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Synthesis of Bicyclo[2.2.1]heptan-2-ones by Thermal Cyclization of 3-Allylcyclopentanones

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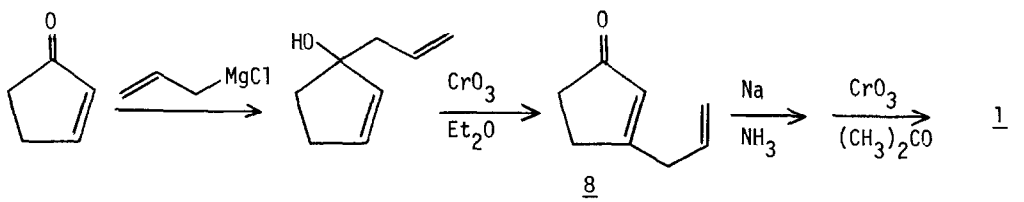
Abstract: Pyrolysis of 3-allylcyclopentanones affords endo-6-substituted bicyclo[2.2.1]heptan-2-ones.

The development of the intramolecular ene reaction of unsaturated ketones into an important and versatile method for the synthesis of carbocycles is largely due to the extensive investigations of Conia.[1] Although a wide variety of bicyclo[3.2.1],[2] [3.3.1],[3] and [4.3.1][4] alkanones have been prepared by this method, there has been almost no application of the procedure for the construction of moderately strained norbornanones. We are aware only of the conversion of (+)-dihydrocarvone into (+)-camphor.[5] We report now the facile preparation of bicyclo[2.2.1]heptan-2-ones by thermal cyclization of 3-allylcyclopentanones. The use of the latter as substrates not only extends the range of compounds known to undergo this reaction, but also permits stereospecific synthesis of endo-6-substituted norbornanones.

Cyclopentanones 2, 3, and 4 were obtained originally in photochemical studies;[6,7] an alternative synthesis of 2 has also been described.[6] 3-Allylcyclopentanone (1)[8,9] was prepared following the sequence shown below. Addition of allylmagnesium chloride to

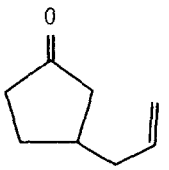
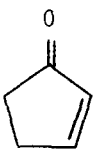
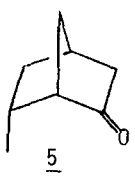
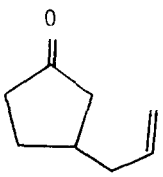
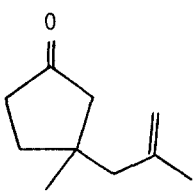
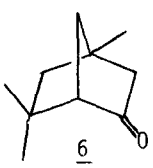
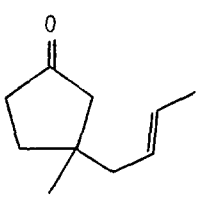
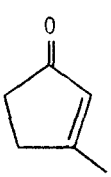
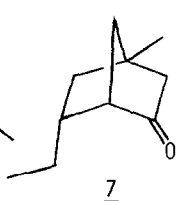
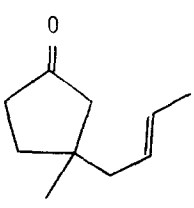
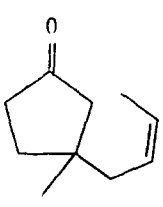
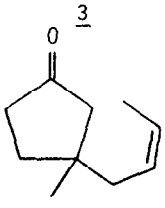


2-cyclopentenone afforded the tertiary alcohol which was subsequently treated with acidic chromium trioxide to give, after allylic rearrangement and oxidation,[10] 3-allylcyclopent-2-enone (8).[8,11] Reduction of the dienone in sodium/liquid ammonia and oxidation of the

