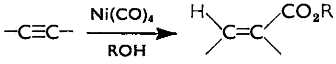
63. *The Stereochemistry of Hydrocarboxylation of Olefins: Reaction of Bicycloheptene and Other Strained Olefins with Acidic Nickel Carbonyl.*

By C. W. Bird, R. C. Cookson, J. Hudec, and R. O. Williams.

Strained olefins, particularly bicyclo[2,2,1]heptene derivatives, undergo hydrocarboxylation at atmospheric pressure and temperature. Nickel carbonyl in a deuterated solvent converts bicyclo[2,2,1]heptene itself into 3-*exo*-deuterobicyclo[2,2,1]heptane-2-*exo*-carboxylic acid: *cis*-addition to olefins from the less hindered side is probably general.

Of the carbonylations developed by Reppe and his colleagues [1] one of the most widely used is the conversion by nickel carbonyl of an acetylene into an acrylic acid or its derivative.[2,3] The elements of formic acid are added *cis* to the triple bond:



Acetylenes react at atmospheric temperature and pressure, but olefins usually require much more drastic conditions: for example, Reppe and Kröper [4] heated cyclohexene with nickel carbonyl at 270°/100 atm. to obtain cyclohexanecarboxylic acid (terminal olefins react more easily). Nevertheless, for an investigation of the mechanism of the reaction olefins are in some ways preferable to acetylenes, and their products contain a third dimension, which may make a stereochemical test more revealing. We thought that the lack of reactivity might be overcome by the use of strained olefins, which add so many

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[1] Reppe, " Neue Entwicklungen auf dem Gebiet der Chemie des Acetylens und Kohlenoxyds," Springer-Verlag, Berlin, 1949.

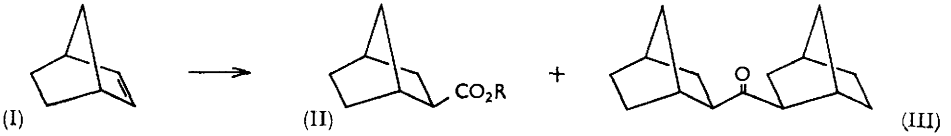
[2] Jones, Whitham, and Whiting, *J.*, 1957, 4628; Jones, Shen, and Whiting, *J.*, 1950, 230; 1951, **48**, 763, 766.

[3] Sternberg, Markby, and Wender, *J. Amer. Chem. Soc.*, 1960, **82**, 3638.

[4] Reppe and Kröper, *Annalen*, 1953, **582**, 38.

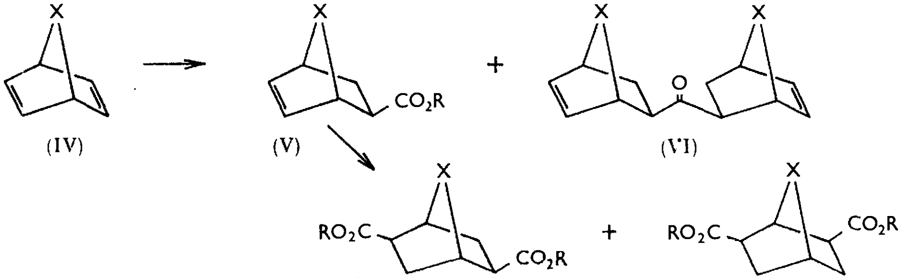
reagents more rapidly than unstrained ones. The bicyclo[2,2,1]hept-2-ene (I) system seemed specially suitable, since it is highly reactive, the two sides of its double bond are geometrically different, and it betrays carbonium ion intermediates by its notorious propensity for rearrangement.

In fact bicyclo[2,2,1]heptene (I) reacted with nickel carbonyl in ethanol–water–acetic acid at atmospheric pressure and 50° to give in almost quantitative yield the *exo*-acid and ester (II; R = H and Et), accompanied by a ketone. The structure of the ketone * (III) was proved by oxidation with peracetic acid to a lactone that was hydrolysed to *exo*-bicycloheptanol and the *exo*-acid (II; R = H). Both the acid and the alcohol were further degraded to norcamphor. When bicyclo[2,2,1]heptadiene (IV; X = CH_2) in excess was treated with nickel carbonyl under the same conditions, analogous products were formed, namely, the *exo*-acid and ester (V; X = CH_2, R = H and Et) and a ketone (VI; X = CH_2) which on hydrogenation took up two mol. of hydrogen to produce the ketone (III). In dioxan–water–acetic acid, only the acid (V; X = CH_2, R = H) and the ketone (VI; X = CH_2) were produced; the less the proportion of water in the solvent the higher the proportion of ketone in the product.



(I) (II) (III)

With an excess of nickel carbonyl and a higher proportion of ethanol to water, bicycloheptadiene yielded a saturated diester, $C_{13}H_{20}O_4$, and a small amount of the corresponding diacid. Treatment of the unsaturated ester (V; X = CH_2) with more nickel carbonyl gave the same diester, which gas-chromatography showed to be a mixture of two components in the ratio of about 93 : 7. They must be the two isomers (VII and VIII; X = CH_2), the second ester group being assumed in each case to be also *exo* by analogy.



(IV) (V) (VI)
(VII) (VIII)

Other bicycloheptenes that underwent the reaction under the same mild conditions were hexachlorobicyclo[2,2,1]heptadiene (IX), giving the acid (X), isodrin (XI), giving an acid (XII; R = H), and aldrin (XIII), giving an acid (XIV). The first product (X) is probably identical with the adduct of the same m. p. from acrylic acid and hexachlorocyclopentadiene.[5] In the mixed solvent containing ethanol, dicyclopentadiene (XV) gave an 80% yield of an unsaturated ester and some of the corresponding acid. The infrared spectrum showed, as expected, that the bicycloheptene double bond was no longer present. The existence of the cyclopentene double bond, which evidently reacts very much more slowly, was proved chemically by oxidation of the ester with selenium dioxide to an alcohol, which was further oxidised with manganese dioxide to a cyclopentenone [6] ($\nu_{max.}$ 1710 and

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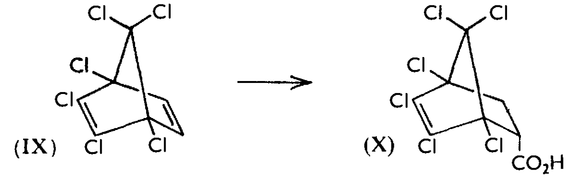
* There is no evidence whether the ketones (III) and (VI) are *meso* (as shown) or, perhaps more likely, racemic forms.

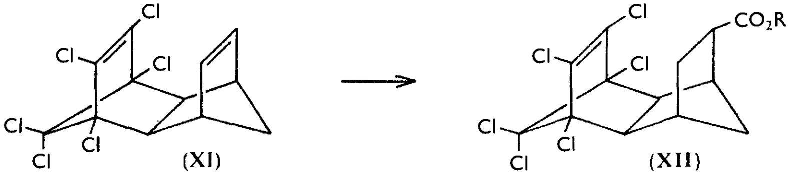
[5] U.S.P. 2,758,918/1956.

