Alkenylation employing Lithium Alkenyls. Part VIII. Studies on Alkadienyl Derivatives.*

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The scope of the method of direct alkenylation with lithium alkenyls has been extended by demonstrating the formation of alkadienyl derivatives.

*iso*Phorone is converted by phosphorus pentachloride into, mainly, the chloro*cyclo*hexadiene (IV), formerly regarded as (II), and the phosphonic acid (V). Metallation of the chloro-diene with lithium, followed by carboxylation, gives the two 3 : 5 : 5-trimethyl*cyclo*hexadienecarboxylic acids (VI) and (VII), the structures of which are established spectroscopically and by hydrogenation.

Chloro*cyclo*heptadiene, similarly prepared from *cyclo*heptenone, is unreactive towards lithium, in contrast to 1-chloro*cyclo*heptene. The acyclic chloro-diene (XVI), derived from mesityl oxide, undergoes metallation and carboxylation, but instead of the expected diene-acid (XVII), a cyclic dimeric product regarded as (XIX) and formed by Diels–Alder addition with the starting chloride, is obtained.

IT has been shown in previous papers that lithium alkenyls can be obtained from a considerable range of alkylated vinyl halides and will undergo many useful reactions. This paper describes an extension of this approach to another type of substituted vinyl halide, namely, alkadienyl-lithium derivatives containing lithium directly attached to a conjugated diene system.

With the expectation (subsequently confirmed) that a cyclic alkadienyl-lithium derivative would have a better chance of survival for a useful life-time than an acyclic one, we selected the readily available *iso*phorone (I) for a first investigation. The conversion, by means of phosphorus pentachloride in chloroform, of *iso*phorone into a chloro-diene formulated as (II) was described by Knoevenagel and Fischer (*Annalen*, 1897, **297**, 191). When 1 molar proportion of phosphorus pentachloride is used, the yields obtained under these conditions are very low and much unchanged ketone is recovered, but somewhat better yields (up to 30%) can be attained in the absence of solvent. The chloro-diene obtained in this way boils over a very narrow range, but shows three distinct ultra-violet absorption maxima, at 2370, 2680, and 2780 Å, which are of varying relative intensity and almost certainly belong to three separate species.† The location of the 2680 Å band is that expected for the direct reaction product (II), formed by addition of phosphorus pentachloride to the carbonyl group followed by 1 : 2 elimination of $HO{\cdot}PCl_4$ (cf. Braude and Forbes, *J.*, 1951, 1755); the wave-length displacement with respect to *cyclo*hexa-1 : 3-diene ($\lambda_{max.}$ 2560 Å) corresponds almost exactly to the sum of the bathochromic effects of an α-methyl substituent (+Δλ 70 Å) and β-chloro-substituent (+Δλ 60 Å) in a diene system (Bowden, Braude, and Jones, *J.*, 1946, 948). The location of the 2780 Å band is that expected for the isomer (III), the slightly greater wave-length displacement with respect to *cyclo*hexa-1 : 3-diene being due to the relatively larger bathochromic effect of a chloro-substituent attached to the terminal position of the diene system.† Lastly, the 2370 Å band must belong to the isomer (IV) containing one exocyclic double bond, the wave-length displacement with respect to 3-methylene*cyclo*hexene (2280 Å; Braude and Wheeler, unpublished work; cf. β-phellandrene, $\lambda_{max.}$ 2320, Macbeth, Smith, and West, *J.*, 1938, 119) again being due the terminal chloro-substituent. The intensity of the 2370 Å band in the chloro-diene mixture is always much higher (ε ~ 9000) than that of the other two bands which are of similar intensity (ε ~ 2000); assuming the extinction coefficients of the pure compounds to be in the same ratio as those of 3-methylene*cyclo*hexene (ε 10,000) and *cyclo*hexa-1 : 3-diene (ε 8000) gives the average proportions of (II),

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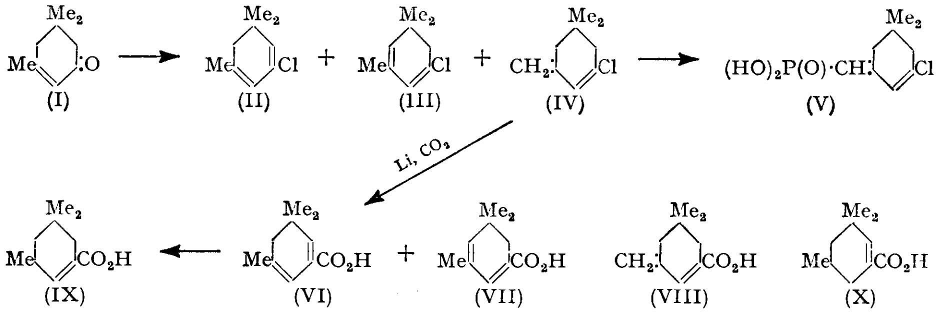
* Part VII, *J.*, 1952, 1425.

† The possibility that the 2680 and 2780 Å bands belong to one species, (II) or (III), cannot be excluded.

(III), and (IV) in the crude reaction product as *ca.* 1 : 1 : 8. The three chloro-dienes may be regarded as derived from the three possible enols of *iso*phorone, although (III) and (IV) may actually be formed from (II) by prototropic double-bond migration. On treatment with Brady's reagent, the chloro-diene mixture gave *iso*phorone 2 : 4-dinitrophenylhydrazone, though only in 30% yield. Treatment with aqueous silver nitrate also gave *iso*phorone, whereas with ethanolic silver nitrate a ketone was obtained which had physical properties identical with those of *iso*phorone but formed a 2 : 4-dinitrophenylhydrazone of much lower m. p. This may be an isomeric derivative of *iso*phorone, as observed in other cases (cf. Dirscherl and Nahm, *Ber.*, 1940, **73**, 448; Theilacker, *ibid.*, 1949, **82**, 190; Braddock and Willard, *J. Amer. Chem. Soc.*, 1951, **73**, 5866); alternatively, it may be the derivative of 2 : 4 : 4-trimethyl*cyclo*hex-2-enone produced by reverse hydration of the vinyl chloride grouping.



