Preparation and Properties of a Series of Alkyl-4,4-dimethylcyclohexa-2,5-dienones, and Related Cyclohexenones and Cyclohexanones

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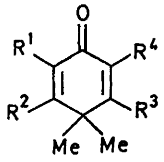
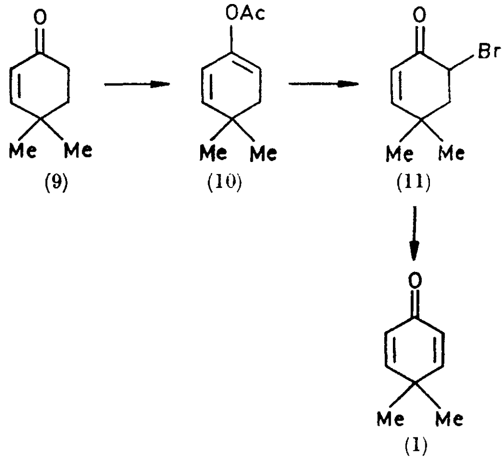
The preparations and spectroscopic properties are described of 4,4-dimethyl-, 3,4,4-trimethyl-, 3-ethyl-4,4-dimethyl-, 3,4,4,5-tetramethyl-, 3,5-diethyl-4,4-dimethyl-, 2,4,4-trimethyl-, and 2,4,4,5-tetramethylcyclohexa-2,5-dienones, and related cyclohexenones and cyclohexanones. The stereochemistry of the related series of 2,6-dibromocyclohexanones is discussed, and various stereochemical criteria are compared. Spectroscopic data for 3,4,4-trimethylcyclohex-2-enone are given; n.m.r. solvent shift and other data were used to confirm that the major product in a recently reported preparation of this compound is in fact 3,6,6-trimethylcyclohex-2-enone.

In connection with studies of the dienone–phenol rearrangement[1] we needed pure samples of the cyclohexa-2,5-dienones (1)—(7). We report the preparations and properties of these dienones, of a bromo-dienone (8), and of related intermediate compounds. The stereochemistry of some 2,6-dibromocyclohexanones in the series is discussed.



	R^1	R^2	R^3	R^4
(1)	H	H	H	H
(2)	H	Me	H	H
(3)	H	Et	H	H
(4)	H	Me	Me	H
(5)	H	Et	Et	H
(6)	Me	H	H	H
(7)	Me	H	Me	H
(8)	Br	H	Et	H

The dienone (1) has been made previously by dehydrogenation of 4,4-dimethylcyclohexenone with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) in benzene,[2] dioxan,[3] or carbon tetrachloride,[4] or with selenium dioxide in t-butyl alcohol catalysed by acetic acid.[5,6] The DDQ route, with dioxan as solvent, gave clean but incomplete reaction (*ca.* 90% conversion) and the dienone could not be completely freed of traces of unchanged cyclohexenone. The use of selenium dioxide gave impure dienone which was not adequately freed of selenium-containing impurities by the conventional ammonium sulphide[6,7] or Raney nickel[8] treatments. Bordwell and Wellman[9] made the dienone by dehydrobromination with calcium carbonate of *cis*-2,6-dibromo-4,4-dimethylcyclohexanone, formed by bromination of 4,4-dimethylcyclohexanone in acetic acid.[10] This route, with slight modification, gave good yields of dienone of high purity, but traces of a bromine-containing impurity could not be removed by preparative g.l.c. A further route, based on a method developed by Plieninger and his co-workers[11] (Scheme), was more satisfactory.† This gave crude dienone *ca.* 95% pure, contaminated mainly with solvent dimethylformamide. Preparative g.l.c. gave pure material. Attempts to prepare the bromide (11) from compound (9) by treatment with copper(II) bromide in ethyl acetate–chloroform[12] which, like copper(II) bromide in methanol[13] is



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† A similar route has been used to prepare the 4,4-diphenyldienone.[3]

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often able selectively to brominate ketones at the α-position, gave impure samples from which only a little pure bromo-ketone (11) was isolated. The use of pyrrolidone hydrobromideperbromide,[14] which might have achieved selective bromination,[15] also gave unsatisfactory results.

For the preparation of 3,4,4-trimethylcyclohexadienone (2) it was not practicable to use 3,4,4-trimethylcyclohex-2-enone as starting material (see later). The 3-methyl group was introduced into 4,4-dimethylcyclohexenone (9), to give 3,4,4-trimethylcyclohexanone, or into the dienone (1) to give 4,4,5-trimethylcyclohex-2-enone, by use of lithium dimethylcuprate, which effects clean β-methylation of αβ-unsaturated ketones.[16-18] The cyclohexanone, with bromine in acetic acid, gave the diequatorial 2,6-dibromide, which was dehydrobrominated with calcium carbonate in dimethylformamide to the dienone (2). This has been made before, in small yield, in a similar way but has been only briefly described.[19] The 4,4,5-trimethylcyclohexenone was dehydrogenated with DDQ in dioxan or (more satisfactorily) in benzene to give a high yield of the dienone (2), which could be freed of traces of unchanged enone by preparative g.l.c. or alumina chromatography. Attempts to dehydrogenate 3,4,4-trimethylcyclohexanone directly to the dienone (2) with DDQ in dioxan were not completely successful. Mixtures of *ca.* 70% dienone, unchanged cyclohexanone, and 4,4,5-trimethyl- and 3,4,4-trimethyl-cyclohex-2-enones were obtained: further conversion of the enones into the dienone was slow, and resulted in lower yields (<30%).

3-Ethyl-4,4-dimethylcyclohexa-2,5-dienone was also prepared from 4,4-dimethylcyclohex-2-enone. This was ethylated with lithium diethylcuprate [20] to give 3-ethyl-4,4-dimethylcyclohexanone, which was brominated to give a mixture of two crystalline 2,6-dibromides (see later). Dehydrobromination of a crude bromination mixture, which probably contained some tribromoketone also, gave the desired dienone (3) and appreciable quantities of 6-bromo-3-ethyl-4,4-dimethylcyclohexa-2,5-dienone (8), which were separated by chromatography.

In the synthesis of 3,4,4,5-tetramethylcyclohexa-2,5-dienone (4), the dienone (1) was methylated to give first 4,4,5-trimethylcyclohex-2-enone, then 3,4,4,5-tetramethylcyclohexanone, with lithium dimethylcuprate. Bromination then give the 2,6-diequatorial dibromide, and dehydrobromination the dienone (4) as a crystalline solid. Attempts at dehydrogenation of the cyclohexanone with DDQ in benzene gave poor results, with either incomplete conversion (dienone, cyclohexenone, and unchanged ketone obtained) or destruction of all volatile products after prolonged reaction. The bromination was also achieved with pyrrolidone hydrobromide perbromide in tetrahydrofuran. Use of 1 equiv. of this reagent gave 2-bromo-3,4,4,5-tetramethylcyclohexanone, which was dehydrobrominated to 3,4,4,5-tetramethylcyclohex-2-enone. The same tetramethylcyclohexenone was made by addition of lithium dimethylcuprate to 3,4,4-trimethylcyclohexa-2,5-dienone (2). This reaction showed that the methyl addition occurred specifically at the unsubstituted (5,6) olefinic group; analogous results have been reported in alkylations of similarly substituted dienones.[17,18]

