Rearrangements of 8-Chloro-8-methylbicyclo[4.2.0]oct-2-en-7-one

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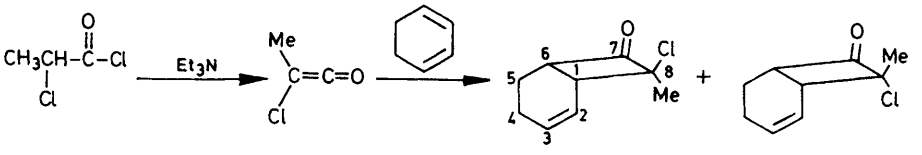
The *endo*- and *exo*-methyl isomers of 8-chloro-8-methylbicyclo[4.2.0]oct-2-en-7-one were separately treated with aqueous sodium carbonate, aqueous sodium hydroxide, silver nitrate in methanol, and sodium methoxide in methanol. A stereospecific ring contraction and an allylic substitution involving the enol form of the bicyclic ketone were found to be dependent on the base. Thermal rearrangement of the title compound resulted in the formation of propiophenone.

RING contraction of α-halogenocyclobutanones with aqueous base to yield cyclopropane derivatives has recently been reviewed.[1] The cycloaddition of halogenated ketens to olefinic compounds provides an excellent source of such α-halogenocyclobutanones and several such cycloadducts have been made from cyclopentadiene.[2] There are several recent reports on the treatment of 7-halogenobicyclo[3.2.0]hept-2-en-6-ones with different bases under various conditions,[3-6] the products being of ring expansions, ring contraction, and substitution. We have found that the *endo*-alkyl isomers of 7-alkyl-7-halogenobicyclo[3.2.0]hept-2-en-6-ones rearrange in base to 2-alkylcyclohepta-2,4,6-trienones and the *exo*-alkyl isomers undergo a stereospecific ring contraction. Garin and Cammack have reported that 7-chloro-7-methylbicyclo[3.2.0]hept-2-en-6-ones undergo stereospecific substitution and rearrangements with nucleophilic bases which depend upon base strength and temperature in 50% yield affording an isomer distribution of 4·9 : 1 *endo* : *exo*-methyl, (I) : (II). The cycloaddition in acetonitrile produced a 45% yield with an isomer distribution of 0·13 : 1 *endo* : *exo*-methyl. The isomers were separated and purified by fractional distillation to the extent of 90—95%. The dependence of the isomer distribution on the polarity of the solvent is apparently due to increased solvation of the halogen substituent in the more polar solvent thus increasing the size of that substituent and producing more *endo*-halogeno-isomer. This is consistent with the sterically favoured orthogonal approach of unsymmetrical keten and cyclopentadiene. The magnitude of the change in isomer distribution in this system is consistent with that in the bicyclo[3.2.0]heptenone system.[8]

Treatment of (I) with sodium methoxide in methanol at reflux yielded an immediate precipitate of sodium chloride and an 80% yield of the 6-methoxy-substitution



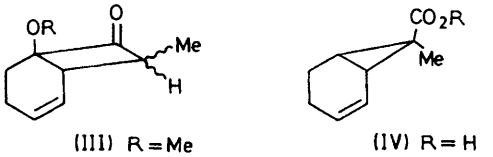
(I) (II)

stereochemistry at C-7 of the starting material. Brook and Harrison report that because of conformational effects in the cyclobutanone ring, 7-*exo*-chloro-7-isopropylbicyclo[3.2.0]hept-2-en-6-one rearranges abnormally on treatment with base to yield hydroxycyclohexenecarboxylic acids.

This paper describes a detailed examination of the rearrangements of 8-chloro-8-methylbicyclo[4.2.0]oct-2-en-7-one. The *endo*-methyl and *exo*-methyl systems were examined separately. This system was selected because of its availability but more importantly because it is not as stereochemically rigid as the bicyclo[3.2.0]heptenone system; *e.g.*, enolization is not as restricted due to the strain of the five-membered ring.

