Acid-catalysed Cyclisations of Cyclo-octenylidene Derivatives to produce Bicyclo[3.3.1]nonanes

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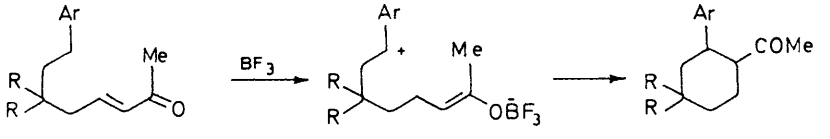
Heating ethyl (cyclo-oct-4-enylidene)acetate (8) with boron trifluoride–ether complex in benzene gives a mixture of ethyl 1-phenylbicyclo[3.3.1]nonane-9-carboxylate (11) and the corresponding acid (12). Reduction of (11) with lithium aluminium hydride followed by dehydration yields 9-methylene-1-phenylbicyclo[3.3.1]nonane (14) whose structure was confirmed by an independent synthesis.

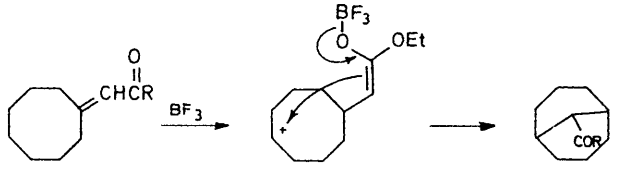
On treatment with boron trifluoride–ether complex or 70% perchloric acid the αβ-unsaturated ketones (1a—c) are transformed into the ketones (2a—c) respectively, by a mechanism involving a 1,5-hydride shift.[1] Seeking to extend this reaction, we considered its application to



(1) a ; Ar = *p*-MeO·C_6H_4, R = Me
b ; Ar = *p*-HO·C_6H_4, R = Me
c ; Ar = *p*-HO·C_6H_4, R = H

(2)

medium rings. In this case, the well known propensity for medium ring compounds to undergo transannular hydride shifts [2] might assist the reaction and intramolecular trapping of the carbonium ion would result in a bridged ring system. Our initial experiments used the cyclo-octylidene ester (3) [3] whose conversion into the bicyclo[3.3.1]nonane (4) was envisaged (Scheme 1). In the event, no bicyclic products of type (4) were obtained from (3) under a variety of acid conditions including those



(3) R = OEt
(5) R = Me

(4) R = OEt
(6) R = Me

Scheme 1

successful for conversion of (1) into (2). The αβ-unsaturated methyl ketone (5), prepared by hydrolysis of (3) followed by treatment with methyl-lithium, also failed to give the methyl ketone (6) under similar conditions. This result was not unexpected in view of the fact that the necessary hydride shift would require formation of a secondary from a tertiary carbonium ion.

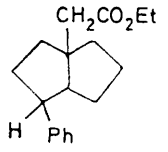
The reactivity of the cyclo-octenylidene esters (7) and (8) towards acid was then examined. Although no homogeneous product was isolated from (7), heating the ester

(7) (8)

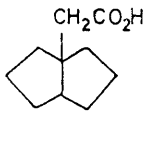
(8) under reflux in 1 : 1 benzene and boron trifluoride–ether complex gave a mixture of an ester (A) and its crystalline acid (B). From the n.m.r. and mass spectra it was obvious that a phenyl ring had been incorporated into (A) and (B). The only other distinctive feature of the n.m.r. spectrum was a broad singlet at τ 6·9. Initially we considered the bicyclo[3.3.0]octane structure (9) as the structure of (A), where acid-catalysed ring-closure was followed by Friedel–Crafts alkylation of benzene. For comparison, the carboxylic acid (10) was prepared by Arndt–Eistert homologation of the known bicyclo-[3.3.0]octane-1-carboxylic acid [4] and characterised as its crystalline amide. A prominent peak in the n.m.r.

[1] R. S. Atkinson, *Chem. Comm.*, 1969, 735; R. S. Atkinson and R. H. Green, *J.C.S. Perkin I*, 1974, 394.
[2] For examples see A. C. Cope, M. M. Martin, and M. A. McKervey, *Quart. Rev.*, 1966, **20**, 119.
[3] J. Wolinsky and K. L. Erickson, *J. Org. Chem.*, 1965, **30**, 2208.
[4] M. A. McKervey, H. A. Quinn, and J. J. Rooney, *J. Chem. Soc. (C)*, 1971, 2430.

spectrum of (10) was a sharp two-proton singlet at τ 7·55. This singlet was absent in the spectrum of the unknown



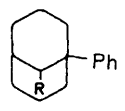
(9)



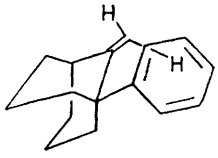
(10)

ester (A), leading us to reject a bicyclo[3.3.0] skeleton for the structure of the latter.

