Thiolan and Monothio-β-diketone Formation through the Use of a Nucleo-electrophilic Thiating Agent

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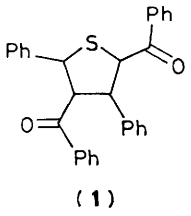
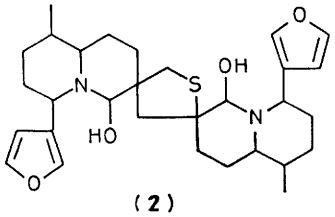
While the treatment of chalcone with anhydrous sodium polysulphide in anhydrous ethanol gave 2,4-dibenzoyl-3,5-diphenylthiolan, which was dehydrogenated to the corresponding thiophen for structure confirmation, the same two reactants in anhydrous 1,2-dimethoxyethane gave 1,3-diphenyl-3-thioxopropan-1-one.

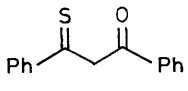
The significance of the reported[1] transformation of chalcone to the thiolan (**1**), by treatment with anhydrous sodium polysulphide, has been largely overlooked. However, it relates to an earlier rationale[2] for the incorporation of sulphur during the biogenesis of the thiaspiran Nuphar alkaloids, (**2**)



(**1**)

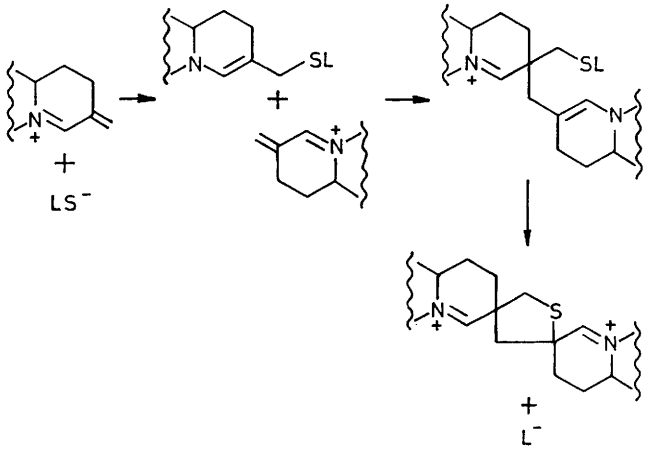


(**2**)



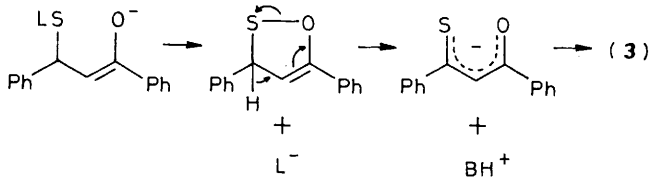
(**3**)

(Scheme 1). According to this rationale, the central thiolan ring was formed when an initially nucleophilic thiating agent



Scheme 1

reacted with a Michael acceptor. Subsequently, the resulting nucleophilic intermediate reacted with a second molecule of the Michael acceptor with consequent carbon–carbon bond formation. Finally, an intramolecular reaction of this second intermediate completed the thiolan ring through the nucleophilic displacement of a leaving group from the sulphenyl sulphur atom. Thus the overall function of such a thiating agent was to act initially as a nucleophile, but once attached to the Michael acceptor, it functioned as an electrophile. The same type of nucleo-electrophilic action of sodium polysulphide on chalcone was offered later to explain[1] the formation of the thiolan (**1**). However, before this transformation could be accepted as a precedent for the Nuphar biogenesis rationale, it was deemed necessary to confirm the thiolan structure, which until now rested on the mechanism for its formation and inconclusive spectral data. At issue was the arrangement of two unbroken chalcone units in the ring. Therefore the thiolan was prepared as reported[1,3] and a sample (2.23 mol, m.p. 205—206 °C) was treated under nitrogen with an excess of dichlorodicyanoquinone in boiling chlorobenzene for 4 days. Rapid chromatography[4] of the crude product mixture on silica gel with hexane–ethyl acetate (10%) gave a white crystalline solid, $C_{30}H_{20}O_2S$ [2.10 mmol, m.p. 158—160 °C (from ethyl acetate–hexane and dried at 0.1 mm Hg at 25 °C), ν_{max} ($CHCl_3$) 1663 cm^{-1}, $M^{+\cdot}$ at *m/z* 444], whose ^{13}C n.m.r. ($CDCl_3$) spectrum demonstrated the presence of two non-equivalent benzoyl groups by the two carbonyl resonances [δ 190.0 (s) and 194.8 (s) p.p.m.] and their two *para*-carbon atoms [δ 132.5 (d) and 133.5 (d) p.p.m.]. Dibenzoyldiphenylthiophens† having C_{2v} symmetry are inconsistent with these results. Therefore the dehydrogenation product is 2,4-dibenzoyl-3,5-diphenylthiophen and its thiolan precursor must be (**1**). Consequently the conversion of chalcone to the thiolan (**1**) does illustrate the action of a nucleo-electrophilic thiating agent.‡ However, it is clear that the over-all nucleo-electrophilic action may take other pathways. When the reaction of chalcone (14.4 mmol) with an excess of sodium



Scheme 2

polysulphide occurred at room temperature using anhydrous 1,2-dimethoxyethane in place of anhydrous ethanol, the known[6] red crystalline 1,3-diphenyl-3-thioxopropane-1-one, (**3**) (10.8 mmol), was obtained by collecting the hexane-eluted, red band from rapid chromatography on silica gel. [(**3**): m.p. 81—84 °C; $M^{+\cdot}$ at *m/z* 270; ν_{max} ($CHCl_3$) 1546, 1183, and 1070 cm^{-1}; ^1H n.m.r. ($CDCl_3$) δ 15.12 (1H, s, thioenol form of monothio-β-diketone) and 7.2—8.2 (11H, m, aromatic and olefinic H); ^{13}C n.m.r. δ 110.8 (d, C-2), 180.2 (s, C-1), and 203.1 (s, C-3) p.p.m.] The formation of the monothio-β-diketone is rationalized in Scheme 2.§

These results not only lend support to the Nuphar alkaloid biogenesis scheme but also have clear implications for the reactions of other Michael acceptors with nucleo-electrophilic thiating agents in organic synthesis.

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† One of these, 2,5-dibenzoyl-3,4-diphenylthiophen, is known (reported m.p. 131.5—132 °C); see reference 5.

‡ The overall role of the nucleo-electrophilic thiating agent is envisaged as follows. Through the nucleophilic attack of the polysulphide dianion on the Michael acceptor chalcone, a sulphur–carbon bond is formed and simultaneously an enolate. If the carbon terminus of this enolate reacts with a second molecule of the Michael acceptor, a carbon–carbon bond and a new enolate are established. The latter attacks the sulphenyl sulphur atom with displacement of the polysulphide chain, formation of the second carbon–sulphur bond, and consequently the completion of the ring.

§ The initiation of this transformation by the nucleophilic action of the polysulphide dianion is envisaged to occur as in thiolan formation. Thereafter, however, the reaction takes a different course. Nucleophilic displacement of the polysulphide chain occurs when the oxygen terminus of the enolate attacks the sulphenyl sulphur atom. Base abstraction of a proton from the resulting intermediate is suggested to promote the formation of the thioenolate form of the monothio-β-diketone, (**3**).