In addition to the chloro-dienes, the reaction of *iso*phorone with phosphorus pentachloride (1 mol.) affords a small amount of a solid, m. p. 139°, $C_9H_{14}O_3ClP$. When, in an attempt to improve the yields of chloro-dienes, the reaction was carried out with 2 molar proportions of phosphorus pentachloride, this solid was the main product. It proved to be a dibasic phosphonic acid and its spectral properties indicate that it has the structure (V) and is formed by the addition of phosphorus pentachloride to the exocyclic double bond in (IV), followed by hydrolysis (cf. Kosolapoff, " Organic Reactions," Vol. VI, 1951, p. 291). The high intensity of the ultra-violet absorption ($\lambda_{max.}$ 2510 Å; ε 28,000) shows that the one double bond is exocyclic while the bathochromic displacement with respect to (IV) is ascribable to the auxochromic effect of the conjugated phosphorus-containing group (cf. Bowden and Braude, *J.*, 1952, 1068); the infra-red spectrum exhibits bands at 1614 and 1573 cm.$^{-1}$ associated with C=C stretching vibrations, and 1022 and 960 cm.$^{-1}$ associated with $-PO(OH)_2$ bending vibrations (cf. Halman and Pinchas, *J.*, 1953, 627; Bellamy and Beecher, *ibid.*, p. 729).

The chloro-dienes are rather unstable compounds and difficult to separate, but the predominating isomer (IV) was obtained nearly pure by fractionation on a small scale. The freshly distilled material reacted fairly readily with almost the theoretical amount of lithium in boiling ether, and on carboxylation furnished a solid acid in up to 15% yield. The conditions of formation of the lithium alkadienyl are considerably more critical than those of similar lithium alkenyls (*e.g.*, *cyclo*hexenyl-lithium; Braude and Coles, *J.*, 1950, 2014); and the alkadienyl derivative is evidently rather unstable, for, if the optimum reaction period was doubled, the yield of acid obtained on carboxylation dropped to 0·5%. The acid, which was also rather unstable, analysed correctly for the expected product (VIII) and had a sharp melting point when freshly purified by vacuum-sublimation or crystallisation, but showed two distinct ultra-violet absorption bands, at 2640 and 2910 Å, in solution. The sum of the intensities of the two bands was approximately constant in different solvents, but the relative intensities depended on the pH (see Table), and the two bands clearly belong to two isomeric species in equilibrium. The location of the 2640 Å band is compatible with structure (VIII) but its low intensity would correspond to the presence of less than 20% of this isomer (cf. sorbic acid which has $\lambda_{max.}$ 2580 Å, ε 25,000, in ethanol). Moreover, the infra-red spectrum of the diene-acid fails to show the C–H bending frequency at 890 cm.$^{-1}$ characteristic of a $CH_2{=}C{<}$ grouping. The

2640 Å band is therefore attributed to structure (VI) containing the " cross-conjugated " *cyclo*hexa-1 : 5-dienecarboxylic acid system which would be expected to exhibit a maximum in this region, although no other examples appear to be known. The 2910 Å band, on the other hand, is attributed to structure (VII) containing the terminally conjugated *cyclo*hexa-1 : 3-dienecarboxylic acid system.

*Ultra-violet light absorption of trimethyl*cyclo*hexadienecarboxylic acids* (VI) $\rightleftharpoons$ (VII), *their salts, and their methyl esters.*

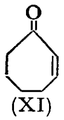
	$\lambda_{max.}$ (Å)	ε	$\lambda_{max.}$ (Å)	ε	$\varepsilon_{2640} + \varepsilon_{2910}$
Acids : in hexane	2640	5200	2910	4800	10,000
,, dioxan	2640	5200	2910	4900	10,100
,, ethanol	2640	5300	2910	4700	10,000
Salts : in ethanol–0·1M-KOH	2610	6000	2910	3800	9,800
Esters : in ethanol	2640	5900	2920	5000	10,900
,, ethanol–0·1M-KOH	2640	5900	2920	5000	10,900

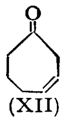
The formation of lithium alkenyls is not normally accompanied by double-bond migration (cf. Braude and Timmons, *J.*, 1950, 2000; Braude and Coles, *J.*, 1950, 2014; 1951, 2078) and it seems probable that the rearrangement of the exocyclic system present in the chloride (IV) to the *cyclo*hexadiene system present in the acids (VI) and (VII) occurs during, rather than before, the carboxylation of the alkadienyl-lithium derivative when the lithium salt of the acid (VIII) is formed. The prototropic mobility of the ethylenic acids and their salts is well known and the exocyclic double-bond arrangement in (VIII) would be expected to be less stable than the more highly hyperconjugated cyclic double-bond arrangements in (VI) and (VII) which should be almost equally stable. The two *cyclo*hexadiene derivatives thus co-exist in about equal proportions, though the exact equilibrium point differs in the acids and their salts, as in other cases (cf. Linstead and Noble, *J.*, 1934, 614, and earlier papers). The predominance of the exocyclic isomer (IV) in the corresponding chlorides may be due to the smaller importance of hyperconjugation in the absence of a carboxyl group, or, more probably, to the fact that the method of preparation does not result in an equilibrium mixture in this case.

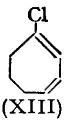
Treatment of the mixture of acids (VI) and (VII) with diazomethane in ether gave a mixture of the corresponding methyl esters which showed very similar spectral properties in the ultra-violet (see Table) and infra-red (see Experimental section) and were also inseparable by small-scale fractionation. Neither the esters nor the acids furnished maleic anhydride adducts under the usual conditions. On hydrogenation over platinum oxide in ethyl acetate, the diene-acids gave a monoene-acid which exhibited a maximum at 2170 Å (ε 9500) and therefore contained the double bond in conjugation with the carboxyl group (cf. *cyclo*hex-1-enecarboxylic acid, $\lambda_{max.}$ 2120 Å, ε 11,000; Braude and Coles, *loc. cit.*). This acid is regarded as (IX), produced by 1 : 4-addition of hydrogen to the *cyclo*hexadiene system in (VI) and 1 : 2-addition in (VII), although the alternative structure (X) is not excluded. Hydrogenation of the diene acids over platinum oxide in acetic acid resulted in the uptake of two mols. of hydrogen and gave 3 : 3 : 5-trimethyl*cyclo*hexanecarboxylic acid. An authentic specimen of the latter was prepared from dihydro*iso*phorone by reduction to the alcohol, conversion into the bromide, and carboxylation of the Grignard derivative.