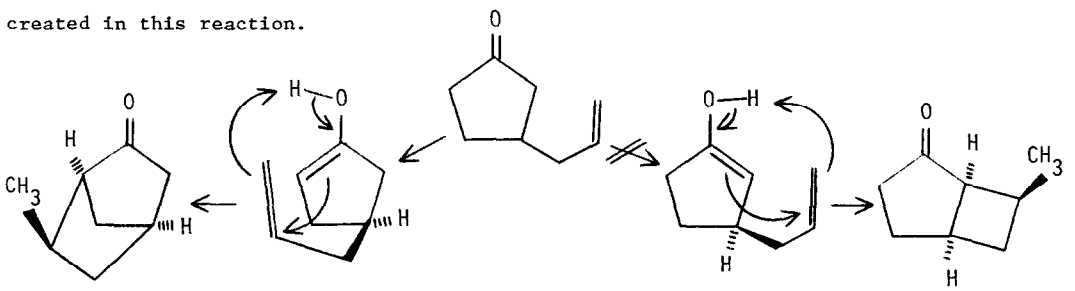
crude reaction mixture with Jones' reagent gave largely desired 1.

Samples of the cyclopentanones (50-100 mg) were pyrolyzed in evacuated sealed tubes (capacity ~20 ml) at 375 °C; results are listed in the table.

Pyrolysis of Cyclopentanones at 375 °C

Cyclopentanone	Time	Products/Yields				
 1	6.5 h	 2%	 5 59%	 4%		
 2	6 h	 6 71%				
 3	18.5 h	 8%	 7 43%	 2%	 8%	
 4	18.5 h	3%	44%	1%	2%	

The structure of 5 was ascertained from IR, ^{1}H and ^{13}C NMR[12] spectra as well as its dinitrophenylhydrazone derivative: mp 130.5-131° (lit. mp 129.4-130.0°).[13] Obtention of only this isomer rigorously demonstrates that the alkyl group formed by transfer of a hydrogen atom is endo, in line with mechanistic expectations.[1] Identification of 6 as (±)-epiisofenchone was accomplished by comparison of IR and NMR spectra with those of an authentic sample.[14] Structure 7 was inferred from spectroscopic data and analogy.[8,15] The simple cyclopentenones formed in minor amounts, presumably via a retro-ene reaction, were identified on the basis of appropriate signals in the NMR spectra of the crude pyrolysate and VPC retention times identical to those of reference samples. There was no evidence for the formation of isomeric bicyclo[3.2.0]heptan-2-ones (arising by cyclization of the alternative enol), a result consistent with the ease with which five-membered rings are created in this reaction.



Thus the thermal cyclization of allylcyclopentanones has been shown to be a valuable and general method for the preparation of endo-6-substituted bicyclo[2.2.1]heptan-2-ones, a set of compounds whose synthesis previously has been arduous and difficult.[13,16]

Footnotes and References

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3. F. Rouessac, P. Le Perchec, and J. M. Conia, Bull. Soc. Chim. Fr., 818 (1967).
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8. Satisfactory elemental analyses and/or measurements of the exact mass of the molecular ion by high resolution mass spectrometry were obtained for all new compounds.
9. Spectral data for 1: IR 3065 (w), 2952(m), 2895 (m), 1747 (s), 1642 (m), 1405 (m), 1150 (m), 985 (m), 913 (s) cm^{-1}; NMR (60 MHz) δ 6.15-5.47 (br m, 1 H), 5.12 (m, 1 H), 4.90 (m, 1 H), 3.03-1.18 (br m, 9 H).
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11. Spectral data for 8: IR 3065 (w), 2905 (w), 1710 (s), 1670 (m), 1618 (s), 1460 (m), 1402 (m), 1168 (m), 982 (m), 912 (s) cm^{-1}; NMR (60 MHz) δ 6.23-5.58 (m, 2 H), 5.27 (m, 1 H), 5.10-4.93 (m, 1 H), 3.13 (d, J = 6 Hz, 2 H), 2.67-2.17 (m, 4 H).
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14. We are indebted to Professor N. H. Werstiuk, McMaster University, for furnishing copies of the IR and NMR spectra of epiisofenchone; N. H. Werstiuk and R. Taillefer, Can. J. Chem., 48, 3966 (1970).
15. Spectral data for 7: IR 2952 (s), 2870 (s), 1750 (s), 1448 (m), 1400 (m), 1375 (m), 1320 (w), 1130 (w), 1070 (w), cm^{-1}; NMR (220 MHz) δ 2.47 (d, J = 5 Hz, 1 H), 2.40-1.67 [br m with s at 1.23 and t (J = 7 Hz) at 0.85].
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