

A NEW APPROACH TO THE SYNTHESIS OF HYDRINDANONECARBOXYLATES

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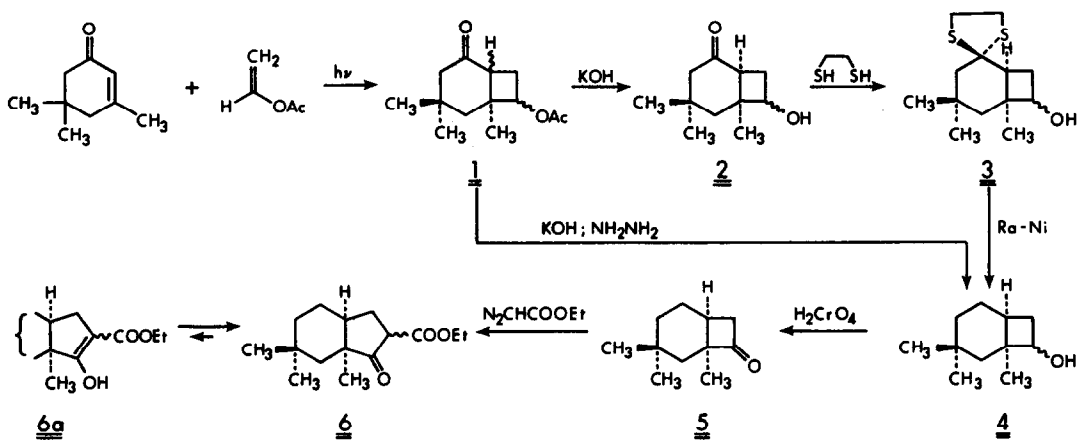
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The application of photoannulation reactions to synthesis has been of growing importance and interest in recent years; by the use of these methods with or without subsequent modification of the so generated cyclobutane rings, a great number of relatively complex organic compounds have been synthesized in remarkably simple fashion (1). This communication reports a convenient and apparently general synthetic route leading to hydrindanonecarboxylates (2) initiated by a photoannulation reaction.

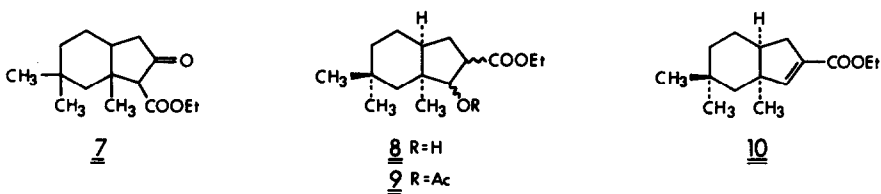
The general synthetic sequence, illustrated with isophorone in the Scheme involves two important stages, first the construction of a bicyclo[4.2.0]octanone system from a cyclohexenone and then the expansion of the derived cyclobutanone ring. Irradiation of isophorone in vinyl acetate and benzene under the usual reaction conditions (3) for 6 hr afforded a diastereomeric mixture of keto acetate 1 (4) in 85% yield (5). Treatment of 1 with aqueous potassium hydroxide in methanol gave, in essentially quantitative yield, keto alcohol 2 as a mixture of epimers. The cis nature of the ring juncture could be readily assigned on the basis of previous observations (6). Thioketalization of 2 using boron trifluoride etherate and 1,2-ethanedithiol followed by desulfurization of the product 3 with Raney nickel (W-7) gave rise to alcohol 4 in 58% yield. Alternatively, direct conversion of 1 to 4 was achieved, in a yield of 40%, by treating the former compound with hydrazine and an excess of potassium hydroxide under modified Wolff-Kishner reduction conditions (7). Oxidation of 4 using Jones reagent (8) in acetone furnished, in a 65% yield, 4,4,6-trimethylbicyclo[4.2.0]octan-7-one (5), homogeneous by tlc and glc; ir (neat) 1780 cm^{-1} ; nmr (CCl_4)