[6] Cf. Alder and Flock, *Chem. Ber.*, 1954, **87**, 1916; Woodward and Katz, *Tetrahedron*, 1959, **5**, 70.

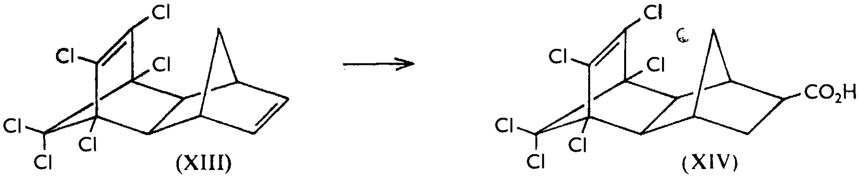
1730 cm.$^{-1}$; $\lambda_{max.}$ 228 mμ, ε 9300). The ester and acid are, therefore, one of the two structural isomers (XVI) arising from *exo*-addition to the bicycloheptene double bond; although the crystalline acid melted over only 1°, it may be a mixture of the two isomers (or one that crystallised from a mixture). When the ethanol in the mixed solvent for hydrocarboxylation was replaced by dioxan, naturally no ester (XVI; R = Et) was formed, but the acid (XVI; R = H) was then accompanied by a ketone, $C_{21}H_{26}O$, containing two double bonds. The ketone was assumed to have a structure analogous to the one (VI) from bicycloheptadiene: three pairs of *exo-exo*-isomers are possible, and the wide melting range of the purified ketone, 124—127°, suggests that it is a mixture.



(IX) (X)

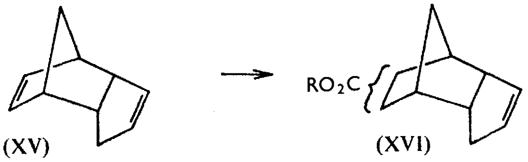


(XI) (XII)

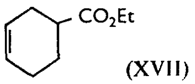


(XIII) (XIV)

Although it reacted rather more slowly, bicyclo[2,2,2]octadiene (an improved synthesis of which is described in the Experimental section) gave under the appropriate conditions a range of products exactly analogous to those from bicyclo[2,2,1]heptadiene (V—VIII; but X = $CH_2{\cdot}CH_2$ instead of CH_2). The acid from hydrocarboxylation (V; X = $CH_2{\cdot}CH_2$, R = H) was identical with that from hydrolysis of the Diels–Alder adduct of ethyl acrylate and cyclohexa-1,3-diene. In agreement with expectation based on the greater distance between the two bridges in the bicyclo-octene (V; X = $CH_2{\cdot}CH_2$, R = Et) than in the bicycloheptene (V; X = CH_2, R = Et), the two isomers (VII and VIII; X = $CH_2{\cdot}CH_2$, R = Et) indicated by gas-chromatography * were produced in more nearly equal quantities (60 : 40). The yields of the various products from bicyclo-octadiene depended very much on the proportions of the reactants, but the over-all conversion of the diene into carbonyl derivatives was again very high.



(XV) (XVI)



(XVII)

After 24 hr. under the usual conditions at atmospheric pressure cyclohexa-1,4-diene gave a low yield of ester, identical with the adduct (XVII) of butadiene and ethyl acrylate. Under the same conditions cyclohexa-1,3-diene (containing 5% of 1,4-diene as impurity)

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* The structure and stereochemistry of the product were not established.

yielded about 4% of the same ester (XVII) as the only carbonyl product. If it had arisen only from the 1,4-diene present as an impurity the conversion of the latter would have been almost quantitative. However, when cyclohexa-1,3-diene was boiled for a few hours in a mixture of ethanol, acetic acid, and water containing nickel acetate, to simulate the conditions of reaction in the absence of carbonyl, the content of 1,4-diene increased from 5% to 11%; so the ester may be derived from the 1,4-diene in equilibrium with the 1,3-diene.

Cyclopentadiene formed no cyclopentenecarboxylic ester. After long reaction the ester (XVI; R = Et) was produced, obviously by prior dimerisation followed by hydrocarboxylation. Some of the nickel complex (XVIII) was also present.

The relatively strain-free olefins, acrylonitrile, cyclohexene, camphene, and 1-phenyl- and 1-methyl-cyclohexene did not react at all at atmospheric pressure, and the last olefin was unchanged when heated with the nickel carbonyl mixture at 140° for 12 hr.

To check whether strain really was the dominant factor in determining reactivity we wanted to try the reaction on a cyclobutene. Since some of the cyclobutene derivative (XIX) was at hand,[7] we treated it with nickel carbonyl. Under the usual mild conditions the ester (XX) was formed in high yield. The infrared spectrum of the product (XX) still had the high-frequency carbonyl band (1752 cm.$^{-1}$) from the strained cyclopentanone units, but the characteristic absorption of the cyclobutene double bond had been replaced by an ester-carbonyl band at 1728 cm.$^{-1}$. The ester group was assumed to have added, as usual, from the less hindered side. When the crystalline ester (XX) was left in the air for a few days it took up one mol. of water. The crystals then depressed the m. p. of the anhydrous ester (XX), and the band at 1752 cm.$^{-1}$ had disappeared, being replaced by new strong peaks characteristic of hydroxyl groups and ethers. The anhydrous diketone (XX) could be regenerated by vacuum-sublimation of the hydrate. Reversible formation of hydrates such as (XXI) is typical of diketones in this and related ring-systems.[8]

In the Table are listed some physical and chemical properties of the relevant olefins, which are at least partly (though none is entirely) dependent on strain in the double bond. Although, as might be expected from inevitable complication by many other factors, no two properties show a strictly linear relationship, bicyclo[2,2,1]heptane is clearly closer in general behaviour to cyclobutene than to cyclopentene. Other variables, such as electron-density and steric hindrance of the double bond, no doubt affect the rate of reaction of olefins with nickel carbonyl, but strain does seem to be most important; the dividing line comes between cyclohexene, which did not react detectably, and cyclopentene, which gave a low yield of ester after prolonged treatment with a large excess of nickel carbonyl. On the other hand, crude correlations of this kind would not have predicted that bicyclo[2,2,2]octene derivatives would have been more reactive to hydrocarboxylation than cyclopentene.

