The bromination of some derivatives of resorcinol

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SYNTHESES OF 5-n-ALKYLRESORCINOL DIMETHYL ETHERS AND 1,14-BIS(3,5-DIMETHOXYPHENYL)TETRADECANE VIA β-KETO SULPHONE INTERMEDIATES

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Abstract

Alkylation of 3,5-dimethoxy-α-(methylsulphonyl)acetophenone followed by reduction of the resulting monoalkylated products with zinc and acetic acid afforded the corresponding 5-n-acylresorcinol dimethyl ethers. Hydrogenolysis of 5-n-undecoylresorcinol dimethyl ether, prepared in this way, yielded 5-n-undecylresorcinol dimethyl ether.

Alkylation of 1-(methylsulphonyl)alkan-3-ones with 3,5-dimethoxybenzyl bromide gave a mixture of mono- and di-substituted products. Clemmensen reduction of the monosubstituted products afforded 5-n-alkylresorcinol dimethyl ethers directly.

These reactions have been adapted to provide two syntheses of 1,14-bis(3,5-dimethoxyphenyl)tetradecane.

INTRODUCTION

Although several methods are available for the preparation of 5-n-alkylresorcinol dimethyl ethers, better syntheses are still being sought in connection with work on constituents of plants belonging to the family Proteaceae.[1]

Recently House and Larson[2] have found that the β-keto sulphone (1), obtained by reaction of methyl benzoate with the anion derived from dimethyl sulphone, may be methylated to yield (2) which on reduction with zinc and acetic acid affords propiophenone (3).

$$\underset{(1)}{PhCOCH_2SO_2Me} \rightarrow \underset{(2)}{PhCOCH(Me)SO_2Me} \rightarrow \underset{(3)}{PhCOCH_2Me}$$

As aryl alkyl ketones are readily reduced to the corresponding arylalkanes, it seemed that this method could be used for the preparation of 5-n-alkylresorcinol dimethyl ethers. It also seemed that the reactions could be adapted to provide a new synthesis of 1,14-bis(3,5-dimethoxyphenyl)tetradecane[1,3] which is an important degradation product of robustol.[4]

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[1] Buddhasukh, D., Cannon, J. R., Metcalf, B. W., and Power, A. J., *Aust. J. Chem.*, 1971, **24**, 2655, and references therein.

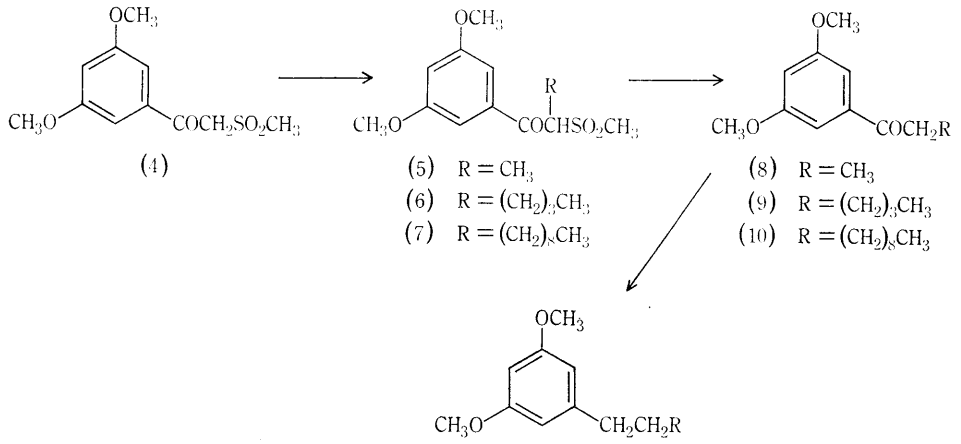
[2] House, H. O., and Larson, J. K., *J. org. Chem.*, 1968, **33**, 61.

[3] Rasmussen, M., Ridley, D. D., Ritchie, E., and Taylor, W. C., *Aust. J. Chem.*, 1968, **21**, 2989.

[4] Cannon, J. R., Chow, P. W., Metcalf, B. W., Power, A. J., and Fuller, M. W., *Tetrahedron Lett.*, 1970, 325.

Syntheses of 5-n-Alkylresorcinol Dimethyl Ethers

The adaptation of the method of House and Larson[2] is set out in Scheme 1. The anion derived from dimethyl sulphone, dissolved in dimethyl sulphoxide, condensed with methyl 3,5-dimethoxybenzoate to form the β-keto sulphone (4) in good yield. Treatment of the sodio derivative of (4) with a number of n-alkyl iodides in



(4)

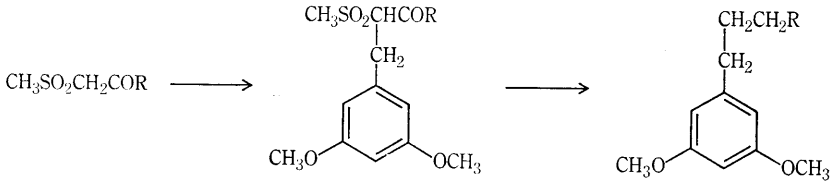
(5) R = CH_3
(6) R = $(CH_2)_3CH_3$
(7) R = $(CH_2)_8CH_3$

(8) R = CH_3
(9) R = $(CH_2)_3CH_3$
(10) R = $(CH_2)_8CH_3$

(11) R = $(CH_2)_8CH_3$

Scheme 1

dimethyl sulphoxide afforded the monoalkylated products (5), (6), and (7). Reduction of these substances with zinc and acetic acid then gave the corresponding 5-n-acylresorcinol dimethyl ethers (8), (9), and (10). Hydrogenolysis of the 5-n-undecoylresorcinol dimethyl ether (10) prepared in this way furnished 5-n-undecylresorcinol dimethyl ether (11).