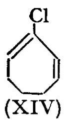
The highest yields of acids obtained from the lithium derivative of (IV) compare favourably with those obtained in similar carboxylations (cf. Braude and Timmons, and Braude and Coles, *locc. cit.*), but none of the corresponding dialkenyl ketone which normally forms the major product could be isolated in the present case. A small quantity of a high-melting ketone $C_{18}H_{30}O_2$ was separated from the neutral fraction, but was not further investigated. No pure products are isolated from the reaction of the alkadienyl-lithium with acetaldehyde, benzaldehyde, or benzophenone, which usually give the expected alcohols in good yields. As has been indicated, even the trimethyl*cyclo*hexadienyl chlorides and carboxylic acids are unstable and the failure to isolate other types of derivatives is undoubtedly due to the high reactivity and ease of isomerisation of this system.

Even greater instability is to be expected for unsubstituted *cyclo*hexadienyl derivatives, but it was hoped that some of the complications just described would be absent in the *cyclo*heptadiene system which is also of particular interest for synthetic purposes (cf. Braude and Forbes, *J.*, 1953, 2208). *cyclo*Hept-2-enone (XI) which has not been previously described although it has been mentioned in the literature (cf. Kötz, *Annalen*, 1913, **400**, 80; Dauben and Ringold, *J. Amer. Chem. Soc.*, 1951, **73**, 876) was prepared by bromination of *cyclo*heptanone with bromine in chloroform in the presence of calcium carbonate, followed by dehydrobromination with collidine at 180°. Even when a deficiency of bromine was used, some dibromo-ketone was produced in the first step and it was necessary to separate the mixture of unchanged *cyclo*heptanone, 1-bromo*cyclo*heptanone, and dibromo-ketone by careful fractionation. Alternatively, chloro*cyclo*heptanone (Kötz, *Annalen*, 1913, **400**, 53) may be employed as intermediate; the monochlorination proceeded in better yield than bromination, but the dehydrochlorination required a higher temperature (cf. Warnhoff and Johnson, *J. Amer. Chem. Soc.*, 1953, **75**, 494) and the overall yield was somewhat lower. The *cyclo*heptanone obtained by either procedure exhibited an absorption band at 2270 Å as expected for (XI), and its skeletal structure was confirmed by catalytic hydrogenation to *cyclo*heptanone. However, the intensity of absorption of the unsaturated ketone was only about half the usual value and the crude semicarbazone showed two bands, one at 2650 Å corresponding to the derivative of an αβ-ethylenic ketone (cf. Evans and Gillam, *J.*, 1943, 565), and another at 2270 Å, corresponding to the derivative of an unconjugated ketone (Braude and Timmons, *J.*, 1953, 3131). *cyclo*Heptenone prepared by this method is thus evidently a mixture of the αβ- (XI) and the βγ-ethylenic isomer (XII), as observed in other cases (cf. Braude, Jones, Koch, Richardson, Sondheimer, and Toogood, *J.*, 1949, 1890, and references there cited). The two isomers could not be separated by small-scale fractionation, and crystallisation of the mixture of semicarbazones gave only the higher-melting derivative of (XII) in a state of purity; on the other hand, treatment with Brady's reagent gave a chromatographically homogeneous 2 : 4-dinitrophenylhydrazone, the light absorption of which ($\lambda_{\max.}$ 3770 Å) indicates that it is the derivative of (XI) (cf. Braude and Jones, *J.*, 1945, 498). With phosphorus pentachloride, *cyclo*heptenone was converted into a mixture of the required chloro*cyclo*hepta-1 : 3-diene (XIII) or (XIV) and 3 : 3-dichloro*cyclo*heptene.


(XI)


(XII)

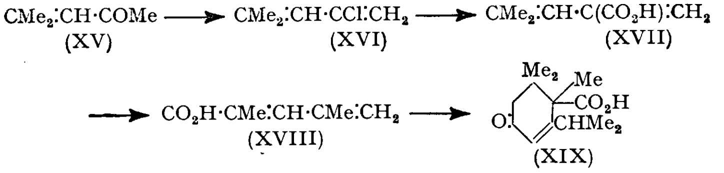

(XIII)


(XIV)

Treatment of the dichloride with ethanolic potassium hydroxide gave the chloro-diene; its ultra-violet light absorption ($\lambda_{\max.}$ 2510 Å) shows the expected small bathochromic shift with respect to *cyclo*heptadiene ($\lambda_{\max.}$ 2480 Å; Pesch and Friess, *J. Amer. Chem. Soc.*, 1950, **72**, 5756), similar to that found in the *cyclo*hexadiene system, but does not distinguish reliably between structures (XIII) and (XIV). The chloro*cyclo*heptadiene proved extremely unreactive towards lithium; only a fraction of the stoicheiometric proportion of metal was consumed and on carboxylation only traces of non-crystalline acidic products were obtained. This lack of reactivity is somewhat surprising since 1-chloro*cyclo*hexene (Braude and Coles, *loc. cit.*) and 1-chloro*cyclo*heptene (Braude, Forbes, and Evans, *J.*, 1953, 2202) are metallated with comparable ease. It is possible that double-bond isomerism in the chloro*cyclo*heptadiene is responsible; the ease of direct metallation reactions is known to be highly sensitive to the homogeneity of the organic halide (cf. Part I, *J.*, 1950, 2000).