	C=C stretch [a] (cm.$^{-1}$)	C–H stretch [a] (cm.$^{-1}$)	$-\Delta H$ hydrogn.[b] at 25° (kcal./mole)	log ($K \times 100$) for Ag^+ complex at 25° [c]	$\lambda_{max.}$ of phenyl derivative in (mμ)
Cyclohexene	1646	3017	27·1	0·27	248 [e]
Cyclopentene	1611	3045	25·4	1·06	254 [e]
Cyclohexa-1,4-diene	1630 [d]	3020 [d]	—	—	—
Cyclobutene	1566	3060	—	—	—
Bicyclo[2,2,2]octene	1614	3040	28·25	0·99	252 [b]
Bicyclo[2,2,2]octadiene	1630 [d]	3040 [d]	28·1 *	—	—
Bicyclo[2,2,1]heptene	1568	3070	33·1	1·43	262·5 [g]
Bicyclo[2,2,1]heptadiene	1546 [d]	3072	36·0 *	—	—

[a] Lord and Walker, *J. Amer. Chem. Soc.*, 1954, **76**, 2518; Schleyer, *ibid.*, 1958, **80**, 1700. [b] Turner, Meador, and Winkler, *ibid.*, 1957, **79**, 4116. [c] Traynham and Schnert, *ibid.*, 1956, **78**, 4025. [d] This paper. [e] Baddeley, Chadwick, and Taylor, *J.*, 1956, 451. [f] Kleinfelter and Schleyer, *J. Amer. Chem. Soc.*, 1961, **83**, 2329. [g] Kleinfelter and Schleyer, *J. Org. Chem.*, 1961, **26**, 3740.

* Values for one double bond.

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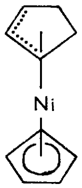
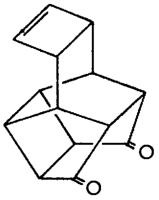
[7] Cookson, Crundwell, and Hudec, *Chem. and Ind.*, 1958, 1003.

[8] Unpublished observations.

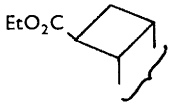
The reaction with bicycloheptene (I) seemed specially suitable for examination of the stereochemistry of addition. Reaction with nickel carbonyl in a mixture of deuterium oxide, deuteroethanol, and deuteroacetic acid, as for the process in isotopically normal solvents, gave a mixture of bicycloheptane-*exo*-carboxylic ester and acid containing (after exchange of active hydrogen) 0·97 atom of deuterium per molecule. The presence of only one atom of deuterium proves that the *exo*-isomer was the primary product of the reaction, not formed by subsequent epimerisation of the *endo*-isomer or of a mixture of the two. The deutero-acid was degraded to the primary amine[10] by the Curtius reaction, through the acid chloride, azide, and isocyanate. Methylation with formaldehyde and formic acid then gave the dimethylamine (XXII). The infrared spectrum confirmed that it was the pure *exo*-isomer: it had the strong band at 1022 cm.$^{-1}$ and medium band at 820 cm.$^{-1}$ reported by Cope *et al.*[11] as characteristic of this isomer, but the strong one at 795 cm.$^{-1}$ shown by the *endo*-isomer[11] was completely absent. Pyrolysis of the *N*-oxide then yielded bicycloheptene (68% yield). The presence of deuterium in all the compounds up to and including the *N*-oxide was checked by infrared spectroscopy (C–D stretching in the region 2200—2300 cm.$^{-1}$) and analysis of the water from combustion. The dimethylamine (XXII) (analysed as its crystalline methiodide) still contained 0·96 atom of deuterium per mol. The bicycloheptene, however, contained no deuterium (less than 0·01 atom per molecule, if any). In confirmation, the bicycloheptene was also converted into its crystalline phenyl azide adduct, in which also no trace of deuterium could be detected. Since Cope *et al.*[12] have established elimination from amine oxides as completely *cis* (XXIII; Z = O), the amine must have both the nitrogen and deuterium in the *exo*-configuration. The original hydrocarboxylation must, therefore, involve a *cis–exo*-addition to the double bond. That isodrin (XI) reacts almost as easily as aldrin (XIII) supports the general *cis*-addition, since the *endo*-side of the double bond of the former is excessively hindered.



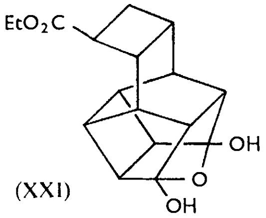
(XVIII)



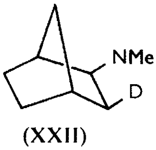
(XIX)



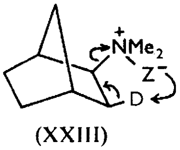
(XX)



(XXI)



(XXII)



(XXIII)

Interestingly, pyrolysis of the trimethylammonium hydroxide (0·96 atom of D per mol.) under the conditions used by Cope *et al.* for the isotopically normal compound (110—135°) also formed bicycloheptene free from deuterium (60% yield), perhaps *via* an ylide intermediate[13] (XXIII; Z = CH_2).

[9] van Tamelen and Shamma, *J. Amer. Chem. Soc.*, 1954, **76**, 2315; Ver Nooy and Rondestvedt, *ibid.*, 1955, **77**, 3583.

[10] Komppa and Beckmann, *Annalen*, 1934, **512**, 172.

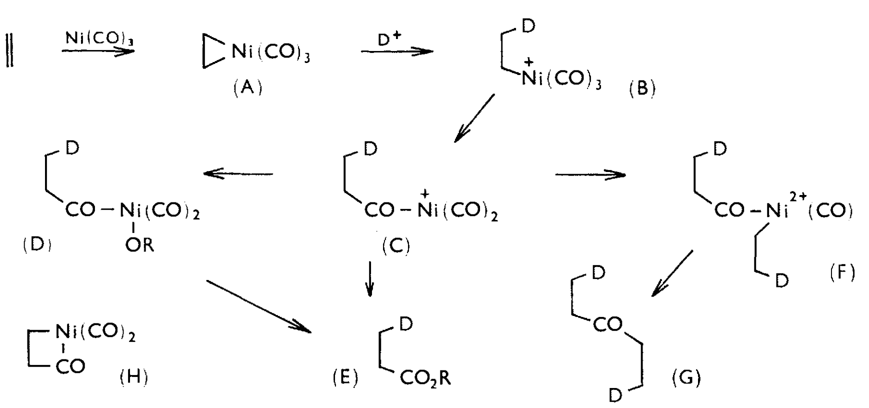
[11] Cope, Ciganek, and LeBel, *J. Amer. Chem. Soc.*, 1959, **81**, 2799.

[12] Cope and Trumbull, " Organic Reactions," Wiley, New York, 1960, Vol. XI, p. 361.

[13] Cf. footnote 19 in ref. 11; but see also De Puy, Thurn, and Morris, *J. Amer. Chem. Soc.*, 1962, **84**, 1314.

The acid and ester (II) from bicycloheptene (I) were pure *exo*-isomers, in which no *endo*-form could be detected spectroscopically. Similarly, no *endo*-isomer could be detected in the *exo*-acid (V; $X = CH_2$, $R = H$) from the diene (IV; $X = CH_2$) by iodolactonisation.[9] By contrast, the Diels–Alder adduct of cyclopentadiene and ethyl acrylate contains 76% of *endo*-ester, and the equilibrium mixture (from treatment with sodium methoxide solution) contains roughly equal amounts of *exo*- and *endo*-isomers.

