

Some Attempts to use the Modified Acyloin Reaction of Schröppler and Rühlmann for the Synthesis of Strained Carbocyclic Systems

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Dimethyl *trans*-cyclopropane-1,2-diacetate (I) and dimethyl *trans*-oct-4-ene-1,8-dioate (II) failed to undergo cyclisation under the conditions of the modified acyloin reaction. Dimethyl *cis*- and *trans*-cyclopropane-1,2-dicarboxylate underwent reductive cleavage with formation of 1,5-dimethoxy-1,5-bis(trimethylsilyloxy)penta-1,4-diene (IV).

SINCE the discovery of Schröppler and Rühlmann¹ that yields in the acyloin condensation could be significantly improved by trapping the intermediate enediolate dianion with chlorotrimethylsilane, the method has been used extensively. Particularly noteworthy applications are the cyclisation of succinate esters to cyclobutane derivatives, even in strained situations.² We have attempted to employ this modified acyloin condensation to a number of esters where cyclisation to strained carbocyclic systems might have occurred. Although the results are mainly negative, they may serve to indicate the scope of the reaction.

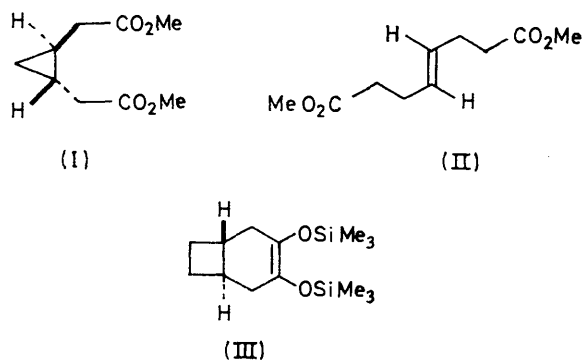
Two cases which failed completely (starting material was recovered efficiently under a variety of reaction conditions) were those of dimethyl *trans*-cyclopropane-

1,2-diacetate (I) and dimethyl *trans*-oct-4-ene-1,8-dioate (II). In the former, it was hoped that a *trans*-fused bicyclo[4.1.0]heptane derivative might be produced, and in the latter the possibility of formation of a *trans*-cyclo-octene was entertained. It is unprofitable to speculate on the reasons for these failures. Control experiments were carried out, involving the efficient cyclisation of diethyl succinate and diethyl adipate, respectively, to minimise the likelihood that we were simply failing to achieve the right reaction conditions. Furthermore, cyclisation of dimethyl *trans*-cyclobutane-1,2-diacetate to give the bistrimethylsilyl ether (III) appeared to be partially successful.

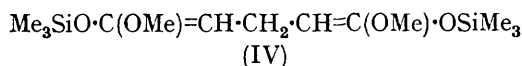
¹ (a) U. Schröppler and K. Rühlmann, *Chem. Ber.*, 1964, **97**, 1383; (b) K. Rühlmann, *Synthesis*, 1971, 236.

² J. J. Bloomfield, *Tetrahedron Letters*, 1968, 587, 591; J. J. Bloomfield, R. A. Martin, and J. M. Nelke, *J.C.S. Chem. Comm.*, 1972, 96; G. E. Gream and S. Worthley, *Tetrahedron Letters*, 1968, 3319.

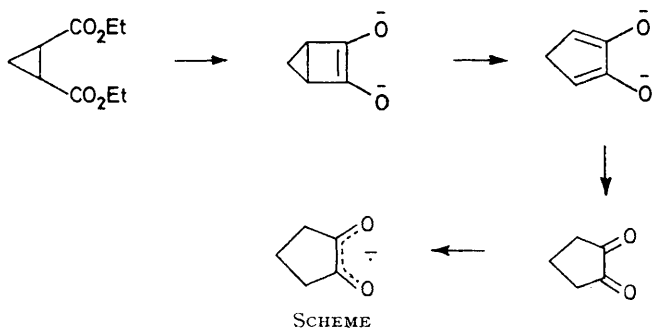
We also investigated the behaviour of *cis*- and *trans*-dimethyl cyclopropane-1,2-dicarboxylate under the conditions of the modified acyloin reaction. In both cases



the bis-enol trimethylsilyl ether (IV) was obtained in moderate yield. Structure (IV) was assigned on the basis of spectroscopic data together with the chemical evidence that methanolysis gave dimethyl glutarate and treatment with deuteriomethanol gave dimethyl [2,4-²H₂]glutarate. Mixed keten acetals of this sort have been isolated previously^{1b,3} and, after the present work was completed, Gassman and Creary briefly reported the same reaction.⁴ Presumably, cleavage of the cyclopropane ring occurs at the radical anion stage, and after addition of a second electron the resulting ester enolate dianion is trapped by chlorotrimethylsilane.



In the light of this reductive cleavage reaction, the suggestion by Russell *et al.*⁵ that cyclopentane-1,2-semidione (detected by e.s.r.) is formed by the Scheme



shown from diethyl *cis*-cyclopropane-1,2-dicarboxylate, involving a bicyclo[2.1.0]pent-2-ene intermediate, appears improbable. A more likely alternative involves initial cleavage, then protonation to give diethyl glutarate, followed by conventional cyclisation to the five-membered semidione.

