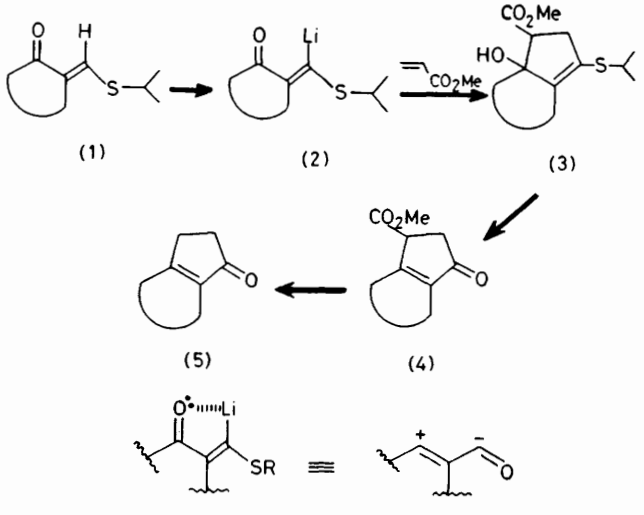
Efficient Pentannelation[1] of *cis*- and *trans*-1-Decalones

By JOSEPH P. MARINO* and LEE C. KATTERMAN
(*Department of Chemistry, University of Michigan, Ann Arbor, Michigan* 48109)

Summary Reactions of 2-isopropylthiomethylene derivatives of 1-decalones (**6**), (**7**), and (**8**) with lithium tetramethylpiperidide and methyl acrylate lead to cycloadducts (**9**), (**12**), and (**15**) which are converted into annelated cyclopentenones.

THE blocking of the α-methylene site of a ketone with the n-butylthiomethylene group is a well established synthetic operation.[2] We here report for the first time the use of a similar α-alkylthiomethylene unit as an activating group for an efficient pentannelation reaction.[1]

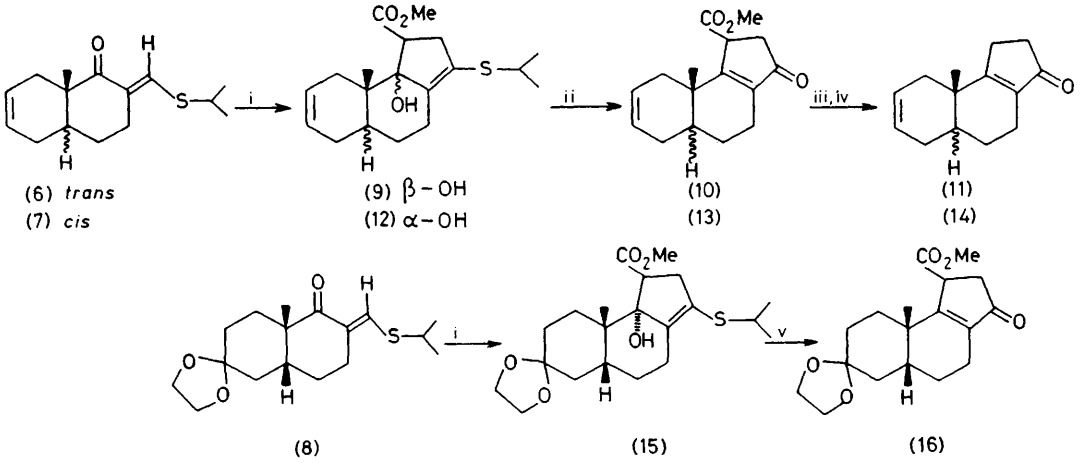
We have found that lithium 2,2,6,6-tetramethylpiperidide (LTMP) selectively removes the vinyl hydrogen in systems such as (**1**) to yield a β-oxo-stabilized species (**2**). In the presence of a Michael acceptor such as an acrylate, species (**2**) undergoes cycloaddition to produce cyclopentenols of general structure (**3**). Since adducts such as (**3**) are efficiently hydrolysed to cyclopentenones (**4**) and (**5**), this new synthetic strategy constitutes an 'umpolung' approach[3] to cyclopentenones, as shown in Scheme 1. After decarboxylation of the cyclopentenones (**4**), the production of



SCHEME 1. General pentannelation sequence.

enones (**5**) represents an overall cycloaddition of an enone system to ethylene.

We have applied this synthetic methodology to the *trans*-1-decalone compound (**6**) and the *cis*-1-decalones (**7**) and (**8**). A mixture of (**6**) and (**7**) was prepared by known procedures[4] and separated by medium pressure liquid chromatography (silica; ethyl acetate–n-hexane) into the pure isomers: (**6**), m.p. 60—61 °C, n.m.r. ($CDCl_3$), δ 0·95 (3H, s), 1·40 (6H, d), 3·25 (1H, heptet), 1·2—2·6 (9H, m), 5·55 (2H, br s), and 7·40 (1H, s); (**7**), oil, δ 1·15 (3H, s) instead of δ 0·95, otherwise n.m.r. data same as for (**6**). Compound (**8**) was also prepared by known procedures:† n.m.r. ($CDCl_3$), δ 1·08 (3H, s), 1·40 (6H, d), 1·1—2·6 (11H, m), 3·15 (1H, heptet), 3·75 (4H, s), and 7·40 (1H, s).



