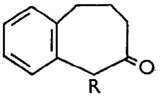
132. *Synthetical Studies Relating to Colchicine. Part II.*[1] *Diethyl* 1,2-*Benzocyclohepta*-1,3-*diene*-4-*acetate*-3-β-*propionate and its* 3′,4′,5′-*Trimethoxy-analogue.*

By T. A. CRABB and K. SCHOFIELD.

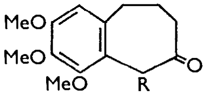
3′,4′,5′-Trimethoxy-1,2-benzocyclohepta-1,3-diene was converted by perbenzoic acid into a glycol monobenzoate which, when distilled, gave benzoic acid and 3′,4′,5′-trimethoxy-1,2-benzocyclohept-1-en-4-one. With pyrrolidine the ketone formed an enamine which reacted with ethyl acrylate to give ethyl β-(3′,4′,5′-trimethoxy-4-oxo-1,2-benzocyclohept-1-en-3-yl)propionate. This keto-ester, and the analogue lacking methoxyl groups,[1] were converted by application of the Reformatsky reaction into the diesters named in the title.

RECENTLY we described a convenient preparation of the ketone (I; R = H), and thence of the keto-ester (I; R = $[CH_2]_2{\cdot}CO_2Et$).[1] We now report the extension of these experiments to the trimethoxylated compounds (II; R = H and $[CH_2]_2{\cdot}CO_2Et$), and the use of these intermediates in synthesising the diesters named in the Title.

3′,4′,5′-Trimethoxy-1,2-benzocyclohept-1-en-4-one (II; R = H) has been obtained in three ways.[2] Of these the route from purpurogallin tetramethyl ether [2b] seemed the most likely to be adaptable for the preparation of considerable amounts of the ketone. The reduction of purpurogallin tetramethyl ether with lithium aluminium hydride, and the formation of the red solution of the cation (III) from the reduction mixture proceeded as described, but in our hands the reduction of the cation by zinc dust gave none of the desired ketone. The solid product was probably the same as the minor product described by the Swiss authors.[2b] Other workers [3] have found the reaction to be capricious, and success may well depend on the quality of the zinc dust used. We were discouraged from using Rapoport and Campion's original synthesis [2a] of the ketone by our finding that the necessary 3,4,5-trimethoxybenzaldehyde was formed in only poor and variable yield by Rosenmund reduction of 3,4,5-trimethoxybenzoyl chloride.



(I)



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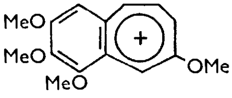

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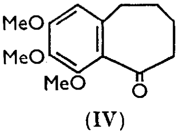

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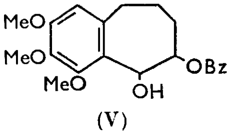

(V)

At this stage we considered the possibility of preparing the ketone (II; R = H) by the method used to obtained its prototype (I; R = H).[1] The essential starting material was the isomeric ketone (IV). A reliable, if tedious, route to this isomer has been described by Koo [4] and this we used successfully. Comments on minor points regarding this preparation will be found in the Experimental section. Reduction of the ketone (IV) with lithium aluminium hydride gave the crystalline alcohol (rather than the oily product obtained by

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[1] Part I, Crabb and Schofield, *J.*, 1958, 4276.

[2] (*a*) Rapoport and Campion, *J. Amer. Chem. Soc.*, 1951, **73**, 2239; (*b*) Eschenmoser and Rennhard, *Helv. Chim. Acta*, 1953, **36**, 290; (*c*) Walker, *J. Amer. Chem. Soc.*, 1955, **77**, 6699.

[3] Buchanan and Sutherland, *J.*, 1957, 2334.

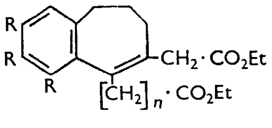
[4] Koo, *J. Amer. Chem. Soc.*, 1953, **75**, 720.