The *in situ* cycloaddition of chloro(methyl)keten to cyclohexa-1,3-diene provided the α-halogenocyclobutanones for this study,[7] and proceeded in hexane at room

products epimeric at C-8, (III). The *exo*-methyl isomer (II) underwent the same substitution reaction yielding, as expected, an identical isomer distribution of (III) (*ca.* 10 : 1 in favour of the thermodynamically more stable



(III) R = Me (IV) R = H
(V) R = H (VI) R = Me

exo-methyl isomer). This substitution must occur through the 6-enol form of the cyclobutanone.

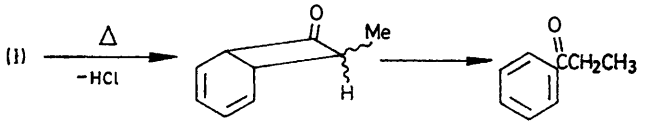
Reaction of (I) with 10% aqueous sodium hydroxide at reflux produced a stereospecific ring contraction product (IV), in *ca.* 65% yield. Treatment of (II) under identical

[1] J. M. Conia and J. R. Salaun, *Accounts Chem. Res.*, 1972, **5**, 33.
[2] W. T. Brady, *Synthesis*, 1971, 415.
[3] W. T. Brady and J. P. Hieble, *J. Amer. Chem. Soc.*, 1972, **94**, 4278.
[4] P. R. Brook and J. M. Harrison, *J.C.S. Chem. Comm.*, 1972, 997.
[5] P. R. Brook and A. J. Duke, *J. Chem. Soc.* (*C*), 1971, 1764.
[6] D. L. Garin and K. L. Cammack, *J.C.S. Chem. Comm.*, 1972, 333.
[7] W. T. Brady and R. Roe, jun., *J. Amer. Chem. Soc.*, 1971, **93**, 1662.
[8] W. T. Brady and R. Roe, jun., *J. Amer. Chem. Soc.*, 1970, **92**, 4618.

conditions produced the *exo*-methyl ring-contracted acid in 21% yield. The reaction mixture from (II) was viscous and polymeric, and no further volatile products could be isolated. The isomeric ring-contracted acids are easily distinguished by the chemical shift of the methyl group in the n.m.r. spectra.

These ring contractions are quite similar to those observed when the corresponding bicycloheptenones are refluxed with aqueous base except that with the *endo*-alkyl-bicycloheptenone isomers a competing ring expansion occurs to yield 2-alkylcyclohepta-2,4,6-trienones. No such ring expansion is observed in the bicyclooctenones, presumably because the attainment of an aromatic system is not as easily accessible as in the bicycloheptenone system.

Ring contraction and substitution both occurred when (I) and (II) were separately refluxed in 20% aqueous



(VII)

sodium carbonate. The substitution product (V) was produced in 60 and 65% yields respectively and only ⩽5% of the stereospecific ring-contracted product (IV) was produced in each case. The *exo*-methyl isomer of (V) predominated to the extent of *ca.* 8 : 1.

Treatment of (I) with silver nitrate in methanol at reflux afforded a 60% yield of a ring-contracted ester (VI). However, (II) reacted much slower under these conditions (24 h *vs.* 8 days) and the *exo*-methyl ester was formed in only a 26% yield along with an unidentified product. This result is consistent with a recent report by Harding and Trotter.[9]

Refluxing (I) and (II) with triethylamine in hexane overnight resulted in no substitution or ring contraction and the starting ketones were unchanged.

The bicyclo-ketones (I) and (II) were treated with sodium borohydride and also with aluminium isopropoxide, in an attempt to prepare the corresponding α-halogenocarbinols for investigation, but rearrangements occurred during the reduction; mixtures of products were produced and the alcohols were not isolated.

