

A Convenient Stereoselective Synthesis of *syn*-Bishomoquinone (Tricyclo[5,1,0,0^{3,5}]octane-2,6-dione)

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Reaction of 4,4-dimethoxycyclohexa-2,5-dienone with dimethylsulphoxonium methylide and subsequent hydrolysis gave exclusively *syn*-bishomoquinone. An attempted double addition of carbene to 3,3,6,6-tetramethoxycyclohexa-1,4-diene produced 1,4-dimethoxybenzene, 1,2,4-trimethoxybenzene, and 2,2',4,5,5'-pentamethoxybiphenyl.

A RECENT publication¹ has described the first preparation of the two bishomoquinones (tricyclo[5,1,0,0^{3,5}]octane-2,6-diones) by debromination of two isomers of 2,4,6,8-tetrabromocyclo-octane-1,5-diones. Although the *anti*-isomer was readily obtainable by this means, the *syn*-isomer was a minor product isolable only by means of a truly Swiss chromatographic separation.

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‡ We thank Dr. Vass, I.C.I. Mond Division, for a gift of this material.

We now report a convenient preparation of this latter isomer.

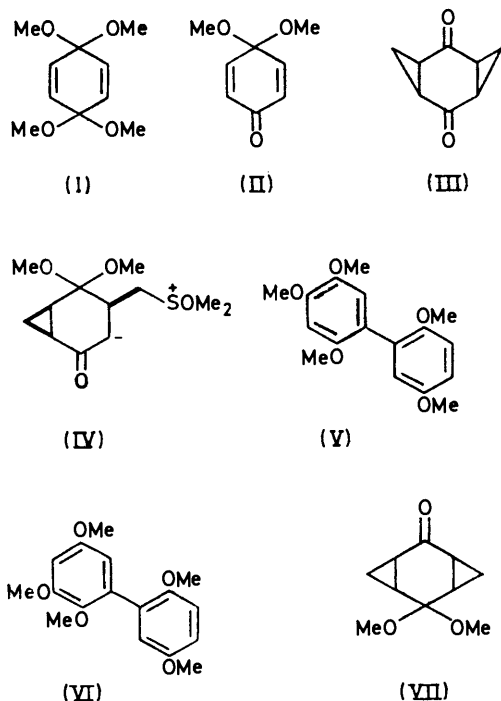
Carefully controlled hydrolysis of the readily available ‡ 3,3,6,6-tetramethoxycyclohexa-1,4-diene² (I) by water alone was found to give the acetal, 4,4-dimethoxycyclohexa-2,5-dienone (II). This cross-conjugated ketone was then subjected to the methylene-transfer

¹ J. Heller, A. Yogev, and A. S. Dreiding, *Helv. Chim. Acta*, 1972, **55**, 1003.

² B. Belleau and N. L. Weinberg, *J. Amer. Chem. Soc.*, 1963, **85**, 2525.

reagent dimethylsulphoxonium methylide.³ Hydrolysis of the resulting acetal gave a single product in high yield which was characterised as *syn*-bishomoquinone (III) by comparison with an authentic sample.* Rigorous examination revealed no trace of the *anti*-isomer. The stereoselectivity of the process may be naively rationalised by the conformation of an intermediate such as (IV); formation of (IV) under thermodynamic control would be expected to produce the energetically more favourable *cis*-1,3-diequatorial adduct.

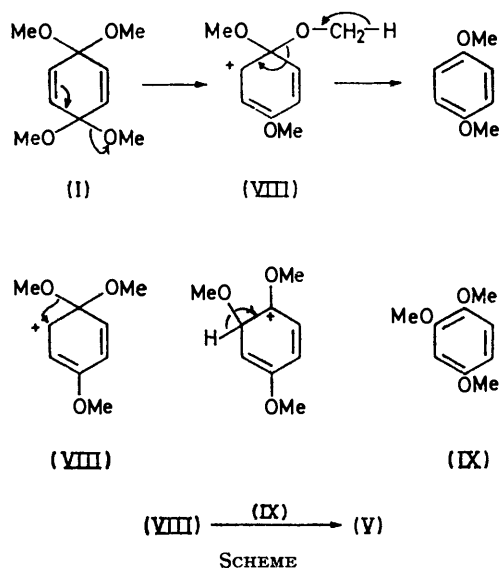
We also studied the addition of carbenes to the bis-acetal (I). Surprisingly the Simmons–Smith reaction on this compound produced three methoxylated benzenoid products only. Two of these were speedily identified as 1,4-dimethoxybenzene and 1,2,4-trimethoxybenzene. The third was a pentamethoxybiphenyl whose n.m.r. spectrum revealed an ABC system and an AB quartet (J 1.5 Hz). This, together with consideration of reasonable modes of formation, narrowed the structure down to the two possibilities, (V) and (VI); the coupling constant is acceptable for either *meta*- or *para*-coupling. The identity of the product was firmly established as (V) by unambiguous synthesis involving a crossed Ullman reaction of 2-iodo-1,4-dimethoxybenzene and 1-iodo-2,4,5-trimethoxybenzene. The same three methoxylated products were obtained from compound