On the basis of the evidence below, structures (11) and (12) have been assigned to (A) and (B) respectively.[5]



(11) R = CO_2Et
(12) R = CO_2H
(13) R = CH_2OH
(15) R = CH_2Cl

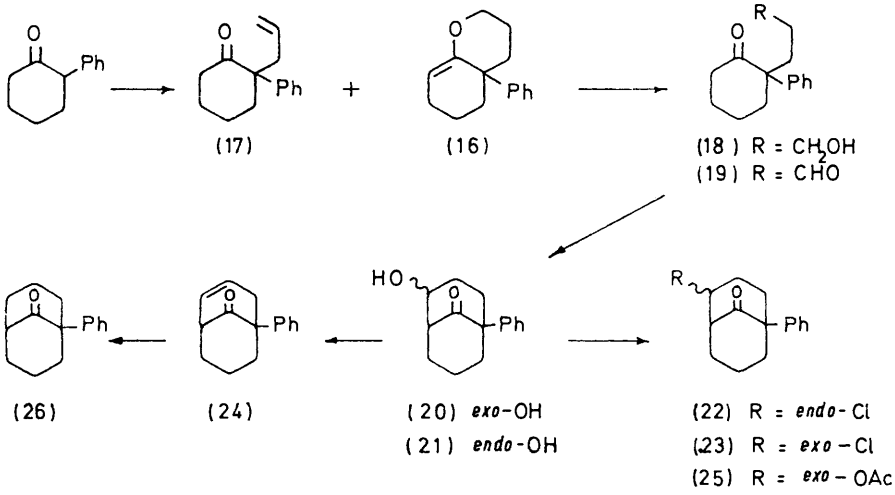


(14)

Reduction of the ester with lithium aluminium hydride gave a crystalline alcohol (13) which was dehydrated with phosphoryl chloride in pyridine to a mixture of an olefin (14) and a crystalline chloride (15); this mixture was wholly converted into the olefin by dehydrohalogenation with potassium hydroxide in ethylene glycol. The n.m.r. spectrum of the olefin was particularly informative: two olefinic protons were visible (τ 5·25 and 5·95), both with coupling constants of 2·2 Hz. Thus the olefin contains an *exo*-methylene group and the ester group in (11) must, therefore, be on a carbon bearing a single proton, presumably the broadened singlet at τ 6·9. In the n.m.r. spectrum of the chloride (15), the protons on the carbon bearing the chlorine appear as the AB part of an ABX system which simplifies to the AB system on double irradiation. Evidently these two protons are diastereotopic and the adjacent carbon atom must be an asymmetric centre. The structure (11) for the ester (A) accommodates all the data above and accounts for the large separation between the two olefinic resonances since that which is closer to the phenyl ring [see (14)] will be more shielded. However, there was little evidence to favour the bicyclo[3.3.1]- over the bicyclo[4.2.1]-nonane skeleton. To settle this point, the olefin (14) was synthesised by an alternative route.

Synthesis of the Olefin (14).—Alkylation of 2-phenylcyclohexanone with 1,3-dibromopropane and sodium hydride in dimethylformamide gave a mixture of the enol ether (16) and the olefin (17) (Scheme 2). It was expedient to separate these two products chromatographically after acid hydrolysis of the enol ether to the keto-alcohol (18). Oxidation of (18) to the aldehyde (19) followed by acid cyclisation gave two crystalline epimeric alcohols (20) and (21) separable by chromatography and identified by the width at half-height of the signal of >C*H*OH.[6]

Attempted dehydration of each of the alcohols (20) and (21) with phosphoryl chloride in pyridine gave the corresponding epimeric chlorides (22) and (23) respectively, in good yield, but none of the required dehydration product. This olefin (24) was obtained, however, by solvolysis of the tosylate from the *exo*-alcohol (20) in buffered acetic acid in 75% yield.[7] A lower yield (22%) of the same olefin was obtained from the *endo*-alcohol (21) by the same method, accompanied by the *exo*-acetate (25). Hydrogenation of the olefin (24) with palladium on charcoal gave a crystalline sample of the ketone (26), identical with a sample prepared by ozonolysis of the olefin (14). Finally, Wittig methylenation of the ketone (26) gave the olefin (14) in excellent yield. Subsequent



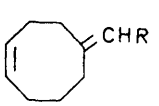
SCHEME 2

[5] Preliminary communication, R. S. Atkinson and R. H. Green, *J.C.S. Chem. Comm.*, 1973, 890.

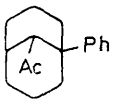
[6] W. Kraus, W. Rothenwöhrer, and R. Chassin, *Tetrahedron Letters*, 1969, 4581.

[7] E. W. Colvin, J. Martin, W. Parker, R. A. Raphael, B. Shroot, and M. Doyle, *J.C.S. Perkin I*, 1972, 860.

to our synthesis of ketone (26), we discovered that this compound had been recently obtained by an alternative route.[8] Comparison with a sample kindly supplied by Professor Nicoletti shows the two samples to be identical.



(27) R = Ac
(29) R = CO_2H



(28)

Boron trifluoride–ether–benzene also converts the αβ-unsaturated methyl ketone (27) into the bicyclic ketone (28) in 25% yield; ketone (27) was obtained by hydrolysis of ester (8) to the corresponding acid (29) followed by treatment with methyl-lithium. The identity of (28) was established by its formation from acid (12) on treatment with methyl-lithium.

Our investigations into the mechanism of the transformation of cyclo-octenylidene ester (8) into the bicyclic ester (11) are continuing.

EXPERIMENTAL

M.p.s were determined with a Kofler hot-stage apparatus and are corrected. The i.r. spectra of crystalline compounds were determined as Nujol mulls and of other compounds as thin films. N.m.r. spectra were measured with a Varian T60 or JEOL-JNM-PS-100 and mass spectra with an A.E.I. MS9 spectrometer. Kieselgel refers to Kieselgel PF_{254} (Merck).