Bicycloheptene invariably undergoes attack from the *exo*-side, because of its smaller hindrance,[14] so the *exo*-configuration of the acid suggests (unless there is a double inversion) that the initial attack controls the configuration of the product. The complete absence of any product formed by reaction of both double bonds of bicycloheptadiene or isodrin with one molecule of nickel carbonyl shows that no large positive charge is developed at the carbon atoms attacked.[15] As in the hydrocarboxylation of acetylenes,[2] the reaction with olefins often exhibits a transient brown coloration before development of the green colour of solvated Ni^{2+}, presumably indicating the formation of intermediate nickel complexes. The annexed scheme explains the *cis*-addition and is consistent with what is known of the chemistry of transition-metal complexes and alkyl-metal carbonyls.[16]



The initial olefin complex (A), which could alternatively be depicted as a π-complex, is supposed to suffer attack by a deuteron (or proton) to give the alkylnickel carbonyl cation (B). We leave open the question of whether it is a direct attack on the C–Ni bond or whether conceivably the complex (A) is in equilibrium with its conjugate acid with a $^+Ni–D$ bond, which then rearranges to (B). In any event the reaction is tantamount to the usual electrophilic displacement on carbon with retention of configuration, and obviously has close affinities with the *cis*-addition of other metal and boron hydrides to olefins. (B) is then supposed to rearrange to the acylnickel cation (C). This step has ample analogy [17] in the chemistry of the alkyl carbonyls of other transition metals: indeed the alkyl-metal carbonyl–acyl-metal equilibrium is beginning to emerge as one of the basic reactions in organic metal-carbonyl chemistry. The acylnickel compound (C) then reacts with the solvent to yield the products (E). Especially when the supply of

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[14] *Inter alia*, Alder, Stein, and Schneider, *Annalen*, 1935, **515**, 185; Alder, Mönch, and Wirtz, *ibid.*, 1959, **627**, 47; Soloway, *J. Amer. Chem. Soc.*, 1952, **74**, 1027; Stille and Frey, *ibid.*, 1959, **81**, 4273; Soloway and Cristol, *J. Org. Chem.*, 1960, **25**, 327; Simmons, *J. Amer. Chem. Soc.*, 1961, **83**, 1657.

[15] Cf. Schmerling, Luvisi, and Welch, *J. Amer. Chem. Soc.*, 1956, **78**, 2819; Winstein and Shatavsky, *Chem. and Ind.*, 1956, 56; Winstein, *J. Amer. Chem. Soc.*, 1961, **83**, 1516; Woods, *J. Org. Chem.*, 1958, **23**, 110; Soloway, Damiana, Sims, Bluestone, and Lidov, *J. Amer. Chem. Soc.*, 1960, **82**, 5377; Bird, Cookson, and Crundwell, *J.*, 1961, 4809.

[16] See Pauson, *Proc. Chem. Soc.*, 1960, 297; Chatt, Pauson, and Venanzi in " Organometallic Chemistry," ed. Zeiss, Reinhold, New York, 1960, p. 468; Bird, *Chem. Rev.*, 1962, **62**, 283.

[17] Coffield, Kozikowski, and Closson, *J. Org. Chem.*, 1957, **22**, 598; Breslow and Heck, *J. Amer. Chem. Soc.*, 1960, **82**, 750; 1961, **83**, 1097, 4023; Booth and Chatt, *Proc. Chem. Soc.*, 1961, 67.

hydroxylic solvent or of carbon monoxide is restricted, the alkyl- (B) or acyl-nickel complex (C) can react with another molecule of olefin to give an intermediate (*e.g.*, F) in which a migration of the alkyl group may be supposed to occur from nickel to the acyl-carbon atom, yielding the ketone (G). This insertion of another molecule of olefin into (C) may be analogous to the polymerisation of olefins by Ziegler–Natta catalysts.

The probable timing of some of the steps is debatable: for example, a cyclic complex (H) might replace (B) as an intermediate in the conversion of (A) into (C). The inevitable reaction of the nickel atom in the intermediates with the solvent or with more carbon monoxide is omitted for simplicity, although it may play an important part in the reaction. For example, migration of the alkyl group from nickel to CO (B ⟶ C) may be concerted with co-ordination of carbon monoxide or solvent to the nickel atom; as well as the likelihood of direct reaction of the solvent with the acyl-carbonyl group in (C) there is the possibility of internal rearrangement of such a solvated form (D). That acetylenes apparently will not react until water is added [2] is hard to understand, merely in view of its greater nucleophilic and solvating power, and does suggest that water takes a more specific part in the reaction. Carboxylic acids may be the primary products, for they are esterified under the conditions of reaction.

Strain in the olefin renders the double bond more nucleophilic and raises the energy of the reactant relative to the transition state.

EXPERIMENTAL

Nickel carbonyl (b. p. 43°) is extremely poisonous and suitable precautions must be taken when it is used.

Ultraviolet spectra of ethanol solutions were recorded on a Unicam S.P. 700 spectrometer, and infrared spectra of Nujol mulls on a S.P. 100 instrument. A diffraction grating was used for measurement of the C–D absorption at 2200—2300 cm.$^{-1}$. Molecular weights were determined by the rise in b. p. of benzene. Dr. J. Nemeth (Urbana, Illinois) analysed samples for deuterium by the falling-drop method.

Mixtures for the hydrocarboxylation of olefins by nickel carbonyl were heated under nitrogen in jacketed flasks by the vapour of boiling acetone (56°). A transient brown colour usually developed. As reaction proceeded the mixture became green, and then black from the deposition of metallic nickel. The cooled mixture was treated with 2N-sulphuric acid and extracted several times with ether. The ether extract was distilled to remove nickel carbonyl with the ether, and the residue was redissolved in ether, which was filtered to free it from nickel (sometimes pyrophoric). The extract was then separated into neutral and acidic fractions in the usual way. The light petroleum used was a fraction of b. p. 60—80°.

Reaction of Bicyclo[2,2,1]*hept-2-ene with Nickel Carbonyl.*—Since reactions with isotopically normal solvents were carried out similarly, the reaction with deuterated solvent is described in detail. Nickel carbonyl (10 ml.) was added to a mixture of the olefin (9·4 g., 0·1 mole), deuteroethanol (30 ml.), deuteroacetic acid (1·5 ml.), and deuterium oxide (1·0 ml.). After 8 hours' heating under reflux the mixture was worked up as usual. Distillation of the neutral fraction gave ethyl 3-*exo*-deuterobicyclo[2,2,1]heptane-2-*exo*-carboxylate (12·2 g., 72%), b. p. 86°/10 mm., n_D^{17} 1·4632, containing 0·94 atoms of D per mol. The acid fraction yielded the corresponding carboxylic acid (1·4 g., 10%), m. p. 55°.