Gardner, Brandon, and Haynes [5]), which was readily dehydrated to 3′,4′,5′-trimethoxy-1,2-benzocyclohepta-1,3-diene. With perbenzoic acid in chloroform the latter did not provide an epoxide, but rather what was probably a glycol monobenzoate (V; or the isomer with hydroxyl and ester groups transposed), for this product gave, upon distillation, first benzoic acid and then the required 3′,4′,5′-trimethoxy-1,2-benzocyclohept-1-en-4-one (II; R = H) in good yield. This sequence of reactions provides a reliable, if laborious, route to the ketone (II; R = H), and it has been used to prepare the ketone in 50 g. batches.

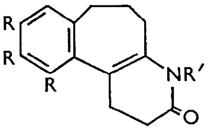
The pyrrolidine enamine from the ketone (II; R = H) reacted readily with acrylonitrile, providing the keto-nitrile (II; $R = [CH_2]_2\cdot CN$). Attempts to convert this into the keto-ester by ethanolic sulphuric acid gave only tars. However, reaction of the enamine with ethyl acrylate gave the keto-ester (II; $R = [CH_2]_2\cdot CO_2Et$) in good yield. The analogous compound (I; $R = [CH_2]_2\cdot CO_2Et$), previously prepared [1] by ethanolysis of the nitrile, was also obtained directly by use of ethyl acrylate.

Our approach to a compound containing the tricyclic colchicine skeleton envisaged the construction of compounds (VI) in which ($n = 2$ or 3) (or their saturated counterparts). In the case ($n = 3$), ring C might result from Dieckmann cyclisation, and in the case ($n = 2$) by acyloin cyclisation. The compounds (I and II; $R = [CH_2]_2\cdot CO_2Et$) have been used as sources of intermediates of the latter type.

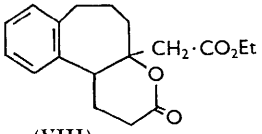
Several reactions were examined in the search for a means of appending the acetic acid side-chain at the site of the ketone group in (I and II; $R = [CH_2]_2\cdot CO_2Et$). The Wittig reaction [6] with ethoxycarbonylmethylenetriphenylphosphorane left the ester (I; $R = [CH_2]_2\cdot CO_2Et$) unchanged. Similarly this ester (I; $R = [CH_2]_2\cdot CO_2Et$) failed to react with ethyl cyanoacetate in presence of piperidine or potassium ethoxide. When the keto-esters were treated in benzene solution with ethyl cyanoacetate and ammonium acetate–acetic acid [7] products having the probable structures (VII; R = H or OMe, R′ = H) resulted. Other workers have reported similar experiences in these reactions.[8] Dev,[8] after a survey of catalysts and conditions suitable for condensations of this kind, recommended the use with keto-esters of piperidine and benzylamine. In the presence of these bases the ester (I; $R = [CH_2]_2\cdot CO_2Et$) did not react with ethyl cyanoacetate, but use of benzylamine converted the analogue (II; $R = [CH_2]_2CO_2Et$) into an amide (VII; R = OMe, $R' = CH_2Ph$). Under a large variety of further conditions useful products could not be obtained from ethyl cyanoacetate or cyanoacetic acid and either of the keto-esters.



(VI)



(VII)



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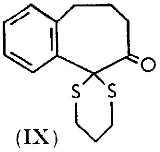

(IX)

These failures threw us back on the Reformatsky reaction. A possible complication was that of attack by the reagent on the ethoxycarbonyl group of the keto-ester,[9] and for this reason we examined the method of Grob and Brenneisen.[10] In this the organometallic reagent is prepared separately before introduction of the ketone. Under these conditions the keto-ester (I; $R = [CH_2]_2\cdot CO_2Et$) gave a 17% yield (allowance being made for recovered starting material) of the diester (VI; R = H, $n = 2$), dehydration of the alcohol

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[5] Gardner, Brandon, and Haynes, *J. Amer. Chem. Soc.*, 1957, **79**, 6334.