Cyclo-octylideneacetone (5).—A solution of methyl-lithium was prepared from lithium (0·6 g) and methyl iodide (6 ml) in ether and was added over 10 min to a well-stirred solution of cyclo-octylideneacetic acid [3] (0·6 g) in dry tetrahydrofuran (THF) (20 ml). The reaction mixture was stirred for a further 1·5 h and then cautiously poured into sodium thiosulphate solution (100 ml; 10%). The aqueous layer was further extracted with ether, and the combined ether extracts were washed with water and dried. Removal of solvent gave a yellow oil (240 mg) whose i.r. indicated the presence of the αβ-unsaturated ketone (5), $\nu_{max.}$ 1680s cm^{-1}. Distillation of this product (75—80° at 0·5 mmHg) resulted in partial isomerisation to a 3 : 2 mixture of αβ- and βγ-isomers, $\nu_{max.}$ 1710s, 1680m, and 1600m cm^{-1}; τ (CCl_4) 3·90 (s, $=CHCOCH_3$), 4·50 (t, *J* 6 Hz, =CH–, βγ-isomer), 7·00 (s, $-CH_2COCH_3$), 7·25 (t, *J* 6 Hz, 2 allylic H, αβ-isomer), 7·90 (s, $CO{\cdot}CH_3$), and 7·5—8·8 (allylic and aliphatic H); *2,4-dinitrophenylhydrazone*, m.p. 100—101·5° (Found: C, 58·55; H, 6·35; N, 16·0. $C_{17}H_{22}N_4O_4$ requires C, 58·95; H, 6·4; N, 16·2%).

Ethyl Cyclo-oct-4-enylideneacetate (8).—Triethyl phosphonoacetate (22·3 g) was added dropwise to a stirred suspension of sodium hydride (2·23 g) in dry THF (100 ml) under nitrogen. The mixture was stirred for 40 h at room temperature before dropwise addition of cyclo-oct-4-enone (12·0 g) in dry THF (150 ml). This mixture was stirred for a further 120 h before pouring into water (500 ml) and extracting with ether. The ethereal extracts were combined, washed successively with water and saturated sodium chloride solution, and dried ($MgSO_4$). Evaporation of the ether yielded a pale yellow oil (18 g), which was distilled under vacuum giving *ethyl cyclo-oct-4-enylideneacetate* (8) as an oil (12·5 g, 65%), b.p. 104—106° at 1 mmHg, $\nu_{max.}$ 1710s, 1640s, and 722m cm^{-1}; τ (CCl_4) 4·25 (m, 3 olefinic H), 5·85 (q, *J* 8 Hz, CH_3CH_2), 6·85—8·90 (m, 10 aliphatic H), and 8·70 (t, *J* 8 Hz, CH_3CH_2); $\lambda_{max.}$ (EtOH) 225 nm (log ε 4·21) (Found: C, 74·3; H, 9·3. $C_{12}H_{18}O_2$ requires C, 74·2; H, 9·35%).

Ethyl 1-Phenylbicyclo[3.3.1]*nonane-9-carboxylate* (11) *and 1-Phenylbicyclo*[3.1.1]*nonane-9-carboxylic Acid* (12).—To ethyl cyclo-oct-4-enylideneacetate (1·12 g), dissolved in dry benzene (50 ml) was added boron trifluoride–ether complex (50 ml) and the solution was heated under reflux for 17 h. The cooled mixture was then cautiously poured into sodium carbonate solution (500 ml; 10%) and shaken until evolution of carbon dioxide had ceased. After separation of the benzene layer the aqueous layer was extracted twice more with benzene, and the combined organic extracts were washed with sodium carbonate solution (50 ml; 10%) and then with water and dried ($MgSO_4$). Evaporation of the solvent gave a dark brown oil (0·74 g). Chromatography (40 g silica; benzene as eluant) gave the *bicyclic ester* (11) as an oil (0·47 g, 30%), b.p. 145—150° at 0·3 mmHg, $\nu_{max.}$ 1740s, 755s, and 695s cm^{-1}; τ (CCl_4) 2·80 (m, 5 aromatic H), 6·1 (q, *J* 7 Hz, CH_3CH_2), 6·90br (s, 9-H), 7·00—9·30 (m, 13 aliphatic H), and 8·90 (t, *J* 7 Hz, CH_3CH_2) (Found: C, 79·4; H, 8·95. $C_{18}H_{24}O_2$ requires C, 79·35; H, 8·9%), *m/e* 272 (35%, M^+), 229 (22), 226 (68), 199 (87), 198 (65), 183 (57), 155 (73), 117 (40), 115 (55), 91 (100), and 77 (30).

The combined basic washings from the extraction were acidified with concentrated hydrochloric acid and extracted with chloroform. The combined chloroform extracts were washed with water, dried ($MgSO_4$), and evaporated to give the *bicyclic acid* (12) as a white solid (0·27 g) which was crystallised from chloroform–light petroleum as colourless flakes (0·22 g, 19%), m.p. 165·5—166·5°, $\nu_{max.}$ 2700s,br, 1705s, and 695s cm^{-1}; τ ($CDCl_3$) −2·03 (s, CO_2H), 2·70 (m, 5 aromatic H), 6·85br (s, 9-H), and 7·10—8·35 (m, 13 aliphatic H) (Found: C, 78·7; H, 8·15. $C_{16}H_{20}O_2$ requires C, 78·7; H, 8·2%).