3-exo-*Deuterobicyclo*[2,2,1]*heptane*-2-exo-*carboxylic Acid.*—The ester (16·8 g., 0·1 mole) was hydrolysed by boiling dilute aqueous-alcoholic alkali to the free acid (II; R = H) (12 g., 86%), m. p. 55° unchanged when mixed with the isotopically normal compound prepared according to Cope *et al.*,[11] containing 0·97 atom of D per mol.

2-exo-*Amino*-3-exo-*deuterobicyclo*[2,2,1]*heptane.*—The acid (14 g., 0·1 mole) was treated with pure thionyl chloride (25 ml.) at room temperature. After the reaction had ceased the excess of thionyl chloride was distilled off and the residue of acid chloride was distilled; it had b. p. 90—92°/16 mm. (14·1 g., 89%).

The acid chloride (15·9 g., 0·1 mole) was boiled with sodium azide (19·5 g., 0·3 mole) in xylene (35 ml.) with stirring for 2 hr. The cooled mixture was filtered and the benzene washings and filtrate were distilled *in vacuo*, leaving the crude isocyanate, which was then dropped into boiling 20% hydrochloric acid (50 ml.). After the solution had been cooled and made alkaline with sodium hydroxide the amine was extracted with ether. Distillation gave the amine, b. p. 79—82°/11 mm. (7·8 g., 64%).

3-exo-*Deutero*-2-exo-*dimethylaminobicyclo*[2,2,1]*heptane*.—The amine (5·55 g., 0·05 mole) was added slowly to a mixture of 85% formic acid (15 ml.) and 40% aqueous formaldehyde (9 ml.) cooled in ice. The mixture was heated on a steam-bath for 8 hr., cooled, acidified to Congo Red, and extracted several times with ether. The dimethylamine was then extracted with ether from the aqueous layer, which had been made strongly alkaline. The dimethylamino-compound boiled at 70—71°/18 mm. (4·8 g., 69%).

Degradation to Bicyclo[2,2,1]*heptene* (cf. ref. 11).—(*a*) The dimethylamino-compound (3·38 g., 0·02 mole) was dissolved in methyl iodide (14 g.) and dry ether (20 ml.). After 24 hr. the methiodide had crystallised in quantitative yield, with m. p. 293° (0·96 atom of D per mol.). This salt (2·81 g., 0·01 mole) was stirred with silver oxide (5 g.) in 50% aqueous methanol (25 ml.) for 24 hr. The filtrate was then evaporated at 40°/0·1 mm. to a syrup, which was decomposed at 60 mm. and a bath temperature of 90—110°. The contents of the two cold traps (carbon dioxide–acetone) that had been connected to the distilling flask were taken up in pentane, which was then washed with dilute sulphuric acid. Distillation of the pentane left bicyclo[2,2,1]heptene (68%), having an infrared spectrum identical with an authentic sample, showing no absorption around 2260 cm.$^{-1}$, and containing no deuterium. The phenyl azide adduct, m. p. 108—109°, also contained no deuterium detectable by combustion.

(*b*) 30% Hydrogen peroxide (7 ml.) was added slowly with stirring to a solution of the dimethylamino-compound (3·38 g., 0·02 mole) in methanol (7 ml.) cooled in ice. After 24 hr. at room temperature the remaining peroxide was decomposed by a trace of 10% platinum–charcoal, and the filtered solution was evaporated *in vacuo*. The syrupy, almost solid *N*-oxide was decomposed at 60 mm. in a bath heated at about 2° per min. Decomposition began at about 110° and was complete at 130°; then the pressure was reduced to 30 mm. The contents of the two cold traps that had been connected to the distilling flask and cooled in carbon dioxide–acetone were then extracted with pentane. The pentane layer was washed twice with dilute sulphuric acid, and again with water. Removal of pentane by distillation through a small column yielded bicyclo[2,2,1]heptene (60%), m. p. 45—46° (sealed tube) (phenyl azide adduct, m. p. 108—109°). Both the olefin and the adduct contained 0·00 atom of D per mol. and did not absorb near 2250 cm.$^{-1}$, as did all the precursors.

Dibicyclo[2,2,1]*heptan-2-yl Ketone* (III).—Bicyclo[2,2,1]heptene (10 g.) was heated for 6 hr. with nickel carbonyl (4 ml.) in ethanol (30 ml.), water (4 ml.), and acetic acid (4 ml.). The acid fraction (0·6 g.) of the product consisted of bicyclo[2,2,1]heptane-2-*exo*-carboxylic acid, m. p. 55—57°. The neutral fraction (mixed ester and ketone) was boiled for 6 hr. with 4N-sodium hydroxide (20 ml.) in ethanol (30 ml.), producing more acid (6·5 g.) and the ketone (III) (3·2 g.), b. p. 129—130°/1·8 mm., $\nu_{\max.}$ 1700 cm.$^{-1}$ (film) (see below).

An identical experiment, but with substitution of dioxan (40 ml.) for ethanol, yielded a total of 2·8 g. of acid and 5·4 g. of ketone.

Reaction of Bicyclo[2,2,1]*heptadiene in Excess with Nickel Carbonyl*.—The diene (100 ml.) was heated for 6 hr. with nickel carbonyl (40 ml.) in ethanol (300 ml.), acetic acid (40 ml.), and water (40 ml.). Two layers were soon formed. [This experiment was done at the beginning of the research (1957): no doubt the yields could be much improved by the use of more ethanol, to prevent separation into two layers.] The product was separated into neutral and acid parts. The acid part (2·5 g.) slowly crystallised, then had m. p. 41—44°, and was identical with authentic bicyclo[2,2,1]hept-2-ene-5-*exo*-carboxylic acid. The neutral part was distilled to give two main fractions: A (5 g.), b. p. 100°/18 mm., and B (17 g.), b. p. 126°/1·5 mm. Alkaline hydrolysis of fraction A gave an acid identical with that described above. The Diels–Alder adduct of ethyl acrylate and cyclopentadiene had the same b. p. as fraction A and a similar infrared spectrum, which became even more similar after equilibration of material A with sodium ethoxide in boiling ethanol. The acid took up one mol. of hydrogen over platinum oxide, to give crude bicyclo[2,2,1]heptane-2-carboxylic acid, m. p. 50—55°, not depressed by a sample of pure *exo*-acid.[18]

Fraction B, consisting of *dibicycloheptenyl ketone* (VI; $X = CH_2$), melted at about room temperature (probably not stereochemically quite pure) and had $\nu_{\max.}$ 1700 cm.$^{-1}$ (film of liquid) (Found: C, 83·75; H, 8·4. $C_{15}H_{18}O$ requires C, 84·1; H, 8·5%).

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[18] Berson and Ben-Efraim, *J. Amer. Chem. Soc.*, 1959, **81**, 4083.

The ketone (5·65 g.) in ethanol (50 ml.), when shaken in the presence of platinum oxide, took up 1150 ml. of hydrogen (calc. for 2 mol., 1180 ml.). The residue from evaporation of the filtered solution was treated with a little potassium permanganate in acetone to remove any unsaturated material. The recovered *tetrahydro-ketone* (III) boiled at 129—130°/1·8 mm. and had $\nu_{\max.}$ 1700 cm.$^{-1}$ (film) (Found: C, 82·8; H, 10·1. $C_{15}H_{22}O$ requires C, 82·5; H, 10·2%).