[6] Wittig and Schollkopf, *Chem. Ber.*, 1954, **87**, 1318.

[7] Cope, Hofmann, Wyckoff, and Hardenbergh, *J. Amer. Chem. Soc.*, 1941, **63**, 3452; Cragoe, Robb, and Sprague, *J. Org. Chem.*, 1950, **15**, 38.

[8] Pfau and Plattner, *Helv. Chim. Acta*, 1940, **23**, 768; Mukharji, *J. Indian Chem. Soc.*, 1947, **24**, 91; Dev, *ibid.*, 1953, **30**, 443.

[9] *Organic Reactions*, Vol. I, p. 4.

[10] Grob and Brenneisen, *Helv. Chim. Acta*, 1958, **41**, 1184.

initially formed occurring during distillation. The ultraviolet absorption spectrum of the diester showed it to consist predominantly of the endocyclic double-bond compound, but crude preparations may have contained small quantities of the exocyclic isomer and of the lactone (VIII). Small and variable amounts of the lactone could sometimes be isolated. Attempts to raise the yield of the diester by carrying out the Reformatsky reaction in boiling xylene gave a different, unidentified product (see Experimental section), which also resulted from application of conventional Reformatsky conditions and was certainly a mixture. The diester (V; R = H, $n = 2$) was obtained in slightly better yield (26%) by reaction of the ester (I; R = $[CH_2]_2{\cdot}CO_2Et$) with ethoxyethynylmagnesium bromide.[11] The somewhat higher intensity of the ultraviolet absorption shown by this product, compared with material from the Reformatsky reaction, suggested that the former was exclusively the endocyclic isomer.

In view of these results, it was pleasantly surprising to find that the Reformatsky reaction, in Grob and Brenneisen's modification,[10] converted the keto-ester (II; R = $[CH_2]_2{\cdot}CO_2Et$) into the diester (V; R = OMe, $n = 2$) in 57% yield. Again the double bond was in the endocyclic position.

We are attempting the cyclisation of the diesters described above, and the synthesis of their higher homologues.

It is convenient to report here another sequence of reactions attempted with 1,2-benzocyclohept-1-en-4-one. We described earlier[1] the conversion of this ketone into an aldehyde (I; R = CHO). This compound, with propane-1,3-dithiol ditoluene-*p*-sulphonate,[12] gave the dithioketal (IX). Attempts to nitrosate this compound failed; it did not react with pentyl nitrite–sodium ethoxide or sodium nitrite–acetic acid, and pentyl nitrite–hydrogen chloride merely liberated sulphur.

EXPERIMENTAL

Reduction of Purpurogallin Tetramethyl Ether.—To a suspension of purpurogallin tetramethyl ether (7·5 g.) in absolute ether (100 ml.) was added dropwise during 20 min. a suspension of lithium aluminium hydride (1·3 g.) in ether (150 ml.). The mixture was stirred at 0° for 3 hr. and then for 30 min. at room temperature. Ice-water was then added, followed by 25% sulphuric acid (200 ml.). The ether solution was extracted with 25% sulphuric acid (3 × 50 ml.), and the combined acid solutions were washed with ether. During 1 hr. zinc dust was added portionwise, with stirring, to 25% sulphuric acid (100 ml.) maintained at 40° in a 3-necked flask. Simultaneously the deep red sulphuric acid solution from the first part of the preparation was added dropwise. The mixture was set aside for 15 min. at room temperature and then filtered from undissolved zinc. The filtrate was extracted thoroughly with ether. Removal of the ether gave a viscous brown oil (3·5 g.), which deposited crystals (2 g.) on trituration with ether–light petroleum (b. p. 40—60°). These separated from ether, then having m. p. 175—177° (Found: C, 67·5; H, 6·4; CH_3O, 45·1%), $\lambda_{max.}$ 315 mμ in 95% ethanol, and strong infrared bands (in carbon tetrachloride) at 3028, 2972, 2867, 1636, 1481, 1452, 1394, 1345, 1166, 1131, 1095, and 923 cm.$^{-1}$.