9-Hydroxymethyl-1-phenylbicyclo[3.3.1]*nonane* (13).—The ester (11) (800 mg) dissolved in dry THF (10 ml) was added dropwise to a stirred suspension of lithium aluminium hydride (250 mg) in dry THF (20 ml). This mixture was refluxed for 2 h, and excess of lithium aluminium hydride was destroyed by addition of ethyl acetate and then water. The usual work-up gave the alcohol (13) (658 mg, 97%), m.p. 78—79° (from light petroleum), $\nu_{max.}$ 3305s,br, 745s, and 695 cm^{-1}; τ ($CDCl_3$) 2·70 (m, 5 aromatic H), 6·2—6·9 (m, $-CH_2OH$), and 7·40—9·00 (m, 15 aliphatic H) (Found: C, 83·4; H, 9·6. $C_{16}H_{22}O$ requires C, 83·45; H, 9·65%).

Dehydration of the Alcohol (13).—The foregoing alcohol (443 mg), phosphoryl chloride (0·7 ml), and dry pyridine (2·0 ml) were heated under reflux for 2 h. The cooled mixture was then poured into ice–water and extracted with ether (× 3). The combined extracts were then washed successively with 2N-hydrochloric acid (× 2), sodium hydrogen carbonate solution, and saturated sodium chloride solution, dried ($MgSO_4$), and the ether removed. Column chromatography (30 g Kieselgel; benzene as eluant) of the residue gave an oil (350 mg) whose g.l.c. (3% OV 17, oven temperature 250 °C, N_2 flow rate 50 ml min^{-1}) showed two components in the ratio of 45 : 55 (t_R 1·3 and 2·9 min). The olefin (14) was obtained by heating the crude mixture (153 mg) with ethylene glycol (4 ml) and potassium hydroxide (400 mg), under nitrogen, for 3 h. The cooled reaction mix-

[8] L. Baiocchi, A. Gambacorta, R. Nicoletti, and V. Petrillo, *Ann. Chim.* (*Italy*), 1971, 744.

ture was poured into water, the solution extracted with ether, and the ethereal extracts dried ($MgSO_4$). Evaporation gave an oil (154 mg) whose n.m.r. spectrum indicated total conversion into the alkene. Minor contaminants were removed by Kieselgel chromatography and distillation, to yield pure 9-*methylene*-1-*phenylbicyclo*[3.3.1]*nonane* (14) (135 mg), b.p. 85° at 0·1 mmHg, $\nu_{max.}$ 1640m, 890s, 745s, and 700s cm^{-1}; τ (CCl_4) 2·70 (3H, m, aromatic), 2·80 (2H, s, aromatic), 5·25 (d, J 2·2 Hz, olefinic H), 5·95 (d, J 2·2 Hz, olefinic H), 7·30br (s, 5-H), and 7·60—8·55 (m, 12 aliphatic H) (Found: C, 90·2; H, 9·65. $C_{16}H_{20}$ requires C, 90·5; H, 9·5%).

1-*Phenylbicyclo*[3.3.1]*nonan*-9-*one* (26) *and* 9-*Chloromethyl*-1-*phenylbicyclo*[3.3.1]*nonane* (15).—The mixture obtained from the phosphoryl chloride dehydration above (180 mg) was dissolved in chloroform (5 ml), cooled to −76°, and ozone was passed through until the i.r. band at 890 cm^{-1} had disappeared. The mixture was then slowly warmed to ambient temperature and chloroform was removed on a rotary evaporator. This gave a viscous oil which was shaken for 10 min with water (10 ml) and then extracted into ether. The ethereal extract was dried ($MgSO_4$), the solvent removed, and the residue (176 mg) chromatographed (12 g Kieselgel; benzene as eluant) to give 9-*chloromethyl*-1-*phenylbicyclo*[3.3.1]*nonane* (15) (80 mg) as cubes, m.p. 74·5—75·5° (from ethanol), $\nu_{max.}$ 1595m, 1025s, 775s, 755s, and 735s cm^{-1}; τ ($CDCl_3$) 2·75 (m, 5 aromatic H), 6·31 (d, J 11 Hz), and 6·73 (dd, J 11 and 4 Hz) ($-CH_2Cl$) [upon double irradiation at τ 7·55 ($CHCl_3$ as lock) this system simplified to dd, J 11 Hz], and 7·30—8·65 (13 aliphatic H) (Found: C, 76·9; H, 8·25. $C_{16}H_{21}Cl$ requires C, 77·25; H, 8·5%).

The next eluted fraction was 1-*phenylbicyclo*[3.3.1]*nonan*-9-*one* (26) (20 mg) which crystallised from ethanol as needles, m.p. 81·5—83·0°. The i.r., mass spectrum, and mixed m.p. were identical with those of the material synthesised by the method described below.

