Thermal Rearrangements of 2-Cyclopropylcycloalk-2-enones

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Thermolysis of 2-(2,2-dimethylcyclopropyl)cyclopent-2-enone (2) and 2-cyclopropylcyclohex-2-enone (6) is shown to produce 2-(3-methylbut-2-enylidene)cyclopentanone (10) and 2-propylphenol (14), respectively, *via* homo[1,5]sigmatropic H-migration and isomerisation. Heating 2-cyclopropylcyclopent-2-enone (8) under a variety of conditions led only to decomposition; no products [*e.g.* (11)] resulting from vinylcyclopropane–cyclopentene rearrangement were detected.

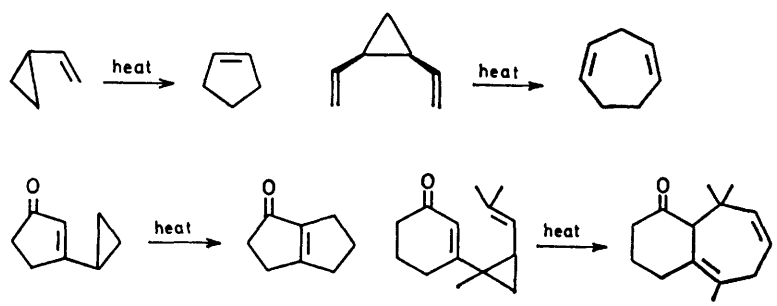
THERMAL rearrangements of vinylcyclopropanes and divinylcyclopropanes to cyclopentenes and cycloheptadienes, respectively (Scheme 1), provide useful methods for the annulative formation of functionalised cyclopentanes and cycloheptanes found amongst natural products. In general, the methods are limited only by the shortage of efficient synthetic routes to suitably functionalised vinyl- and divinyl-cyclopropanes. In one solution to this problem, several workers have explored the use of cyclopropylcuprates and β-halogeno-α,β-unsaturated cycloalkenones in the synthesis of a range of 3-cyclopropyl and 3-vinylcyclopropyl-cycloalkenones (Scheme 1). Almost without exception, these substrates undergo smooth thermal rearrangement, in the expected sense, leading to fused-ring cyclopentene and cycloheptadiene compounds.[1] To our knowledge no investigations have been made of the synthesis of cyclopentenes and cycloheptadienes by thermal rearrangement of the corresponding 2-cyclopropyl- and 2-(vinylcyclopropyl)-cycloalkenones. In this paper we describe a study of the synthesis, and thermal rearrangement of 2-cyclopropylcycloalk-2-enones, which has led to products resulting from exclusive homo[1,5]sigmatropic H-migration in the vinylcyclopropanes rather than to cyclopentene products from vinylcyclopropane–cyclopentene rearrangement.

During other investigations, we have demonstrated that irradiation of prop-2-enyl-substituted cyclopent-2-enones provides a useful route to certain 2-cyclopropylcyclopent-2-enones by photochemical di-π-methane rearrangement, *e.g.* (1) ⟶ (2).[2] From a synthetic viewpoint the method is limited by the sensitivity of the rearrangement to changes in the substituents on the 1,4-diene substrate (1), and in some cases by the paucity of synthetic routes to this class of compound.[3] We have now found that 2-cyclopropylcycloalk-2-enones are easily synthesised from Grignard additions of cyclopropylmagnesium bromide to the monoalkyl enol ethers of cycloalkane-1,2-diones, followed by hydrolysis and dehydration. Thus, reaction between the isobutyl ether (3) of cyclohexane-1,2-dione and cyclopropylmagnesium bromide led to the tertiary carbinol (4), which on treatment with dilute hydrochloric acid in ether led to the cyclohexanol (5). Treatment of (5) with toluene-*p*-sulphonic acid in benzene under Dean–Stark conditions then gave the enone (6). In a similar manner, the isobutyl ether (7) derived from cyclopentane-1,2-dione led to 2-cyclopropylcyclopent-2-enone (8).