3′,4′,5′-Trimethoxy-1,2-benzocyclohept-1-en-3-one.—The following observations relate to some of the steps in Koo's preparation of this ketone.[4] 3,4,5-Trimethoxybenzoyl chloride was obtained from the acid by the action of phosphorus pentachloride.[13] The average yield of 15 preparations was 55%. In distillations of quantities greater than 100 g., sudden decomposition often occurred with evolution of hydrogen chloride and formation of a black pitch. This occurred only very rarely with smaller quantities.

To obtain moderate-to-good yields of ethyl β-(3,4,5-trimethoxybenzoyl)acetoacetate strict adherence to Koo's procedure[4] was essential, with the use of freshly prepared absolute ethanol and freshly distilled acid chloride. In nine experiments on the 100—200 g. scale the average yield was 65% (Koo claimed 90%).

For converting the acetoacetate into ethyl 3,4,5-trimethoxybenzoylacetate it was essential to grind the former very finely and to shake the reaction mixture very vigorously (yield, 86%).

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[11] Raphael, "Acetylenic Compounds in Organic Synthesis," Butterworths, London, 1955, p. 82.
[12] Woodward, Patchett, Barton, Ives, and Kelly, *J.*, 1957, 1131.
[13] Perkin and Weizmann, *J.*, 1906, 1649.

*3′,4′,5′-Trimethoxy-*1,2-*benzocyclohept*-1-*en*-3-*ol.*—The ketone (15 g.) in ether (500 ml.) was added during 1½ hr. to a stirred mixture of lithium aluminium hydride (7 g.) in ether (500 ml.). After being boiled for 1 hr. the mixture was decomposed with water and dilute sulphuric acid. The usual methods gave the *alcohol* (13 g.), which formed needles, m. p. 170° (Found: C, 66·9; H, 7·2. $C_{14}H_{20}O_4$ requires C, 66·7; H, 8·0%), from ether.

*3′,4′,5′-Trimethoxy-*1,2-*benzocyclohepta*-1,3-*diene.*—Dehydration of the alcohol[5] gave an oil, b. p. 120°/0·3 mm., in 68% yield.

*3′,4′,5′-Trimethoxy-*1,2-*benzocyclohept*-1-*en*-4-*one.*—The foregoing diene (10 g.), in chloroform (50 ml.), was treated with perbenzoic acid (7 g.) in chloroform (250 ml.) at 0—5°. The reaction was complete in 2 hr.; then the solution was washed with N-sodium hydroxide and with water, and dried (Na_2SO_4). Concentration gave a viscous oil [strong peaks at 3530 (OH) and 1716 cm.$^{-1}$ (ester)], which on distillation gave benzoic acid and the ketone (7 g.), b. p. 150°/0·1 mm. [a liquid film gave strong peaks at 2966, 2855, 1706 (C=O), 1598, 1494, 1120, and 990 cm.$^{-1}$], which during cold weather crystallised and had m. p. 46—47°. The 2,4-dinitrophenylhydrazone formed silky yellow needles, m. p. 177—178° (Found: C, 55·4; H, 5·4. Calc. for $C_{20}H_{22}O_7N_4$: C, 55·8; H, 5·2%), from methanol (reported,[2] m. p. 177—178°).

3-(2-*Cyanoethyl*)-3′,4′,5′-*trimethoxy*-1,2-*benzocyclohept*-1-*en*-4-*one.*—The ketone (2 g.) was boiled under reflux with pyrrolidine (0·8 g.) in benzene (20 ml.), in an apparatus provided with a water-separator. The mixture was boiled for 2 hr. and the benzene was then removed under reduced pressure. The crude enamine was dissolved in dioxan (20 ml.) and boiled with acrylonitrile (2 g.) for 2 days. Water was added to the cooled mixture which was then kept overnight, before being extracted with chloroform. Removal of the chloroform, followed by distillation of the crude residue (2·2 g.), gave starting ketone (0·7 g.) and an oil (1 g.), b. p. 150°/0·1 mm. On trituration with ether–light petroleum this gave the required *keto-nitrile* (0·6 g., 24%) as platelets, m. p. 92—93° (Found: C, 66·9; H, 7·2. $C_{17}H_{21}O_4N$ requires C, 67·3; H, 7·0%), from ether.