The bicyclic ketones (I) and (II) underwent an interesting rearrangement upon heating neat at 165—170° for 2½ days; propiophenone was produced in 60% yield. This reaction is similar to the thermal decomposition of 2-chlorocyclobutanone as recently reported by Metcalfe and Lee.[10] If dehydrochlorination and isomerization occurred, the conjugated diene (VII) might be produced. An aliquot portion of the reaction mixture after a short period of heating revealed two extra doublets in the n.m.r. spectrum at δ 1·2 and 1·3 which could correspond to the *endo*- and *exo*-isomers of the isomerized dehydrochlorinated product. Also, these two extra doublets were observed whenever (I) was vacuum distilled and the oil-bath temperature exceeded 120°. Further isomerization and ring opening of the isomerized dehydrochlorination product would be expected to lead to the aromatic ketone.

The ketones (I) and (II) upon refluxing in dilute or concentrated sulphuric acid also produced propiophenone.

EXPERIMENTAL

^{1}H n.m.r. spectra were recorded on a Jeolco PS-100 spectrometer employing tetramethylsilane as an internal standard and carbon tetrachloride as the solvent. G.l.c. was performed on an F. & M. Scientific model 700 gas chromatograph with a 10 ft × ¼ in column packed with 10% SE-30 on acid washed Chromosorb W (80—100).

8-Chloro-8-methylbicyclo[4.2.0]*oct-2-en-7-one* (I) *and* (II).—To a refluxing solution of cyclohexa-1,3-diene (0·4 mol) and triethylamine (0·3 mol) in hexane or acetonitrile (200 ml) was added 2-chloropropanoyl chloride (0·25 mol) in hexane or acetonitrile (25 ml). After the addition was completed, reflux was maintained for 4 h. The amine salt was removed by filtration and washed with the solvent. The filtrate was concentrated on a rotatory evaporator and the residue vacuum distilled to yield the adduct. A distribution of 4·9 : 1 *endo* : *exo*-methyl isomer was produced in hexane (50% yield) and 0·13 : 1 in acetonitrile (45% yield). The isomers were separated by fractional distillation at reduced pressure employing a 12 in Vigreux column. This distillation provided material of isomeric purity 90—95%; *endo*-methyl isomer b.p. 45° at 0·05 mmHg and *exo*-methyl isomer b.p. 48—50° at 0·05 mmHg.

6-Methoxy-8-methylbicyclo[4.2.0]*oct-2-en-7-one* (III).—A mixture of methanol (150 ml) and sodium (4 g) was vigorously refluxed while a solution of the *exo*-chloro-ketone (I) (5 g) in methanol (10 ml) was added. There was an immediate precipitation of sodium chloride. Refluxing was continued for 1 h and then the mixture was added to water (100 ml) and extracted with chloroform. The combined extracts were dried, the solvent was removed on a rotatory evaporator, and the residue was distilled in vacuum to yield the isomeric ketones (III) (both ketones epimeric at C-8), b.p. 41—42° at 0·05 mmHg (80% yield), m.p. 57—59° (both isomers) (from ethanol) (Found: C, 71·75; H, 8·4. Calc. for $C_{10}H_{14}O_2$: C, 72·3; H, 8·45%); $\nu_{max.}$ 1780 cm^{-1} (C=O); δ 1·1 (*endo*-Me) and 1·2 (*exo*-Me) (3H, d), 2·0 (5H, m), 2·6 (1H, quintet), 3·3 (3H, s), and 5·9 (2H, m) (the isomer distribution was determined on the crude product and found to be *ca.* 10 : 1 in favor of the *exo*-methyl isomer). Treatment of (II) (5 g) under the same conditions yielded an identical mixture of methoxy-substituted products.

7-Methylbicyclo[4.1.0]*hept-2-en-7-carboxylic Acid* (IV).—The *exo*-chloro-ketone (I) (5 g) was refluxed with aqueous 10% sodium hydroxide solution (150 ml) for 4—6 h. The mixture was cooled, acidified, and extracted with chloroform, and the combined extracts were dried, and concentrated on a rotatory evaporator. Distillation in vacuum afforded the endo-*methyl acid* (65%), b.p. 96—97° at 0·05 mmHg; m.p. 81—83°. The *exo*-methyl isomer (II) produced the exo-*methyl acid* (21%) b.p. 86—90° at 0·01 mmHg; m.p. 86—88°. No other volatile products could be obtained from the reaction mixture (Found: C, 70·7; H, 8·0.