Despite this discouraging result, the metallation of an acyclic chloro-diene was next attempted. A suitable example appeared to be 2-chloro-4-methylpenta-1 : 3-diene (XVI) obtainable from mesityl oxide and phosphorus pentachloride (Baeyer, *Annalen*, 1866, **140**, 298). This chloro-diene reacted quite readily with lithium but on carboxylation did not give the expected diene-acid (XVII). Instead, an acid $C_{13}H_{20}O_3$ was obtained, the spectral properties ($\lambda_{\max.}$ 2430 A, ε 10,000; $\nu_{\max.}$ 1654, 1580 cm.$^{-1}$) of which indicated the presence of the carboxyl group but also of a keto-group conjugated with *one* ethylenic double bond;

this, together with the high melting point (187°) leads to the conclusion that the acid contains one alicyclic ring. The molecular formula corresponds to an adduct of the expected diene-acid (XVII; $C_7H_{10}O_2$) and one molecule of mesityl oxide (XV; $C_6H_{10}O$), which would be the hydrolysis product of the starting chloride (XVI). The most probable structure of the keto-acid is (XIX), formed by Diels–Alder addition of the lithium salt of the diene-acid in its isomeric form (XVIII) to the starting chloride, followed by prototropic shift of the double bond into the ring and hydrolysis of the vinyl chloride grouping during the working-up. The occurrence of this type of side-reaction severely restricts the potential synthetic usefulness of acyclic alkadienyl-lithium derivatives and, not unexpectedly, no pure products could be isolated from the reactions with other carbonyl compounds, such as formaldehyde and benzophenone.



EXPERIMENTAL

M. p.s were taken on a Kofler block and are corrected.

Analytical data were determined by Mr. F. H. Oliver and the staff of the microanalytical laboratory of this Department. Ultra-violet light absorptions were determined by Mrs. A. I. Boston using Hilger–Spekker and Unicam S.P. 500 instruments. Infra-red spectra were kindly determined by Dr. E. S. Waight, using a single-beam Grubb–Parsons instrument. The intensities of infra-red absorption bands are indicated qualitatively by vs (very strong), s (strong), or m (medium).

1-*Chloro*-5 : 5-*dimethyl*-3-*methylene*cyclo*hexene* (IV).—*iso*Phorone (200 g.) was added slowly to phosphorus pentachloride (300 g.) with rapid stirring and external cooling. Stirring was continued overnight, and the mixture was then added to ice-water (2 l.) and extracted with ether (1 l.). The ethereal extract was dried (Na_2SO_4) and the solvent removed under reduced pressure. On cooling to 0°, a solid (9·8 g.) separated which was filtered off and after recrystallisation from ethyl acetate had m. p. 138—139°, undepressed on admixture with the phosphonic acid (V) described below.

The liquid product was fractionated through an 8″ Dufton column, giving a mixture of 1-chloro-5 : 5-dimethyl-3-methylene*cyclo*hexene, and 3-chloro-1 : 5 : 5- and 1-chloro-3 : 5 : 5-trimethyl*cyclo*hexa-1 : 3-diene (58 g., 26%), b. p. 65—66°/17 mm., n_D^{21} 1·4910—1·4920 (Found: C, 69·2; H, 8·4; Cl, 22·4. Calc. for $C_9H_{13}Cl$: C, 69·0; H, 8·3; Cl, 22·7%). Light absorption in hexane: $\lambda_{max.}$ 2360, 2680, and 2780 Å; ε 9000, 2000, and 1500 respectively. The yield quoted is the best obtained; in other runs it ranged from 8 to 26%, the average yield in 8 runs being 16%. When the reaction was carried out in chloroform solution the yield was reduced (cf. Knoevenagel and Fischer, *Annalen*, 1897, **297**, 191). The composition of the chloro-diene mixture as indicated by the intensities of the three ultra-violet absorption bands also showed some variation.

Higher-boiling fractions consisted of mixtures of the chloro-diene, unchanged *iso*phorone, and 1 : 1-dichloro-3 : 3 : 5-trimethyl*cyclo*hexane.

Refractionation of the above chloro-diene mixture gave 1-*chloro*-5 : 5-*dimethyl*-3-*methylene*-cyclo*hexene*, b. p. 70°/16 mm., n_D^{19} 1·4921, $\lambda_{max.}$ 2360, ε 10,500 in hexane (Found: Cl, 22·2%).

Hydrolysis of 1-*Chloro*-5 : 5-*dimethyl*-3-*methylene*cyclo*hexene*.—(*a*) The chloro-diene (1 g.) was refluxed with 2 : 4-dinitrophenylhydrazine (1 g.) and sulphuric acid (3 g.) in methanol (15 ml.) and water (5 ml.) for 30 min. On cooling, *iso*phorone 2 : 4-dinitrophenylhydrazone (0·5 g.) separated which after one crystallisation from ethyl acetate had m. p. and mixed m. p 146°.

(*b*) The chloro-diene (1·2 g.) was refluxed with silver nitrate (3 g.), water (50 ml.), and 1 drop of sulphuric acid for 3 hr. The silver chloride (0·25 g., 7%) was filtered off and the solution extracted with ether, giving *iso*phorone, identified as in (*a*).

(*c*) The chloro-diene (3 g.) was refluxed with silver nitrate (4 g.) in ethanol (30 ml.) containing 1 drop of nitric acid for 1 hr. Water was added and the precipitate of silver chloride

(0·9 g., 7%) filtered off. Extraction of the filtrate with ether and fractionation gave a ketone (1·2 g.), b. p. 93—94°/17 mm., n_D^{22} 1·4855, $\lambda_{max.}$ 2340 Å, ε 11,700 in EtOH. It formed a 2 : 4-*dinitrophenylhydrazone* which crystallised from ethyl acetate in plates, m. p. 124°, and had $\lambda_{max.}$ 3900 Å, ε 28,600 in EtOH (Found : C, 57·0; H, 6·0; N, 17·3. $C_{15}H_{18}O_4N_4$ requires C, 56·6; H, 5·7; N, 17·6%). This is presumably an isomer of *iso*phorone 2 : 4-dinitrophenylhydrazone or the derivative of 2 : 4 : 4-trimethyl*cyclo*hex-2-enone.