Ethyl β-(3′,4′,5′-*Trimethoxy*-4-*oxo*-1,2-*benzocyclohept*-1-*en*-3-*yl*)*propionate.*—The pyrrolidine-enamine from 3′,4′,5′-trimethoxy-1,2-benzocyclohept-1-en-4-one (10 g.) was boiled for 48 hr. with ethyl acrylate (15 g.) in dioxan (100 ml.). Water was added to the cooled solution, and the mixture was left. Working up as described above gave the desired *keto-ester* (9·5 g., 68%), b. p. 175°/0·1 mm., n_D^{20} 1·5262 (Found: C, 65·6; H, 7·2. $C_{19}H_{26}O_6$ requires C, 65·1; H, 7·5%), $\lambda_{max.}$ (in 95% ethanol) at 280 mμ (log ε 3·17), strong infrared bands (liquid film) 1736 (ester) and 1710 cm.$^{-1}$ (C=O). The 2,4-*dinitrophenylhydrazone* crystallised as yellow needles, m. p. 127° (Found: C, 57·7; H, 5·3. $C_{25}H_{30}O_9N_4$ requires C, 56·6; H, 5·7%), from methanol.

Ethyl β-(4-*Oxo*-1,2-*benzocyclohept*-1-*en*-3-*yl*)*propionate.*—The pyrrolidine-enamine from 1,2-benzocyclohept-1-en-4-one (20 g.)[1] was boiled with ethyl acrylate (30 g.) in dioxan (200 ml.) for 60 hr. The mixture was shaken with water (200 ml.) and kept at room temperature overnight. Extraction with ether, followed by distillation, gave the keto-ester (15 g.), identical with the compound previously described,[1] and starting ketone (6 g.).

The Lactams (VII).—(*a*) Ethyl β-(4-oxo-1,2-benzocyclohept-1-en-3-yl)propionate (5·2 g.), ethyl cyanoacetate (6 g.), ammonium acetate (0·3 g.), acetic acid (4 ml.), and benzene (20 ml.) were boiled under reflux for 20 hr. in an apparatus fitted with a water-separator. Water was then added, the mixture was extracted with ether, and the extract was dried (Na_2SO_4). Evaporation gave the *lactam* (0·34 g.) (VII; R = R′ = H) which formed needles, m. p. 190° (Found: C, 78·6; H, 7·5; N, 7·0. $C_{14}H_{15}ON$ requires C, 78·8; H, 7·1; N, 6·6%), from ethanol [$\lambda_{max.}$ 286 mμ (log ε 4·4) in 95% ethanol; $\nu_{max.}$ 1680s and 1650s cm.$^{-1}$]. The remaining material from the experiment was the starting ester.

(*b*) A similar experiment using the trimethoxy-keto-ester gave the *lactam* (VII; R = OMe, R′ = H), which separated from ethanol as needles, m. p. 194—195° (Found: C, 67·1; H, 6·9; N, 4·8. $C_{17}H_{21}O_4N$ requires C, 67·3; H, 7·0; N, 4·6%), $\lambda_{max.}$ 287 mμ (log ε 4·6) in 95% ethanol.

