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PREPARATION AND THERMAL REARRANGEMENT OF β-CYCLOPROPYL-α,β-UNSATURATED KETONES. CONVENIENT CYCLOPENTANE ANNELATIONS.

Edward Piers*, Cheuk Kun Lau, and Isao Nagakura
Department of Chemistry, University of British Columbia,
2075 Wesbrook Place, Vancouver, B.C., Canada V6T 1W5

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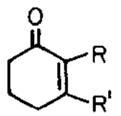
Although the now well-known thermal rearrangement of vinylcyclopropanes to cyclopentenes[1] has been extensively studied, most of the reports have been concerned with a delineation of the mechanism of the reaction[2]. However, a number of recent papers have included results of work which has dealt with this type of transformation mainly from a synthetic point of view.[3] We report herein an efficient synthesis of β-cyclopropyl-α,β-unsaturated ketones and the thermal rearrangement of some of these substances to afford the corresponding cyclopentane systems. Overall, in conjunction with previously reported results[4], these conversions constitute new and potentially useful cyclopentane annelation reactions which can be represented in general terms as follows:

Treatment of 3-bromo-2-cyclohexen-1-one (1)[4] with 1.5 equiv. of lithium phenylthio(cyclopropyl)cuprate[5] in ether-THF at 0° for 2.5 h gave, in 93% yield, 3-cyclopropyl-2-cyclohexen-1-one[7,8]. In similar fashion, the following conversions were carried out: 3[7,9] into 4[7] (m.p. 31-33°; 97%); 5[4] into 6[7] (86%); 7[4] into 8[7] (m.p. 36-37°; 78%); 9[7,10,11] into 10[7,11,12] (82%); 11[7,11,13] into 12[7] (91%, 1:1 mixture of geometric isomers); 13[7,11,14] into 14[7,11] (65%). Clearly, the reaction of lithium phenylthio(cyclopropyl)cuprate with β-halo-α,β-unsaturated ketones is a very convenient and efficient method for preparing the corresponding β-cyclopropyl enones[15]. It should be noted that, in each case where a comparison was made, the β-iodo enone was superior (better yield, milder reaction conditions, less recovered starting material) to the β-bromo enone as a starting material. Furthermore, in no case were we able to detect a product resulting from a second addition of a cyclopropyl moiety to the initially formed β-cyclopropyl enone.

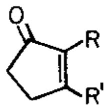
Thermolysis[16] of 3-cyclopropyl-2-cyclohexen-1-one (2), followed by passing the initially formed product mixture through a short column of basic alumina, gave (83% yield) a mixture of the bicyclic enone 15[7,17] and the monocyclic compound 16[7,18], in a ratio of about 92:8. Similarly, cyclopropyl enone 17[7,19] gave, in 79% yield, compound 18[7]. Thermolysis of 4 afforded somewhat less of the annelated product, giving (80%) a mixture of 19[7] and 20[7] in a ratio of about 60:40.

Although thermal rearrangement of compounds 10, 12 and 14 gave somewhat more complex product mixtures, modest yields of the corresponding spiroannelated compounds (21, 32%; 22, 25%; 23, 26%, respectively) were formed. In each case, the annelation product was accompanied by an aromatic compound (tetralin, 5-methyltetralin, indane, respectively) and a mixture of monocyclic dienones[21]. Very recently, however, we have been able to effect a considerable improvement in the conversion of 10 into 21. Thus, successive treatment of 10 with lithium diisopropylamide (DME) and $(CH_3)_3SiCl$ gave the enol silyl ether 24. Thermolysis of the latter, followed by hydrolysis and simple distillation of the crude product afforded the pure spiro compound 21 in 50% overall yield.

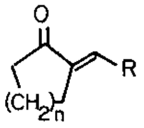
Work in this area is continuing.[22]



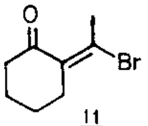
1 $R=H, R'=Br$
2 $R=H, R'=\underline{c}\text{-}C_3H_5$
7 $R=CH_3, R'=I$
8 $R=CH_3, R'=\underline{c}\text{-}C_3H_5$



3 $R=H, R'=I$
4 $R=H, R'=\underline{c}\text{-}C_3H_5$
5 $R=CH_3, R'=I$
6 $R=CH_3, R'=\underline{c}\text{-}C_3H_5$



9 $n=2, R=I$
10 $n=2, R=\underline{c}\text{-}C_3H_5$
13 $n=1, R=I$
14 $n=1, R=\underline{c}\text{-}C_3H_5$



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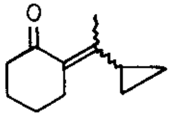

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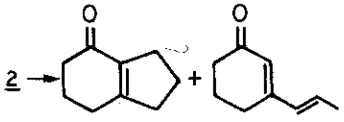
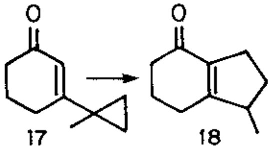
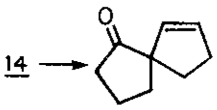