Synthesis of 9-*Methylene*-1-*phenylbicyclo*[3.3.1]*nonane* (14).—2-Phenylcyclohexanone [9] (12 g) was dissolved in dry dimethylformamide (50 ml) and sodium hydride (1·9 g) was added with vigorous stirring. The mixture was warmed to 43° and stirred for 25 min. 1,3-Dibromopropane (14 g) was then added dropwise over 5 min, followed by more sodium hydride (1·9 g). After stirring at 43° for 2 h, and at ambient temperature for a further 1 h, the mixture was cautiously poured into water (750 ml) and extracted with benzene (× 4). The combined benzene extracts were washed with water (× 3), with sodium chloride solution, and dried ($MgSO_4$). Removal of the solvent gave a yellow oil (18·5 g) which was used directly.

This yellow oil (0·5 g) was chromatographed on Kieselgel (1 : 2 benzene–light petroleum as eluant) to give the enol ether (16) (140 mg, 35%) as an oil which could not be distilled without decomposition, $\nu_{max.}$ 1670s, 1145s, 760s, and 700s cm^{-1}; τ (CCl_4) 2·70 (5 aromatic H), 4·65 (t, J 3 Hz, olefinic H), 5·75—6·65 (m, $-OCH_2-$), and 7·35—9·20 (m, 10 × aliphatic H).

Further elution gave 2-*phenyl*-2-(*prop*-2-*enyl*)*cyclohexanone* (17) (139 mg, 35%) as an oil, b.p. 126—129° at 0·25 mmHg, $\nu_{max.}$ 1635m, 915s, 760s, and 705s cm^{-1}; τ (CCl_4) 2·80 (m, 5 × aromatic H), 4·10—5·40 (m, 3 olefinic H), and 7·10—8·80 (m, 10 aliphatic H) (Found: C, 84·1; H, 8·55. $C_{15}H_{18}O$ requires C, 84·0; H, 8·4%).

[9] M. S. Newman and M. D. Farbman, *J. Amer. Chem. Soc.*, 1944, **66**, 1551.

[10] R. Ratcliffe and R. Rodehorst, *J. Org. Chem.*, 1970, **35**, 4000.

2-(3-*Hydroxypropyl*)-2-*phenylcyclohexanone* (18).—The crude product from the previous reaction (18·0 g) was dissolved in acetone (200 ml) and water (10 ml), and concentrated sulphuric acid (10 ml) was cautiously added. The mixture was then stirred at room temperature for 18 h, reduced in volume on a rotary evaporator, saturated with water, and extracted with ethyl acetate. After neutralising the aqueous layer with solid sodium hydrogen carbonate and extracting twice more with ethyl acetate, the combined extracts were washed with sodium hydrogen carbonate solution, dried ($MgSO_4$), and evaporated to yield a brown oil (17·0 g). A yellow oil was first eluted on passing through silica in benzene; elution with ethyl acetate gave the crude hydroxy-ketone (9·6 g). This was purified by chromatography on Kieselgel with 3 : 2 benzene–ethyl acetate as eluant giving the pure *hydroxy-ketone* (18) as an oil (4·36 g), b.p. 175—180° at 0·3 mmHg, $\nu_{max.}$ 3385s,br, 1700s, 1060s, and 760s cm^{-1}; τ (CCl_4) 2·80 (m, 5 aromatic H), 6·65 (t, J 6 Hz, $-CH_2OH$), 6·90 (s, disappears on shaking with D_2O, OH) and 7·05—9·30 (m, 12 aliphatic H) (Found: C, 77·55; H, 8·5. $C_{15}H_{20}O_2$ requires C, 77·55; H, 8·7%).

Oxidation of the Hydroxy-ketone (18).[10]—Chromium trioxide (9·9 g) was added to a stirred mixture of purified dichloromethane (130 ml) and dry pyridine (16 ml), and the resulting deep red solution was stirred at room temperature for 15 min. The foregoing hydroxy-ketone (18) (0·99 g) was added in one portion and the reaction mixture stirred at room temperature for a further 5 min. After decanting the dichloromethane, the residual chromium salts were washed with dichloromethane (× 3). Hydroquinone (10 mg) was added to the combined dichloromethane layers, and these were then washed successively with 2N-sodium hydroxide solution (× 3), dilute hydrochloric acid (10%), sodium hydrogen carbonate solution, and water, before drying ($MgSO_4$). Removal of the solvent gave a light brown oil (700 mg, 71%) whose i.r. spectrum indicated complete oxidation to the aldehyde (19). This product was used in the next step without further purification, $\nu_{max.}$ 2710w, 1720s, 1705s, 740s, and 710s cm^{-1}; τ (CCl_4) 0·5br (s, −CHO), 2·75 (m, 5 aromatic H), and 7·00—9·10 (m, 12 aliphatic H).

exo- *and* endo-4-*Hydroxy*-1-*phenylbicyclo*[3.3.1]*nonan*-9-*one* (20) *and* (21).—The aldehyde above (870 mg) was dissolved in dioxan (5 ml), and a solution of hydrochloric acid (6N; 3 ml) in dioxan (5 ml) was added dropwise with stirring, at 0°, under nitrogen. The mixture was stirred for 24 h at ambient temperature in the dark, and then saturated with water and extracted with ether. The ethereal solution was washed with sodium hydrogen carbonate solution and sodium chloride solution, dried ($MgSO_4$), and evaporated, to yield a yellow oil (700 mg). Column chromatography (65 g Kieselgel; 3 : 2 benzene–ethyl acetate as eluant) gave endo-4-*hydroxy*-1-*phenylbicyclo*[3.3.1]*nonan*-9-*one* (21) which crystallised as needles from ethyl acetate–light petroleum (210 mg), m.p. 98—99°, with a second crop (23 mg) with m.p. 96·5—98·0°, $\nu_{max.}$ 3500s,sh, 1705s, 1060s, 760s, and 700s cm^{-1}; τ (CCl_4) 2·75 (m, aromatic H), 5·75—6·25 (m, $W_{\frac{1}{2}}$ 15 Hz, C*H*OH), 6·80 (s, OH), and 7·05—8·20 (m, 11 aliphatic H) (Found: C, 78·0; H, 7·65. $C_{15}H_{18}O_2$ requires C, 78·25; H, 7·9%).