The synthesis of 3,5-diethyl-4,4-dimethylcyclohexadienone (5) was similar, *via* 5-ethyl-4,4-dimethylcyclohex-2-enone, 3,5-diethyl-4,4-dimethylcyclohexanone, and the 2,6-dibromo-derivative of the latter. However, the conjugate addition of lithium diethylcuprate was less clean than the analogous methylation reaction, and gave alcoholic by-products. In the subsequent addition ethylmagnesium bromide in the presence of copper(I) iodide was used.*

4,4,6-Trimethylcyclohex-2-enone was made in poor yield from the piperidine enamine of isobutyraldehyde and methyl isopropenyl ketone, or, more easily, by direct condensation of the aldehyde and ketone in alkali.[22] Dehydrogenation with DDQ in benzene gave 2,4,4-trimethylcyclohexadienone (6), previously made by the bromination route.[23] The trimethylcyclohexenone was also converted into its enol acetate, 2-acetoxy-1,5,5-trimethylcyclohexa-1,3-diene, but this could not be converted satisfactorily into 6-bromo-4,4,6-trimethylcyclohex-2-enone by a route similar to that shown in the Scheme. Methylation of the trimethylcyclohexenone gave 2,4,4,5-tetramethylcyclohexanone, which was dehydrogenated directly to the dienone (7). The reaction with DDQ in benzene was very slow, but addition of a trace of toluene-*p*-sulphonic acid greatly accelerated it.† Complete conversion into dienone was

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* For analogous additions of ethyl groups in the presence of copper(II) acetate, see ref. 21; for analogous methylations see refs. 16*a*—*c*, 19, and 21, and references cited therein.

† Catalysis of DDQ dehydrogenations (presumably by increasing the rate of enolisation of the ketone) by traces of acid [18,24,25] or base [24] has been reported previously.

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not achieved, and the crude product contained some unchanged saturated ketone; longer reaction times caused loss of product and the overall yield of dienone was poor.

Spectroscopic data for the compounds studied are presented in the Experimental section and in Tables 1 and 2. All the dienone i.r., u.v., and n.m.r. peaks fall in the normal positions established previously.[26,27]

TABLE 1

N.m.r. data for cyclohexa-2,5-dienones

Compound	2-Subst.			3-Subst.			4-Me		5-Subst.			6-Subst.		
		τ[a]	Δ[b]		τ	Δ	τ	Δ		τ	Δ		τ	Δ
(1)	H	3·93[c]	−0·21	H	3·24[c]	0·54	8·73	0·50	H	3·24[c]	0·54	H	3·93[c]	−0·21
(2)	H	4·04[d,e]	−0·18	Me	8·02[d]	0·51	8·75	0·49	H	3·37[f]	0·40	H	3·97[e,]	−0·20
(3)	H	4·01[g]	−0·15	CH_2	7·66[h]	0·55	8·76	0·47	H	3·38[i]	0·43	H	3·96[g,i]	−0·20
				Me	8·82[h]	0·38								
(4)	H	4·17[d]	−0·33	Me	7·98[d]	0·54	8·73	0·51	Me	7·98[d]	0·54	H	4·17[d]	−0·33
(5)	H	4·05		CH_2	7·70[j]		8·75		CH_2	7·70[j]		H	4·05	
				Me	8·81[j]				Me	8·81[j]				
(6)	Me	8·19[l]	−0·08	H	3·51[l,m]	0·38	8·77	0·45	H	3·31[m,n]	0·49	H	3·94[n]	−0·14
(7)	Me	8·19[d]	−0·02	H	3·52[d]	0·32	8·80	0·44	Me	8·03[d]	0·52	H	4·02[d]	−0·12
(8)	Br			H	2·89	0·39	8·70	0·69	CH_2[j]	7·69	0·68	H	3·88	0·00
									Me[j]	8·79	0·55			

[a] Solutions in CCl_4. [b] $\Delta = \tau(C_6H_6) - \tau(CCl_4)$. [c] $J_{2,3}$ 10·3—10·5.Hz. [d] $J_{H,Me}$ 1·2–1·4 Hz. [e] $J_{2,6}$ 1·8—1·9 Hz. [f] $J_{5,6}$ 9·9 Hz. [g] $J_{2,6}$ *ca.* 1·6 Hz. [h] J 7 Hz. [i] $J_{5,6}$ 10·0 Hz. [j] J 7·4 Hz. [l] $J_{H,Me}$ 1·4 Hz. [m] $J_{3,5}$ 2·9—3·0 Hz. [n] $J_{5,6}$ 9·7 Hz.

TABLE 2

N.m.r. data for cyclohex-2-enones

Substituents	2-Subst.			3-Subst.			4-Subst.			5-Subst.			6-Subst.		
		τ[a]	Δ[b]		τ	Δ		τ	Δ		τ	Δ		τ	Δ
4,4-Dimethyl-	H	4·31[c]	−0·12	H	3·44[c]	0·48	Me	8·84	0·42	H	8·15[d]	0·46	H	7·65[d]	0·14
2-Bromo-4,4-dimethyl-	Br			H	2·93		Me	8·76		H	8·10[d]		H	7·39[d]	
6-Bromo-4,4-dimethyl-	H	4·06[c]		H	3·29[c,e]		Me	8·75		H	*ca.* 7·6		H	5·16	
							Me	8·77							
4,4,5-Trimethyl-	H	4·27[c]	−0·14	H	3·49[c]	0·37	Me	8·86	0·41	H	*g*		H	*g*	
							Me	9·00	0·41	Me[h]	9·03	0·39			
3,4,4-Trimethyl-	H	4·33[i]	−0·12	Me	8·10[i]	0·48	Me	8·81	0·47	H	8·16[d]	0·43	H	7·77[d]	0·07
3,6,6-Trimethyl-	H	4·34[i]	−0·12	Me	8·09[i]	0·46	H[d]	7·74	0·55	H[d]	8·22	0·37	Me	8·97	0·00
3,6,6-Trimethyl-[j]	H	4·33		Me	8·08		H	7·71		H	8·23		Me	8·99	
5-Ethyl-4,4-dimethyl-	H	4·25[c]		H	3·47[c]		Me	8·83		CH_2	*k*		H	*k*	
							Me	8·99		Me	9·04[k]				
3,4,4,5-Tetramethyl-	H	4·34[i]	−0·20	Me[i]	8·08	0·52	Me	8·83	0·46	H	*l*		H	*l*	
							Me	8·90	0·45	Me	9·00[l]	0·39			
4.4,6-Trimethyl-	H	4·29[m]	−0·09	H	3·47[m,n]	0·38	Me	8·79	0·38	H	8·28[o]		H[o]	7·57	
							Me	8·86	0·38				Me	8·93[p]	0·01

[a] Solutions in CCl_4. [b] $\Delta = \tau(C_6H_6) - \tau(CCl_4)$. [c] $J_{2,3}$ 10 Hz. [d] Triplets, J 6·7—7·0 Hz. [e] $J_{3,5}$ 1·2 Hz. [f] X part of ABX pattern, $J_{AX} + J_{BX}$ 18·5 Hz. [g] Complex, τ 7·64—8·09 in CCl_4, 7·64—8·57 in C_6D_6. [h] Doublet, $J \ngtr 6$ Hz. [i] J(allylic) *ca.* 1·2 Hz. [j] Lit. data from L. Eberson, *Tetrahedron Letters*, 1966, 223; the spectrum in J. M. Conia and F. Rouessac, *Bull. Soc. chim. France*, 1963, 1925, is very similar. [k] Complex, τ 7·36—8·64 includes 5- and 6- protons; Me, doublet J 7 Hz. [l] Complex, τ 7·5—8·1 in CCl_4 includes 5- and 6-H: Me, doublet I 6·2 Hz. [m] $J_{2,3}$ 9·7—9·8 Hz. [n] Doublet, J 1·7 Hz. [o] Complex. [p] Doublet, J 6·8 Hz.