3-*Chloro*-5 : 5-*dimethyl*cyclo*hex-2-enylidenemethylphosphonic Acid* (V).—*iso*Phorone (28 g.) was caused to react with phosphorus pentachloride (78 g.), and the products were worked up as above. After the removal of ether, solid material (15 g.) separated and was filtered off. Crystallisation from ethyl acetate gave the *phosphonic acid*, m. p. 139° (Found : C, 45·6; H, 6·2; P, 12·7; Cl, 15·1. $C_9H_{14}O_3PCl$ requires C, 45·7; H, 6·0; P, 13·1; Cl, 15·0%). A solution in aqueous ethanol was acid to litmus and liberated carbon dioxide from sodium carbonate. The equivalent weight, kindly determined alkalimetrically by Dr. H. Coates (Albright and Wilson, Ltd.), was 118 (Calc.: 118) and no orthophosphoric acid was produced on fusion with potassium hydroxide; hence the acid is a dibasic phosphonic acid and not a phosphoric acid monoester. Ultra-violet light absorption : $\lambda_{max.}$ 2510 and 2560 Å (ε 28,300) in EtOH. Infra-red light absorption : $\nu_{max.}$ 1614 (m), 1573 (m), 1022 (s), and 960 (s) cm.$^{-1}$ (Nujol mull).

3 : 3 : 5-*Trimethyl*cyclo*hexa*-1 : 5- (VI) *and* 3 : 5 : 5-*Trimethyl*cyclo*hexa*-1 : 3-*dienecarboxylic Acid* (VII).—Freshly distilled 1-chloro-5 : 5-dimethyl-3-methylene*cyclo*hexene (50 g.) in anhydrous ether (100 ml.) was added to a vigorously stirred, finely divided suspension of lithium (13·1 g.) in ether (1 l.) under nitrogen. After about 20 min. the solution became cloudy and was then heated to gentle reflux. Heating was continued for 15 hr. during which the mixture first became red, then brown and finally orange; these characteristic colour changes are different from those observed with monoethylenic lithium alkenyls (cf. Braude and Coles, *J.*, 1950, 2014; Braude and Forbes, *J.*, 1951, 1755). The solution of alkadienyl-lithium was filtered under nitrogen through glass wool into a flask containing excess of solid carbon dioxide (1500 g.). The amount of unchanged lithium recovered from the residue was 9·4 g.; the amount consumed was therefore 3·7 g., or 82% based on the chloro-diene. After the filtrate had attained room temperature, N-hydrochloric acid (500 ml.) was added, the ethereal layer was separated, and the aqueous layer extracted with ether. The combined ethereal extracts were shaken with saturated aqueous sodium carbonate (3 × 100 ml.), and the ethereal (A) and the aqueous layer (B) were separated.

The ethereal layer was concentrated under reduced pressure and, on being kept, deposited a crystalline *ketone* (0·5 g.) which after sublimation at 160°/10^{-5} mm. had m. p. 166°, $\lambda_{max.}$ 2850 Å, $E^{1\%}_{1\,cm.}$ 2·4 in EtOH (Found: C, 77·6; H, 10·9. $C_{18}H_{30}O_2$ requires C, 77·7; H, 10·8%). Treatment with Brady's reagent gave a 2 : 4-*dinitrophenylhydrazone* which was crystallised from ethyl acetate and had m. p. 261—262° (decomp.), $\lambda_{max.}$ 3680 Å, $E^{1\%}_{1\,cm.}$ 700 in $CHCl_3$ (Found : C, 54·3; H, 6·5; N, 15·6%).

Acidification of the aqueous layer (B) with hydrochloric acid precipitated a brown gum which was extracted with ether. The ethereal solution was dried (Na_2SO_4) and evaporated, and the residue (10 g.) was slowly sublimed in a short-path sublimation apparatus at 80°/10^{-5} mm., giving a mixture of the diene-acids (7·4 g., 14%), m. p. 88° (Found : C, 72·1; H, 8·5. Calc. for $C_{10}H_{14}O_2$: C, 72·3; H, 8·5%). Ultra-violet light absorption : see Table. Infra-red light absorption (Nujol mull) : $\nu_{max.}$ 1682 (s; C=O stretching), 1646 and 1575 cm.$^{-1}$ (m; C=C stretching).

The above conditions of metallation are those which gave the highest yields of diene-acids. The results of other typical runs are tabulated below.

Li used (atom proportions)	5·8	4·6	2·4	2·7
Li consumed (atom proportions)	1·6	2·0	1·4	1·1
Reaction time (hr.)	15	15	15	36
Yield of acids (%)	14	5	5	0·5

Esterification of Diene-acids.—Treatment of the acids (0·9 g.) with excess of diazomethane in ether afforded the methyl esters (1·0 g.), b. p. 53°/0·5 mm., n_D^{23} 1·4934 (Found : C, 73·1; H, 9·0. Calc. for $C_{11}H_{16}O_2$: C, 73·3; H, 8·95%). Ultra-violet light absorption : see Table. Infra-red light absorption (liquid film) : $\nu_{max.}$ 1740 (vs; C=O stretching), 1652, 1626, 1606, 1585 (m; C=C stretching), 1266, 1240, 1198 (s; C–O stretching), 1078 (s), and 824, 804 cm.$^{-1}$ (m; CR_2=CR–H bending).

Hydrogenation of Diene-acids.—(*a*) Hydrogenation of the above diene-acids (0·5 g.) in methanol (15 ml.) in the presence of platinum oxide resulted in the uptake of 65 ml. of hydrogen during 4 hr. (at 20°/760 mm. Calc. for 1 mol., 72 ml.), giving 3 : 3 : 5-*trimethyl*cyclo*hex*-1-*ene*-

carboxylic acid (0·3 g.), m. p. 65° (Found: C, 71·0; H, 9·7. $C_{10}H_{16}O_2$ requires C, 71·4; H, 9·6%). Light absorption in EtOH: $\lambda_{max.}$ 2170 Å, ε 9200.

(*b*) Hydrogenation of the diene-acids (0·3 g.) in glacial acetic acid (25 ml.) in the presence of platinum oxide resulted in the uptake of 87 ml. of hydrogen (at 20°/761 mm. Calc. for 2 mols., 87 ml.). There was a marked decrease in the rate of uptake after 1 mol. had been absorbed. Dilution with water and extraction with ether gave an oil which was treated with thionyl chloride followed by aniline, to give 0·2 g. of 3 : 3 : 5-trimethyl*cyclo*hexylacetanilide, m. p. 115—116°, undepressed on admixture with the authentic specimen described below.