(*c*) The trimethoxy-keto-ester (2 g.), ethyl cyanoacetate (1·3 g.), benzene (20 ml.), benzylamine (0·5 ml.), and acetic acid (0·5 ml.) were heated under reflux for 2 hr. with use of a water-separator. The solution was washed with hydrochloric acid and water, and then dried (Na_2SO_4). Distillation gave a viscous oil (0·9 g.), b. p. 190—210°/0·3 mm. From ethanol it gave needles of the *benzyl lactam*, m. p. 149° (Found: C, 73·5; H, 7·0; N, 3·5. $C_{25}H_{27}O_4N$ requires C, 74·0; H, 6·7; N, 3·5%), $\lambda_{max.}$ 285 mμ (log ε 4·31) in 95% ethanol, $\nu_{max.}$ 1670s and 1620s cm.$^{-1}$.

Diethyl 1,2-*Benzocyclohepta*-1,3-*diene*-4-*acetate*-3-β-*propionate.*—(*a*) Ethyl bromoacetate (3·4 g.) in 1 : 1 ether–benzene (5 ml.) was added dropwise to finely divided zinc (1 g.) stirred in benzene (20 ml.). After two-thirds of the bromo-ester had been added, zinc (0·5 g.) was added followed by the same amount when all the ester had been admitted. The mixture was heated under reflux for 2 hr., cooled to 20°, and treated dropwise with the keto-ester (2·6 g.). Boiling was carried on for 3 hr. more. The mixture was poured on ice and dilute sulphuric acid, and extracted with ether. Distillation of the washed and dried extract gave starting material (1·2 g.) and a viscous oil (0·2 g.), b. p. 180—185°/0·1 mm. The latter, when triturated with ether, deposited the *lactone* (VIII) (50 mg.), which formed needles (from ether), m. p. 108° (Found: C, 71·8; H, 7·3; OEt, 14·4. $C_{18}H_{22}O_4$ requires C, 71·5; H, 7·3; OEt, 14·9%), $\lambda_{max.}$ 263 mμ (log ε 2·51) in 95% ethanol, $\nu_{max.}$ 1732s cm.$^{-1}$ in carbon tetrachloride. Redistillation of the residue from the lactone gave the *diester*, b. p. 180—185°/0·1 mm., n_D^{18} 1·5390 (Found: C, 71·7; H, 7·3. $C_{20}H_{26}O_4$ requires C, 72·7; H, 7·9%), $\lambda_{max.}$ 258 mμ (log ε 3·68) in 95% ethanol, $\nu_{max.}$ 1734s cm.$^{-1}$ with a subsidiary band at 1714 cm.$^{-1}$ (liquid film).

Increasing the reaction time did not affect the yield of diester. In five preparations on 7·8 g. batches of the keto-ester the average recovery of keto-ester was 5 g. and the average yield of diester was 0·6 g. (6% conversion, 17% yield).

(*b*) Activated zinc (4 g.), keto-ester (4 g.), ethyl bromoacetate (2·8 g.), benzene (25 ml.), and a crystal of iodine were boiled for 3 hr. Three additions of zinc (3 × 2 g.) and ethyl bromoacetate (3 × 2 g.) were made at hourly intervals and, after the final addition, boiling was continued for a further 3 hr. Working up as before gave the diester (0·5 g.), b. p. 180—184°/0·5 mm. No keto-ester was recovered but an oil (2·6 g.), b. p. 152°/0·1 mm., n_D^{17} 1·5620 (Found: C, 80·1; H, 8·1%), was obtained. The oil, which was also formed when the reaction was carried out as in (*a*) but in xylene, showed $\lambda_{max.}$ 231—240 mμ in 95% ethanol, and strong bands at 1726, 1707, and 1671 cm.$^{-1}$. With 2,4-dinitrophenylhydrazine the oil (0·4 g.) gave a dark-red product (0·4 g.; m. p. 75—88°). The ethanol-soluble portion of this product separated from that solvent as yellow-orange needles (0·2 g.), m. p. 188° (Found: C, 63·6; H, 5·3; N, 14·2%). The ethanol-insoluble portion gave dark-red crystals (0·06 g.), m. p. 190° (Found: C, 63·5; H, 4·1%), from chloroform–ethanol. Neither of these derivatives showed ester bands in the infrared spectrum (Nujol mull).