Stereochemistry of 2,6-*Dibromocyclohexanones*.—Previous n.m.r. studies on compounds which were shown, or strongly believed, to have their cyclohexanone ring in an essentially normal chair conformation have given the following results. Axial 2-protons in 2-bromocyclohexanones have $J_{AX} + J_{BX}$ 17·8—19·9 Hz,[*,29–33] with $J_{ax,ax}$ 12·2—13·4 Hz, $J_{ax,eq}$ 5·7—7·1 Hz,[31–33] and τ 5·17—5·42.[30,31,33–36] In two examples of *cis*-2,6-dibromocyclohexanones the 2- and 6-axial protons show similar coupling constants,[32,33] but the τ value is less (5·05);[33] in *trans*-2,6-dibromo-compounds the axial protons again have similar couplings,[29,30] but τ values are 4·21—4·79 owing to deshielding by the axial bromine atom.[30,34] For equatorial 2-protons, $J_{AX} + J_{BX}$ is

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[*] When the compound has a methylene group at position 3 the 2-proton is the X part of an ABX spin-system, for which $J_{AX} + J_{BX}$ is accurately known from the line-spacings of the X part of the n.m.r. spectrum.[28]

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5·6—6·0 Hz,[29,30,32,33] with τ 5·33—6·25 in 2-bromo- or *cis*- or *trans*-2,6-dibromo-ketones.[30,31,33-36] It has been stated recently that a τ value of 5·82—6·04 may be taken as a fair indication of an equatorial bromomethine proton, and that τ 5·32 may be taken as an upper limit for an axial 2-proton in a 2-bromocyclohexanone.[34]

The n.m.r. spectrum of 2,6-dibromo-4,4-dimethylcyclohexanone shows the 2- and 6-proton signals at τ 5·14, with $J_{AX} + J_{BX}$ 18·9 Hz; treating the system as AMX gives individual coupling constants 12·5 and 6·3 Hz, which may be, respectively, somewhat smaller and larger than the true values.*[,32] These data confirm the conclusion [23b] from the i.r. carbonyl peak (40 cm^{-1} to higher wavenumber than the parent dimethylcyclohexanone) that this compound has H-2 and H-6 axial. For 2,6-dibromo-3,4,4-trimethylcyclohexanone, the H-2 signal is a doublet (J 12·4 Hz) of doublets (J 1·2 Hz) † at τ 5·49. The larger coupling is consistent with H-2 and H-3 both axial, but the τ value is rather high—this will be discussed later. The 6-proton, τ 5·19, has $J_{AX} + J_{BX}$ 19·8 Hz; from treatment as AMX the individual values are 13·8 and 6·1 Hz. These signals are also doublets, J 1·2 Hz.† The n.m.r. and i.r. data ($\nu_{max.}$ 1760 cm^{-1}; *cf.* 1723 cm^{-1} for the parent ketone) confirm that H-6 is also axial.

Two isomers of 2,6-dibromo-3-ethyl-4,4-dimethylcyclohexanone were isolated. One of these ($\nu_{max.}$ 1757 cm^{-1}; *cf.* 1720 cm^{-1} for the parent ketone) should [37,38] have both the 2- and 6-protons axial. The 6-proton, with $J_{AX} + J_{BX}$ 20 Hz (individual values 13·3 and 6·7 Hz) must be axial, but resonates at high field (τ 5·36). The 2-proton coupling, J 11·9 Hz, shows it and H-3 to be essentially axial, but the τ value (5·52) is much closer to that expected for an equatorial proton. The other isomer has $\nu_{max.}$ 1742 cm^{-1}, consistent [37,38] with H-2 and H-6 *trans*. The 2-proton signal (doublet, J *ca.* 3·4 Hz) at τ 5·50 is typical of an equatorial proton, where H-3 may be axial or equatorial; H-6, with $J_{AX} + J_{BX}$ 20·1 Hz (individual values *ca.* 6·1 and 14·1 Hz) and τ 4·61, is typically axial. 2,6-Dibromo-3,4,4,5-tetramethylcyclohexanone ($\nu_{max.}$ 1763 cm^{-1}; *cf.* 1720 cm^{-1} for the parent ketone) has the 2-proton n.m.r. signal as a doublet, J 11·8 Hz, indicating that H-2 and H-3 are both axial; the τ value, 5·57, is again abnormally high. The 6-proton doublet, J 4·5 Hz at τ 4·81 (rather low), indicates that H-6 is axial and H-5 equatorial.

The inconsistent chemical shifts of some of the 2- or 6-protons in the foregoing spectra may be explained in terms of diamagnetic shielding of the cyclohexanone ring by the alkyl substituents. The effects of alkyl groups on the chemical shifts of axial or equatorial carbinol ring protons in substituted cyclohexanols have been correlated with their nature, position, and stereochemistry. Of particular significance is the finding that a methyl or ethyl group *cis* and adjacent to such a proton exerts a shielding effect of 0·35—0·47 p.p.m.[39] If the established additive quantities are used to estimate the bromomethine proton shifts in the dibromo-ketones, taking 2,6-dibromo-4,4-dimethylcyclohexanone as an arbitrary standard, the following values are obtained. For the axial 2-protons in the 3,4,4-trimethyl, 3-ethyl-4,4-dimethyl (isomer with $\nu_{max.}$ 1757 cm^{-1}), and 3,4,4,5-tetramethyl compounds τ values (calculated) are 5·61, 5·49, 5·61; for the axial 6-protons the values are 5·19, 5·19, and 5·00, respectively. These estimates agree quite well with the experimental values (mean deviation $<$0·1 p.p.m.).

Comments on 3,4,4-*Trimethylcyclohex*-2-*enone*.—The obvious precursor of 3,4,4-trimethylcyclohexa-2,5-dienone is 3,4,4-trimethylcyclohex-2-enone, which one would expect to be formed by alkaline condensation of methyl isopropyl ketone (3-methylbutan-2-one) and methyl vinyl ketone (but-3-en-2-one). Conia and Rouessac have reported the condensation with sodium pentyl oxide in benzene to give *ca.* 30% of a mixture containing *ca.* 5% of the desired cyclohexenone and 95% of 3,6,6-trimethylcyclohex-2-enone.[40] More recently, Dauben and his co-workers [22] used the conventional conditions [41] and claimed to obtain 3,4,4-trimethylcyclohexenone as the product. When we repeated this preparation we obtained a product with spectroscopic data similar to those reported,[22] but with chemical properties inconsistent with the structure assigned. Preparative g.l.c. resulted in separation into three compounds; a saturated ketone (not studied), 3,6,6-trimethylcyclohexenone (major product), and 3,4,4-trimethylcyclohexenone. There is insufficient difference between the b.p.s and i.r. and u.v. spectra of the two isomers to allow one of them to be identified in the absence of the other, and the n.m.r. spectra of solutions in $CDCl_3$ or CCl_4 are very similar. Although a brief correction has appeared,[42] the original data [22] do not distinguish between the two isomers. It is clear, however, that this route does not offer an easy synthesis of the 3,4,4-trimethyl isomer. N.m.r. solvent shifts allow the two isomers to be readily distinguished. The n.m.r. spectra of saturated and unsaturated ketones in benzene solution are different from those of solutions in $CDCl_3$ or CCl_4. Protons lying on the 'oxygen side' of an imaginary plane surface through the carbonyl carbon atom, and perpendicular to the carbon–oxygen bond, resonate at lower field in benzene than in $CDCl_3$ or CCl_4, whereas protons lying on the opposite

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* See footnote on page 531.