3 : 3 : 5-*Trimethyl*cyclo*hexanecarboxylic Acid*.—*iso*Phorone (100 g.) in ethyl acetate (200 g.) was hydrogenated over platinic oxide, to give 3 : 3 : 5-trimethyl*cyclo*hexanone (90 g., 89%), b. p. 68°/15 mm., n_D^{16} 1·4492 (cf. Skita, *Ber.*, 1909, **42**, 1630). The 2 : 4-*dinitrophenylhydrazone* crystallised from methanol in plates, m. p. 115—116° (Found: C, 56·0; H, 6·4; N, 17·3. $C_{15}H_{20}O_4N_4$ requires C, 56·2; H, 6·3; N, 17·5%). (Morgan and Hardy, *Chem. and Ind.*, 1933, 518, give m. p. 145—147°, presumably due to an isomer; alternatively, it seems possible that their derivative was, in fact, that of *iso*phorone and not of dihydro*iso*phorone.)

The ketone (30 g.) was reduced with lithium aluminium hydride (7 g.) in ether (350 ml.) at 0°, and then at 20°, to 3 : 3 : 5-trimethyl*cyclo*hexanol (26 g., 85%), b. p. 83°/10 mm., n_D^{20} 1·4558. Knoevenagel, *loc. cit.*, gives b. p. 92°/12 mm., n_D^{16} 1·4550, for the *cis*-isomer; this stereochemical assignment is now confirmed, since reduction by lithium aluminium hydride will give the thermodynamically more stable *cis*-isomer (cf. Barton, *J.*, 1953, 1027) with both the 1-hydroxyl and the 3-methyl group equatorial. The 3 : 5-*dinitrobenzoate* crystallised from light petroleum (b. p. 40—60°) in needles, m. p. 71° (Found: C, 57·5; H, 6·1; N, 8·6. $C_{16}H_{20}O_6N_2$ requires C, 57·2; H, 6·0; N, 8·3%).

A mixture of the alcohol (21·2 g.) and phosphorus tribromide (40·6 g.) was kept overnight at 20° and then refluxed for 3 hr. After this had cooled, water (100 ml.) was added and the product extracted with ether. Fractionation gave 3-bromo-1 : 1 : 5-trimethyl*cyclo*hexane (14 g., 46%), b. p. 79°/10 mm., n_D^{22} 1·4823 (Found: C, 52·8; H, 8·3; Br, 39·4. $C_9H_{17}Br$ requires C, 52·7; H, 8·3; Br, 39·0%).

A solution of the foregoing bromide (7·65 g.) in ether (80 ml.) was stirred and refluxed with magnesium (0·95 g.) and a trace of iodine and methyl iodide. Reaction set in after about 1 hr. and was complete after 3 hr. Excess of solid carbon dioxide (50 g.) was added, then, after 2 hr., 2N-sulphuric acid (50 ml.), and the ethereal layer was separated and extracted with aqueous sodium carbonate. The alkaline extract was acidified with hydrochloric acid and extracted with ether. This ethereal extract was dried (Na_2SO_4) and distilled, giving 3 : 3 : 5-*trimethyl*cyclo*hexanecarboxylic acid* (1·9 g., 30%), m. p. 43°, b. p. 90°/0·5 mm., n_D^{24} 1·4571 (Found: C, 70·5; H, 10·8. $C_{10}H_{18}O_2$ requires C, 70·6; H, 10·7%). The *methyl ester*, prepared in quantitative yield by treatment with excess of diazomethane in ether, had b. p. 46°/0·5 mm., n_D^{25} 1·4452 (Found: C, 72·0; H, 11·1. $C_{11}H_{20}O_2$ requires C, 71·7; H, 10·9%). The *anilide*, prepared *via* the acid chloride as above, crystallised from aqueous methanol in plates, m. p. 118—119° (Found: N, 5·8. $C_{16}H_{23}ON$ requires N, 5·7%).

2-*Bromo*cyclo*heptanone*.—Bromine (240 g.) in chloroform (150 ml.) was added during 2 hr. to a stirred mixture of *cyclo*heptanone (168 g.), chloroform (100 ml.), water (300 ml.), and calcium carbonate (75 g.). The flask was initially warmed to start the reaction and later cooled when necessary. Stirring was continued for 5 hr. after all the bromine had been added and the mixture was then extraced with ether (2 × 250 ml.). The ethereal extract was washed with water, dried (Na_2SO_4), and fractionated, giving (i) a mixture of unchanged *cyclo*heptanone and 2-bromo*cyclo*heptanone (55 g.), b. p. 60—78°/2 mm., n_D^{23} 1·4665—1·4800, (ii) 2-bromo*cyclo*heptanone (75 g., 28%), b. p. 80—84°/2 mm., n_D^{23} 1·5100, (iii) dibromo*cyclo*heptanone (3 g.), b. p. 94—98°/1 mm., n_D^{23} 1·5385, and higher-boiling residues. Redistillation of fraction (ii) gave pure 2-*bromo*cyclo*heptanone*, b. p. 105°/10 mm., n_D^{22} 1·5137 (Found: C, 44·5; H, 6·0; Br, 41·5. $C_7H_{11}OBr$ requires C, 44·0; H, 5·8; Br, 41·8%). On treatment with 2 : 4-dinitrophenylhydrazine in methanol–sulphuric acid it gave 2-*methoxy*cyclo*heptanone* 2 : 4-*dinitrophenylhydrazone* which after chromatography on alumina in benzene–chloroform crystallised from ethyl acetate–methanol in yellow needles, m. p. 109° (Found: C, 52·4; H, 6·0; N, 17·5. $C_{14}H_{18}O_5N_4$ requires C, 52·2; H, 5·6; N, 17·4%). [Since the present work was done, the preparation of 2-bromo*cyclo*heptanone in unstated yield by the use of *N*-bromosuccinimide has been reported by Corey (*J. Amer. Chem. Soc.*, 1953, **75**, 2301).]