(*c*) Ethoxyacetylene (1·3 g.) in ether (10 ml.) was added to ethylmagnesium bromide [from magnesium (0·4 g.)] in dry ether (20 ml.), and the mixture was boiled for 2½ hr. After the mixture had been cooled, the keto-ester (4 g.) in ether (10 ml.) was added during 30 min. Boiling was continued for 2 hr., during which the mixture became almost solid. It was cooled to 0°, decomposed with aqueous ammonium chloride, and extracted with ether. The extract (200 ml.) was shaken with 10% sulphuric acid (100 ml.) for 10 min. Distillation of the washed and dried ether layer gave unchanged keto-ester (2·8 g.) and the diester (0·4 g.), b. p. 192°/0·5 mm., n_D^{18} 1·5452 (Found : C, 72·5; H, 7·7%), $\lambda_{max.}$ 258 mμ (log ε 3·74) in 95% ethanol.

The diester (0·2 g.) was boiled for 3 hr. with potassium hydroxide (1 g.) in 1 : 1 ethanol–water (10 ml.). Acidification with dilute hydrochloric acid and ether-extraction gave the *diacid* which formed needles (from ether), m. p. 220° (decomp.) (Found: C, 68·3; H, 6·7. $C_{16}H_{18}O_4,\frac{1}{2}H_2O$ requires C, 68·1; H, 6·7%), $\lambda_{max.}$ 260 mμ (log ε 4·04) in 95% ethanol.

Similar hydrolysis of the diester from the Reformatsky reaction gave a waxy oil (0·15 g.). Trituration with ether–light petroleum (b. p. 40—60°) at 0° gave a solid (0·06 g.) which formed needles, m. p. 84° (Found: C, 65·9; H, 7·0. $C_{16}H_{20}O_5$ requires C, 65·7; H, 6·9%), from ether. This compound was probably the *hydroxy-diacid* corresponding to the lactone described above. The residual oil showed $\lambda_{max.}$ 260 mμ (log ε 3·52) in 95% ethanol.

Diethyl 3′,4′,5′-Trimethoxy-1,2-benzocyclohepta-1,3-diene-4-acetate-3β-propionate.—Ethyl bromoacetate (4 g.), zinc (3 g.), benzene (20 ml.), and a crystal of iodine were boiled and stirred, and three additions of ethyl bromoacetate (3 × 1 g.) and zinc (3 × 1 g.) were made at hourly intervals. Boiling was continued for 2 hr. more, and the keto-ester (9 g.) in benzene (10 ml.) was added dropwise. After 5 hr. more of boiling, the usual working up gave an oil which underwent dehydration (as shown by rise in pressure) on distillation, leaving the *diester* (6·2 g.), b. p. 220°/0·3 mm., n_D^{17} 1·5455 (Found: C, 66·3; H, 7·3. $C_{23}H_{32}O_7$ requires C, 65·7; H, 7·7%), $\lambda_{max.}$ 272 mμ (log ε 3·75) in 95% ethanol, $\nu_{max.}$ 1728s cm.$^{-1}$.

The Dithio-ketal (IX).—The formyl compound (I; R = CHO) (0·5 g.), propane-1,3-dithiol ditoluene-*p*-sulphonate (1·6 g.), anhydrous potassium acetate (2·3 g.), and absolute ethanol (32 ml.) were boiled for 7 hr. and then kept at room temperature overnight. Ethanol was removed under reduced pressure and the residue was dissolved in water and extracted with ether. Removal of the ether gave an oil (1·2 g.) which was passed, in benzene solution, over alumina. Removal of the benzene gave the *dithio-ketal* (0·4 g.) which formed platelets, m. p. 96—97·5° (Found: C, 64·4; H, 6·2. $C_{14}H_{16}OS_2$ requires C, 63·6; H, 6·1%), from ethanol.

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