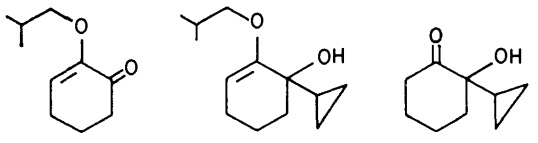
(1) (2)

Thermolysis of the vinylcyclopropane (2) in benzene at 300 °C resulted in smooth rearrangement to one major product which was isolated in 64% yield. U.v. and i.r. spectral data revealed the presence of a five-membered ring ketone ($\nu_{max.}$ 1 696 cm^{-1}) in conjugation with two double bonds [$\lambda_{max.}$ 308 nm (ε 8 050)], and ^1H and ^{13}C n.m.r. spectral data showed that both the C=C bonds were trisubstituted with one having geminal-methyl substitution. The combined spectral data were consistent with the dienone structure (10) resulting from homo[1,5]sigmatropic H-migration in (2), leading to (9), followed by isomerisation. Only one geometrical isomer was detected by spectral data, and this is almost certainly the *E*-isomer shown.

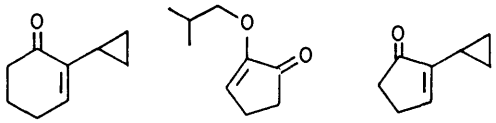
We next turned to the thermolysis of the vinylcyclo-



SCHEME 1

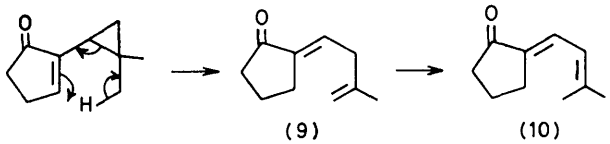


(3) (4) (5)

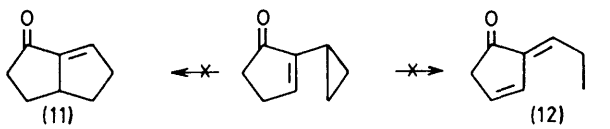


(6) (7) (8)

propane (8), which lacked additional methyl substituents in the cyclopropane ring capable of taking part in [1,5]-H-migration. Heating the vinylcyclopropane at various temperatures under a wide range of conditions resulted either in complete recovery of starting material or in total decomposition; we were unable to detect the



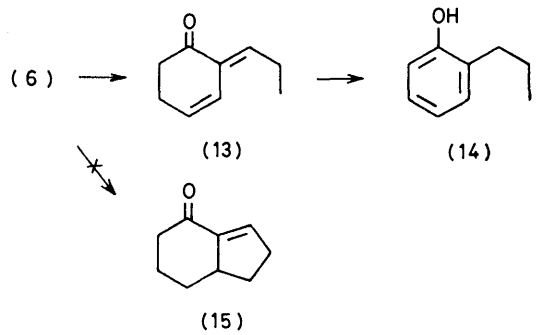
(9) (10)



(11) (12)

transient formation of the bicyclo[3.3.0]octenone (11) or products resulting from the formation of the reactive dienone (12) from an alternative homo[1,5]sigmatropic H-migration. This is to be contrasted with the corresponding thermolysis of 2-cyclopropylcyclohex-2-enone (6) which, at 300 °C, was cleanly transformed into 2-propylphenol (14), presumably *via* stepwise 1,5-H-migration [to (13)] and isomerisation; once again we were unable to detect the formation of products [*e.g.* (15)] resulting from vinylcyclopropane–cyclopentene rearrangement in (6).

The foregoing observations clearly reflect a limitation to the vinylcyclopropane–cyclopentene rearrangement when applied to 2-cyclopropylcycloalkenones. Since it is likely that a number of these rearrangements proceed by discrete radical intermediates, it is possible that the differing behaviour of 2- and 3-cyclopropyl-substituted cycloalkenones [compare (8) with Scheme 1] is associated with the additional stabilisation of the allyl radical centre in the latter, through the carbonyl group [*cf.* (16), Scheme 2]. Closure of the diradical (17) produced from (8) leading to a bridgehead conjugated double bond [in (11)] is probably also significant, since it is well known that such systems are quite strained.[4]