2-*Chloro*cyclo*heptanone*.—Chlorine was passed through a mixture of *cyclo*heptanone (52 g.), water (40 ml.), and calcium carbonate (24 g.) until all the carbonate had disappeared (*ca.* 2 hr.) (cf. Kötz, *Annalen*, 1913, **400**, 53). Throughout the reaction, the mixture was cooled in ice and shaken at frequent intervals. Extraction with ether and fractionation gave 2-chloro*cyclo*heptanone (40 g., 59%), b. p. 100—103°/15 mm., n_D^{21} 1·4861 (Found : Cl, 24·2. Calc. for $C_7H_{11}OCl$: Cl, 24·2%). Treatment with Brady's reagent under the condition used for the bromo-ketone gave the 2 : 4-*dinitrophenylhydrazone* which crystallised from ethyl acetate in yellow needles, m. p. 140—141° (Found : C, 48·0; H, 4·65; N, 16·9; Cl, 10·6. $C_{13}H_{15}O_4N_4Cl$ requires C, 47·8; H, 4·65; N, 17·15; Cl, 10·85%). Light absorption in $CHCl_3$: $\lambda_{max.}$ 3580 Å, ε 24,800.

If the reaction mixture is not cooled or if chlorine is passed for a longer time, mainly 2 : 2(?)-*dichloro*cyclo*heptanone* (52 g., 62%), b. p. 128—130°/17 mm., n_D^{21} 1·5025 (Found : Cl, 38·9. $C_7H_{10}OCl_2$ requires Cl, 39·0%), is obtained.

cyclo*Hept-2-enone*.—(*a*) A rapidly stirred mixture of 2-bromo*cyclo*heptanone (100 g.) and collidine (85 g.) was heated to 180—185° for a few minutes in an oil-bath. As soon as the separation of collidine hydrobromide was complete, the bath was removed and benzene (300 ml.) was added to the now viscous reaction mixture when it had cooled to *ca.* 100°. The collidine hydrobromide was then filtered off and washed with hot benzene (200 ml.). The combined filtrates were washed with 2N-hydrochloric acid (200 ml.), the benzene layer was separated and dried (Na_2SO_4), and the solvent removed under reduced pressure. Fractionation of the residue gave a mixture of *cyclo*hept-2- (XI) and -3-enone (XII) (39 g., 68%), b. p. 31°/0·5 mm., n_D^{20} 1·491—1·500, $\lambda_{max.}$ 2270 Å (ε 5000—8000) in EtOH or C_6H_{14} (Found : C, 76·4; H, 9·3. Calc. for $C_7H_{10}O$: C, 76·3; H, 9·1%). The mixture of ketones (9 g.) formed a semicarbazone which after one recrystallisation from aqueous methanol formed plates (5 g.), m. p. 136—137°, $\lambda_{max.}$ 2270 (ε 9000) and 2650 Å (ε 7700) in EtOH (Found : C, 57·4; H, 7·7; N, 25·0. Calc. for $C_8H_{13}ON_3$: C, 57·5; H, 7·8; N, 25·1%). On further recrystallisation from aqueous methanol, the m. p. slowly rose and after 7 operations the *semicarbazone*, m. p. 155—156°, of *cyclo*hept-3-enone, was obtained; it had $\lambda_{max.}$ 2260 Å (ε 18,500) in EtOH (Found : C, 57·4; H, 7·8; N, 24·8%). Treatment of the mixture of ketones with Brady's reagent gave the 2 : 4-*dinitrophenylhydrazone* of *cyclo*hept-2-enone which, after chromatography on alumina in benzene–chloroform, crystallised from ethyl acetate–methanol in red plates, m. p. 122°, $\lambda_{max.}$ 3770 Å (ε 21,000) in $CHCl_3$ (Found : C, 53·7; H, 5·2; N, 19·0. $C_{13}H_{14}O_4N_4$ requires C, 53·8; H, 4·9; N, 19·3%).

(*b*) A rapidly stirred mixture of 2-chloro*cyclo*heptanone (25 g.) and collidine (25 g.) was heated to about 220° and kept under gentle reflux. After about 2 hr., collidine hydrochloride began to separate and eventually the whole reaction mixture became viscous. After 2 hr., it was allowed to cool and worked up as above, giving *cyclo*heptenone (5 g., 27%), b. p. 26°/0·3 mm., n_D^{21} 1·4913, $\lambda_{max.}$ 2270 Å (ε 4800) in EtOH.

Hydrogenation of *cyclo*hept-2-enone (1·1 g.) in methanol (25 ml.) in the presence of platinic oxide resulted in the uptake of 240 ml. of hydrogen (at 20°/756 mm. Calc., 240 ml.), giving *cyclo*heptanone (1 g.), b. p. 71°/10 mm., n_D^{24} 1·4607; the 2 : 4-dinitrophenylhydrazone had m. p. and mixed m. p. 148°.

3-*Bromo*cyclo*heptene*.—*cyclo*Heptene (32 g.; prepared from *cyclo*heptanone in nearly quantitative yield by reduction of lithium aluminium hydride in ether followed by dehydration with naphthalene-2-sulphonic acid; cf. Kohler *et al.*, *J. Amer. Chem. Soc.*, 1939, **61**, 1057), *N*-bromosuccinimide (54·8 g.), benzoyl peroxide (0·2 g.), and carbon tetrachloride (200 ml.) were heated under reflux in nitrogen. An exothermic reaction set in after a few minutes and was complete after 1 hr. After cooling, succinimide was filtered off, the filtrate was washed with 5% sodium carbonate solution (100 ml.) and water, and dried (Na_2SO_4), and the solvent removed under reduced pressure. Fractionation gave 3-*bromo*cyclo*heptene* (25 g., 43%), b. p. 67°/8 mm., n_D^{22} 1·5281 (Found : C, 48·4; H, 6·5; Br, 45·7. $C_7H_{11}Br$ requires C, 48·0; H, 6·3; Br, 45·7%).

Bromo*cyclo*heptene was only partly hydrolysed by concentrated, boiling aqueous sodium carbonate, and oxidation of the product with sodium dichromate and sulphuric acid gave only a trace of *cyclo*heptenone.

cyclo*Hex-2-enone*.—*cyclo*Hexanone (98 g.) was brominated by the procedure used for *cyclo*heptanone, giving 2-bromo*cyclo*hexanone (51 g., 36%), b. p. 116°/15 mm. A rapidly stirred mixture of the bromo-ketone (8 g.) and collidine (8 g.) was heated to 175° for 3 min. Working up as in the case of *cyclo*hept-2-enone afforded *cyclo*hex-2-enone (1·8 g., 42%), b. p. 61—62°/10 mm., n_D^{22} 1·4897 (2 : 4-dinitrophenylhydrazone, m. p. 165°) (cf. Rigby, *J.*, 1949, 1587; Born, Pappo, and Szmuszkovicz, *J.*, 1953, 1779; Treibs, Franke, Leichsenring, and Rüder, *Ber.*, 1953, **86**, 616). When the dehydrobromination was carried out on a larger scale, however, extensive aromatisation took place and the product consisted of a mixture of *cyclo*hexenone and phenol.

