Bicycloannulation with Isopropenyltriphenylphosphonium Bromide. The Synthesis of Trachyloban-19-oic Acid†

By ROBERT M. CORY,* YOUSRY M. A. NAGUIB, and MARY H. RASMUSSEN
(*Department of Chemistry, University of Western Onrario, London, Ontario* N6A 5B7, *Canada*)

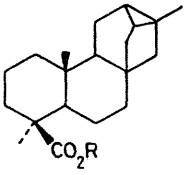
Summary 1-Methyltricyclo[3.2.1.$0^{2,7}$]octan-6-ones can be prepared in one step from the α'-enolates of $\alpha\beta$-cyclohexenones and isopropenyltriphenylphosphonium bromide; this reaction has been employed as the key step in

† For the previous paper in the series Bicycloannulation see R. M. Cory and F. R. McLaren, *J.C.S. Chem. Comm.*, 1977, 587.

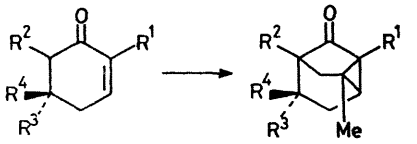
a synthesis of trachyloban-19-oic acid from podocarpic acid.

BICYCLOANNULATION of $\alpha\beta$-cyclohexenones by treatment of the corresponding α'-enolates with vinyltriphenylphosphonium bromide (VTB) is a synthetically useful reaction in spite of the relatively low yields obtained,[1] since three new carbon–carbon σ-bonds are formed, resulting in the construction of a tricyclic system from a monocyclic precursor in a single step.‡ We now report that the corresponding isopropenylphosphonium salt provides much higher yields of tricyclo[3.2.1.$0^{2,7}$]octan-6-ones. We have also demonstrated the utility of this new method in a synthesis of a diterpenoid, trachyloban-19-oic acid (**1**), the enantiomer of which has been isolated from the common sunflower, *Helianthus annuus*.[2]

In contrast to VTB, which failed to give the expected tricyclo-octanones from cyclohex-2-enone itself (**3a**) and 6-methylcyclohex-2-enone (**3b**), isopropenyltriphenylphosphonium bromide[3] (ITB) not only reacted in the desired manner with the α'-enolates from (**3a**) and (**3b**) to give (**4a**) and (**4b**) in 17 and 44% yield, respectively (g.l.c.), but also led to much higher yields of the tricyclo-octanones (**4c**) and (**4d**), 42 and 45% isolated yields, respectively from the cyclohexenones (**3c**) and (**3d**).§ Furthermore, although bicycloannulation with VTB required reflux in tetrahydrofuran (THF) for completion, that with ITB was complete at room temperature.¶ As with VTB, in the case of (+)-carvone (**3d**), bicycloannulation proceeded stereoselectively, attack of ITB occurring exclusively from the side opposite to the isopropenyl group of the enolate.

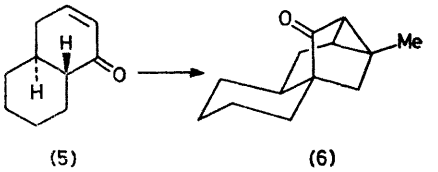


(1) R = H
(2) R = Me



(3) (4)

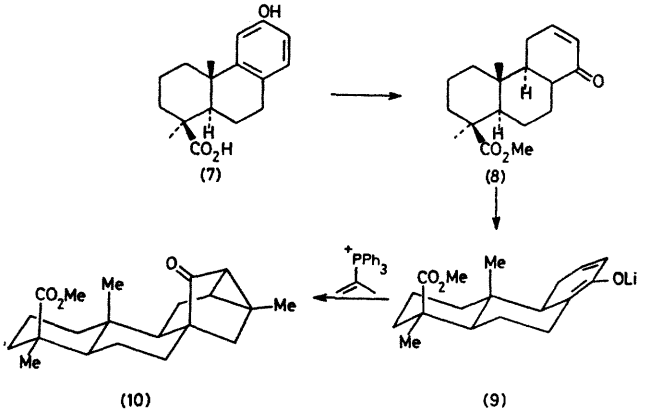
a; $R^1 = R^2 = R^3 = R^4 = H$
b; $R^1 = H, R^2 = Me, R^3 = R^4 = H$
c; $R^1 = R^2 = H, R^3 = R^4 = Me$
d; $R^1 = Me, R^2 = H, R^3 = C(Me)=CH_2, R^4 = H$



(5) (6)

In a model study more closely related to our proposed synthesis of (**1**), the octalone (**5**) (prepared from 1-decalone *via* the 2-toluene-*p*-sulphinyl derivative) was subjected to bicycloannulation with ITB under the same conditions. A single product, (**6**), was obtained in 36% yield (g.l.c.), arising from stereoselective attack of the phosphonium salt in the desired sense.