7.02, 7.15 (d,d,2H,-CH₂-C(=O)-), 8.83 (s,3H,-CH₃), and 9.08τ (s,6H,CH₃-C(CH₃)₂); mass spec. M⁺ 166.1354 (Calcd. for C₁₁H₁₈O:166.1358). When 5 was treated with 1.5 equiv each of boron trifluoride etherate and ethyl diazoacetate (9) in ether at room temperature for 3 hr it was easily transformed to hydrindanonecarboxylate 6 (10) (89% yield; existing partially in its enol form 6a); ir (neat) 1755, 1728, 1660, and 1625 cm⁻¹; nmr (CCl₄) 5.82 (q,2H,-C(=O)-CH₂-), 6.68 (t,=0.85H,-C(=O)-CH-), 8.70 (t,3H,-C(=O)-CH₂-CH₃), 8.83 - 9.3 (6s,9H,3-CH₃); mass spec. M⁺ 252.1717 (Calcd. for C₁₅H₂₄O₃:252.1724).



SCHEME

The ring expansion could in principle lead to 6 and/or its positional isomer 7. The assigned structure was verified by the following transformations (11). Sodium borohydride reduction of 6 gave, in a 3:1 ratio, two isomeric alcohols 8 which were separated and acetylated by acetic anhydride and pyridine. The nmr spectra of the two acetylation products 9 show in each case a doublet (5.05τ for the major isomer and 5.1τ for the minor) for the methine proton next to the acetate and thus are in full agreement with the depicted structure. Furthermore treatment of both isomers of 9 with sodium hydride gave rise to unsaturated ester 10; ir (neat) 1720 and 1625 cm⁻¹; mass spec. M⁺ 236.1781 (Calcd. for C₁₅H₂₄O₂:236.1776). The fact that the vinylic proton appeared at 3.47τ as a broad singlet in its nmr spectrum may only be accounted for by this structure assignment.



Using essentially the same reaction sequence (via thioketals), bicyclo[4.2.0]octanones 11-15 were synthesized in fair-good yields and were further converted to hydrindanonecarboxylates. The results are summarized in the table.

TABLE Preparation of Hydrindanonecarboxylates

Cyclohexenone	Enol Acetate	Bicyclo[4.2.0]octanone Intermediate(s)	Product(s) (% Yield of Ring Expansion)

It should be noted that the expansion of cyclobutanone rings is highly regioselective and predictable (see table). Where applicable, products formed result either exclusively or predominantly from migration of the less substituted carbon. The general scope and mechanistic aspects of these findings are being investigated.

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REFERENCES AND NOTES

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2. A frequently used approach involves an intramolecular Dieckmann Condensation. For leading references, see J. P. Schaefer and J. J. Bloomfield, *Org. Reactions*, 15, 1 (1967).
3. N. R. Hunter, G. A. MacAlpine, H. J. Liu, and Z. Valenta, *Can. J. Chem.* 48, 1436 (1970).
4. Satisfactory ir, nmr and high resolution mass spectra were obtained for all the new compounds.
5. All the yields given are for isolated products.
6. E. J. Corey, J. D. Bass, R. Le Mathieu, R. B. Mitra, *J. Amer. Chem. Soc.* 86, 5570 (1964).
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8. K. Bowden, I. M. Heilbron, E. R. H. Jones, and B. C. L. Weedon, *J. Chem. Soc.*, 39 (1946).
9. W. T. Tai and E. W. Warnhoff, *Can. J. Chem.*, 42, 1333 (1964).
10. The stereochemistry of the newly introduced labile chiral center remains to be determined.
11. By similar transformations, structures 16-18 were confirmed. These results and chemical proof of the structures assigned for 19-21 will be discussed in the full paper.
12. On the assumption that the ring expansion results in the retention of configuration at the migrating center analogous to the well established Bayer-Villiger oxidation reaction [R. B. Turner, *J. Amer. Chem. Soc.*, 72, 878 (1950)], a cis ring juncture is tentatively assigned to this compound.