† Small long-range couplings between *equatorial* protons at C-2 and C-6 have been reported; [33] these are between two *axial* protons.

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[39] E. L. Eliel, M. H. Gianni, T. H. Williams, and J. B. Stothers, *Tetrahedron Letters*, 1962, 741.

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[41] E. L. Eliel and C. A. Lukach, *J. Amer. Chem. Soc.*, 1957, **79**, 5986.

[42] Corrigenda in *J. Org. Chem.*, 1970, **35**, 4004.

side resonate at higher field in benzene.[43-45] The magnitude of the solvent shift, $\Delta = \tau(C_6H_6) - \tau(CCl_4)$, increases as the protons become more remote from the plane surface. Examples of this effect in cyclohexenones [43,44] and cyclohexanones [45] have been reported: new data from our own compounds are in Table 2. The Δ value for the *gem*-dimethyl group in 3,6,6-trimethylcyclohex-2-enone is zero, confirming its location at C-6. The *gem*-dimethyl group in 3,4,4-trimethylcyclohex-2-enone has Δ 0·47, confirming its location at C-4. An identical, authentic sample of this isomer was made by monobromination of 3,4,4-trimethylcyclohexanone and dehydrobromination as in ref. 19; this gave the desired product, which was separated from 4,4,5-trimethylcyclohex-2-enone and traces of dienone and unchanged cyclohexanone. The 3,6,6-trimethylcyclohexenone gave a dinitrophenylhydrazone whose m.p. agrees with a reported value; hydrogenation gave 2,2,5-trimethylcyclohexanone which was easily distinguished from our two samples of 3,4,4-trimethylcyclohexanone.

EXPERIMENTAL

G.l.c. analyses used a Pye 104 instrument with flame ionisation detector and glass columns (7 ft × ¼ in) of silicone gum (E30), neopentyl glycol succinate (NGS), Ucon fluid LB 550-X (Ucon) or cyanoethylsilicone fluid (XF1150) on silanised Supasorb (B.D.H.). A Pye 105 instrument with glass columns (10, 20, or 30 ft × ⅜ in) was used for preparative g.l.c. I.r. spectra were obtained on a Unicam SP 200G grating instrument, u.v. spectra on a Cary model 14 or a Unicam SP 800, and n.m.r. spectra on a Perkin-Elmer 100 or 60 MHz instrument with tetramethylsilane as internal standard. M.p.s were measured on a microscope hot-stage. ' Evaporation ' denotes removal of solvent with a vacuum rotary evaporator at room temperature. All 2,4-dinitrophenylhydrazones were made by the method of Parrick and Rasburn,[46] with dimethylformamide as solvent. ' Petroleum ' refers to the fraction of b.p. 40—60°.

4,4-*Dimethylcyclohex*-2-*enone* (9).—The method of Eliel and Lukach,[41] modified by using 90% methyl vinyl ketone–water (Koch-Light) and correspondingly less water, could be scaled up to twice molar proportions to give material, b.p. 72—73° at 13 mmHg (33—40%), of >93% purity (lit.,[47] b.p. 72·5—73·5° at 20 mmHg; lit.,[48] 72—73° at 15 mmHg; lit.,[49] 54—56° at 4 mmHg). The n.m.r. data are in Table 2. The 2,4-dinitrophenylhydrazone had m.p. 140—141° (from ethyl acetate) (lit.,[47] 142°; lit.,[48] 143—144°).

4,4-*Dimethylcyclohexanone*.—The cyclohexenone (9) (12·5 g) in ethyl acetate (120 ml) was hydrogenated over 5% Pd–$BaSO_4$; filtration and evaporation gave the dimethylcyclohexanone (11·3 g, 90%), purified by crystallisation from petroleum or sublimation at 15 mmHg, m.p. 41—42° (lit.,[48] 40—42°; lit.,[49] 39—40°), $\nu_{max.}$ (CCl_4) 1725 and 1715 cm^{-1}, τ 8·89 (4-Me), 8·34 (t, *J* 6·9 Hz, 3- and 5-H_2), and 7·74 (t, *J* 6·9 Hz, 2- and 6-H_2).

cis-2,6-*Dibromo*-4,4-*dimethylcyclohexanone*.—*Method A*. Treatment of 4,4-dimethylcyclohexanone (6·92 g) with bromine in glacial acetic acid at 3 °,[10,49] and recrystallisation from petroleum gave the *cis*-dibromo-ketone (7·58 g, 49%), m.p. 96—97° (lit.,[10] 97°; lit.,[9,49] 95—96°).

Method B. 4,4-Dimethylcyclohexenone (102·9 g) in acetic acid (300 ml) was hydrogenated at 1 atm over Adams catalyst (70 mg) for 6·5 h; g.l.c. on NGS (120°) showed reduction to be complete. A portion of the solution (155 ml; 54 g of dimethylcyclohexanone) was stirred well at 10°, and bromine (139 g) in acetic acid (50 ml) was added over 4 h. After 0·25 h further at 10° the mixture was poured into cold water (600 ml) and extracted with ether (3 × 1 l). The combined extracts were washed with water, saturated sodium hydrogencarbonate solution, then water, dried ($MgSO_4$), and evaporated. Recrystallisation from petroleum gave the dibromo-ketone (72·3 g, 59%), m.p. 93—94°, $\nu_{max.}$ (CCl_4) 1762 cm^{-1}, τ 8·89 (4-Me), 8·68 (4-Me), and 7·5—8·0 (m, 3- and 5-H_2); the 2- and 6-proton signals are discussed earlier.

4,4-*Dimethylcyclohexa*-2,5-*dienone* (1).—*Method A*. The foregoing dibromo-ketone (71·2 g) in dry dimethylformamide (400 ml) was stirred at reflux for 5 h with finely powdered calcium carbonate (105 g). After cooling, the supernatant liquid was separated as far as possible by decantation and the residue filtered. The solid salts were washed well with water; the washings were combined with the filtrate and supernatant and diluted with water to 1·3 l. Continuous liquid extraction with boiling petroleum (250 ml) for 6 hr, and drying and evaporation of the extract gave the crude dienone (27·4 g). Distillation gave dienone (14·8 g, 50%) of 90—98% purity (b.p. 65—79° at 12 mmHg), of which the fractions of b.p. 77—79° at 12 mmHg (13·5 g, 44%) were >98% pure by g.l.c. (NGS at 120°) (lit.,[2] b.p. 72° at 12 mmHg; lit.,[3] 41° at 0·15 mmHg; lit.,[9] 90° at 15 mmHg). Dehydrobromination with lithium carbonate gave similar results; preparative g.l.c. separated the major impurity, 2-bromo-4,4-dimethylcyclohex-2-enone, $\nu_{max.}$ (cyclohexane) 249 nm (lit.,[9] 252 nm in MeOH) with n.m.r. data (Table 2) close to those in ref. 9.