(12) R = CH_2CH_3
(13) R = $(CH_2)_2CH_3$
(14) R = $(CH_2)_4CH_3$
(15) R = $(CH_2)_7CH_3$

(16) R = CH_2CH_3
(17) R = $(CH_2)_2CH_3$
(18) R = $(CH_2)_4CH_3$
(19) R = $(CH_2)_7CH_3$

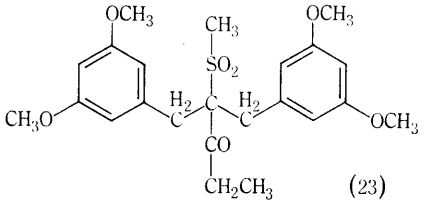
(20) R = CH_2CH_3
(21) R = $(CH_2)_2CH_3$
(22) R = $(CH_2)_4CH_3$
(11) R = $(CH_2)_7CH_3$

Scheme 2

During this work it was noted that, despite the use of dimethyl sulphoxide as solvent, a prolonged reaction time was required to obtain an acceptable yield of the alkylated product (7). In an attempt to overcome this difficulty, the reactions set out in Scheme 2, which involve alkylation of an aliphatic β-keto sulphone with the more reactive halide, 3,5-dimethoxybenzyl bromide, were then investigated.

The β-keto sulphones (12), (13), (14), and (15) were readily obtained by condensation of the appropriate aliphatic esters with the anion derived from dimethyl sulphone in dimethyl sulphoxide.[2] When the sodio derivative of (12) was treated with 3,5-dimethoxybenzyl bromide the major product formed was (16) but it was accompanied by the disubstituted product (23). Similar results were obtained when (13), (14), and (15) were treated in this way.

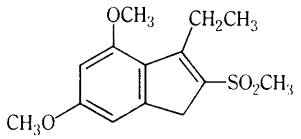
The formation of significant amounts of disubstituted products during the alkylation of other active methylene compounds (e.g. diethyl malonate) with benzyl halides has been discussed previously.[5] In the present work it was found that the mixture of (16) and (23) could be separated by repeated extraction of a solution in ether with 10% aqueous sodium hydroxide. The monosubstituted product (16) was recovered on acidification of the alkaline extract and the neutral disubstituted product (23) was purified by chromatography. The monosubstituted product (17) could also



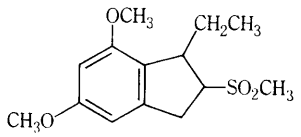
(23)

be separated from the reaction mixture in this way, but the higher homologues, (18) and (19), were not extracted from ethereal solutions by aqueous solutions of sodium hydroxide. Although (18) could be isolated by fractional crystallization of the reaction product, in the case of (19) it was found better to extract this substance from the reaction mixture with Claisen's alkali.[6]

Unlike β-keto sulphones with an aroyl carbonyl which are reduced to the ketone by zinc and acetic acid, (16) was recovered unchanged from this treatment. However, Clemmensen reduction of (16) in the presence of toluene[7] gave a good yield of 5-n-pentylresorcinol dimethyl ether (20) directly. This method was also used successfully to convert (17), (18), and (19) into the corresponding 5-n-alkylresorcinol dimethyl ethers (21), (22), and (11). On the other hand, the one-phase Clemmensen reduction[7] of (16) was not satisfactory as a mixture of products was obtained. One highly crystalline substance which separated from the mixture has been assigned the structure



(24)



(25)

(25), mainly on the basis of its n.m.r. spectrum. It is suggested that the formation of (25) may be due to cyclodehydration of the β-keto sulphone (16) to the indene (24)

[5] Cope, A. C., Holmes, H. L., and House, H. O., *Org. React.*, 1957, **9**, 107.

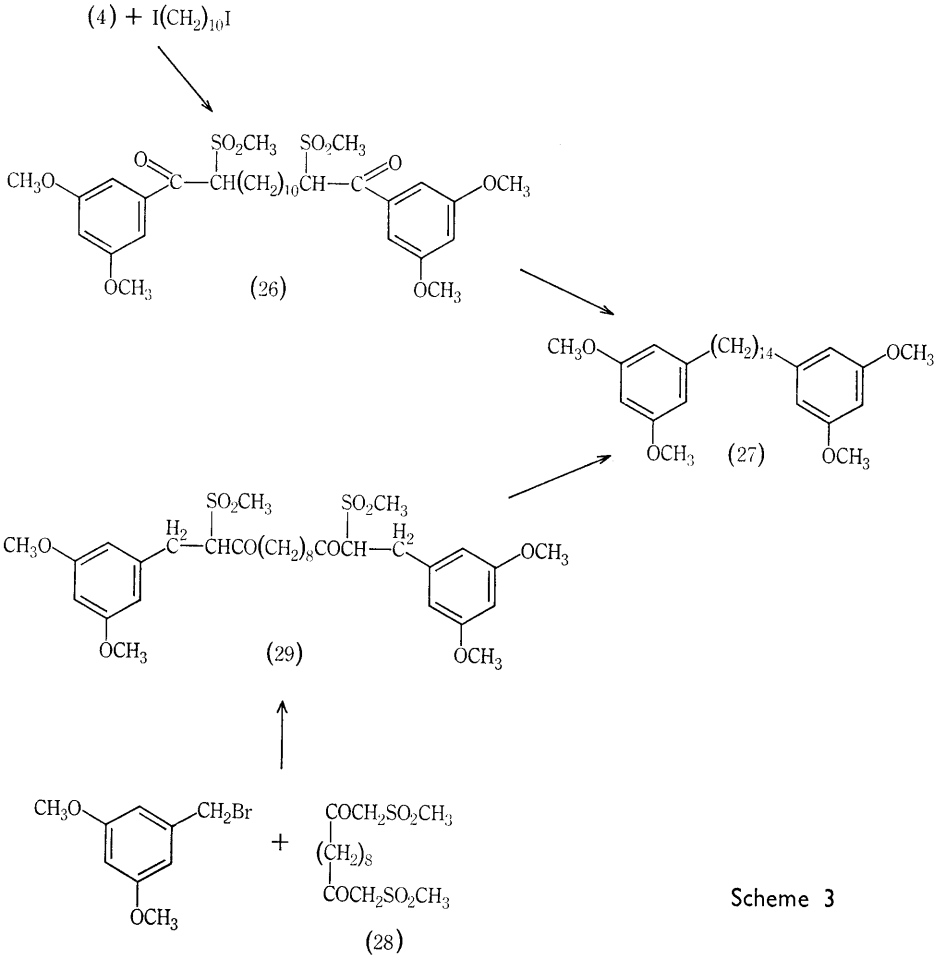
[6] Fieser, L. F., and Fieser, M., "Reagents for Organic Synthesis," p. 153 (John Wiley: New York 1967).