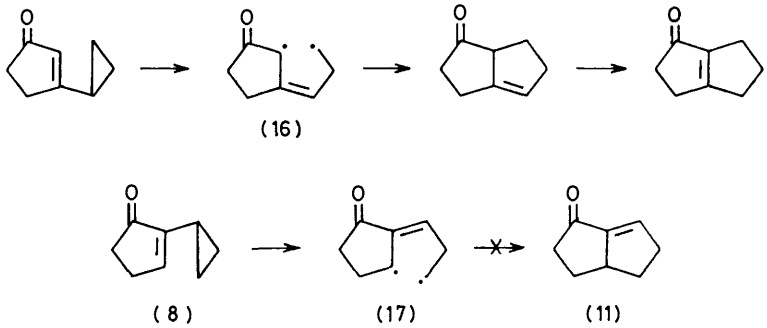


(6) (13) (14) (15)

EXPERIMENTAL

2-*Isobutoxycyclohex*-2-*enone* (3).—A solution of cyclohexane-1,2-dione (10 g) and isobutyl alcohol (22.5 ml) in dry benzene (90 ml) was heated under reflux for 3 h in the presence of toluene-*p*-sulphonic acid (0.13 g) with continuous removal of water (Dean–Stark). The cooled solution was washed with sodium hydrogencarbonate solution, then dried ($MgSO_4$) and evaporated. Distillation of the residue gave the *ether* (13.3 g, 88%) as a colourless liquid, b.p. 71 °C at 0.01 mmHg, $n_D^{20.5}$ 1.4768, $\nu_{max.}$ (film) 1 686 and 1 623 cm^{-1}; τ 4.33 (t, *J* 4.5 Hz, :CH), 6.66 (d, *J* 6 Hz, OCH_2), 7.5—7.8 (m, 4 H), 7.84—8.36 (m, 4 H), and 9.05 (d, *J* 7.5 Hz, $CHMe_2$) (Found: M^+, 168.1142. $C_{10}H_{16}O_2$ requires *M*, 168.1150).

2-*Cyclopropylcyclohex*-2-*enone* (6).—Reaction between 2-isobutoxycyclohex-2-enone (13 g) and cyclopropylmagnesium bromide (from 10.2 g of cyclopropyl bromide), as described for the five-membered ring analogue (8), gave 1-*cyclopropyl*-2-*isobutoxycyclohex*-2-*enol* (4) (80%), $n_D^{20.5}$ 1.4734, $\nu_{max.}$ 3 500 and 1 655 cm^{-1}, τ 5.36 (t, *J* 4 Hz, :CH), 6.62 (d, *J* 6 Hz, OCH_2), 7.69 (OH), 8.0—9.4 (m, 8 H), and 9.4—9.9 (m, 4 H), (Found: M^+, 210.1630. $C_{13}H_{22}O_2$



(16) (8) (17) (11)

SCHEME 2

requires M, 210.1620). Treatment of the alcohol in ether with dilute hydrochloric acid afforded *2-cyclopropyl-2-hydroxycyclohexanone* (5) (50%) as an oil, $\nu_{max.}$ (film) 3 500 and 1 714 cm^{-1}, τ 6.4 (OH), 7.2—9.0 (m, 8 H), and 9.0—9.8 (m, 5 H) (Found: M^+, 154.0995. $C_9H_{14}O_2$ requires M, 154.099 37).

A solution of 2-cyclopropyl-2-hydroxycyclohexanone (0.5 g) in benzene (125 ml) was heated under reflux for 2 h in the presence of toluene-*p*-sulphonic acid (0.1 g) with continuous removal of water (Dean–Stark). The cooled solution was washed with sodium hydrogencarbonate solution, then dried ($MgSO_4$) and evaporated. Chromatography of the residue in 1 : 1 ether–light petroleum (b.p. 40—60°) on silica gel gave the cyclohexanone (6) (0.25 g, 55%) as a colourless oil, $\lambda_{max.}$ 245 nm; $\nu_{max.}$ (film) 1 680 cm^{-1}, τ 3.7 (t, J 4 Hz, :C*H*), 7.4—8.6 (m, 3 H), 7.8—8.4 (m, 4 H), and 9.0—9.8 (m, 5 H) (Found: M^+, 136.0895. $C_9H_{12}O$ requires M, 136.0888), homogeneous in g.l.c. analysis (10% SE-30; 175 °C).