2-*Acetoxy*-5,5-*dimethylcyclohexa*-1,3-*diene* (10).—4,4-Dimethylcyclohex-2-enone (25·1 g, 92% pure), isopropenyl acetate (104 g), and toluene-*p*-sulphonic acid monohydrate (0·7 g) were heated under a 6 in lagged Vigreux column (bath temp. 120°). Acetone and isopropenyl acetate were distilled off at 56—80° during 5—6 h, then isopropenyl acetate at 97—101°. The brown residue was distilled to give the *acetoxy-diene*, b.p. 93—94° at 17 mmHg, 80—82° at 10 mmHg, 77—79° at 7 mmHg, as an oil (>97% pure by g.l.c. on NGS at 120:), $\nu_{max.}$ (film) 3050, 3025, 2950, 1760, 1672, 1665, 1220 cm^{-1}, $\lambda_{max.}$ (EtOH) 258 nm (log ε 3·60), τ 8·92 (5-Me), 7·94 (Ac), 7·79 (d, *J* 4·6 Hz, 6-H_2), 4·75 (t, *J* 4·6 Hz, of t, *J* 1·5 Hz, H-1 coupled to

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[48] J. M. Conia and A. LeCraz, *Bull. Soc. chim. France*, 1960, 1934.

[49] F. G. Bordwell and K. M. Wellman, *J. Org. Chem.*, 1963, **28**, 1347.

H-3 and H-4), and 4·44 (d, *J* 1·5 Hz, H-3 and H-4 coupled to H-1).

6-*Bromo*-4,4-*dimethylcyclohex*-2-*enone* (11).—To the acetoxy-diene (10) (10·93 g) in dry carbon tetrachloride (100 ml) *N*-bromosuccinimide (12·24 g) was added, and the mixture was heated under reflux (nitrogen atmosphere) for 3 h. After cooling, the red oily solid was filtered off and the filtrate evaporated under vacuum to give an orange gum which was extracted with pentane (4 × 100 ml). The combined extracts were washed with saturated sodium hydrogen carbonate solution (twice) and water (thrice), dried ($CaSO_4$), and evaporated under vacuum to an oil (13·1 g) which crystallised on cooling. Recrystallisation from pentane gave the bromocyclohexenone (5·07 g, 38%), needles, m.p. 48—48·5° (lit.,[9] 47·5°), $\nu_{max.}$ (CCl_4) 1705 and 1622 cm^{-1}, $\lambda_{max.}$ (95% EtOH) 228 nm (log ϵ 4·01) [lit.,[9] 225 nm (log ϵ 4·24)]. The n.m.r. (Table 2) and i.r. spectra show the bromine atom to be equatorial.

4,4-*Dimethylcyclohexa*-2,5-*dienone*.—*Method B*. To the bromo-ketone (11) (6·08 g) in dry dimethylformamide (25 ml) was added a slurry of lithium bromide (7·87 g) and lithium carbonate (6·97 g) in dry dimethylformamide (20 ml), and the mixture was heated at reflux with stirring for 25 min. The cooled mixture was filtered and the filtrate diluted with water (150 ml) and continuously extracted with n-pentane (100 ml) for 2 h. The dried ($MgSO_4$) pentane extract was evaporated under vacuum to give the dienone (3·01 g, 83%), 95% pure by g.l.c. (XF 1150 at 140°), contaminated only with dimethylformamide. Preparative g.l.c. (7 ft × $\frac{3}{8}$ in column, with 25% XF 1150 at 176°), followed by drying over Linde 4A molecular sieve and short-path vacuum distillation gave material $\gg$99% pure by g.l.c., $\nu_{max.}$ (film) 1730w, 1720w, 1690s, 1664vs, 1649w, 1630s, 1614w, and 1597m cm^{-1}, $\nu_{max.}$ (CCl_4) 1730w, 1720w, 1683s, 1663vs, 1632s, and 1620w cm^{-1} (agreeing within 5 cm^{-1} with the spectrum quoted in ref. 50), $\lambda_{max.}$ (hexane) 224 nm (log ϵ 4·187), $\lambda_{max.}$ (iso-octane) 225 nm (log ϵ 4·182) [lit.,[30] 224·5 nm (log ϵ 4·17)]. The n.m.r. data are in Table 1. Further spectroscopic data for the dienone and its cation are in ref. 1 (Found: C, 78·4; H, 8·2%; *M*, 122. Calc. for $C_8H_{10}O$: C, 78·6; H, 8·2%; *M*, 122). The 2,4-*dinitrophenylhydrazone* had m.p. 152·5—153° (from ethyl acetate) (lit.,[2] 149—151°) (Found: C, 55·6; H, 4·8; N, 18·4. $C_{14}H_{14}N_4O_4$ requires C, 55·6; H, 4·7; N, 18·5%).

3,4,4-*Trimethylcyclohexanone*.—*Method A*.—To 4,4-Dimethylcyclohex-2-enone (5·21 g) in dry ether was added with stirring, during 10 min, lithium dimethylcuprate,[16] formed from purified[51] copper(I) iodide (15·41 g) and methyl-lithium (0·16 mol of *ca.* 1·0M-solution in ether, from lithium and methyl iodide, standardised by acidometric titration), at 0° in a nitrogen atmosphere. After being stirred for 20 min further at 0° the mixture was poured slowly, with vigorous stirring, into an equal volume of saturated aqueous ammonium chloride. After filtration, and washing of the solid residue with ether, the ether layer was separated. The aqueous layer was extracted with ether, and the combined extracts were dried, concentrated, filtered through a silica gel column, and evaporated to give crude trimethylcyclohexanone (5·08 g, 88%), 98% pure (g.l.c. on NGS at 130°). Distillation at 80—81° and 12 mmHg (with foaming) gave material of purity >99% (lit.,[52] b.p. 80—81° at 13 mmHg); $\nu_{max.}$ (film) 1723 and 1712 cm^{-1}, τ 9·09 (d, *J* 6·9—7·0 Hz, 3-Me), 9·00 (4-Me), 8·96 (4-Me), 8·27 (complex, 3-H and 5-H_2), and 7·78 (complex, 2- and 6-H_2) (Found: C, 76·8; H, 11·2%; *M*, 140. Calc. for $C_9H_{16}O$: C, 77·1; H, 11·4%; *M*, 140). The 2,4-*dinitrophenylhydrazone* (87%) had m.p. 147·8—148·6° (from ethyl acetate) (Found: C, 56·7; H, 6·2; N, 17·7. $C_{15}H_{20}N_4O_4$ requires C, 56·3; H, 6·3; N, 17·5%).

2,6-*Dibromo*-3,4,4-*trimethylcyclohexanone*.—To the preceding ketone (896 mg) in glacial acetic acid (10 ml) at 15° was added bromine (1·98 g) in acetic acid (10 ml) during 15 min. After being stirred for 5 min further the mixture was poured into water (50 ml) and extracted with ether; the extracts were washed ($NaHCO_3$ solution, then water), dried ($MgSO_4$), and evaporated to a semicrystalline mass (1·71 g). Crystallisation from pentane gave the *dibromo-ketone* (629 mg, 33%) as needles, m.p. 83·5—84·5° (lit.,[53] m.p. 81·2—81·7° for material prepared similarly, but assigned the 6,6-dibromo-ketone structure), $\nu_{max.}$ (CCl_4) 1760 cm^{-1}, τ 8·91 (4-Me), 8·87 (4-Me), 8·79 (d, *J* 6·3—6·5 Hz, 3-Me), 8·2 (complex, 5-H_2), 7·71 (q, *J* 6·3—6·5 Hz, of d, *J* 12·4 Hz, 3-H); the 2- and 6-proton signals and the stereochemistry are discussed earlier (Found: C, 36·2; H, 4·4; Br, 53·6. $C_9H_{14}Br_2O$ requires C, 36·2; H, 4·7; Br, 53·7%) *m/e* 300, 298, and 296 (M^+), intensities 1 : 2 : 1 as calc. for the ^{81}Br and ^{79}Br isotopes. Further crystalline material was obtained by low-temperature crystallisation. Both the crystalline product and oily residues could be used for the next step.