[7] Martin, E. L., *Org. React.*, 1942, **1**, 155.

followed by reduction of the conjugated double bond of (24). The ready cyclodehydration of 1-benzyl-1-(hydroxymethylene)propan-2-one to form 2-acetylindene[8] may be an analogous reaction; the reduction of conjugated double bonds during the Clemmensen reduction is well known.[7]

Syntheses of 1,14-Bis(3,5-dimethoxyphenyl)tetradecane

Both of the above methods were adapted to the preparation of 1,14-bis(3,5-dimethoxyphenyl)tetradecane (27) as set out in Scheme 3.



Scheme 3

Condensation of 2 mol of the sodio derivative of (4) with 1,10-diiododecane in dimethyl sulphoxide proceeded slowly and only a low yield of (26) was obtained. Two-phase Clemmensen reduction[7] of (26) proceeded smoothly and yielded 1,14-bis-(3,5-dimethoxyphenyl)tetradecane (27) directly.

[8] Rupe, H., and Müller, H., *Helv. chim. Acta*, 1921, **4**, 841.

In a second synthesis of (27), dimethyl sebacate was first treated with 2 mol of the anion derived from dimethyl sulphone in dimethyl sulphoxide, whereupon 1,12-bis-(methylsulphonyl)dodecane-2,11-dione (28) was obtained. The disodio derivative of (28) was then alkylated with 2 mol of 3,5-dimethoxybenzyl bromide in dimethyl sulphoxide. Two-phase Clemmensen reduction of the major product (29) of this reaction then gave (27) directly.

EXPERIMENTAL

The relevant general instructions given previously[9] also apply to the present work.

Dimethyl sulphoxide was distilled from calcium hydride; tetrahydrofuran was distilled from hydroquinone, and then from sodium hydride. Pure sodium hydride was obtained by washing the calculated quantity of its dispersion in oil (B.D.H., 50%, w/w) with light petroleum, by decantation, and then evaporating the residual solvent. All reactions involving sodium hydride were carried out under dry nitrogen.

Thin-layer chromatography was carried out on plates of Merck silica gel G, 250 μm thick. The plate was sprayed with a 3% solution of ceric sulphate in 1M aq. H_2SO_4 and then heated to 140° in order to produce visible spots. Preparative t.l.c. was carried out on a layer of Merck silica gel G 750 μm thick.

(*a*) *3,5-Dimethoxy-α-(methylsulphonyl)acetophenone* (*4*)

A mixture of sodium hydride (9·78 g), dimethyl sulphone (38·4 g), and dimethyl sulphoxide (150 ml) was stirred at 65° until evolution of hydrogen ceased (1·5 hr). The suspension was cooled to room temperature and diluted with tetrahydrofuran (150 ml), then a solution of methyl 3,5-dimethoxybenzoate[10] (40·0 g) in tetrahydrofuran (200 ml) was added. After stirring at 65° for 1 hr the solution was cooled, poured into ice (1 kg) and 10% aq. HCl (500 ml), then filtered. The precipitate was washed with sat. aq. $NaHCO_3$ and water, then dried. Crystallization of the product (42·0 g) from ethyl acetate–light petroleum afforded *3,5-dimethoxy-α-(methylsulphonyl)acetophenone* (4) as needles, m.p. 136·5–137·0° (Found: C, 51·2; H, 5·6; S, 12·3. $C_{11}H_{14}O_5S$ requires C, 51·2; H, 5·5; S, 12·4%). N.m.r. spectrum ($CDCl_3$): d, 2, 7·11 (ArH): t, 1, 6·75 (ArH); s, 2, 4·59 (CH_2); s, 6, 3·86 (OCH_3); s, 3, 3·15 (SO_2CH_3).

Acidification of the sat. aq. $NaHCO_3$ washings afforded 3,5-dimethoxybenzoic acid (5·0 g), m.p. and mixed m.p. 184·5–185·0°.

(*b*) *Alkylation of 3,5-Dimethoxy-α-(methylsulphonyl)acetophenone*

(i) A mixture of 3,5-dimethoxy-α-(methylsulphonyl)acetophenone (4) (30·0 g), dimethyl sulphoxide (150 ml), and sodium hydride (2·8 g) was stirred at room temperature until evolution of hydrogen had ceased, then methyl iodide (17·7 g) was added. After stirring for 1·5 hr at room temperature, the solution was poured into cold 10% aq. HCl (600 ml) and the mixture was extracted with chloroform. The extract was washed with aq. $Na_2S_2O_3$ and brine, then evaporated. Crystallization of the solid residue (28·0 g) from ethyl acetate gave *3,5-dimethoxy-α-(methylsulphonyl)-propiophenone* (5) as needles, m.p. 123·0–123·5° (Found: C, 53·2; H, 6·1; S, 12·0. $C_{12}H_{16}O_5S$ requires C, 52·9; H, 5·9; S, 11·8%). N.m.r. spectrum ($CDCl_3$): d, 2, 7·15 (ArH); t, 1, 6·73 (ArH); m, 1, 5·04–4·58, ($COCHSO_2$), 7; s, 6, 3·85 (OCH_3); s, 3, 3·00 (SO_2CH_3); d, 3, 1·73, (CH_3), 7.