(I) by the action of dichlorocarbene produced by thermal decomposition of sodium trichloroacetate but not by dibromocarbene produced by bromoform and potassium *t*-butoxide. It is tempting to suggest that the carbene in a neutral medium is acting as a Lewis acid, in keeping with its electrophilic character. Production from com-

* We thank Professor A. Dreiding for a specimen of this compound.

ound (I) of the carbonium ion (VIII) can then readily be envisaged and the formation of all three aromatic products can then be rationalised by the processes shown in the Scheme.



The action of boron trifluoride on compound (I) has been reported² to produce compounds (IX) and (V), although no evidence was presented to support the latter structure. Repetition of this reaction, and comparison of the pentamethoxybiphenyl with our sample, showed that they are identical.

EXPERIMENTAL

4,4-Dimethoxycyclohexa-2,5-dienone (II).—3,3,6,6-Tetramethoxycyclohexa-1,4-diene (5 g) dissolved in water (500 ml) was stirred at 37° in a water-bath. After 4 h, the solution was extracted with ether (400 ml); the extract was dried and evaporated to give the crude product (4.1 g). Column chromatography of the mixture on alumina gave starting material (650 mg) and the dienone (3.1 g), uncontaminated with *p*-benzoquinone; ν_{\max} (film) 1695 and 1650 cm^{-1} ; τ (CDCl_3) 3.55 (4H, q, J 10 Hz) and 6.68 (6H, s); g.l.c. on 1% APL at 150° showed components with the following retention times: 3,3,6,6-tetramethoxycyclohexa-1,4-diene, 2.50 min; 4,4-dimethoxycyclohexa-2,5-dienone, 4.40 min.

Attempted hydrolysis under literature conditions² gave only *p*-benzoquinone.

Reaction of the Dienone (II) with Dimethylsulphoxonium Methylide.—Trimethylsulphoxonium iodide (1320 mg, 6 mmol) was added carefully to a suspension of sodium hydride (150 mg, 6 mmol) in dry dimethylformamide (30 ml). The mixture was stirred at room temperature for 1 h, then 4,4-dimethoxycyclohexa-2,5-dienone (II) (308 mg, 2 mmol) in dimethylformamide (10 ml) was added during 15 min. The resulting clear solution was stirred under nitrogen for 16 h, then poured into water (100 ml); the aqueous solution was extracted with chloroform (150 ml). The extract was washed thoroughly with water and then brine (100 ml). Drying and removal of the chloroform gave the crude product (96 mg), containing two compounds

³ E. J. Corey and M. Chaykovsky, *J. Amer. Chem. Soc.*, 1962, **84**, 867.

(t.l.c.). Separation by t.l.c. (50% ethyl acetate-petroleum) afforded the less polar component (VII), ν_{CO} (CCl_4) 1690 cm^{-1} ; τ (CCl_4) 6.61 and 6.62 (6H, singlets), 8.05 (4H, m), and 8.80 (4H, m).

On attempting to remove a yellow impurity by boiling the total product in ethanol containing animal charcoal, the less polar component was converted to the more polar component (III), purified by vacuum sublimation, m.p. $100-101^\circ$ (Found: C, 70.95; H, 6.2. Calc. for $\text{C}_8\text{H}_8\text{O}_2$: C, 70.6; H, 5.9%), ν_{CO} (CCl_4) 1695 cm^{-1} ; τ (CDCl_3) 7.8 (4H, m), 8.15 (2H, m), and 8.85 (2H, m); m/e 136 (M^+), 107, 91, 79, 68, 40, and 39, and identical (g.l.c. and mixed m.p. with an authentic specimen of compound (III) supplied by Professor Dreiding.