3,4,4-*Trimethylcyclohexa*-2,5-*dienone* (2).—*Method A*. The foregoing crystalline dibromo-ketone (1·22 g) in dry dimethylformamide (10 ml) was stirred and heated at reflux with finely powdered calcium carbonate for 1 h. The cooled solution was decanted from inorganic salts, which were washed (on a filter) with water; the washings were combined with the solution, which was then diluted with more water (50 ml). Extraction with n-pentane (8 × 40 ml), and drying ($MgSO_4$) and evaporation of the pentane solution gave the crude dienone (370 mg, 66%; 88% pure by g.l.c. on NGS at 183°) as a pale yellow oil. Distillation at 110—112° and 22 mmHg, or alumina chromatography (elution with petroleum, then up to 7% ether–petroleum) gave material >95% pure, further purified to >98% by preparative g.l.c. (XF 1150 at 180°), identical with samples made by method C.

Method B. The oily residue from the crystallisation of the foregoing dibromo-ketone (3·27 g) in dimethylformamide was similarly treated with calcium carbonate, to give crude dienone (800 mg, 53%; *ca.* 90% pure by g.l.c.).

4,4,5-*Trimethylcyclohex*-2-*enone*.—To lithium dimethylcuprate from purified copper(I) iodide[51] (15·80 g) and methyl-lithium (140 ml of 1·1M-solution) in ether was added 4,4-dimethylcyclohexa-2,5-dienone (5·00 g) in ether. Treatment as in the preparation of 3,4,4-trimethylcyclohexanone gave the trimethylcyclohexenone (5·38 g, 94%), 95% pure by g.l.c. (NGS at 130°). Distillation (b.p. 86—87° at 14 mmHg) gave material (4·78 g, 85%) >97% pure; $\nu_{max.}$ (film) 1687, 1677, 1667sh, and 1613w cm^{-1}, $\lambda_{max.}$ (95% EtOH) 227 (log ϵ 4·026) and *ca.* 320 nm (*ca.* 1·48) [lit.,[19] $\nu_{max.}$ (film) 1680 cm^{-1}]. The n.m.r. data are in Table 2 (Found: C, 78·1; H, 10·4%; *M*, 138. Calc. for $C_9H_{14}O$: C, 78·2; H, 10·2%; *M*, 138). The mass

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[52] E. R. Buchman and H. Sargent, *J. Org. Chem.*, 1942, **7**, 140.

[53] E. R. Buchman and H. Sargent, *J. Org. Chem.*, 1942, **7**, 148.

spectrum agreed with that published in ref. 19. The 2,4-*dinitrophenylhydrazone* had m.p. 143—144° (from ethyl acetate) (Found: C, 56·3; H, 5·7; N, 17·4. $C_{15}H_{18}N_4O_4$ requires C, 56·6; H, 5·7; N, 17·6%).

3,4,4-*Trimethylcyclohexanone*.—*Method B*. The foregoing cyclohexenone, hydrogenated over Adams catalyst in ethyl acetate at 1 atm gave 81% (after distillation) of trimethylcyclohexanone, identical with that made earlier.

3,4,4-*Trimethylcyclohexa*-2,5-*dienone* (2).—*Method C*. 4,4,5-Trimethylcyclohex-2-enone (1·23 g) in dry benzene (65 ml) was stirred with DDQ (3·00 g) at reflux, under nitrogen, for 11 days. At this stage (>90% conversion) the cooled mixture was filtered, the solid residue washed with ether, and the combined solutions evaporated to dryness below 0°. The residual oil was stirred well and boiled with petroleum four times; the petroleum solution was washed with aqueous sodium sulphite until this no longer became coloured, then water, and dried ($MgSO_4$). Evaporation gave the dienone (448 mg, 37%) better than 90% pure. Filtration of an ether–petroleum (1 : 5) solution through alumina, and preparative g.l.c. (XF 1150 at 146°) gave the *dienone* as a liquid >99·7% pure (chromatography on alumina afforded material *ca.* 95% pure), $\nu_{max.}$ (film) 1746w, 1665vs, 1640m, 1625s, and 1603m cm^{-1}, $\nu_{max.}$ (CCl_4) 1742w, 1672vs,br, 1634s, and 1610sh, cm^{-1}, $\lambda_{max.}$ (hexane or iso-octane) 227 nm (log ε 4·150), $\lambda_{max.}$ (H_2O) 241 nm (log ε 4·172). The n.m.r. spectra are reported in Table 1 (Found: C, 79·1; H, 9·2%; *M*, 136. $C_9H_{12}O$ requires C, 79·4; H, 8·9%; *M*, 136). The 2,4-*dinitrophenylhydrazone*, m.p. 145·4—146·2° (from ethyl acetate), was identical (mixed m.p.) with a sample made by Method A, m.p. 146·2—147° (Found: C, 56·8; H, 5·1; N, 17·8. $C_{15}H_{16}N_4O_4$ requires C, 57·0; H, 5·1; N, 17·7%). Both samples contained both yellow and red crystals; the former were converted into the red form near the m.p.

Mixture of 3,4,4- *and* 3,6,6-*Trimethylcyclohex*-2-*enones*.—Dry, redistilled methyl vinyl ketone (70 g; b.p. 23—24° at 61 mmHg) and isopropyl methyl ketone (86 g) were condensed in the presence of aqueous methanolic potassium hydroxide, by the procedure of Eliel and Lukach,[41] and of Dauben and his co-workers.[22] The five fractions collected between 81 and 86° at 10 mmHg (total 29·3 g, 21%) contained three components; that identified as 3,6,6-trimethylcyclohexenone comprised 68—75% of each, and 3,4,4-trimethylcyclohexenone (total yield 3—4%) was concentrated more in the later fractions (7—25% of each). Preparative g.l.c. (25% XF 1150 or 25% Ucon at 150°) gave a saturated ketone (not studied further), and the two cyclohexenones. The 3,6,6-trimethyl isomer showed $\nu_{max.}$ (film) 2965s, 2925s, 2865m, 1675s,br (with fine structure), 1650sh, and 1638s, n.m.r. chemical shift and solvent shift data in Table 2, $\lambda_{max.}$ (95% EtOH) 234 and 320 nm (relative ε *ca.* 100 : 1) [lit.,[40] $\nu_{max.}$ (film) 1674 and 1645 cm^{-1}; lit.,[54] 1660 and 1632 cm^{-1}; lit.,[40] $\lambda_{max.}$ (EtOH) 235 nm (log ε 4·21); lit.,[54] 234 and 317 nm]. The 2,4-dinitrophenylhydrazone had m.p. 207·5—208° (from ethyl acetate) (lit.,[40] 203—204°; lit.,[54] 204—205°) (Found: C, 56·5; H, 5·8; N, 17·4. Calc. for $C_{15}H_{18}N_4O_4$; C, 56·6; H, 5·7; N, 17·6%). The 3,4,4-trimethyl isomer was identical (g.l.c., i.r. and n.m.r.) with the sample made by the following alternative route.