Degradation of the Tetrahydro-ketone to Norcamphor.—The ketone (III) (5·6 g.) was treated with peracetic acid (40 ml.; 0·456 g./ml.) and toluene-*p*-sulphonic acid (0·15 g.) in acetic acid (20 ml.). After 12 days the product was isolated by ether-extraction of the diluted solution. The ester could not be separated by chromatography from the unchanged ketone that the infrared spectrum showed was also present, so the product was hydrolysed by 6 hours' boiling with 4N-sodium hydroxide (20 ml.) in ethanol (60 ml.). Sublimation of the neutral fraction gave norborneols (1·4 g.) and a residue of unchanged ketone (0·73 g.). Oxidation of the norborneols with chromium trioxide (0·8 g.) in acetic acid containing a little water produced the very volatile norcamphor, characterised as the 2,4-dinitrophenylhydrazone, m. p. and mixed m. p. 131—132°. The acid fraction (2·4 g.) was converted into the amine hydrochloride, *via* the azide and isocyanate, essentially as described above, and the amine hydrochloride in water was treated with sodium nitrite (1·5 g.) and acetic acid (1·3 ml.). The resulting norborneol (0·4 g.) was purified by sublimation before oxidation to norcamphor, again recognised as its 2,4-dinitrophenylhydrazone, m. p. 131—132°.

Hydrocarboxylation of Ethyl Bicyclo[2,2,1]*hept-5-ene-2-carboxylate.*—The *exo*-ester (8·3 g., 0·05 mole) was heated for 6 hr. with nickel carbonyl (10 ml.) in ethanol (30 ml.), water (2 ml.), and acetic acid (2 ml.). The neutral product (VII + VIII; R = Et) was a sweet-smelling liquid (10 g., 83%), b. p. 161°/13 mm., n_D^{17} 1·4692 (Found: C, 64·9; H, 8·3. Calc. for $C_{13}H_{20}O_4$: C, 65·0; H, 8·3%). Gas-chromatography revealed two peaks in the ratio of 93 : 7.

Reaction of Bicyclo[2,2,1]*heptadiene with an Excess of Nickel Carbonyl.*—The diene (9·2 g., 0·1 mole) was heated for 6 hr. with nickel carbonyl (10 ml.) in ethanol (35 ml.), water (2 ml.), and acetic acid (2 ml.), more carbonyl (10 ml.) being added after 3 hr. Distillation of the neutral fraction gave a diester (VII + VIII; R = Et) (19·1 g.), b. p. 160—162°/13 mm., n_D^{18} 1·4690, with an infrared spectrum indistinguishable from that of the previous sample. The acid fraction, after recrystallisation from aqueous ethanol, had m. p. 262—264° (Found: C, 59·0; H, 6·7. $C_9H_{12}O_4$ requires C, 58·6; H, 6·5%). It was *bicyclo*[2,2,1]*heptane-*2,5- or -2,6-*dicarboxylic acid*, or perhaps a mixture of the two (VII, VIII; R = H).

Reaction of 1,2,3,4,7,7-*Hexachlorobicyclo*[2,2,1]*heptadiene.*—Under the usual conditions much of the diene was recovered. The 1,4,5,6,7,7-*hexachlorobicyclo*[2,2,1]*hept-*5*-ene-*2*-carboxylic acid* (X) produced (assumed to be the *endo*-epimer) was purified by chromatography on silica gel and recrystallisation from ether–light petroleum; it had m. p. 183—184° (Found: C, 28·2; H, 1·45; Cl, 61·7. $C_8H_4Cl_6O_2$ requires C, 27·9; H, 1·2; Cl, 61·7%).

Reaction of Cyclopentadiene.—The monomeric diene (10 ml.), ethanol (30 ml.), water (2 ml.), acetic acid (2 ml.), and nickel carbonyl (10 ml.) were heated for 24 hr. The mixture soon became red, and then black owing to deposition of nickel. The deep red product, isolated as usual, was chromatographed on silica gel in light petroleum, yielding red crystals of dicyclopentadienylnickel[19] (XVIII) (0·4 g.), m. p. 41—42°. Light petroleum containing 5% of benzene eluted the ester (XVI) as an oil (1·5 g.) with an infrared spectrum identical with that of the sample described below.

In a similar experiment, after 24 hours' heating, more nickel carbonyl (10 ml.) was added, and the mixture was heated for a further 24 hr. During the latter period the red colour vanished, and the complex must have suddenly decomposed, for some of the mixture had been blown out of the condenser. The neutral fraction of the product was distilled, to give *ethyl tricyclo*-[5,2,1,0^{2,6}]*dec-*3- or -4-*ene-*exo-8-*carboxylate* (XVI; R = Et) (14·2 g., 69%), b. p. 131—132°/10 mm., n_D^{16} 1·4982 (Found: C, 75·6; H, 8·7%; *M*, 204. $C_{13}H_{18}O_2$ requires C, 75·7; H, 8·75%; *M*, 206). Hydrogenation showed the presence of one double bond.

Recrystallisation of the acid fraction from water produced the corresponding *carboxylic acid* (XVI; R = H), m. p. 74—75° (Found: C, 73·6; H, 8·11. $C_{11}H_{14}O_2$ requires C, 74·1; H, 7·9%).

Reaction of Dicyclopentadiene.—(*a*) The dimer (13·2 g., 0·1 mole) was heated in a similar solvent with nickel carbonyl (10 ml.) for 2 hr., more carbonyl (10 ml.) was added and heating continued for 6 hr. more. The neutral fraction yielded ester (16·4 g., 80%) with the same

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[19] Dubeck and Filbey, *J. Amer. Chem. Soc.*, 1961, **83**, 1257; Fischer and Werner, *Tetrahedron Letters*, 1961, No. 1, 17; Jones, Parshall, Pratt, and Wilkinson, *ibid.*, 1961, No. 2, 48.

infrared spectrum as the previous sample (XVI; R = Et) and b. p. 132—133°/11 mm., n_D^{17} 1·4981. The acid fraction yielded the carboxylic acid (XVI; R = H) (0·8 g.).