(ii) 3,5-Dimethoxy-α-(methylsulphonyl)acetophenone (4) (5·0 g) was treated with sodium hydride (0·47 g) in dimethyl sulphoxide as in (i). 1-Iodobutane (4·27 g) was then added and the mixture was stirred at 50–55° for 3 hr. The oil obtained on working up the reaction mixture as before was crystallized from aqueous methanol whereupon *3,5-dimethoxy-α-(methylsulphonyl)hexanophenone* (6) was obtained as needles (4·5 g), m.p. 85–86° (Found: C, 57·0; H, 7·1; S, 9·9. $C_{15}H_{22}O_5S$ requires C, 57·3; H, 7·1; S, 10·2%). N.m.r. spectrum ($CDCl_3$): d, 2, 7·17 (ArH); t, 1, 6·68 (ArH);

[9] Cannon, J. R., and Metcalf, B. W., *Aust. J. Chem.*, 1971, **24**, 1925.

[10] Ridley, D. D., Ritchie, E., and Taylor, W. C., *Aust. J. Chem.*, 1968, **21**, 2979.

m, 1, 4·95–4·58 ($COCHSO_2$); s, 6, 3·85 (OCH_3); s, 3, 2·97 (SO_2CH_3); m, 6, 2·33–1·05 (CH_2); m, 3, 1·05–0·75 (CH_3).

(iii) The suspension prepared from 3,5-dimethoxy-α-(methylsulphonyl)acetophenone (4) (8·84 g) and sodium hydride (0·82 g) in dimethyl sulphoxide (55 ml) as in (i) was treated with 1-iodononane[11] (10·4 g) and the mixture was stirred at 50–55° for 19 hr. The reaction mixture was worked up as before and the oily product (13·3 g) was chromatographed on silicic acid (450 g). Elution of the column with benzene yielded *3,5-dimethoxy-α-(methylsulphonyl)undecanophenone* (7) as an oil, b.p. 205° (bath)/0·1 mm (Found: C, 62·1; H, 8·2; S, 8·2. $C_{20}H_{32}O_5S$ requires C, 62·5; H, 8·4; S, 8·3%). N.m.r. spectrum (CCl_4): d, 2, 7·08, (ArH); t, 1, 6·61 (ArH); m, 1, 5·00–4·53 ($COCHSO_2$); s, 6, 3·78 (OCH_3); s, 3, 2·83 (SO_2CH_3); m, 2, 2·38–1·82 (CH_2CHSO_2); m, 14, 1·82–1·02 (CH_2); m, 3, 1·02–0·69 (CH_3).

(c) Preparation of 5-n-Acylresorcinol Dimethyl Ethers

(i) A mixture of 3,5-dimethoxy-α-(methylsulphonyl)propiophenone (5) (1·0 g), zinc dust (2·1 g), glacial acetic acid (6 ml), and dry ethanol (7 ml) was stirred for 2 hr at room temperature, then filtered, poured into water, and extracted with ether. The extract was washed with sat. aq. $NaHCO_3$ and brine, and then evaporated whereupon 3,5-dimethoxypropiophenone (8) was obtained as an oil (0·67 g) (lit.[12] m.p. 34–35°). ν_{max} (Nujol) 1690s cm^{-1} (CO). N.m.r. spectrum (CCl_4): d, 2, 6·93 (ArH); t, 1, 6·48 (ArH); s, 6, 3·75 (OCH_3); q, 2, 2·85 (CH_2), 7; t, 3, 1·15 (CH_3), 7.

(ii) 3,5-Dimethoxy-α-(methylsulphonyl)hexanophenone (6) (1·0 g) was reduced with a mixture of zinc dust (1·0 g), glacial acetic acid (5 ml), and dry ethanol (7 ml) for 4 hr at room temperature. The reaction product (0·7 g), isolated as above, crystallized from aqueous methanol whereupon 3,5-dimethoxyhexanophenone (9) was obtained as needles, m.p. 49–51° (lit.[13] 53°). ν_{max} (Nujol) 1690s cm^{-1} (CO). N.m.r. spectrum (CCl_4); d, 2, 7·08 (ArH); t, 1, 6·71 (ArH); s, 6, 3·78 (OCH_3); t, 2, 2·89 (CH_2CO), 8; m, 6, 1·91–1·10 (CH_2); m, 3, 1·10–0·69 (CH_3).

(iii) 3,5-Dimethoxy-α-(methylsulphonyl)undecanophenone (7) (5·62 g) was stirred with zinc dust (4·35 g), glacial acetic acid (25 ml), and dry ethanol (35 ml) for 12 hr at room temperature. The product (4·0 g) was isolated as above, and was crystallized from light petroleum whereupon *3,5-dimethoxyundecanophenone* (10) was obtained as needles, m.p. 43·0–43·5° (Found: C, 74·8; H, 9·9. $C_{19}H_{30}O_3$ requires C, 74·5; H, 9·9%). ν_{max} (Nujol) 1690s cm^{-1} (CO). N.m.r. spectrum (CCl_4): d, 2, 6·98 (ArH); t, 1, 6·50 (ArH); s, 6, 3·75 (OCH_3); t, 2, 2·81 ($COCH_2$); m, 16, 1·92–1·10 (CH_2); m, 3, 1·10–0·70 (CH_3).

(d) 5-n-Undecylresorcinol Dimethyl Ether (11)

A solution of 3,5-dimethoxyundecanophenone (10) (170 mg) in ethyl acetate (100 ml) containing 2 drops of conc. H_2SO_4 was shaken with 10% Pd/C (200 mg) under 5·5 atm of hydrogen for 5 hr. On working up in the usual manner 5-n-undecylresorcinol dimethyl ether (11) was obtained as an oil. The n.m.r. and i.r. spectra were identical with those of an authentic specimen.[1]

(e) Preparation of the β-Keto Sulphones (12), (13), (14), and (15)

(i) A solution of dimethyl sulphone (75 g) in dimethyl sulphoxide (350 ml) was added to sodium hydride (38·5 g) and the mixture was stirred at 60–65° until the evolution of hydrogen had ceased. After the mixture had cooled to room temperature tetrahydrofuran (250 ml) was added followed by a solution of methyl propionate (35 g) in tetrahydrofuran (150 ml). The mixture was stirred at 60–65° for 3 hr, then poured into a mixture of ice and aq. HCl and extracted with chloroform. The extract was washed cautiously with water, sat. aq. $NaHCO_3$, and brine, then dried and evaporated. A solution of the residue in benzene was passed through a short column of silicic acid (30 g). The eluate was evaporated and the residue was distilled whereupon *1-(methylsulphonyl)butan-2-one* (12) was obtained as a pale oil (46·8 g), b.p. 91–92°/0·5 mm, which solidified on cooling; m.p. 44·5–45·5° (Found: C, 40·0; H, 6·7. $C_5H_{10}O_3S$ requires C, 40·0; H, 6·7%). N.m.r. spectrum ($CDCl_3$): s, 2, 4·14 ($COCH_2SO_2$); s, 3, 3·08 (SO_2CH_3); q, 2, 2·77 (CH_2CO), 7; t, 3, 1·13 (CH_3), 7.