³ Y.-N. Kuo, F. Chen, C. Ainsworth, and J. J. Bloomfield, *Chem. Comm.*, 1971, 136.

⁴ P. G. Gassman and X. Creary, *J.C.S. Chem. Comm.*, 1972, 1214.

⁵ G. A. Russell, J. J. McDonnell, P. R. Whittle, R. S. Givens, and R. G. Keske, *J. Amer. Chem. Soc.*, 1971, **93**, 1452.

EXPERIMENTAL

Dimethyl trans-Cyclopropane-1,2-diacetate.—A zinc-copper couple⁶ (16.5 g, 0.25 g atom), a crystal of iodine, and methylene iodide (53.6 g, 0.20 mol) in anhydrous ether (100 ml) were slowly stirred with external heating until bubbles were evolved from the surface of the couple. Heating was discontinued and the reaction was allowed to proceed. When the exothermic reaction was complete, dimethyl *trans*-hex-3-ene-1,6-dioate⁷ (10.0 g, 0.06 mol) and more methylene iodide (40.0 g; 0.35 mol total) in anhydrous ether (50 ml) were added to the pre-formed reagent. The mixture was stirred and heated under reflux for 2 days after which the red-brown solid was filtered off. The ethereal solution was then washed successively with cold aqueous hydrochloric acid, water, and saturated brine. Evaporation of the dried (MgSO₄) solution gave a residue which was shown by n.m.r. to contain the excess of methylene iodide, 67% of unchanged starting material, and 33% of the dimethyl *trans*-cyclopropane-1,2-diacetate. This material was recycled twice more and finally distillation gave a pale yellow liquid (7.2 g), b.p. 98–100° at 20 mmHg, that contained 67% of the desired ester (n.m.r., g.l.c.).

The mixture of esters was dissolved in carbon tetrachloride (20 ml) and the solution was cooled to –20 to –25° in an acetone–solid carbon dioxide bath. Meanwhile ozone was bubbled through the solution until a blue colouration was observed. The excess of ozone was removed by bubbling nitrogen through the solution. Sodium hydroxide solution (10% w/w aqueous; 10 ml) was added to decompose the ozonide and the mixture was allowed to warm to 20°. The organic layer was separated, washed with water and saturated brine solution, dried (MgSO₄), and evaporated. Distillation then gave a liquid (3.5 g), b.p. 98–100° at 2 mmHg, which was shown by n.m.r. to consist of a mixture of the dimethyl and diethyl esters of *trans*-cyclopropane-1,2-diacetic acid.

Transesterification of the mixed esters (3.5 g) was accomplished by heating under reflux with methanolic sodium methoxide. Isolation in the usual way gave dimethyl *trans*-cyclopropane-1,2-diacetate (2.0 g, 20%), b.p. 87–89° at 3 mmHg, τ (CCl₄) 6.37 (6H, s, CH₃), 7.75–7.85 (4H, q, CH₂), 8.90–9.32 (2H, m, cyclopropane CH), and 9.48–9.70 (2H, m, cyclopropane CH₂), one peak on g.l.c. (15% PEGS; 147°).

Attempted Acyloin Cyclisation of Dimethyl trans-Cyclopropane-1,2-diacetate.—In a 250 ml flask fitted with nitrogen inlet, condenser, and separating funnel, was placed freshly powdered sodium (4.0 g, 0.17 g atom) in anhydrous benzene (100 ml). A constant flow of oxygen-free nitrogen was maintained throughout the reaction. The temperature of the mixture was increased to 80° and a solution of dimethyl *trans*-cyclopropane-1,2-diacetate (8.0 g, 0.04 mol) and chlorotrimethylsilane (18.6 g, 0.17 mol) in benzene (100 ml) was added. The mixture was gently stirred and heated under reflux for 7 days after which the solid material was carefully filtered off. The filtrate was concentrated and the residue was distilled *in vacuo*. The starting material was recovered quantitatively. The Table lists other conditions which were used. In all cases starting material was recovered.

⁶ R. S. Shank and H. Schechter, *J. Org. Chem.*, 1959, **24**, 1825.

⁷ R. P. Linstead, L. N. Owen, and R. F. Webb, *J. Chem. Soc.*, 1953, 1225.

