Triacetic Acid[†] Lactone and 2,6-Dimethyl-γ-pyrone as Polyketide Synthons: Syntheses of Torachrysone and Eleutherinol Derivatives

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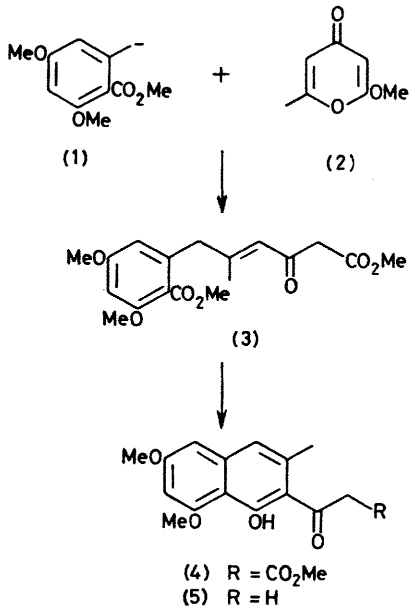
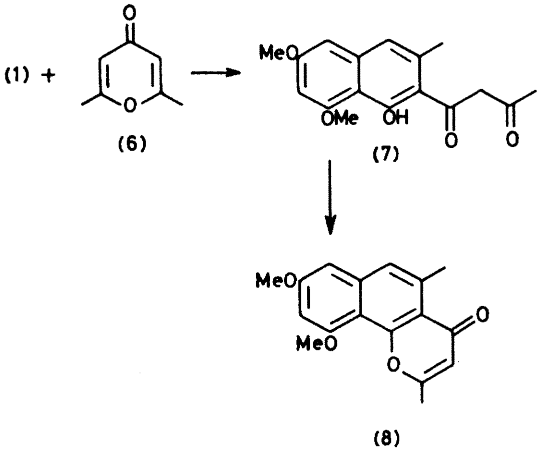
Summary Derivatives of torachrysone and eleutherinol have been made by reaction of a carbanion of an orsellinic acid derivative with γ-pyrones.

[†] 4-Hydroxy-6-methylpyran-2-one.

In the preceding communication we described the reaction of the anion (**1**) with a methyl ether of triacetic acid lactone† to give a product resulting from Michael addition rather than direct attack at the carbonyl group. In the hope that Michael addition might be the normal mode of attack of this benzylic carbanion with pyrones, we have investigated the possibility of altering the site of the attack on the triacetic acid lactone nucleus by using the isomeric methyl ether (**2**).[1]



The addition of (**1**) to (**2**) in tetrahydrofuran (THF) at −78 °C for 3 h is essentially regiospecific leading, after work-up with 2% sulphuric acid, to the formation of (**3**), the product of attack at C-6 of the triacetic acid lactone nucleus. The compound existed in solution as a tautomeric mixture of enol and keto forms and so the structure could not be rigorously established from its spectroscopic properties. Fortunately, the following reactions which were carried out to demonstrate its synthetic potential, incidentally confirm the assigned structure. Treatment of (**3**) with lithium di-isopropylamide (3 equiv.) in THF at −15 °C followed by warming to room temperature and acidification with 2% sulphuric acid after 20 min gave (**4**)‡ (70%; m.p. 105 °C, decomp.) This naphthalene derivative can be prepared more conveniently by allowing the mixture produced by reaction of (**1**) with (**2**) to warm to room temperature so that the intermediate (**3**) cyclizes *in situ* in the presence of excess of base. When treated with 6N-hydrochloric acid in methanol under reflux for 45 min (**4**) undergoes hydrolysis and decarboxylation to give a product (m.p. 94—98 °C) which had spectroscopic properties identical to those reported[2] for torachrysone methyl ether (**5**), a constituent of the seeds of *Karwinskia humboldtiana.*



This is the fourth class of polyketide structure which has been prepared in this and preceding communications by reaction of the carbanion (**1**) with variously methylated derivatives of triacetic acid lactone. The success of these syntheses has hinged on the strong tendency of the anion to add 1,4- rather than 1,2- to the enone system. This tendency is further demonstrated in the reaction of (**1**) with 2,6-dimethyl-γ-pyrone (**6**). As in the reaction with (**2**) the addition is virtually regiospecific to give (**7**), the product of Michael addition at −78 °C followed by a cyclization on warm up (79%). On treatment with trifluoracetic acid at room temperature for 30 min this diketone was converted into (**8**), the dimethyl ether of eleutherinol,‡ (89%), m.p. 185—187 °C (lit.,[3] 186—186·5 °C).

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‡ For this compound n.m.r., u.v., i.r., and mass spectra as well as microanalysis or high resolution mass measurement were in agreement with the assigned structure.

[1] P. Beak and J. K. Lee, *J. Org. Chem.*, 1978, **43**, 1367.
[2] S. Shibata, E. Morishita, M. Kaneda, Y. Kimura, M. Takido, and S. Takahashi, *Chem. and Pharm. Bull.* (*Japan*), 1969, **17**, 454.
[3] H. Frei and M. Schmid, *Annalen*, 1957, **603**, 169.