[11] Stallberg-Stenhagen, S., *Ark. Kemi Miner. Geol.* (*A*), 1949, **26**(12), 1.
[12] Mauthner, F., *Chem. Abstr.*, 1924, **18**, 1656.
[13] Suter, C. M., and Weston, A. W., *J. Am. chem. Soc.*, 1939, **61**, 232.

(ii) A solution of dimethyl sulphone (54 g) in dimethyl sulphoxide (250 ml) was added to sodium hydride (30 g) and the mixture was stirred at 60–68° until the evolution of hydrogen had ceased. After cooling, ether (100 ml), and then a solution of methyl butyrate (41 g) in ether (200 ml), were added, and the mixture was refluxed for 2 hr before being set aside at room temperature for 16 hr. The mixture was then poured into ice and aq. HCl, extracted with chloroform, and chromatographed as above. The solid product (46 g) was recrystallized from light petroleum to yield *1-(methylsulphonyl)pentan-2-one* (13) as needles (40 g), m.p. 46–47° (Found: C, 43·7; H, 7·7. $C_6H_{12}O_3S$ requires C, 43·9; H, 7·4%). N.m.r. spectrum (CCl_4) : s, 2, 4·05 ($COCH_2SO_2$); s, 3, 2·92 (SO_2CH_3); t, 2, 2·55 (CH_2CO); m, 2, 1·90–1·30 (CH_2); t, 3, 0·84 (CH_3).

(iii) A solution of dimethyl sulphone (130 g) in dimethyl sulphoxide (200 ml) and tetrahydrofuran (250 ml) was added to sodium hydride (33·1 g) and the mixture was heated at 60–68° until the evolution of hydrogen had ceased. Methyl hexanoate (90·7 g) was then added and stirring and heating at 60–68° were continued for 3 hr. The mixture was then worked up as before. Distillation of the crude product (83 g; b.p. 108–115°/0·5 mm) and crystallization of the distillate from chloroform–light petroleum yielded 1-(methylsulphonyl)heptan-2-one (14) as needles (60 g), m.p. 38–40° (lit.[2] 37–38°) (Found: C, 50·5; H, 8·7; S, 16·5. Calc. for $C_8H_{16}O_3S$: C, 50·0; H, 8·4; S, 16·6%). N.m.r. spectrum (CCl_4); s, 2, 3·95 ($COCH_2SO_2$); s, 3, 2·95 (SO_2CH_3); t (b), 2, 2·69 (CH_2CO); m, 6, 2·00–1·12 (CH_2); m, 3, 1·12–0·70 (CH_3).

(iv) A solution of dimethyl sulphone (38·2 g) in dimethyl sulphoxide (300 ml) was added to sodium hydride (9·7 g) and the mixture was stirred at 65° until evolution of hydrogen had ceased. After cooling, tetrahydrofuran (150 ml) and then a solution of methyl nonanoate (35 g) in tetrahydrofuran (100 ml) were added. The mixture was stirred at 65° for 3 hr, then cooled, and poured into ice containing 10% aq. HCl. The precipitate was filtered, washed copiously with water, 10% aq. Na_2CO_3, and finally water. After drying the precipitate by azeotropic distillation with benzene in a Dean and Stark apparatus, a pale solid (38·2 g) was obtained. Recrystallization of this material from ethyl acetate–light petroleum gave *1-(methylsulphonyl)decan-2-one* (15) as needles, m.p. 62·5–63·0° (Found: C, 56·3; H, 9·3; S, 13·5. $C_{11}H_{22}O_3S$ requires C, 56·4; H, 9·5; S, 13·7%). N.m.r. spectrum ($CDCl_3$): s, 2, 4·06 ($COCH_2SO_2$); s, 3, 3·04 (SO_2CH_3); t (distorted), 2, 2·71 ($COCH_2$), 6·5; m, 12, 2·00–1·10 (CH_2); m, 3, 1·10–0·60 (CH_3).

(*f*) *Alkylation of the β-Keto Sulphones (12), (13), (14), and (15) with 3,5-Dimethoxybenzyl Bromide*

(i) A solution of 1-(methylsulphonyl)butan-2-one (12) (30 g) in dimethyl sulphoxide (250 ml) was stirred with sodium hydride (4·8 g) at 65° until evolution of hydrogen had ceased. The suspension was then treated with a solution of 3,5-dimethoxybenzyl bromide[14] (46 g) in dimethyl sulphoxide (100 ml) and the mixture was stirred at 55° for 2 hr. When the reaction was worked up by pouring into ice and aq. HCl followed by extraction with chloroform, an orange oil was obtained. This product was redissolved in ether and the solution was extracted exhaustively with 10% aq. NaOH.

Acidification of the alkaline extract yielded a solid (36 g) which crystallized from aqueous methanol whereupon *1-(3,5-dimethoxyphenyl)-2-(methylsulphonyl)pentan-3-one* (16) was obtained as prisms, m.p. 97·0–97·5° (Found: C, 55·8; H, 6·8; S, 10·6. $C_{14}H_{20}O_5S$ requires C, 56·0; H, 6·7; S, 10·7%). N.m.r. spectrum ($CDCl_3$): m, 3, 6·40–6·21 (ArH); m, 1, 4·40–4·07 ($COCHSO_2$); s, 6, 3·77 (OCH_3); m, 2, 3·48–3·10 ($ArCH_2$); s, 3, 2·92 (SO_2CH_3); m, 2, 2·73–2·00 ($COCH_2$); t, 3, 0·92 (CH_3), 7.