The enone-ester (**8**) was readily available by a known sequence from podocarpic acid (**7**).[4] Attack by an electrophile such as ITB on the corresponding kinetic enolate (**9**) must occur on the α-face of the molecule, this direction being at least partly due to the severe steric hindrance afforded by the 10(β)-methyl group.[5] In the event, treatment of the dienolate (**9**) with ITB produced, stereoselectively, the desired pentacyclic oxo-ester (**10**) [m.p. 143—145 °C; ^{1}H n.m.r. spectrum ($CDCl_3$) δ 0·53 (s, 10-Me), 1·14 (s, 4-Me), 1·25 (s, 16-Me), and 3·61 (s, OMe)] in 20% yield.



(7) (8)

(10) (9)

Wolff–Kishner reduction[6] of (**10**) with concomitant hydrolysis, followed by esterification of the crude acid (**1**) with diazomethane, gave methyl trachyloban-19-oate (**2**), identical with an authentic sample of methyl *ent*-trachyloban-19-oate derived from sunflower heads, except for its o.r.d. (opposite in sign to that of the natural product).

‡ Following the publication of our results, it was reported that methyl α-bromocrotonate can be employed in a similar manner (H. Hagiwara, T. Kodama, H. Kosugi, and H. Uda, *J.C.S. Chem. Comm.*, 1976, 413).

§ Satisfactory ^{1}H and ^{13}C n.m.r., i.r., and mass spectra as well as precise masses, were obtained for all new compounds. The ^{13}C n.m.r. data have been reported (R. M. Cory and J. B. Stothers, *Org. Magnetic Resonance*, 1978, **11**, 252).

¶ To a solution of the α'-enolate in THF, formed by slow addition of the ketone to a solution of lithium di-isopropylamide in THF at 0 °C, was added dropwise a solution of ITB in pyridine. The mixture was stirred for several hours at room temperature and then subjected to an aqueous work-up.

The bicycloannulation reactions described here and previously provide savings in time, effort, and materials. The analogous transformations carried out by Herz[5] and Kelly[7] and their coworkers in previous syntheses of trachylobane terpenoids, although elegant, required a minimum of eight and twelve steps, respectively.

We thank Professor R. A. Bell, McMaster University, for a supply of podocarpic acid, Professor R. McCrindle, University of Guelph, for a sample of methyl *ent*-trachyloban-19-oate, and the Research Corporation (U.S.A.) and the National Research Council (Canada) for financial support.

(*Received*, 16*th March* 1979; *Com.* 268.)

[1] R. M. Cory and D. M. T. Chan, *Tetrahedron Letters*, 1975, 4441.
[2] J. St. Pyrek, *Tetrahedron*, 1970, **26**, 5029; Z. Kasprzyk, W. Janiszewska, and M. Papaj, *Bull. Acad. Polon. Sci., Ser. Sci. biol.*, 1974, **22**, 1.
[3] E. E. Schweizer, A. T. Wehman, and D. M. Mycz, *J. Org. Chem.*, 1973, **38**, 1583.
[4] R. C. Cambie and A. W. Missen, *Austral. J. Chem.*, 1972, **25**, 973.
[5] W. Herz, R. N. Mirrington, H. Young, and Y. Y. Lin, *J. Org. Chem.*, 1968, **33**, 4210; K. Mori and M. Matsui, *Tetrahedron*, 1968, **24**, 3095; R. B. Turner, K. H. Gänshirt, P. E. Shaw, and J. D. Tauber, *J. Amer. Chem. Soc.*, 1966, **88**, 1776.
[6] D. H. R. Barton, D. A. Ives, and B. R. Thomas, *J. Chem. Soc.*, 1955, 2056.
[7] R. B. Kelly, B. A. Beckett, J. Eber, H.-K. Hung, and J. Zamecnik, *Canad. J. Chem.*, 1975, **53**, 143 and references therein.