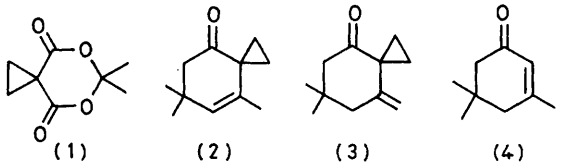
Homoconjugate Addition to Spiro[2.5]octen-4-ones

By P. HUGH HELFERTY, PAUL MAHLER, and PETER YATES*
(*Lash Miller Chemical Laboratories, University of Toronto, Toronto, Ontario, Canada* M5S 1A1)

Summary 6,6,8-Trimethylspiro[2.5]oct-7-en-4-one (**2**) and 6,6-dimethyl-8-methylenespiro[2.5]octan-4-one (**3**) undergo homoconjugate addition with the anion derived from isophorone and with morpholine; the reactions of (**3**) are much more rapid than those of (**2**), reflecting greater spiroactivation in the case of (**3**).

DANISHEFSKY and SINGH[1] have found that homoconjugate addition to cyclopropanes with two activating groups is remarkably facilitated when the activating groups form part of the spirocyclic acylal (**1**). They have proposed that this facilitation or 'spiroactivation' results from increased delocalization of the developing carbanion in the transition state by the carbonyl groups in (**1**) which, unlike those of non-spiro analogues, are held in an optimal orientation for such delocalization. We have observed that the monocarbonyl compounds (**2**) and (**3**) undergo homoconjugate addition and propose that these reactions also involve such spiroactivation.

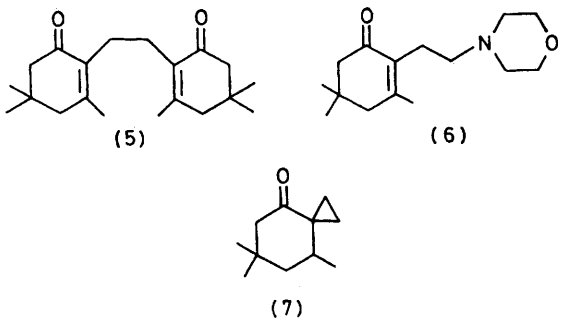


(1) (2) (3) (4)

Reaction of isophorone (**4**) with 1,2-dibromoethane and sodium amide in liquid ammonia gave a mixture of (**2**), (**3**), and unconsumed (**4**).[2] Treatment of this mixture with alkaline hydrogen peroxide[3] removed (**4**) to give a mixture of (**2**) and (**3**) (54%).† Treatment of the latter mixture with toluene-*p*-sulphonic acid in boiling ethanol isomerized (**3**) to (**2**), and permitted the isolation of the latter. Compound (**2**) has ν_{max} ($CHCl_3$) 1693 and 1658 cm^{-1}; δ ($CDCl_3$) (^1H) 1·08 (s, 6H), 1·13 (m, 2H), 1·53 (m, 2H), 1·48 (d, *J* 2 Hz, 3H), 2·37 (s, 2H), and 5·55 (m, 1H), and compound (**3**) has δ ($CDCl_3$) (^1H) 1·07 (s, 6H), 2·30 (m,2H), 2·42 (s, 2H), 4·48 (m, 1H), and 4·63 (m, 1H).

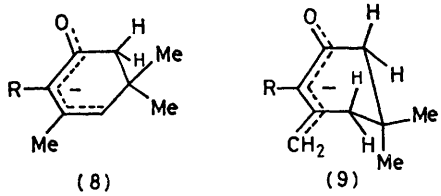
Reaction of (**2**) with (**4**) and sodium hydride in boiling toluene gave (**5**) (41%), m.p. 181—182 °C; ν_{max} ($CHCl_3$) 1658 and 1637 (sh) cm^{-1}; λ_{max} (EtOH) 244·5 nm (16,600); δ ($CDCl_3$) (^1H) 1·02 (s, 12H), 2·02 (s, 6H), and 2·22 (s) and 2·27 (s) (12H); δ (C_6H_6) (^1H) 0·80 (s, 12H), 1·68 (s, 4H), 1·88 (s, 6H), 2·08 (s, 4H), and 2·58 (s, 4H); δ ($CDCl_3$) (^{13}C) 21·3 (q), 24·6 (t), 28·3 (q), 32·8 (s), 47·1 (t), 51·5 (t), 134·0 (s), 153·5 (s), and 199·0 p.p.m. (s). A similar reaction of a 1:3·5 mixture of (**2**) and (**3**) with (**4**) showed that (**3**) was also converted into (**5**) and that this conversion was considerably more rapid than in the case of (**2**).

Treatment of (**2**) with morpholine at reflux gave (**6**) (58%); ν_{max} ($CHCl_3$) 1647 and 1629 cm^{-1}; λ_{max} (EtOH) 245·5 nm (ε 9400); δ ($CDCl_3$) (^1H) 1·00 (s, 6H), 1·93 (s, 3H),



(5) (6) (7)

2·22 (s, 4H), 2·3—2·6 (m, 8H), and 3·7 (m, 4H); δ (C_6H_6) (^1H) 0·80 (s, 6H), 1·53 (s, 3H), 1·72 (s, 2H), 2·07 (s, 2H), 2·2—2·8 (m, 8H), 3·6 (m, 4H); δ ($CDCl_3$) (^{13}C) 21·3, 22·4, 28·2, 32·7, 47·1, 51·2, 53·7, 57·7, 67·1, 132·5, 153·3, and 198·5 p.p.m. Similar treatment of a 1:4 mixture of (**2**) and (**3**) showed that (**3**) was also converted into (**6**). Furthermore, while 95% conversion of (**2**) into (**6**) required 110 h, the conversion of (**3**) into (**6**) was complete within 3·5 h.



(8) (9)

Thus homoconjugate addition occurs much more slowly for the endocyclic (**2**) than for the exocyclic isomer (**3**), and indeed the reaction of morpholine with (**2**) is only twice as rapid as its reaction with (**7**). The strong spiroactivation for (**3**) in contrast to the very weak spiroactivation for (**2**) is interpretable in terms of the delocalization of the developing anion in the transition states for the two reactions. Full delocalization of the anion from (**2**) requires coplanarity of all the ring atoms with concomitant angle strain at C-5 and -6 and eclipsing of the C-5 methyl groups by the C-6 hydrogen atoms [*cf.* (**8**)], whereas full delocalization of the anion from (**3**) does not require coplanarity of C-5 with the other ring atoms [*cf.* (**9**)]. While this difference will only be partially developed in the transition states, it seems likely that it can account for the very much more rapid reaction of (**3**). Even in the case of (**3**) the conditions required for homoconjugate addition are much more vigorous than in that of (**1**), reflecting that only one of the activating groups is a carbonyl group while the other is the more weakly activating ethylenic double bond.

We thank the National Science and Engineering Research Council of Canada for support.

(*Received, 2nd August* 1979; *Com.* 848.)

† Yields have not been optimized.

[1] S. Danishefsky and R. K. Singh, *J. Amer. Chem. Soc.*, 1975, **97**, 3239; *J. Org. Chem.*, 1975, **40**, 3807; R. K. Singh and S. Danishefsky, *ibid.*, p. 2969; 1976, **41**, 1668; *cf.* also T. Livinghouse and R. V. Stevens, *J. Amer. Chem. Soc.*, 1978, **100**, 6479.
[2] *Cf.* M. S. Newman, V. DeVries, and R. Darlak, *J. Org. Chem.*, 1966, **31**, 2171.
[3] *Cf.* R. D. Temple, *J. Org. Chem.*, 1970, **35**, 1275.