The remaining ether solution was evaporated. The resulting yellow gum was purified by use of preparative t.l.c. whereupon *2-(3,5-dimethoxybenzyl)-1-(3,5-dimethoxyphenyl)-2-(methylsulphonyl)pentan-3-one* (23) was obtained as a colourless gum which decomposed on attempted distillation (Found: C, 60·9; H, 6·8; S, 7·3. $C_{23}H_{30}O_7S$ requires C, 61·3; H, 6·7; S, 7·1%). N.m.r. spectrum (CCl_4): s, 6, 6·20 (ArH); s, 12, 3·67 (OCH_3); s (b), 4, 3·37 ($ArCH_2$); q, 2, 2·79 ($COCH_2$), 7; s, 3, 2·48 (SO_2CH_3); t, 3, 1·12 (CH_3), 7.

(ii) A solution of 1-(methylsulphonyl)pentan-2-one (13) (5 g) in dimethyl sulphoxide was added to sodium hydride (1·7 g) and the mixture was heated to 60° until evolution of hydrogen had ceased, then cooled to room temperature. 3,5-Dimethoxybenzyl bromide[14] (6·90 g) was then added. The mixture was stirred at 60° for 2 hr, then worked up as above. A solution of the reaction product

[14] Bhati, A., *Tetrahedron*, 1962, **18**, 1519.

(7·1 g) in ether (400 ml) was shaken exhaustively with 10% aq. NaOH (30 × 100 ml). Acidification of the alkaline extracts gave *1-(3,5-dimethoxyphenyl)-2-(methylsulphonyl)hexan-3-one* (17) which crystallized from light petroleum as needles, m.p. 81·5–82·5° (Found: C, 57·1; H, 7·3. $C_{15}H_{22}O_5S$ requires C, 57·3; H, 7·1%). N.m.r. spectrum (CCl_4): s, 3, 6·23 (ArH); s, 6, 3·74 (OCH_3); m, 1, 4·35–4·00 ($COCHSO_2$); m, 2, 3·30–3·00 ($ArCH_2$); s, 3, 2·82 (SO_2CH_3); m, 2, 2·46–2·12 ($COCH_2$); m, 2, 1·65–1·18 (CH_2); m, 3, 0·94–0·64 (CH_3).

(iii) A solution of 1-(methylsulphonyl)heptan-2-one (14) (55·5 g) in dimethyl sulphoxide (50 ml) was added to sodium hydride (6·95 g). The mixture was stirred at room temperature until evolution of hydrogen had ceased, then added to a solution of 3,5-dimethoxybenzyl bromide[14] (66·7 g) in tetrahydrofuran (250 ml). This mixture was stirred at 60° for 8 hr, then the solvents were evaporated under reduced pressure; the residue was treated with aq. HCl and extracted with chloroform. Evaporation of the chloroform afforded a semi-solid product (95 g) which on fractional crystallization from methanol yielded *1-(3,5-dimethoxyphenyl)-2-(methylsulphonyl)octan-3-one* (18) as needles (33 g), m.p. 62·5–63·0° (Found: C, 59·8; H, 7·5; S, 9·1. $C_{17}H_{26}O_5S$ requires C, 59·6; H, 7·7; S, 9·3%). N.m.r. spectrum (CCl_4): s, 3, 6·22 (ArH); m, 1, 4·40–3·90 ($COCHSO_2$); s, 6, 3·73 (OCH_3); m, 2, 3·32–3·06 ($ArCH_2$); s, 3, 2·81 (SO_2CH_3); m, 8, 2·75–1·00 ($COCH_2$ and CH_2); m, 3, 1·00–0·67 (CH_3).

(iv) A solution of 1-(methylsulphonyl)decan-2-one (15) (20 g) in dimethyl sulphoxide (150 ml) was stirred with sodium hydride (4·12 g) until evolution of hydrogen had ceased. A solution of 3,5-dimethoxybenzyl bromide[14] (19·75 g) in dimethyl sulphoxide (100 ml) was added dropwise and the mixture was stirred at 55° for 3 hr, then poured into ice and aq. HCl, and extracted with chloroform. The chloroform extract was washed with water and 10% aq. Na_2CO_3, then evaporated. The resulting yellow oil (34 g) was chromatographed on alumina (200 g). Evaporation of the light petroleum–benzene (1 : 1) eluate gave the product (26·4 g) which travelled as two, almost coincident, spots on t.l.c. A portion (18·4 g) of this product was dissolved in light petroleum–benzene (3 : 2) and extracted exhaustively with Claisen's alkali[6] (12 × 50 ml). Acidification of the extract gave a pale oil (14 g) which crystallized slowly. Recrystallization from light petroleum then afforded *1-(3,5-dimethoxyphenyl)-2-(methylsulphonyl)undecan-3-one* (19) as needles, m.p. 63–64° (Found: C, 62·6; H, 8·2; S, 8·4. $C_{20}H_{32}O_5S$ requires C, 62·5; H, 8·4; S, 8·3%). N.m.r. spectrum (CCl_4): s (b), 3, 6·32 (ArH); m, 1, 4·43–4·00 ($COCHSO_2$); s, 6, 3·76 (OCH_3); m, 2, 3·40–3·10 ($ArCH_2$); s, 3, 2·93 (SO_2CH_3); m, 17, 2·75–0·70 ($COCH_2$, CH_2, and CH_3).

(*g*) *Reduction of the β-Keto Sulphones (16), (17), (18), and (19)*

(i) A mixture of 1-(3,5-dimethoxyphenyl)-2-(methylsulphonyl)pentan-3-one (16) (1·5 g), zinc dust (1·63 g), glacial acetic acid (12 ml), and dry ethanol (14 ml) was stirred at 65° for 2 hr. Unchanged (16), m.p. and mixed m.p. 97·0–97·5°, was recovered when the mixture was worked up in the usual way.