15 16



17 18



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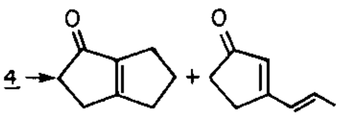
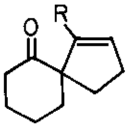
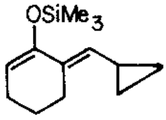


19 20



10 → 21 $R = H$
12 → 22 $R = CH_3$



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References and Notes

1. C.D. Gutsche and D. Redmore, "Carbocyclic Ring Expansion Reactions", Academic Press, New York, N.Y., 1968. p. 163.
2. For a very recent report, see M.J.S. Dewar, G.J. Fonken, S. Kirschner, and D.E. Minter, *J. Am. Chem. Soc.*, **97**, 6750 (1975).
3. E.J. Corey and S.W. Walinsky, *J. Am. Chem. Soc.*, **94**, 8932 (1972); B.M. Trost and M.J. Bogdanowicz, *ibid.*, **95**, 5311 (1973); S.A. Monti, F.G. Cowherd, and T.W. McAninch, *J. Org. Chem.*, **40**, 858 (1975); E.J. Corey and R.H. Wollenberg, *ibid.*, **40**, 2265 (1975); B.M. Trost and D.E. Keeley, *J. Am. Chem. Soc.*, **98**, 248 (1976).
4. E. Piers and I. Nagakura, *Synth. Commun.*, **5**, 193 (1975).
5. Prepared by adding an ethereal solution of freshly prepared cyclopropyllithium to a slurry of phenylthiocopper[6] in THF at -78°, followed by warming to -20° for 10 min.
6. G.H. Posner, D.J. Brunelle, and L. Sinoway, *Synthesis*, 662 (1974).
7. All products exhibited spectral data in full accord with assigned structures. New compounds gave satisfactory elemental analysis and/or molecular weight determinations (high resolution mass spectrometry).
8. Previously prepared in two steps (∿ 10% yield) from cyclopropyl methyl ketone: R.C. Hahn and G.W. Jones, *J. Am. Chem. Soc.*, **93**, 4232 (1971).
9. M.p. 67-68°. Prepared in 85% yield by reaction of 1,3-cyclopentanedione with $(C_6H_5)_3PI_2$ in reluxing CH_3CN containing 1 equiv. of Et_3N.
10. Prepared in 93% yield by reaction (r.t., 15h) of 2-hydroxymethylenecyclohexanone with $(C_6H_5)_3PI_2$ in 6:1 CH_3CN-HMPA containing 1 equiv. of Et_3N.
11. The stereochemical assignments for compounds **9**, **10**, **11**, **13** and **14** were made mainly on the basis of spectral data. A discussion of this point is deferred to a detailed paper.
12. S. Danishefsky and G. Rovnyak, *J. Org. Chem.*, **39**, 2924 (1974)
13. Prepared in 80% yield by reaction (r.t., 21h) of 2-acetylcyclohexanone with $(C_6H_5)_3PBr_2$ in 5:1 CH_3CN-C_6H_6 containing 1 equiv. of Et_3N.
14. M.p. 31.5°. Prepared in 73% yield by reaction (r.t., 3 days) of hydroxymethylenecyclopentanone with $(C_6H_5)_3PI_2$ in 6:1 CH_3CN-HMPA containing 1 equiv. of Et_3N.
15. For the reaction of β-halo enones with other cuprate reagents, see E. Piers and I. Nagakura, *J. Org. Chem.*, **40**, 2694 (1975).

16. Thermal rearrangement of the β-cyclopropyl enones was accomplished by dropwise addition of a hexane solution of the compound onto a vertical column (∿ 32 cm) packed with glass helices and heated to ∿ 450°. The pyrolysate was collected in a receiving tube cooled in a dry ice-acetone bath.
17. Cf. R.L. Cargill and T.E. Jackson, *J. Org. Chem.*, **38**, 2125 (1973).
18. A.F. Kluge and C.P. Lillya, *J. Org. Chem.*, **36**, 1977 (1971).
19. Prepared by 1,6-addition of dimethyloxosulfonium methylide[20] to 3-isopropenyl-2-cyclohexen-1-one. The latter was prepared by reaction of isopropenylmagnesium bromide with 3-methoxy-2-cyclohexen-1-one followed by acid hydrolysis of the product.
20. E.J. Corey and M. Chaykovsky, *J. Am. Chem. Soc.*, **87**, 1353 (1965).
21. A discussion concerning the structure of these materials is deferred to the full paper.
22. Financial support for this work from the National Research Council of Canada and a N.R.C.C. Scholarship (to C.K.L.) are gratefully acknowledged.