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EFFICIENT PREPARATION AND THERMAL REARRANGEMENT OF β-(2-VINYLCYCLOPROPYL)-α,β-UNSATURATED KETONES. CONVENIENT CYCLOHEPTANE ANNELATIONS.

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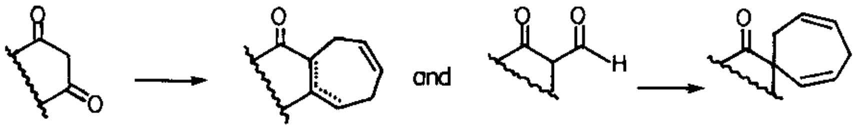
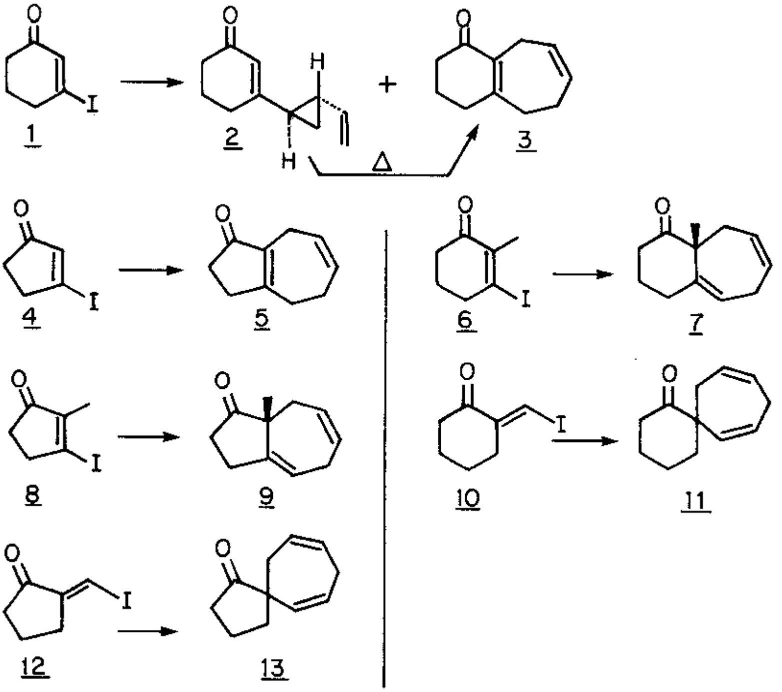
The thermal Cope rearrangement of 1,2-divinylcyclopropane systems to afford the corresponding cycloheptadienes is, particularly if the vinyl substituents are cis-oriented, a very facile process which has been the subject of considerable study[1]. However, this type of conversion has received relatively little application in synthetic organic chemistry. Clearly, the very common occurrence of seven-membered rings in many different classes of natural products provides impetus for investigations regarding the possibility of using this type of transformation in synthesis.

Recently, Marino and Kaneko have demonstrated the use of thermal rearrangement of substituted 3-(2-vinylcyclopropyl)-2-cyclohexen-1-ones[2] and 2-methyl-3-(2-vinylcyclopropyl)-2-cyclopentene-1-ones[3] for the preparation of ring-fused cycloheptadiene compounds. These workers obtained the β-cyclopropyl enones via a 4-step sequence from the corresponding 1,3-cycloalkanediones and, particularly for the synthesis of the hydroazulene compounds[3], the overall yields were modest. We report herein preliminary results of complementary work which shows that the reaction of β-iodo-α,β-unsaturated ketones with lithium phenylthio-(2-vinylcyclopropyl) cuprate[4], followed by thermal rearrangement of the resulting β-(2-vinylcyclopropyl) enones provides a short, efficient synthesis of the corresponding cycloheptadiene systems. Overall, in conjuction with previously reported results[5,6], these conversions represent seven-membered ring annelation reactions which can be represented in general terms as follows.



Treatment of 3-iodo-2-cyclohexen-1-one (1)[5] with 1.5 equiv. of lithium phenylthio(2-vinylcyclopropyl)cuprate[7] in THF-ether-pentane (-78° for 1 h, -20° for 1h and 0° for 1h), followed by work-up and distillation (air-bath temperature 62-88°, 0.4 Torr) of the crude product gave an oil in 90% yield. Analysis (p.m.r., g.l.c.) of



this material indicated that although the bulk of the mixture was the annelation product **3**[10,2], a significant amount of β-(2-vinylcyclopropyl)enone (presumably the trans compound **2**) was also present. When this mixture was heated (neat) at 180° for 30 min. and then redistilled and purified, the annelation product **3** could be isolated in 75% overall yield. In similar fashion, the following conversions were accomplished: **4**[5] into **5**[10] (80%); **6**[5,11] into **7**[10] (82%); **8**[5,11] into **9**[10] (84%).

Seven-membered spiroannelations could also be carried out *via* the general methodology outlined above. Thus, treatment of the iodomethylenecyclohexanone **10**[6] with lithium phenylthio(2-vinylcyclopropyl)cuprate[7] under conditions identical with those used for compound **1**, followed by thermolysis (180°, 15 min.) of the initially isolated product, gave the spiro dienone **11**[10] in 77% yield. In similar fashion, the iodomethylenecyclopentanone **12**[6] was converted (64% yield) into the spiro compound **13**[10].

We are currently studying the reaction of β-iodo enones with more highly substituted (vinylcyclopropyl)cuprate reagents and hope to apply this methodology to the synthesis of some natural products.[12]

References and Notes

1. S.J. Rhoads and N.R. Raulins, *Org. Reactions*, **22**, 54 (1975).
2. J.P. Marino and T. Kaneko, *Tetrahedron Lett.*, 3975 (1973).
3. J.P. Marino and T. Kaneko, *J. Org. Chem.*, **39**, 3175 (1974).
4. For the reaction of β-halo enones with simpler cuprate reagents, see E. Piers and I. Nagakura, *J. Org. Chem.*, **40**, 2694 (1975).
5. E. Piers and I. Nagakura, Synth. Commun., **5**, 193 (1975).
6. E. Piers, C.K. Lau, and I. Nagakura. Preceding communication.
7. This reagent was prepared as follows. To a solution of 2-vinylcyclopropyl bromide[8] (cis:trans = 7:3) in ether at -78° was added a solution of 2 equiv. of t-butyllithium in pentane. The resulting mixture was stirred for 1h (a white precipitate formed) and then diluted with THF. Solid phenylthiocopper[9] (1 equiv.) was added and the resulting suspension was stirred and warmed to -20° for 10 min. A clear yellow solution resulted.

8. J.A. Landgrebe and L.W. Becker, *J. Org. Chem.*, **33**, 1173 (1968).

9. G.H. Posner, D.J. Brunelle and L. Sinoway, *Synthesis*, 662 (1974).

10. 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).

11. In this case, 2 equiv. of cuprate reagent were employed, and the reaction was allowed to proceed at -20° for 1h and at 0° for 2h.

12. Financial support for this work from the National Research Council of Canada is gratefully acknowledged.