3,4,4-*Trimethylcyclohex*-2-*enone*.— 3,4,4-Trimethylcyclohexanone (1·77 g) in glacial acetic acid was treated with bromine (1 equiv.) in acetic acid at 10°. Work-up as for the earlier bromo-ketones gave a crude bromo-ketone mixture which was dehydrobrominated in the usual way with calcium carbonate in dimethylformamide. The usual work-up gave an oil which was separated by alumina chromatography into unchanged trimethylcyclohexanone (190 mg), 4,4,5-trimethylcyclohex-2-enone (220 mg), 3,4,4-trimethylcyclohex-2-enone (440 mg), and mixtures of the latter with 3,4,4-trimethylcyclohexa-2,5-dienone. The 3,4,4-trimethylcyclohexenone (95% pure), after molecular distillation, had $\nu_{max.}$ (film) 3023w, 2960s, 2920s, 2865m, 1712sh, 1673s,br, and 1616m cm^{-1}, $\lambda_{max.}$ (95% EtOH) 236 nm (log ε 4·13), n.m.r. data given in Table 2, *M* 138 (as calc.) [lit.,[19] $\nu_{max.}$ (film) 1660 cm^{-1}; dinitrophenylhydrazone lit.,[40,52] m.p. 167°; lit.,[55] 168°].

3-*Ethyl*-4,4-*dimethylcyclohexanone*.—To lithium diethylcuprate [from purified copper(I) iodide (15·37 g) in ether and ethyl-lithium (160 ml; *ca.* 1·0M; from ethyl chloride)] at 0 °C under nitrogen was added 4,4-dimethylcyclohex-2-enone (5·05 g) in ether (40 ml) during 10 min. After a further 20 min at 0°, work-up as in the preparation of 3,4,4-trimethylcyclohexanone (method A) gave the crude ketone (5·51 g) of *ca.* 80% purity. Distillation (foaming) gave a *liquid*, b.p. 88—90° at 12 mmHg, >95% pure, $\nu_{max.}$ (film) 1720s and 1710s cm^{-1} (doublet), τ 9·01 and 8·96 (4-Me) (Found: C, 77·9; H, 11·5%; *M*, 154. $C_{10}H_{18}O$ requires C, 77·9; H, 11·8%; *M*, 154). The 2,4-*dinitrophenylhydrazone* formed needles, m.p. 155—157° (Found: C, 57·2; H, 6·5; N, 16·7. $C_{16}H_{22}N_4O_4$ requires C, 57·5; H, 6·6; N, 16·8%).

2,6-*Dibromo*-3-*ethyl*-4,4-*dimethylcyclohexanone*.— Treatment of the foregoing ketone (910 mg) in acetic acid with bromine, as in the preparation of the dibromotrimethylcyclohexanone, gave a semicrystalline mass (1·86 g) which was dissolved in n-hexane (25 ml) and cooled to 0°, giving the cis-*dibromo-ketone* (428 mg), m.p. 82—85°, *m*/*e* 310, 312, and 314 (intensity ratio 1 : 2 : 1) (Found: M^+, 309·9602. $C_{10}H_{16}Br_2O$ requires *M*, 309·9569), $\nu_{max.}$ (CCl_4) 1757s and 1722w cm^{-1}, τ 8·92 (t, *J* 7 Hz, CH_2Me), 8·88 and 8·86 (4-Me), and *ca.* 8·43 and 7·9 (complex) (the bromomethine proton signals are discussed earlier). Concentration of the liquors from the crystallisation, addition of a little ether–hexane and cooling at −80° gave the *trans*-dibromo-ketone (160 mg), m.p. 87—90°, $\nu_{max.}$ (CCl_4) 1742s and 1708w cm^{-1}, τ 9·03 (t, *J ca.* 6·5 Hz, CH_2Me), 8·97 and 8·71 (4-Me), and 8·45—7·53 (complex) (the bromomethine proton signals are discussed earlier), *m*/*e* 310, 312, and 314 (intensity 1 : 2 : 1). The evaporated residues from the crystallisation (1·06 g) were used in the next step.

3-*Ethyl*-4,4-*dimethylcyclohexa*-2,5-*dienone* (3).—The foregoing crude residual bromo-ketone mixture (1·06 g) was dehydrobrominated with calcium carbonate (2·0 g) in dimethylformamide (15 ml) for 3 h in the usual way. Work-up gave an oil (508 mg). Alumina chromatography gave 2-bromo-5-ethyl-4,4-dimethylcyclohexa-2,5-dienone (214 mg) as a solid, m.p. 76·8—77·8° (from petroleum), $\nu_{max.}$ (CCl_4) 1665s, 1630w, and 1610m cm^{-1}, $\lambda_{max.}$ (95% EtOH) 247 nm (log ε 4·15), *m*/*e* 228 and 230 (intensity 1 : 1) (M^+) n.m.r. data in Table 1. The later fraction was 3-*ethyl*-4,4-*dimethylcyclohexa*-2,5-*dienone* (110 mg), needles, m.p. 42·5—43° (from petroleum), >99% pure (g.l.c. on NGS at 150°), $\nu_{max.}$ (CCl_4) 1666s, 1631, and 1608 cm^{-1}, $\lambda_{max.}$ (95% EtOH) 237 nm, $\lambda_{max.}$ (H_2O) 242 nm (log ε 4·18), n.m.r. data in Table 1 (Found: C, 79·7; H, 9·1%; *M*, 150. $C_{10}H_{14}O$ requires C, 80·0; H, 9·4%; *M*, 150).

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5-*Ethyl*-4,4-*dimethylcyclohex*-2-*enone*.—4,4-Dimethylcyclohexa-2,5-dienone (1·14 g) was treated with lithium diethylcuprate [from copper(I) iodide (9·373 g) and ethyl-lithium] in the usual way. The usual work-up gave an oil which on alumina chromatography gave 5-ethyl-4,4-dimethylcyclohexenone (760 mg, 54%) as a liquid, $\nu_{max.}$ 1678 and 1610 cm^{-1}, $\lambda_{max.}$ (95% EtOH) 227 nm (log ε 4·04), *m/e* 152 (M^+) n.m.r. data in Table 2. The 2,4-*dinitrophenylhydrazone* had m.p. 131—132° (from ethyl acetate) (Found: C, 57·6; H, 6·4; N, 16·9. $C_{16}H_{20}N_4O_4$ requires C, 57·8; H, 6·1; N, 16·9%).

3,5-*Diethyl*-4,4-*dimethylcyclohexanone*.—To stirred purified copper(I) iodide (2·83 g) in dry ether (50 ml) at −80°, under nitrogen, was added ethylmagnesium bromide in ether (14·1 ml of 2M-solution). After 10 min at −78° the mixture was warmed to 0° and 4,4-dimethylcyclohexadienone (840 mg) in ether was added during 30 min. After a further 30 min at 0° the usual work-up gave 5-ethyl-4,4-dimethylcyclohex-2-enone (910 mg; 70% pure by g.l.c.) as before. The ethylation was repeated in the same way on this material, and the product separated on alumina to give 3,5-diethyl-4,4-dimethylcyclohexanone (306 mg, 25%; *ca.* 90% pure), $\nu_{max.}$ (film) 1722 and 1712 cm^{-1}.

3,5-*Diethyl*-4,4-*dimethylcyclohexa*-2,5-*dienone* (5).—The foregoing ketone in acetic acid (10 ml) was treated with bromine (548 mg) in acetic acid (10 ml) in the usual way, and the product dehydrobrominated with calcium carbonate in dimethylformamide as in the preparation of the 3,4,4-trimethyl-dienone (method A). Alumina chromatography gave the *dienone*, crystals (121 mg, 41%), m.p. 68—71°, $\nu_{max.}$ (CCl$_4$) 1693m, 1683sh, 1672s,sh, 1665vs, 1658sh, 1649m,sh, 1625s,sh, and 1601 cm^{-1}, $\lambda_{max.}$ (H_2O) 247 nm (log ε 4·26) (Found: M^+, 178·1355. $C_{12}H_{18}O$ requires *M*, 178·1358), n.m.r. data in Table 1. Since all this material was needed for physical studies it was not analysed.

