suspension of sodium hydride (1 g, 0.02 mol) in dry dimethylformamide (15 ml) at 50–55 °C and the reaction mixture was stirred for 3 h. Work-up and purification as described above yielded 3-methylthio-2-methylmethyl-1-phenylprop-2-en-1-one (2a) (0.45, 36%) (superimposable i.r. and n.m.r.).

When the same reaction was carried out in the presence of hydroquinone (0.2 g) instead of diphenyliodicrylhydrazyl, the yield of (2a) was 0.4 g (33%).
Presence of cross-over products (particularly (24) and/or (25)) in the mixture.

**Reaction of 1-(p-Methoxyphenyl)-3-methylthio-2-methylthiomethylprop-2-en-1-one (2c) with Sodium Hydride in the Presence of Ethanethiol.---A** solution of ethanethiol (0.6 g, 0.01 mol) and sodium hydride (1 g, 0.02 mol) in dry dimethylformamide (2 ml) was added slowly (5 min) to a well stirred suspension of sodium hydride (1 g, 0.02 mol) in dry dimethylformamide (10 ml) under a nitrogen blanket at 5—10 °C. A solution of (2c) (0.8 g, 0.003 mol) in dry dimethylformamide (3 ml) was added slowly to the reaction mixture with stirring, the reaction temperature was raised to 50 °C, and the stirring was continued at this temperature and under the nitrogen blanket for a further 30 min. After the usual work-up, the crude product showed a single spot (major) on t.l.c. and it was purified by column chromatography over silica gel using hexane—EtOAc (4 : 1) as eluant. The pure orange oil (t.l.c. single spot) thus obtained was a mixture of four products, (2c), (2a), (24), and (25) (superimposable i.r. and n.m.r., and mass spectra).

**Attempted Rearrangement of the Dimethyl Dithioacetal (1a) to (2a).---(a) In benzene.** A suspension of (1a) (1.2 g, 0.005 mol) and sodium hydride (1 g, 0.02 mol) in dry benzene (25 ml) was refluxed with stirring for 10 h. The reaction mixture after usual work-up and purification yielded (1a) (1.0 g, 85%) (superimposable i.r. and n.m.r.) along with starting material (lb) (0.8 g, 30%) (mixed m.p., superimposable i.r. and n.m.r.).

**Reaction of the Diketone (30) with Sodium Hydride.---A** suspension of compound (30) (1.64 g, 0.005 mol) and sodium hydride (1 g, 0.02 mol, 50% suspension) in dry dimethylformamide (15 ml) was stirred at 35—40 °C for 6 h. Work-up and purification of the reaction mixture as described in earlier experiments yielded (17) (0.9 g, 80%) (superimposable i.r., n.m.r., and mixed m.p.) and benzoic acid (0.25 g, 40%) (mixed m.p. and superimposable i.r.).

**Reaction of the Chalcone (14) with Sodium Hydride.---A** suspension of (14) (1.6 g, 0.005 mol) and sodium hydride (0.75 g, 0.015 mol) in dry dimethylformamide (15 ml) was stirred under nitrogen for 4 h. The reaction mixture after usual work-up and purification yielded the products (13) (80 mg, 5%), (14) (0.9 g, 55%), and (15) (0.4 g, 25%) (superimposable i.r. and n.m.r.). When a similar reaction was carried out in the absence of nitrogen, for 8 h, the reaction mixture after usual work-up and purification yielded products (16) (0.2 g, 10%) and (17) (0.7 g, 65%) (mixed m.p., superimposable i.r. and n.m.r.).

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**References**


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