Reaction of 3,3,6,6-Tetramethoxycyclohexa-1,4-diene with Simmons-Smith Reagent.—Zinc-copper couple (20 g) and a crystal of iodine were added to anhydrous ether (150 ml), and the mixture was stirred until the brown colour of the iodine disappeared. The diene (5 g) and freshly distilled methylene iodide (15 g) were added and the mixture was refluxed for 24 h. After cooling and filtering, the organic solution was washed with saturated ammonium chloride solution ($2 \times 100 \text{ ml}$), saturated sodium hydrogen carbonate solution (100 ml) and distilled water ($2 \times 100 \text{ ml}$). Drying and removal of the solvent afforded a crude oily product (3.2 g), which was shown by t.l.c. (30% ethyl acetate-petroleum) to consist of several components, none of which was starting material. Separation was achieved by column chromatography on silica gel with ethyl acetate-petroleum as eluant.

The major component (1.25 g) was 1,2,4-trimethoxybenzene (IX) (Found: C, 64.15; H, 7.2. Calc. for $\text{C}_9\text{H}_{12}\text{O}_3$: C, 64.25; H, 7.2%), τ (CDCl_3) 3.3–4.0 (3H, ABX multiplet), and 6.36, 6.42, and 6.45 (9H, singlets), m/e 168 (M^+), 153, 125, 110, 95, 79, 69, and 52.

The least polar component was shown to be the dimethyl ether of hydroquinone by comparison with an authentic sample.

The most polar component was 2,2',4,5,5'-pentamethoxybiphenyl (V), m.p. $120-121^\circ$ (Found: C, 66.9; H, 6.65. $\text{C}_{17}\text{H}_{20}\text{O}_5$ requires C, 67.1; H, 6.6%), τ (CDCl_3) 3.2 (3H, m), 3.23 (1H, m), 3.41 (1H, s), and 6.11–6.40 (15H, series of

five singlets), m/e 304 (M^+), 299, 258, 243, 231, 152, 126, and 115; g.l.c. on 5% QF1, temperature programming from 30° to 220° at 4° per min as follows:

Component	t_R/min	%
Hydroquinone dimethyl ether	9.5	14
1,2,4-Trimethoxybenzene	15.7	63
Pentamethoxybiphenyl	18.4	12

Ullmann Reaction.—A mixture of 2-iodo-1,4-dimethoxybenzene⁴ (250 mg) and 1-iodo-2,4,5-trimethoxybenzene⁵ (275 mg) was heated to 210° and copper-bronze (500 mg) was added in small portions. The mixture was then maintained at 230° for 30 min. After cooling, the residue was dissolved in ether (25 ml) and filtered; t.l.c. (30% ethyl acetate-petroleum) showed the presence of three components, which were separated by preparative t.l.c. The middle component was identical with the foregoing pentamethoxybiphenyl (V).

Reaction of the Tetramethoxy-diene with Sodium Trichloroacetate.—A solution of 3,3,6,6-tetramethoxycyclohexa-1,4-diene (200 mg) and anhydrous sodium trichloroacetate (1.65 g) in a mixture of tetrachloroethylene (20 ml) and dry bis-(2-methoxyethyl) ether (5 ml) was refluxed for 2 h at 130° . Excess of solvent was then distilled off under water pump pressure and a solution of the residue in ether (50 ml) was washed with brine (25 ml), dried, and evaporated. The crude product (165 mg) was shown by t.l.c. (30% ethyl acetate-petroleum) to consist of ca. ten components, some of which were minor. Preparative t.l.c. gave 1,2,4-trimethoxybenzene (70 mg), hydroquinone dimethyl ether (22 mg), and the pentamethoxybiphenyl (V) (25 mg).

Action of Boron Trifluoride-Ether Complex on the Diene (I).—This was carried out by the method of Weinberg;² the components of the crude product were separated by t.l.c. (30% ethyl acetate-petroleum) giving 1,2,4-trimethoxybenzene and the same pentamethoxybiphenyl (V), m.p. and mixed m.p. 120° .

[2/1711 Received, 20th July, 1972]

One of us (R. T.) acknowledges financial support from the S.R.C.

⁴ H. Kaufmann and I. Fritz, *Ber.*, 1908, **41**, 4416.

⁵ G. K. Hughes, K. G. Neill, and F. Ritchie, *Austral. J. Sci. Res.*, 1950, **3A**, 497.