(*b*) *Reaction in dioxan.* A mixture of dimer (13·2 g., 0·1 mole), purified dioxan (30 ml.), water (2 ml.), acetic acid (3 ml.), and nickel carbonyl (10 ml.) was heated for 5 hr., and then, after addition of more carbonyl (5 ml.), for 5 hr. more. Nickel acetate had crystallised. The infrared spectrum of the crude neutral fraction (8·2 g.) had peaks at 1700, 1730, and 1800 cm.$^{-1}$. Chromatography on silica gel gave, with light petroleum containing 10% of benzene, *di-(2β,6β,7α-tricyclo*[5,2,1,$0^{2,6}$]*dec*-3- or -4-*en*-8β-*yl) ketone* (2·1 g.), having m. p. 125—127° after recrystallisation from light petroleum and vacuum-sublimation (Found: C, 85·7; H, 8·9%; *M*, 296. $C_{21}H_{26}O$ requires C, 85·7; H, 8·85%; *M*, 294), $\nu_{max.}$ 743, 948, 1115, 1160, 1620, and 1713 cm.$^{-1}$. Two mol. of hydrogen were quickly taken up over platinum. The 2,4-*dinitrophenylhydrazone* of the unsaturated ketone melted at 156—160° (Found: C, 68·1; H, 6·2; N, 11·7. $C_{27}H_{30}O_4N_4$ requires C, 68·4; H, 6·3; N, 11·8%).

Continued elution (50% benzene) of the column gave the acid (XVI; R = H), m. p. 74—75°, more of which (9·2 g.) was obtained from the acidic fraction. The acid in the neutral fraction must have been present originally as the mixed anhydride with acetic acid (band at 1800 cm.$^{-1}$).

Oxidation of the Ethyl Ester (XVI; R = Et).[6]—The ester (2·06 g., 0·01 mole) in purified dioxan (5 ml.) was treated with potassium dihydrogen phosphate (0·2 g.) in water (0·5 ml.). Freshly sublimed selenium dioxide (0·57 g., 0·0052 mole) was added to the hot solution, which was then boiled under reflux for 6 hr. The cooled solution was filtered, and the filtrate and ether washings were washed with brine (3 × 40 ml.), with 16% aqueous sodium hydroxide, and again with brine. The residue from distillation of the ether was chromatographed on alumina, providing unchanged ester (0·31 g.) (25% of benzene in light petroleum) and the *hydroxy-derivative* (1·3 g.) (benzene). The latter distilled at 126—128°/0·5 mm. (Found: C, 69·8; H, 8·1. $C_{13}H_{18}O_3$ requires C, 70·3; H, 8·1%).

This alcohol (0·444 g., 0·002 mole) was stirred with active manganese dioxide (3 g.) in light petroleum (b. p. 60—80°) for 18 hr. Chromatography (benzene) of the filtrate and washings on alumina afforded the *tricyclo-ketone* (0·22 g.), purified by sublimation at 100°/0·5 mm. (Found: C, 70·7; H, 7·3. $C_{13}H_{16}O_3$ requires C, 70·9; H, 7·3%).

Reaction of Isodrin.—Water (5 ml.), acetic acid (2 ml.) and nickel carbonyl (5 ml.) were added to a solution of isodrin (XI) (10 g.) in ethanol (200 ml.) and dioxan (50 ml.). After 6 hours' heating, the product was separated and chromatographed on silica gel, yielding isodrin (0·9 g.) with light petroleum, and the *ester* (XII; R = Et) (7 g.) (with 1 : 1 benzene–light petroleum), m. p. 93° (from light petroleum) (Found: C, 41·2; H, 3·1; Cl, 48·5. $C_{15}H_{14}Cl_6O_2$ requires C, 41·0; H, 3·2; Cl, 48·5%). Finally benzene–ethyl acetate (1 : 1) eluted 1,8,9,10,11,11-*hexachlorotetracyclo*[6,2,1,$1^{3,6}$,$0^{2,5}$]*dodec*-9-*ene*-exo-4-*carboxylic acid* (XII; R = H) (1·5 g.), m. p. 305° (decomp.) (from benzene) (Found: C, 38·25; H, 2·6; Cl, 52·6. $C_{13}H_{10}Cl_6O_2$ requires C, 38·0; H, 2·45; Cl, 51·8%).

Reaction of Aldrin.—Under the same conditions aldrin (XIII) (10 g.) gave an ester that was very soluble in light petroleum and did not crystallise. Alkaline hydrolysis converted it into the *carboxylic acid* (XIV) [stereoisomer of XII] (8·2 g.), m. p. 218—220° (from chloroform) (Found: C, 37·7; H, 2·55; Cl, 53·2%).

Synthesis of Bicyclo[2,2,2]*octadiene.*—The following synthesis is a modification of that of Grob *et al.*[20] Cyclohexa-1,3-diene was made *via* cyclohexene dibromide by the method of Hine *et al.*[21] rather than *via* 3-chlorocyclohexene according to Grob *et al.*,[20] because the reactions can easily be carried out on a large scale and avoid the preparation of t-butyl hypochlorite. Grob's method (which does not use strong base) yields pure 1,3-diene, while Hine's (involving sodium hydroxide in ethylene glycol at 230°) gives the 1,3-diene contaminated with a few per cent of 1,4-diene, *not* benzene as reported (identified by gas chromatography). For the present synthesis traces of 1,4-diene are, of course, unimportant.

Crude acryloyl chloride was distilled during 3 hr. from a mixture of acrylic acid (432 g., 6 moles), benzoyl chloride (1642 g., 12 moles), and quinol (1 g.). On redistillation from a small amount of quinol the fraction, b. p. 72—78°, was collected (396 g., 73%).

The reaction between acryloyl chloride (361 g., 4 moles), cyclohexa-1,3-diene (240 g., 3 moles) and quinol (1 g.) was kept under control by cooling the flask in ice-water. After reaction had

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[20] Grob, Kny, and Gagneux, *Helv. Chim. Acta*, 1957, **40**, 130.

[21] Hine, Brown, Zalkow, Gardner, and Hine, *J. Amer. Chem. Soc.*, 1955, **77**, 594.

subsided, the mixture was heated at 100° for 2 hr. and then distilled. The adduct was collected at 99—102°/17 mm. (395 g., 77%).

The adduct (170·5 g., 1 mole) was stirred with sodium azide (130 g., 2 moles) in boiling xylene (350 ml.) for 2 hr. The cooled mixture was filtered to remove the sludge, which was then washed with benzene. Distillation of the combined filtrates under reduced pressure left the crude isocyanate. It was hydrolysed by dropwise addition to boiling 20% hydrochloric acid (500 ml.). The solution was cooled, and made strongly alkaline with sodium hydroxide solution. The amine layer was separated, and the aqueous layer extracted with ether (3 × 400 ml.). The combined amine layer and extracts were dried and distilled, to give 5α-amino-1α,4α-bicyclo[2,2,2]oct-2-ene, b. p. 98—101°/10 mm. (80 g., 65%) (picrate m. p. 210—211°).

This amine (123 g., 1 mole) was added dropwise with cooling to a mixture of 85% formic acid (275 ml.) and 40% aqueous formaldehyde (180 ml.). The mixture was then heated on a steam-bath under reflux for 8 hr. The cooled solution was made acid to Congo Red with hydrochloric acid and extracted with ether (4 × 500 ml.). The ether extract yielded bicyclo[2,2,2]oct-5-en-2-one (27 g., 22%), m. p. 78—79° (after sublimation). After addition of ether (1 l.), the acidic aqueous layer was made strongly alkaline with sodium hydroxide, and the organic layer was separated and combined with further ether extracts (2 × 500 ml.) of the aqueous layer. Distillation afforded the dimethylamino-compound, b. p. 78—82°/12 mm. (104 g., 70%).