2-Cyclopropylcyclopent-2-enone (8).—A solution of 2-isobutoxycyclopent-2-enone [5] (2 g) in dry tetrahydrofuran (10 ml) was added dropwise over 0.5 h to a stirred solution of the Grignard reagent formed from cyclopropyl bromide (2.5 g) and activated magnesium [prepared from magnesium chloride (2.4 g), potassium iodide (3.7 g) and potassium metal (1.95 g)] [6] in tetrahydrofuran (150 ml) under nitrogen. The mixture was stirred at 25 °C for 1 h, and then treated with saturated aqueous ammonium chloride (20 ml) and extracted with ether. The combined organic extracts were washed with saturated sodium chloride solution, then dried ($MgSO_4$) and evaporated. Chromatography of the residue in 1 : 1 ether–light petroleum (b.p. 40—60 °C) on silica gel gave 1-cyclopropyl-2-isobutoxycyclopent-2-enol (1.95 g, 77%) as a colourless oil, n_D^{20} 1.4785, $\nu_{max.}$ (film) 3 400 and 1 645 cm^{-1}; τ 5.6 (m, :CH), 6.58 (m, OCH_2CH), 7.56—8.19 (m, 4 H), 8.0 (OH), 9.01 (d, J 8 Hz, $CHMe_2$), and 9.4—9.85 (m, 5 H).

A solution of the alcohol (1.6 g) in ether (16 ml) was stirred with dilute hydrochloric acid (16 ml) at 25 °C for 3 h. The ether layer was separated, then washed with saturated sodium chloride solution, dried ($MgSO_4$), and evaporated. Chromatography of the residue in 1 : 1 ether–light petroleum (b.p. 40—60 °C) on silica gel gave the *cyclopentenone* (8) (0.36 g, 42%) as a colourless oil, n_D^{22} 1.5025, $\lambda_{max.}$ (EtOH) 239 nm (ε 6 300); $\nu_{max.}$ (film) 1 694 and 1 630 cm^{-1}; τ 3.0 (t, J 6 Hz, :CH), 7.4—7.9 (m, 4 H), 8.28—8.6 (m, 1 H), and 8.96—9.6 (m, 4 H) (Found: M^+, 122.0729. $C_8H_{10}O$ requires M, 122.0716), homogeneous in g.l.c. analysis (10% SE-30; 180 °C).

2-(3-Methylbut-2-enylidene)cyclopentanone (10).—A solution of 2-(2,2-dimethylcyclopropyl)cyclopent-2-enone (0.05 g) [2] in benzene (1 ml) was heated at 300 °C in a sealed tube for 0.5 h, and then evaporated to dryness. Chromatography of the residue in 1 : 1 ether–light petroleum on silica gel gave the *diene* (32 mg) as an oil, $\lambda_{max.}$ (EtOH) 243 (ε 4 050) and 308 nm (8 050); $\nu_{max.}$ ($CHCl_3$) 1 696 and 1 620 cm^{-1}; τ 2.9 (dt, J 16 and 2.5 Hz, CH:C·CH_2), 4.1 (d, J 16 Hz, :CH), 7.2—7.5 (m, 2 H), 7.5—7.8 (m, 2 H), 7.8—8.2 (m, 2 H), and 8.09 (:CMe_2); δ_C 148.1 (s), 134.2 (s), 128.0 (d), and 122.2 (d) p.p.m. (Found: M^+, 150.1043. $C_{10}H_{14}O$ requires M, 150.1045), which was homogeneous in g.l.c. (50 ft SCOT capillary, OV-17; 145 °C)

2-n-Propylphenol (14).—A solution of 2-cyclopropylcyclohex-2-enone (0.055 g) in benzene (0.5 ml) was heated at 300 °C in a sealed tube for 0.25 h, and then dissolved in ether (10 ml) and extracted with aqueous sodium hydroxide solution (2%; 5 ml). The aqueous layer was separated, then acidified and extracted with ether. Evaporation gave the phenol (36 mg) τ 2.8—3.4 (m, 4 H), 4.7 (OH), 7.4 (t, J 7 Hz, CH_2), 8.3 (sextet, J *ca.* 7 Hz, CH_2), and 9.08 (t, J 7 Hz, CH_3) (Found: M^+, 136.0895. $C_9H_{12}O$ requires M, 136.0888), which showed spectral data identical with those of, and did not separate in g.l.c. (10% SE-30; 175 °C) from, an authentic sample synthesised by Claisen rearrangement of allyl phenyl ether followed by hydrogenation.

We thank the S.R.C. for a fellowship (to D. W.) and the Royal Society for an equipment grant.

[1/737 *Received*, 11*th May*, 1981]

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