Diester (mol)	Sodium (g atom)	Potassium (g atom)	Solvent	Temperature
0.04	0.17		Benzene	Reflux
0.05	0.20		Toluene	Reflux
0.04	0.13	0.07	Benzene	Room
0.05	0.30	0.10	Toluene	Reflux
—	0.02	0.01	Benzene	Reflux

Acyloin Reaction on Dimethyl trans-Cyclobutane-1,2-diacetate.—To a stirred suspension of freshly powdered sodium (1.5 g, 0.065 g atom) in anhydrous benzene (10 ml) was added a solution of the dimethyl ester⁸ (4.8 g, 0.024 mol) and chlorotrimethylsilane (6.0 g, 0.056 mol) in anhydrous benzene (10 ml). The mixture was then stirred and refluxed under oxygen-free nitrogen for 4 days, after which the sodium chloride was filtered off. Removal of the solvent and vacuum distillation gave material (1.5 g), b.p. 86—88° at 1 mmHg, whose properties showed the presence of trimethylsilyl groups [ν_{\max} (film) 880—830 cm^{-1} (OSiMe), τ (CCl₄) 9.85—9.93 (m, OSiMe₃)] and also the presence of some starting diester, τ 6.43 (s, CO₂Me).

A solution of this material (1.5 g) in methanol (20 ml) was heated for 4 h under nitrogen. After removal of the methanol by distillation, vacuum distillation gave a fraction (0.14 g), b.p. 75—76° at 1.3 mmHg, ν_{\max} (film) 3460—3420 cm^{-1} (OH), 1700—1740 (CO), and 1375—1070 cm^{-1} (C—O str.), τ (CCl₄) 6.43 (s, OCH₃), 7.61—7.66 (m, CH₂), and 8.00—8.40 (m, cyclobutane), indicating the presence of the acyloin and the starting diester. The mass spectrum showed a very strong peak at *m/e* 140 corresponding to the parent ion of the acyloin.

1,5-Dimethoxy-1,5-bis(trimethylsilyloxy)penta-1,4-diene (IV).—(a) To a stirred suspension of freshly powdered sodium (5.5 g, 0.24 g atom) in dry benzene (100 ml) was added a mixture of dimethyl *trans*-cyclopropane-1,2-dicarboxylate⁹ (10.0 g, 0.06 mol) and chlorotrimethylsilane (27.1 g, 0.24 mol) in dry benzene (20 ml). The mixture was stirred and heated under reflux in an atmosphere of oxygen-free nitrogen for 4 days, after which all the sodium had reacted. The sodium chloride was filtered off and the filtrate was concentrated. Distillation gave the

⁸ E. Casadevall, C. Largeau, and P. Moreau, *Bull. Soc. chim. France*, 1968, 1514.

bis-enol ether (IV) (7.1 g, 39%), b.p. 98—104° at 0.65 mmHg (Found: C, 51.0; H, 9.2. C₁₃H₂₈O₄Si₂ requires C, 51.25; H, 9.25%), ν_{\max} (film) 1665s (C=C), 1250—1060 (several strong broad peaks, CO str), 980m, and 900—840br (OSiMe₃) cm^{-1} , τ (CCl₄) 6.38—6.48 (2H, m, —CH=C), 6.57 (6H, s, CH₃), 7.40—7.85 (2H, m, CH₂), and 9.75—9.95 (18H, m, 2 OSiMe₃). Another fraction (3.9 g), b.p. 92—98° at 0.65 mmHg, of similar material was obtained.

(b) In a similar way dimethyl *cis*-cyclopropane-1,2-dicarboxylate^{5,10} gave the bistrimethylsilyl ether (25%), identical with material prepared in (a).

Dimethyl Glutarate.—1,5-Dimethoxy-1,5-bis(trimethylsilyloxy)penta-1,4-diene (7.1 g, 0.02 mol) was added dropwise to anhydrous methanol (50 ml). The solution was heated under reflux in an atmosphere of nitrogen for 2 h. Removal of the methanol and distillation of the residue gave dimethyl glutarate (1.9 g, 51%), b.p. 71—73° at 0.8 mmHg, as shown by comparison (i.r., n.m.r., g.l.c.) with an authentic sample prepared from glutaric acid.

Deuteriolysis of 1,5-Dimethoxy-1,5-bis(trimethylsilyloxy)penta-1,4-diene.—The silyl ether (0.04 g) was added to tetradeuteriomethanol (0.5 ml) and an n.m.r. spectrum was recorded immediately after mixing. The mixture was then heated in a sealed tube at 60—64° for 4 h and a second n.m.r. spectrum was recorded. The two spectra were identical, and corresponded to that expected for dimethyl [2,4-²H₂]glutarate: τ (CD₃OD) 6.45 (6H, s, 2 CH₃), 7.63—7.85 (2H, m, 2 CHD·C=O), and 8.06—8.32 (2H, m, CH₂).

In a control experiment the n.m.r. spectrum of dimethyl glutarate (0.08 g) in tetradeuteriomethanol (0.5 ml) was recorded immediately upon mixing and after heating the solution at 60—64° for 4 h. The spectra were identical: τ (CD₃OD) 6.45 (6H, s, 2 CH₃), 7.60—7.82 (4H, m, 2 CH₂·C=O), and 8.08—8.35 (2H, m, CH₂).

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⁹ A. T. Blomquist and D. L. Longone, *J. Amer. Chem. Soc.*, 1959, **81**, 2012.

¹⁰ G. Bonavent, M. Causse, M. Guitard, and R. Fraissé-Jullien, *Bull. Soc. chim. France*, 1964, 2462.