Further elution gave a mixture of epimers (49·4 mg) followed by the exo-*isomer* (20), as long needles (from chloroform–light petroleum) (124 mg), m.p. 130—131°, $\nu_{max.}$ 3300m,br, 3240m,br, 1725s,sh, 935s, 750s, and 705s cm^{-1}; τ (CCl_4) 2·70 (m, 5 aromatic H), 5·50—5·80 (m, $W_{\frac{1}{2}}$ 8 Hz, C*H*OH), 7·00 (s, OH), and 7·10—8·50 (m, 11 aliphatic H)

(Found: C, 77·95; H, 7·7. $C_{15}H_{18}O_2$ requires C, 78·25; H, 7·9%). The total yield of (20) and (21) was 47%.

Attempted Dehydration of the Hydroxy-ketones (20) *and* (21) *with Phosphoryl Chloride–Pyridine*.—The *exo*-isomer (20) (37·0 mg) was dissolved in dry pyridine (3 ml), phosphoryl chloride (0·1 ml) was added, and the solution heated at 100° for 2 h. The cooled mixture was poured into ice–water, the solution was extracted twice with ether, and the combined organic layers were washed with dilute hydrochloric acid (10%) (× 2), with saturated sodium chloride solution, dried ($MgSO_4$), and evaporated to yield a white solid. Crystallisation from light petroleum gave endo-4-*chloro*-1-*phenylbicyclo*[3.3.1]*nonan*-9-*one* (22) as long rods (33·9 mg, 85%), m.p. 115—116°, $\nu_{max.}$ 1710s, 745s, and 695s cm^{-1}; τ ($CDCl_3$) 2·70 (m, 5 aromatic H), 5·25—5·85 (m, $W_{\frac{1}{2}}$ 20 Hz, CHCl), and 6·70—8·60 (m, 12 aliphatic H) (Found: C, 72·4; H, 6·9. $C_{15}H_{17}ClO$ requires C, 72·5; H, 6·85%).

Treatment of the *endo*-isomer (21) (36·8 mg) as above gave an oily white solid. Crystallisation from chloroform–light petroleum gave the exo-4-*chloro-isomer* (23) (34 mg, 82%) as cubes, m.p. 99—99·5°, $\nu_{max.}$ 1715s, 750s, and 700s cm^{-1}; τ ($CDCl_3$) 2·70 (m, 5 aromatic H), 5·10—5·40 (m, $W_{\frac{1}{2}}$ 7 Hz, CHCl), and 6·75—9·30 (m, 12 aliphatic H) (Found: C, 72·6; H, 7·1. $C_{15}H_{17}ClO$ requires C, 72·5; H, 6·85%).

1-*Phenylbicyclo*[3.3.1]*non*-3-*en*-9-*one* (24).—The *endo*-alcohol (21) (0·104 g) was added to a solution of toluene-*p*-sulphonyl chloride (0·110 g) in dry pyridine (0·55 ml) at 0 °C, and then kept at room temperature for 30 h. The mixture was poured into water and extracted with ether (× 3), and the combined organic layers were washed successively with dilute hydrochloric acid (10%) (× 2), and water, dried ($MgSO_4$), and evaporated to give an oil (0·1 g, 59%) whose i.r. spectrum showed the disappearance of the OH stretching band.

This crude tosylate (0·182 g) was added to a suspension of sodium acetate (39·6 mg; fused) in glacial acetic acid (5·7 ml) and the mixture was heated under reflux under nitrogen for 28 h. The cooled mixture was poured into water, the solution was extracted with ether (× 3), and the combined ether layers were washed with sodium carbonate solution, then with saturated sodium chloride solution, dried ($MgSO_4$), and evaporated to give a light brown oil (0·132 g). Column chromatography (10 g Kieselgel; 4 : 1 benzene–ethyl acetate as eluant) gave 1-phenylbicyclo[3.3.1]non-3-en-9-one (24) (22·4 mg, 22%), b.p. 155—160° at 1 mmHg, $\nu_{max.}$ 1720s, 1660s, 750s, and 700s cm^{-1}; τ (CCl_4) 2·70 (m, 5 aromatic H), 3·80—5·40 (m, 2 olefinic H), 6·80—7·25 (m, 2-H_2 and H-5), and 7·55—8·45 (m, 6 aliphatic H); *m/e* 212 (100%, M^+), 184 (27), 169 (29), 141 (38), 129 (24), 128 (24), 115 (30), 91 (38), and 77 (23).