(ii) Zinc amalgam, prepared from mossy zinc[7] (150 g), conc. aq. HCl (265 ml), and water (113 ml) were warmed until vigorous evolution of hydrogen took place. A solution of (16) (23·5 g) in toluene (200 ml) was added and the mixture was refluxed briskly for 30 hr. Additional portions (45 ml) of conc. aq. HCl were added every 6 hr. The mixture was cooled and extracted with ether. The extract was washed with sat. aq. $NaHCO_3$ and water, then dried. The ether was evaporated then the residue was fractionated under reduced pressure. 5-n-Pentylresorcinol dimethyl ether (20) was obtained as an oil (11 g), b.p. 110–112°/1 mm (lit.[15] 114°/2 mm). N.m.r. spectrum (CCl_4): s, 3, 6·20 (ArH); s, 6, 3·75 (OCH_3); t (b), 2, 2·50 ($ArCH_2$); m, 6, 1·90–1·15 (CH_2); t (b), 3, 0·90 (CH_3).

(iii) A mixture of the β-keto sulphone (16) (1 g), zinc amalgam, prepared from mossy zinc (12 g), conc. aq. HCl (17·5 ml), and ethanol (20 ml) was refluxed for 10 hr. The product, isolated in the usual manner, formed a yellow oil (0·8 g) which slowly deposited some prisms (82 mg). Recrystallization from light petroleum afforded *1-ethyl-2-(methylsulphonyl)-5,7-dimethoxyindane* (25) as prisms, m.p. 134–135° (Found: C, 59·0; H, 7·1; S, 11·4. $C_{14}H_{20}O_4S$ requires C, 59·1; H, 7·1; S, 11·3%). N.m.r. spectrum ($CDCl_3$): q (AB), 2, ν_A 6·50, ν_B 6·32 (ArH), 2; s, 3, 3·82 (OCH_3); s, 3, 3·80 (OCH_3); m and s, 9, 3·40–1·80 and 2·80, respectively (CH, CH_2, and SO_2CH_3); t, 3, 0·84 (CH_3), 7.

[15] Asahina, Y., and Nogami, H., *Ber. dt. chem. Ges.*, 1935, **68**, 1500.

(iv) When the reduction of (16) was carried out as described in (iii), except that the mixture was stirred at room temperature for 28 hr, (25) (0·18 g), m.p. 134–135°, was again obtained.

(v) Reduction of the β-keto sulphone (17) as described in (ii) afforded 5-n-hexylresorcinol dimethyl ether (21) as an oil, b.p. 114–115°/1·0 mm (lit.[13] 120–122°/4 mm). N.m.r. spectrum (CCl_4): s, 3, 6·19 (ArH); s, 6, 3·67 (OCH_3); t, 2, 2·49 ($ArCH_2$); m, 8, 1·65–1·12 (CH_2); m, 3, 1·05–0·81 (CH_3).

(vi) Reduction of the β-keto sulphone (18) as described in (ii) afforded 5-n-octylresorcinol dimethyl ether (22) as an oil, b.p. 130°/0·3 mm, n_D^{20} 1·5005 (lit.[16] b.p. 164–168°/4 mm, n_D^{20} 1·4995). N.m.r. spectrum (CCl_4): s (b), 3, 6·22 (ArH); s, 6, 3·68 (OCH_3); t (b), 2, 2·50 ($ArCH_2$); m, 12, 1·80–1·10 (CH_2); m, 3, 1·10–0·73 (CH_3).

(vii) 1-(3,5-Dimethoxyphenyl)-2-(methylsulphonyl)undecan-3-one (19) (0·9 g) was reduced as described in (ii). Distillation of the product (0·67 g) afforded 5-n-undecylresorcinol dimethyl ether (11) as an oil, b.p. 108–110° (bath)/0·01 mm (lit.[1] 110°/0·01 mm). The n.m.r., i.r., and mass spectra of this substance were identical with those of an authentic specimen.[1]

(*h*) *Synthesis of 1,14-Bis(3,5-dimethoxyphenyl)tetradecane (27)*

(i) Decane-1,10-diol (25 g) and potassium iodide (96 g) were added to a stirred mixture of 85% orthophosphoric acid (56 g) and phosphorus pentoxide (20 g) at room temperature. The resulting mixture was stirred at 115–120° under nitrogen for 5 hr, then cooled, diluted with water, and extracted with ether. The extract was washed with aq. $NaHSO_3$ and water, then dried and evaporated under reduced pressure. When the dark oily residue (50·6 g) was distilled, 1,10-diiododecane was obtained as a pale solid (46 g), b.p. 186–188°/2 mm, m.p. 28·0–28·5° (lit.[17] 28–30°). N.m.r. spectrum (CCl_4): t, 4, 3·14 (CH_2I), 6·5; m, 16, 2·10–1·10 (CH_2).

(ii) A solution of 1,10-diiododecane (3·82 g) in dimethyl sulphoxide (25 ml) was added to the stirred suspension prepared as in (*b*) from a solution of 3,5-dimethoxy-α-(methylsulphonyl)acetophenone (4) (5·00 g) in dimethyl sulphoxide (30 ml), and sodium hydride (0·465 g). The mixture was stirred at 55° for 9 hr, then cooled, poured into ice and conc. aq. HCl, and extracted with chloroform. The extract was washed with 10% aq. $NaHSO_3$ and water, then dried, and evaporated to yield a pale yellow viscous oil (7·8 g). This product was chromatographed on silicic acid (100 g).

Elution of the column with ether–benzene (1 : 19) gave a pale yellow solid (2·4 g) which crystallized from ethyl acetate–light petroleum to yield *1,12-bis(3,5-dimethoxybenzoyl)-1,12-bis(methylsulphonyl)dodecane* (26) as fine needles, m.p. 89–90° (Found: C, 59·0; H, 7·2; S, 9·5. $C_{32}H_{46}O_{10}S_2$ requires C, 58·7; H, 7·1; S, 9·8%). I.r. spectrum (Nujol): ν_{max} 1672s (CO), 1295s, and 1150s cm^{-1} (SO_2). N.m.r. spectrum ($CDCl_3$): d, 4, 7·15 (ArH); t, 2, 6·72 (ArH); t, 2, 4·87 ($SO_2CH(CO)CH_2$), 7; s, 12, 3·82 (OCH_3); s, 6, 2·95, (SO_2CH_3); m, 4, 2·50–1·90 (SO_2CHCH_2); m, 16, 1·50–1·00 (CH_2).