SCHEME 2. Pentannelations of 1-decalones (**6**), (**7**), and (**8**); i, 1·1 equiv. LTMP, −78 °C (1 h), 1·5 equiv. methylacrylate, −78 °C to room temperature overnight; ii, 5% HCl–THF, room temperature; iii, Me_3SiI neat, 80 °C (5 h); iv, HCl, reflux toluene; v, *p*-$MeC_6H_4SO_3H$, wet benzene, heat.

Each of the α-isopropylthiomethylene decalones (**6**), (**7**), and (**8**) was treated with 1·1 equiv. of LTMP in tetrahydrofuran (THF) at −78 °C. After 1 h, 1·5 equiv. of methyl acrylate was added at −78 °C and the mixture slowly warmed to room temperature overnight. It appears from quenching experiments that the acrylate trap must be in the mixture during the deprotonation for optimum results. Work-up included the addition of a saturated ammonium chloride solution and ether. After washing the ether layer several times with water, it was dried with anhydrous Na_2SO_4 and concentrated to an oil. Trituration of the oil with cold light petroleum usually resulted in the crystallization of the cycloadducts.

Compounds (**9**), m.p. 146·5—147·5 °C, δ 0·70 (3H, s), 1·22 (6H, d), 1·4—3·2 (13H, m), 3·20 (1H, heptet), 3·65 (3H, s), 3·53 (2H, s); (**12**), m.p. 121·5—123·0 °C, δ 1·0 (3H, s), 1·20 (6H, d), 1·2—2·9 (13H, m), 3·20 (1H, heptet), 3·70 (3H, s), and 5·48 (2H, br s), crystallized in *ca.* 50% yield upon trituration, while the cycloadduct (**15**) was isolated as an oil in 75% yield.‡ Column chromatography of the mother liquors from the crystallizations of (**9**) and (**12**) yielded 20—25% more of the cycloadducts. In addition to the cyclopentenols (**9**) and (**12**), small amounts of the corresponding dehydration products were isolated by chromatography.

Hydrolysis of the cycloadducts (**9**), (**12**), and (**15**) with 5% HCl in THF at room temperature yielded the respective enones (**10**), (**13**), and (**16**). These methoxycarbonylenones were not easily hydrolysed to their corresponding acids with dilute acid or base. Treatment of (**10**) with trimethylsilyl iodide, neat, at 80 °C, yielded the carboxylic acid, which was then decarboxylated in refluxing toluene to the enone (**11**). The overall conversion of (**6**), (**7**), and (**8**) into the enones (**10**), (**13**), and (**16**) could be accomplished in 70—75% yield without isolation of the cyclopentenols.

The cycloaddition reactions described herein for the *cis*- and *trans*-1-decalones represent a new approach to tricyclic and tetracyclic systems containing a cyclopentenone.

We thank the N.I.H. for a training grant to the Department of Medicinal Chemistry, School of Pharmacy at the University of Michigan (L. C. K.).

(*Received, 27th June* 1979; *Com.* 678.)

† Compound (**8**) was prepared from the corresponding keto-acetal by Ireland's procedure (ref. 4). The starting keto-acetal was obtained from hydrogenation of the monoacetal of the Wieland–Mischler ketone. The m.p. of the saturated diketone with the *cis* configuration was compared to that of the known compound (S. Swaminatham and M. S. Newman, *Tetrahedron*, 1958, **2**, 88).

‡ All new compounds were characterized by ^1H n.m.r., i.r., and mass spectral and microanalytical data. The relative stereochemistry of the angular methyl groups and the hydroxy groups in the cycloadducts (**9**), (**12**), and (**15**) has tentatively been assigned as shown on the basis of steric arguments for the *cis* and *trans* decalins.

[1] We use the term pentannelation to describe the direct elaboration of a fused five-membered ring. The original report by us of this process (J. P. Marino and Wm. B. Mesbergen, *J. Amer. Chem. Soc.*, 1974, **96**, 4051) was incorrectly interpreted to yield a different type of cycloadduct. The correct cycloaddition process, which forms the basis of this work, was first presented at the 175th ACS National Meeting, Anaheim, California, March 1978, ORGN 22.

[2] R. E. Ireland and J. A. Marshall, *J. Org. Chem.*, 1962, **27**, 1615.
[3] For a recent review of methods of reactivity umpolung, see D. Seebach, *Angew. Chem. Internat. Edn.*, 1979, **18**, 239.
[4] R. E. Ireland and J. A. Marshall, *J. Org. Chem.*, 1962, **27**, 1620.