30% Hydrogen peroxide (336 ml.) was dropped into a stirred ice-cooled solution of the amine (151 g., 1 mole) in methanol (290 ml.). 24 hr. later the remaining peroxide was decomposed by addition of a little platinum black, and the solvents were removed from the filtered solution. The residue was distilled into a receiver cooled in solid carbon dioxide-acetone. At 10 mm. the *N*-oxide began to decompose at a bath temperature of 120° and finished at 140°. The distillate, dissolved in ether (400 ml.), was washed with 2N-hydrochloric acid (800 ml.), and the aqueous layer was extracted with ether (2 × 400 ml.). Distillation of the combined ether layers gave bicyclo[2,2,2]octadiene (80 g., 75·5%), m. p. 51—55°.

Reaction of Bicyclo[2,2,2]*octadiene in Excess with Acidic Nickel Carbonyl.*—(*a*) The diene (10 g.), ethanol (30 ml.), water (2 ml.), acetic acid (2 ml.), and nickel carbonyl (5 ml.) were heated for 12 hr. The neutral fraction of the product consisted of *ethyl bicyclo*[2,2,2]*oct-5-ene-*exo-2-*carboxylate* (V; $X = CH_2{\cdot}CH_2$, $R = Et$) (10 g.), b. p. 90—92°/9 mm., n_D^{17} 1·4787 (Found: C, 72·9; H, 8·9. $C_{11}H_{16}O_2$ requires C, 73·3; H, 8·9%).

Recrystallisation of the acidic fraction from water gave the corresponding *carboxylic acid* as colourless needles (0·4 g.), m. p. 54—55° (Found: C, 71·0; H, 7·8%; *M*, 159. $C_9H_{12}O_2$ requires C, 71·1; H, 7·9%; *M*, 152). It contained one double bond per mol. (hydrogenation).

(*b*) *Reaction with an excess of nickel carbonyl.* The reaction mixture was the same as in the last experiment, but for the use of 5 ml. more each of nickel carbonyl and of ethanol. After 5 hr. more nickel carbonyl (10 ml.) was added. Distillation of the neutral product separated it into two fractions, b. p. 80—160°/10 mm. (2·5 g.), and b. p. 164—166°/10 mm. (14·9 g., 60%), n_D^{17} 1·4740 (Found: C, 66·3; H, 8·7. Calc. for $C_{14}H_{22}O_4$: C, 66·1; H, 8·65%). Gas-chromatography of the second fraction showed that it was a mixture of two isomeric esters in the proportion 40 : 60, presumably (VII + VIII; $X = CH_2{\cdot}CH_2$).

The acidic product was recrystallised from water, to give a mixture of diacids (0·8 g.), m. p. 193—198° (Found: C, 60·1; H, 7·1. Calc. for $C_{10}H_{14}O_4$: C, 60·6; H, 7·1%).

(*c*) *Reaction in dioxan.* The diene (5 g.), dioxan (25 ml.), water (1·0 ml.), acetic acid (1·0 ml.), and nickel carbonyl (5 ml.) were heated for 12 hr. Chromatography of the neutral product on silica gel gave (light petroleum) bicyclo-octadiene (0·3 g.), followed (25% of benzene in light petroleum) by *di*(*bicyclo*[2,2,2]*octen-2-yl*) *ketone* (stereochemistry not determined), m. p. 99—100° after sublimation or recrystallisation from light petroleum (Found: C, 84·6; H, 9·4%; *M*, 240. $C_{17}H_{22}O$ requires C, 84·3; H, 9·1%; *M*, 242). The acidic fraction (4·5 g.) consisted of the above carboxylic acid, m. p. 53—54° (after sublimation at 100°/12 mm.), having an infrared spectrum identical with that of the previous sample.

Reaction of Cyclohexa-1,4-*diene.*—The diene (10 g.), ethanol (30 ml.), water (2 ml.), acetic acid (2 ml.), and nickel carbonyl (10 ml.) were heated for 24 hr. Distillation of the neutral fraction gave unchanged diene (8 g.) and the ester (XVII) (1·1 g.), b. p. 194—196°, n_D^{17} 1·4590. The infrared spectrum was identical with that of a sample made by heating buta-1,3-diene (0·2 mole) and ethyl acrylate (0·25 mole) at 100° for 24 hr. (85% yield); it had n_D^{18} 1·4589, d_4^{20} 0·969.

Reaction of Cyclohexa-1,3-*diene.*—The reaction, carried out as for the 1,4-diene, yielded the same ester (0·8 g.), identified by its infrared spectrum, b. p. 194—198°, and n_D^{17} 1·4595.

The 1,3-diene (10 ml.), ethanol (25 ml.), water (2 ml.), acetic acid (2 ml.), and nickel acetate (1 g.) were boiled for 4 hr. Gas-chromatography showed that the proportion of 1,4-diene had increased from 5% to 11%.

The Cage Compound (XIX).—The olefin (424 mg.), made by photo-isomerisation [7] of the adduct of cyclo-octatetraene and benzoquinone, was heated for 48 hr. with ethanol (15 ml.), water (0·3 ml.), acetic acid (0·3 ml.), and nickel carbonyl (3 ml.). After filtration from nickel the solution was evaporated to dryness *in vacuo*. Sublimation of the residue at 120°/0·1 mm. gave the *ester* (XX) (489 mg., 85%), m. p. 113—114° (from benzene–light petroleum), $\nu_{max.}$ 1049, 1192, 1209, 1728, and 1752 cm.$^{-1}$ (Found: C, 71·1; H, 6·5. $C_{17}H_{18}O_4$ requires C, 71·3; H, 6·3%).

On exposure to the air the form of the crystals and their infrared spectrum gradually changed. After a week no further change occurred. The *hydrate* (XXI) then melted at 111—111·5°, depressed by the anhydrous ketone. The infrared spectrum had become much more complex, $\nu_{max.}$ 908, 1140, 1208, 1303, 1728, and 3250 cm.$^{-1}$ (Found: C, 66·9; H, 6·6. $C_{17}H_{20}O_5$ requires C, 67·1; H, 6·6%). When the hydrate was heated at 130° *in vacuo* the original diketo-ester slowly sublimed.

Reaction of Cyclopentene.—Nickel carbonyl (15 ml.) was added dropwise to a mixture of cyclopentene (13·6 g., 0·2 mole), ethanol (40 ml.), acetic acid (2 ml.), and water (1 ml.). After 4 hr. at 56° more nickel carbonyl (10 ml.) was added and heating was continued for 20 hr. Distillation of the neutral fraction gave ethyl cyclopentanecarboxylate (6·1 g., 21·5%), b. p. 171—173°, n_D^{20} 1·4370.

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