Further elution gave exo-4-*acetoxy*-1-*phenylbicyclo*[3.3.1]-*nonan*-9-*one* (25) (91·2 mg, 70%) as an oil which solidified. Crystallisation from ethyl acetate–light petroleum gave long needles, m.p. 105—105·5°, $\nu_{max.}$ 1730s, 1715s, 1250s, 1240s, 1230s, 760s, and 700s cm^{-1}; τ ($CDCl_3$) 2·65 (m, 5 aromatic H), 4·40—4·70 (m, $W_{\frac{1}{2}}$ 8 Hz, C*H*OAc), and 6·90—8·40 (m, 14 aliphatic H, including s, CH_3CO_2, at τ 8·00) (Found: C, 74·75; H, 7·3. $C_{17}H_{20}O_3$ requires C, 74·95; H, 7·5%).

The *exo*-tosylate was prepared from the *exo*-alcohol (20) as described above in 59% yield. Buffered acetolysis of the *exo*-tosylate (100·6 mg) gave a brown oil (58·2 mg) which was purified by column chromatography (6 g Kieselgel; 8 : 1 benzene–ethyl acetate as eluant) to give 1-phenylbicyclo-[3.3.1]non-3-en-9-one (41·6 mg, 75%) identical with that prepared above.

1-*Phenylbicyclo*[3.3.1]*nonan*-9-*one* (26).—1-Phenylbicyclo-[3.3.1]non-3-en-9-one (52·7 mg) was dissolved in glacial acetic acid (5 ml) and hydrogenated at normal temperature and pressure in the presence of 5% palladium on charcoal (6 mg) until the uptake of hydrogen ceased. The usual work-up and chromatography of the residue (6 g Kieselgel; benzene as eluant) gave a solid. Crystallisation from ethanol gave 1-*phenylbicyclo*[3.3.1]*nonan*-9-*one* (26) (36·4 mg, 69%) as needles, m.p. 81·5—83·0°, $\nu_{max.}$ 1715s, 750s, and 700s cm^{-1}; τ ($CDCl_3$) 2·70 (m, 5 aromatic H) and 6·75—8·90 (m, 13 aliphatic H) (Found: C, 84·15; H, 8·3. $C_{15}H_{18}O$ requires C, 84·05; H, 8·45%). This compound was identical with the product isolated by ozonolysis of 9-methylene-1-phenylbicyclo[3.3.1]nonane; it was also identical with a sample of this ketone (after crystallisation from ethanol) kindly supplied by Professor Nicoletti.

Wittig Methylenation of the Ketone (26).—Methyltriphenylphosphonium bromide (368 mg) was suspended in dry ether (3 ml) with stirring, and n-butyl-lithium (1·45 ml of a 0·705M solution in pentane) was added over 5 min. The solution was stirred for 10 min at ambient temperature and the ketone (26) (200 mg) in ether (5 ml) was added. The mixture was heated under reflux for 3 h, stirred overnight at ambient temperature, and poured into water and extracted with ether. The combined ether extracts were washed with water, dried ($MgSO_4$), and evaporated, and the residue was distilled to give 9-methylene-1-phenylbicyclo[3.3.1]nonane (14) (0·180 g, 91%), identical with the product derived by dehydration of 9-hydroxymethyl-1-phenylbicyclo[3.3.1]-nonane (13).

Cyclo-oct-4-*enylideneacetic Acid* (29).—Ethyl cyclo-oct-4-enylideneacetate (1·0 g) was added to sodium hydroxide solution (20 ml; 2N) and brought to reflux. Sufficient ethanol was added to dissolve the ester and the solution was heated under reflux for 6 h. The cooled mixture was poured into water (100 ml) and extracted twice with ether. Acidification of the basic, aqueous solution with concentrated hydrochloric acid, followed by extraction with chloroform, drying ($MgSO_4$) of the chloroform layer, and removal of solvent gave an oil which solidified. This was crystallised from aqueous ethanol to give *cyclo-oct*-4-*enylideneacetic acid* (29) (0·63 g, 74%) as a microcrystalline powder, m.p. 80—81°, $\nu_{max.}$ 2660m,br, 1685s, and 1630s cm^{-1}; τ ($CDCl_3$) —2·30 (s, disappears on addition of D_2O, CO_2H), 4·20—4·45 (m, olefinic 4- and 5-H), 4·70 (s, $=CH\cdot CO_2H$,), and 6·90—8·55 (m, 10 aliphatic H) (Found: C, 72·05; H, 8·65. $C_{10}H_{14}O_2$ requires C, 72·25; H, 8·5%).

Cyclo-oct-4-*enylideneacetone* (27).—The foregoing acid (1·8 g) was dissolved in dry ether (50 ml) and to this stirred solution was added methyl-lithium [prepared from lithium (1·4 g) and methyl iodide (14 ml) in dry ether (100 ml)] over 20 min at room temperature. The solution was stirred for 1·2 h, cautiously poured into sodium thiosulphate solution, and the ether layer was separated. The aqueous layer was extracted twice with ether, and the combined ether layers were washed with water and dried ($MgSO_4$). Removal of the solvent gave a yellow oil which was purified by column chromatography (60 g Kieselgel; benzene as eluant) and distillation to give the required *ketone* (27) (1·0 g, 51%) as an oil, b.p. 85—90° at 1·5 mmHg, $\nu_{max.}$ 1680s, 1610s, and 715m cm^{-1}; τ (CCl_4) 3·90, 4·05 (s, $=CHCOCH_3$), 4·10—4·80 (m, olefinic 4- and 5-H), and 7·00—8·80 (m, 13 aliphatic H, including s, $-COCH_3$, at τ 7·90) (Found: C, 80·3; H, 9·8. $C_{11}H_{16}O$ requires C, 80·45; H, 9·85%).