[9] K. E. Harding and J. W. Trotter, Southwestern Regional Meeting, American Chemical Society, December, 1973, El Paso, Texas.

[10] E. K. C. Lee and J. Metcalfe, *J. Amer. Chem. Soc.*, 1973, **95**, 4316.

$C_9H_{12}O_2$ requires C, 71·05; H, 7·9%); $\nu_{max.}$ 1690 cm^{-1} (C=O); δ 1·18 (*endo*-methyl) and 1·38 (*exo*-methyl) (3H, s), 2·0 (6H, m), 5·85 (2H, m), and 10—11 (OH, s).

6-Hydroxy-8-methylbicyclo[4.2.0]*oct-2-en-7-one* (V).—The *exo*-chloro-ketone (I) (5 g) in aqueous 20% sodium carbonate solution was refluxed for 10 h. Upon cooling, the mixture was extracted with chloroform, and the combined extracts were dried, and concentrated on a rotatory evaporator. Vacuum distillation afforded the isomeric hydroxy-ketones (V) (60%), b.p. 77—79° at 0·5 mmHg (both isomers); m.p. 67—70° (Found: C, 70·95; H, 7·8. Calc. for $C_9H_{12}O_2$: C, 71·05; H, 7·9%); $\nu_{max.}$ 1765 (C=O) and 1635 cm^{-1} (C=C); δ 1·02 (*endo*-methyl) and 1·09 (*exo*-methyl) (3H, d), 1·8 (m 5H), 3·3 and 2·7 (1H, quintet), 4—5 (s, OH), and 5·9 (2H, m).

The *exo*-methyl isomer (II) produced the same mixture of isomers (65%). The ratio of isomers in both cases was *ca.* 8 : 1 in favour of the *exo*-methyl isomer. Also, with both (I) and (II), a small amount (<5%) of the stereospecific ring contracted product (IV) was produced.

Methyl 7-Methylbicyclo[4.1.0]*hept-2-ene-7-exo-carboxylate* (VI).—Upon the addition of the *exo*-chloro-ketone (I) (10 g) to a refluxing solution of silver nitrate (15 g) in methanol (150 ml), a white precipitate was formed immediately and the reaction was continuously refluxed for 24 h. The salt was removed by filtration and the filtrate concentrated on a rotatory evaporator. The residue was diluted with water and extracted with chloroform, and the combined extracts were concentrated and distilled affording the *bicyclic ester* (VI) (60%), b.p. 52—54° at 0·05 mmHg; $\nu_{max.}$ 1720 cm^{-1} (C=O); δ 1·10 (3H, s), 1·80 (6H, m), 3·55 (3H, s), and 5·62 (2H, m) (Found: C, 72·45; H, 8·45%; M^+, 166. $C_{10}H_{14}O_2$ requires C, 72·3; H, 8·45%; *M*, 166).

Methyl 7-Methylbicyclo[4.1.0]*hept-2-ene-7-endo-carboxylate*.—The *endo*-chloro-ketone (II) was treated with silver nitrate in methanol as described above, for 8 days to give the *ester* (26%), b.p. 39—40° at 0·1 mmHg (Found: C, 71·4; H, 8·5%; M^+, 166); $\nu_{max.}$ 1720 cm^{-1} (C=O); δ 1·30 (3H, s), 1·85 (6H, m), 3·50 (3H, s), and 5·50 (2H, m).

Thermal Rearrangement of (I).—The *exo*-chloro-ketone (I) (5 g) was heated neat for 2·5 days on an oil-bath (165—170°). Vacuum distillation afforded propiophenone (2 g, 60%), b.p. 52—56° at 0·05 mmHg.[11] Comparison with an authentic sample revealed identical retention times on g.l.c. and identical n.m.r. spectra.

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[11] K. Auwers, *Ber.*, 1912, **45**, 996.