3 : 3-*Dichloro*cyclo*heptene and Chloro*cyclo*hepta*-1 : 3-*diene*.—*cyclo*Hept-2-enone (60 g.) was added dropwise, with mechanical stirring, to phosphorus pentachloride (130 g.). Hydrogen chloride was vigorously evolved and the mixture was cooled in ice-water. After all the ketone had been added, stirring was continued for 2 hr. at 20° and for a further 2 hr. at 35—40°. The mixture was then added to ice-water (2 l.), and the products were extracted with ether. Distillation gave a range of fractions (total 50 g.), b. p. 56—104°/10 mm., n_D^{19} 1·513—1·518, consisting of chloro*cyclo*hepta-1 : 3-diene and mainly 3 : 3-dichloro*cyclo*heptene. They were added to a solution of potassium hydroxide (20 g.) in ethanol (100 ml.) at 35° and the mixture was then kept at 0° for 4 hr. The precipitate of potassium chloride (12 g.) was filtered off and washed with ether, and the filtrate was diluted with water (500 ml.) and extracted with ether. The combined ethereal solutions were dried (Na_2SO_4) and fractionated through a 6″ Fenske column, giving 1(or 2)-*chloro*cyclo*hepta*-1 : 3-*diene* (XIII or XIV) (18 g.), b. p. 61°/10 mm., n_D^{21} 1·5133, $\lambda_{max.}$ 2510 and 2570 Å, ε 4900 in C_6H_{14} (Found : C, 65·2; H, 7·4; Cl, 26·8. C_7H_9Cl requires C, 65·4; H, 7·0; Cl, 27·6%), and 3 : 3-*dichloro*cyclo*heptene* (11 g.), b. p. 102°/10 mm., n_D^{22} 1·5136 (Found : Cl, 42·4. $C_7H_{10}Cl_2$ requires Cl, 43·0%). Re-treatment of the dichloride with ethanolic potassium hydroxide gave a further 4 g. of 1-chloro*cyclo*hepta-1 : 3-diene, making a total yield of 22 g. (32%).

*Attempted Metallation of Chloro*cyclo*hepta*-1 : 3-*diene*.—The chloride (8 g.) was added to a stirred suspension of lithium (1·5 g.) in ether (170 ml.). After 2 hr., the solution became green and was then refluxed for 15 hr. Only 20—50% of the theoretical amount of lithium reacted in several experiments, and on carboxylation with solid carbon dioxide only traces of gummy, acidic products were obtained, the majority of the chloride being recovered unchanged.

2-*Chloro*-4-*methylpenta*-1 : 3-*diene* (XVI).—Mesityl oxide (98 g.) was added to a stirred solution of phosphorus pentachloride (250 g.) in carbon disulphide (150 ml.) at 0° (cf. Baeyer, *Annalen*, 1866, **140**, 298). The solution was then kept at 55—58° for 40 min. and poured on ice (100 g.). The carbon disulphide layer was separated, washed with sodium carbonate and water, dried ($CaCl_2$), and evaporated at ordinary pressure. The product was fractionated through an 8″ Dufton column, giving (i) 2-chloro-4-methylpenta-1 : 3-diene (27 g.), b. p. 34—36°/12 mm., n_D^{20} 1·4638, $\lambda_{max.}$ 2330 Å, ε 8100 in C_6H_{14} (Found : Cl, 29·8. Calc. for C_6H_9Cl : Cl, 30·4%), and (ii) 4 : 4-dichloro-2-methylpent-2-ene (31 g.), b. p. 60°/1 mm., n_D^{21} 1·4778.

Treatment of the dichloride with potassium hydroxide (10 g.) in ethanol (50 ml.) as above gave a further 12 g. of 2-chloro-4-methylpenta-1 : 3-diene, making a total yield of 39 g. (33%).

Metallation and Carboxylation of 2-*Chloro*-4-*methylpenta*-1 : 3-*diene*.—The chloro-diene (11 g.) in ether (10 ml.) was added dropwise to a vigorously stirred suspension of finely divided lithium (1·4 g.) in ether (170 ml.). After a few minutes, the solution became green and the lithium surface assumed a bright, metallic appearance. The mixture was gently refluxed for 14 hr. and then filtered through glass-wool into a flask containing excess of solid carbon dioxide (600 g.). About half of the theoretical amount of lithium had reacted. When the solution had attained room temperature, 0·1N-hydrochloric acid (100 ml.) was added, and the ethereal layer was separated and extracted with saturated aqueous sodium carbonate. The alkaline extract was acidified with hydrochloric acid and extracted with ether. Removal of the ether under reduced pressure gave a semi-solid product (1·5 g.) which could not be sublimed at 10^{-5} mm., but was purified by low-temperature crystallisation (−60°) from aqueous methanol. This afforded (?) 1 : 6 : 6-*trimethyl*-4-*oxo*-2-iso*propyl*cyclo*hex*-2-*enecarboxlic acid* (XIX) (0·35 g., 1%), m. p. 187° (Found : C, 69·5; H, 9·2%; *M*, in camphor, 206; equiv. wt., by titration with sodium hydroxide, 246. $C_{13}H_{20}O_3$ requires C, 69·6; H, 9·0%; *M*, 224). Ultra-violet light absorption : $\lambda_{max.}$ 2430 Å, ε 10,300 in EtOH. Infra-red light absorption (Nujol mull) : $\nu_{max.}$ 1654 (vs; conjugated C=O stretching) and 1580 cm.$^{-1}$ (C=C stretching).

The yield of acid was consistently 1—1·5% in several runs. Only unchanged chloro-diene could be recovered from the neutral products and from attempted reactions of the lithium derivative with formaldehyde and benzophenone.

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