Further elution of the column with ether–benzene (1 : 9) gave a solid (2·21 g), recrystallization of which from ethyl acetate–light petroleum afforded unchanged 3,5-dimethoxy-α-(methylsulphonyl)-acetophenone (4), m.p. and mixed m.p. 136–137°.

(iii) A solution of dimethyl sulphone (82 g) in dimethyl sulphoxide (500 ml) was added to sodium hydride (21 g) and the mixture was stirred at 65° under nitrogen until evolution of hydrogen ceased (2 hr). The fawn suspension was cooled and diluted with tetrahydrofuran (200 ml), then a solution of dimethyl sebacate (50 g) in tetrahydrofuran (100 ml) was added slowly. The mixture was stirred at 65° under nitrogen for 2 hr, then cooled and poured into ice and conc. aq. HCl. The precipitate was filtered, washed with sat. aq. $NaHCO_3$ and water, then dried by azeotropic distillation of the remaining water with benzene. Crystallization of this product from ethyl acetate–light petroleum afforded *1,12-bis(methylsulphonyl)dodecane-2,11-dione* (28) as needles (56 g), m.p. 128·5–129·5° (Found: C, 47·9; H, 7·6; S, 18·0. $C_{14}H_{26}O_6S_2$ requires C, 47·5; H, 7·4; S, 18·1%). I.r. spectrum (Nujol): ν_{max} 1705s (CO); 1305s and 1130s cm^{-1} (SO_2). N.m.r. spectrum ($CDCl_3$): s, 4, 4·04 (SO_2CH_2CO); s, 6, 3·04 (CH_3SO_2); t, 4, 2·69 (CH_2CO), 6·5; m, 12, 1·90–1·10 (CH_2).

(iv) A solution of 3,5-dimethoxybenzyl bromide[14] (7·0 g) in dimethyl sulphoxide (50 ml) was added to the stirred suspension prepared as in (*f*) from a solution of 1,12-bis(methylsulphonyl)-

[16] Adams, R., Loewe, S., Jelinek, C., and Wolff, H., *J. Am. chem. Soc.*, 1941, **63**, 1971.
[17] Masayuki, O., *Chem. Abstr.*, 1955, **49**, 10960.

dodecane-2,11-dione (28) (5·0 g) in dimethyl sulphoxide (50 ml) and sodium hydride (0·68 g). The mixture was stirred under nitrogen at room temperature for 1·5 hr, then at 55° for 2·5 hr. The cooled mixture was poured into ice and conc. aq. HCl and the resulting precipitate was extracted with chloroform. The extract was washed with water, sat. aq. $NaHCO_3$, and water, then dried and evaporated. The resulting pale viscous oil (10·6 g) was chromatographed on silicic acid (100 g).

The fraction eluted with ether–benzene (1 : 9) yielded a solid (3·6 g) which crystallized from ethyl acetate–light petroleum to afford *1,14-bis(3,5-dimethoxyphenyl)-2,13-bis(methylsulphonyl)-tetradecane-3,12-dione* (29) as needles, m.p. 113–115° (Found: C, 58·9; H, 7·5; S, 9·7. $C_{32}H_{46}O_{10}S_2$ requires C, 58·7; H, 7·1; S, 9·8%). ν_{max} (Nujol): 1700s (CO); 1290s and 1152s cm^{-1} (SO_2). N.m.r. spectrum ($CDCl_3$): s (b), 6, 6·35 (ArH); m, 2, 4·45–4·00 ($ArCH_2CHSO_2$); s, 12, 3·78 (OCH_3); m, 4, 3·42–3·15 ($ArCH_2CHSO_2$); s, 6, 2·93 (SO_2CH_3); m, 16, 2·90–0·90 ($COCH_2$ and CH_2).

The fractions eluted with ether–benzene (3 : 7) yielded a solid (1·71 g) which crystallized from ethyl acetate–light petroleum to afford unchanged 1,12-bis(methylsulphonyl)dodecane-2,11-dione (28) as needles, m.p. and mixed m.p. 128–129°.

(v) Zinc amalgam was prepared by shaking mossy zinc (20 g), mercuric chloride (2 g), water (30 ml), and conc. aq. HCl (1·2 ml) together for 5 min. The aqueous layer was decanted, then 1,12-bis(3,5-dimethoxybenzoyl)-1,12-bis(methylsulphonyl)dodecane (26) (1 g), water (15 ml), conc. aq. HCl (35 ml), and toluene (50 ml) were added to the amalgam. The mixture was refluxed for 4 hr, then a further portion of zinc amalgam was added. After 48 hr the reaction mixture was cooled and extracted with ether. The extract was washed with sat. aq. $NaHCO_3$ and water, then dried and evaporated. The residue (0·83 g) was dissolved in benzene and passed through a short column of silicic acid (5 g). Evaporation of the eluate and crystallization of the residue from light petroleum afforded 1,14-bis(3,5-dimethoxyphenyl)tetradecane (27) as needles (0·72 g), m.p. 64–65° undepressed on admixture with an authentic sample (lit.[3] 65–66°). The n.m.r., i.r., and mass spectra of the two samples were identical.

(vi) 1,14-Bis(3,5-dimethoxyphenyl)-2,13-bis(methylsulphonyl)tetradecane-3,12-dione (29) (0·91 g) was treated with zinc amalgam as described in (v). The crude product was purified by chromatography as before. Recrystallization of the resulting solid (0·66 g) from light petroleum then afforded 1,14-bis(3,5-dimethoxyphenyl)tetradecane (27) as needles, m.p. and mixed m.p. 64–65°.

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