9-*Acetyl*-1-*phenylbicyclo*[3.3.1]*nonane* (28).—The ketone

(27) (250 mg) was dissolved in a mixture of boron trifluoride–diethyl ether complex (5 ml) and dry benzene (5 ml) and heated under reflux for 17 h. The solution was cautiously poured into sodium carbonate solution and the benzene layer separated. The aqueous layer was extracted twice with benzene and the combined benzene extracts were washed with water and dried ($MgSO_4$). Removal of solvent gave a pale yellow oil which was chromatographed (alumina; 1 : 1 benzene–light petroleum as eluant) to give, as the first fraction, a paraffinic oil (148 mg), and then 9-*acetyl*-1-*phenylbicyclo*[3.3.1]*nonane* (27) (92 mg, 25%) as an oil, b.p. 160—170° at 0·3 mmHg, $\nu_{max.}$ 1705s, 750s, and 690s cm^{-1}, τ (CCl_4) 2·85 (m, 5 aromatic H), 6·75br (s, 9-H), and 7·45—8·50 (m, 16 aliphatic H, including s, $-COCH_3$, at τ 8·05) (Found: C, 84·0; H, 9·05. $C_{17}H_{22}O$ requires C, 84·25; H, 9·15%).

Conversion of 1-*Phenylbicyclo*[3.3.1]*nonane*-9-*carboxylic Acid* (12) *into* 9-*Acetyl*-1-*phenylbicyclo*[3.3.1]*nonane* (28).—A solution of methyl-lithium was prepared by adding methyl iodide (230 mg) in dry diethyl ether (4 ml) to lithium wire (23 mg) suspended in dry ether (1 ml) and stirring at room temperature for 30 min. The acid (12) (100 mg) dissolved in dry ether (2 ml) was added rapidly and the mixture was stirred for a further 30 min, poured into sodium thiosulphate solution, and extracted with ether. The ether extract was washed with water, dried ($MgSO_4$), and evaporated to give a yellow oil which was chromatographed (10 g Kieselgel; 1 : 1 benzene–light petroleum as eluant) to afford the title ketone (89 mg, 90%) as an oil, identical with the sample obtained from the previous reaction.

Bicyclo[3.3.0]*oct*-1-*ylacetic Acid* (10).—Bicyclo[3.3.0]octane-1-carboxylic acid (3·8 g) was refluxed with thionyl chloride (4 ml) for 30 min, and the thionyl chloride was then removed under vacuum. Traces of thionyl chloride remaining were removed by azeotroping with dry benzene, and the acid chloride obtained was dissolved in dry ether (10 ml). An ethereal, alcohol-free solution of diazomethane [prepared from *N*-methyl-*N*-nitrosotoluene-4-sulphonamide (21 g)] was then cooled to 0°, the acid chloride solution added dropwise and the mixture was allowed to warm to room temperature, and set aside for 2 h. Ether and the excess of diazomethane were removed under reduced pressure and the resulting orange oil was dissolved in chloroform, washed twice with sodium carbonate solution, and dried ($MgSO_4$). Removal of the solvent gave the intermediate diazo-ketone (1·0 g) ($\nu_{max.}$ 2100s cm^{-1}) which was decomposed [11] by adding it dropwise to a refluxing mixture of benzyl alcohol (9 ml) and *s*-collidine (9 ml). The solution was heated until all the nitrogen had been evolved (7 min), cooled, and poured into dilute hydrochloric acid (2N). Extraction with ether, followed by a further washing of the ether extracts with dilute hydrochloric acid and drying ($MgSO_4$), gave, after removal of the solvent, the benzyl ester dissolved in benzyl alcohol. The crude benzyl ester was immediately hydrolysed by heating under reflux for 10 h with sodium hydroxide solution (75 ml; 2N) with sufficient ethanol to ensure a homogeneous solution. The cooled solution was extracted with ether, and the basic, aqueous layer acidified (concentrated hydrochloric acid), and extracted with chloroform. The chloroform layer was washed with water, dried ($MgSO_4$), and evaporated and the residue distilled to give pure *bicyclo*[3.3.0]*oct*-1-*ylacetic acid* (0·85 g, 20%) as an oil, b.p. 125—130° at 0·4 mmHg, $\nu_{max.}$ 2660m,br and 1700s cm^{-1}; τ ($CDCl_3$) −3·25 (s, disappears upon addition of D_2O, $-CO_2H$) and 7·30—8·85 (m, 15 aliphatic H, including s, $-CH_2 \cdot CO_2H$, at τ 7·55).

A small sample of this acid was converted into the *amide*, m.p. 91—94° (from ethyl acetate–light petroleum) (Found: C, 71·8; H, 10·3; N, 8·65. $C_{10}H_{17}NO$ requires C, 71·8; H, 10·25; N, 8·4%).

We thank the S.R.C. for a research studentship (to R. H. G.)

[4/1809 *Received, 2nd September,* 1974]

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