3,4,4,5-*Tetramethylcyclohexanone*.—4,4,5-Trimethylcyclohex-2-enone (5·38 g) and lithium dimethylcuprate [from copper(I) iodide (14·71 g) and methyl-lithium (140 ml of 1·1M-solution)] in the usual way gave the crude *tetramethylcyclohexanone* (5·36 g, 94%; 95% pure by g.l.c.). Distillation gave material, b.p. 96—98° at 12 mmHg, 97% pure (NGS at 140°), $\nu_{max.}$ (film) 1720 and 1713 cm^{-1}, τ 9·10 (d, *J* 6·5 Hz, 3- and 5-Me), 8·97 (4-Me), and 7·59—8·20 (m, 2-, 3-, 5-, 6-H) (Found: C, 78·1; H, 11·4%; *M*, 154. $C_{10}H_{18}O$ requires C, 77·9; H, 11·8%; *M*, 154). The 2,4-*dinitrophenylhydrazone* had m.p. 133—133·5° (from ethyl acetate) (Found: C, 57·8; H, 6·6; N, 17·0. $C_{16}H_{22}N_4O_4$ requires C, 57·5; H, 6·6; N, 16·8%).

cis-2,6-*Dibromo*-3,4,4,5-*tetramethylcyclohexanone*.— The preceding ketone (5·55 g) in acetic acid (18 ml) was treated with bromine (11·55 g) in acetic acid during 105 min at *ca.* 10°. Work-up in the usual way gave crude crystalline product (8·40 g); recrystallisation twice from ether–petroleum gave pure *dibromo-ketone* (5·44 g, 48%), needles, m.p. 125·5—126·5°, $\nu_{max.}$ (CCl$_4$) 1763vs, 1736sh,m, and 1720sh,m cm^{-1}, τ 9·02 (d, *J* 7·2 Hz, 5-Me), 8·80 (d, *J* 6·2 Hz, 3-Me), 8·86 and 8·71 (4-Me), 7·89 [q (*J* 6·2 Hz) of d (*J* 11·8 Hz), 3-H], 7·82 [q (*J* 7·2 Hz) of d (*J* 4·5 Hz) 5-H], 5·57 [d (*J* 11·8 Hz) of d (*J* 1·1 Hz) 2-H], and 4·81 [d (*J* 4·5 Hz) of d (*J* 1·1 Hz)] (Found: C, 38·8; H, 5·4; Br, 50·9. $C_{10}H_{16}Br_2O$ requires C, 38·5; H, 5·2; Br, 51·2%), *m/e* 310, 312, and 314 (M^+, relative intensities 1 : 2 : 1).

3,4,4,5-*Tetramethylcyclohexa*-2,5-*dienone* (4).—The foregoing dibromo-ketone (5·44 g) was treated with calcium carbonate (7·00 g) in dimethylformamide (50 ml) at reflux for 3 h. The usual work-up, with continuous petroleum extraction, gave crude dienone (2·59 g), which was crystallised twice from petroleum at 0° (yield 1·59 g, 61%). Short-path distillation gave >99% pure *dienone*, m.p. 46·5—47·5°, $\nu_{max.}$ (CCl$_4$) 1673 and 1668 (vs doublet), 1660sh, 1650w, 1630, and 1615 cm^{-1}, $\lambda_{max.}$ (hexane) 230·5 nm (log ε 4·22), $\lambda_{max.}$ (iso-octane) 230·8 nm (log ε 4·21), (H_2O) 246 nm (log ε 4·25), n.m.r. data in Table 1 (Found: C, 80·3; H, 9·2%; *M*, 150. $C_{10}H_{14}O$ requires C, 80·0; H, 9·4%; *M*, 150). The 2,4-*dinitrophenylhydrazone* had m.p. 178·5—179·5° (from ethyl acetate) (Found: C, 58·5; H, 5·2; N, 16·9. $C_{16}H_{18}N_4O_4$ requires C, 58·2; H, 5·5; N, 17·0%).

2-*Bromo*-3,4,4,5-*tetramethylcyclohexanone and* 3,4,4,5-*Tetramethylcyclohex*-2-*enone*.—To 3,4,4,5-tetramethylcyclohexanone (400 mg) in chloroform (50 ml) was added, with stirring during 1 hr, pyrrolidone hydrobromide perbromide [14] (1·346 g) in chloroform (40 ml). After a further 15 min the solution was washed (H_2O, then $NaHCO_3$, then H_2O), dried ($CaSO_4$) at 0°, and evaporated to leave the crude bromo-ketone (536 mg) as a semicrystalline mass. This was treated with calcium carbonate (1·0 g) in refluxing dimethylformamide (10 ml) for 2 h in the usual way, to give an oil containing some unchanged cyclohexanone, and the cyclohexenone and corresponding dienone (ratio *ca.* 4 : 1), from which the dinitrophenylhydrazone of the enone was obtained [m.p. 132·6—133·4° (from ethyl acetate)].

3,4,4,5-*Tetramethylcyclohex*-2-*enone*.—To lithium dimethylcuprate [from copper(I) iodide (987 mg) and ethereal methyl-lithium (8·0 ml; 1·1M)] was added 3,4,4-trimethylcyclohexa-2,5-dienone (225 mg) in the usual way. Work-up and chromatography on a short alumina column, gave the cyclohexenone (230 mg, 91%), identical with that prepared before. A distilled sample (*ca.* 97% pure by g.l.c.) had $\nu_{max.}$ (film) 1672, 1666 (doublet), and 1620 cm^{-1}, $\lambda_{max.}$ (95% EtOH) 236 nm (log ε 4·13), *m/e* 152 (M^+), n.m.r. data in Table 2. The 2,4-*dinitrophenylhydrazone* (82%) (from ethyl acetate) had m.p. 134·4—135·0° (Found: C, 58·0; H, 6·1; N, 17·2. $C_{16}H_{20}N_4O_4$ requires C, 57·8; H, 6·1; N, 16·9%). In the preparation, no evidence was obtained of the presence of the possible contaminant 4,4,5,5-tetramethylcyclohex-2-enone.

Isopropenyl Methyl Ketone (3-*Methylbut*-3-*en*-2-*one*).—The method described here is a more reliable and convenient modification of the combined procedures of refs. 56 and 57. Ethyl methyl ketone (450 ml) and paraformaldehyde (30 g) were stirred at 40°, and a mixed pH indicator (Phenol Red and Bromothymol Blue) was added. Aqueous N-sodium hydroxide was added until the colour turned just to pale blue, from yellow (much indicator is adsorbed on the paraformaldehyde), then more alkali (2·0 ml) was added. When no solid paraformaldehyde remained (usually *ca.* 40 min) and a Tollens test showed the absence of free formaldehyde in the solution, it was just neutralised with glacial acetic acid–ethyl methyl ketone solution and excess of ethyl methyl ketone was evaporated off at *ca.* 30 mmHg. The residue was dehydrated with syrupy phosphoric acid and copper powder,[57] the fractions b.p. 82—98° being collected, dried ($CaSO_4$), and redistilled.

4,4,6-*Trimethylcyclohex*-2-*enone*.—*Method A*. To the piperidine enamine of isobutyraldehyde [58] (4·107 g), stirred

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at 0° under nitrogen, isopropenyl methyl ketone (2·67 g) was added dropwise during 5 min. No reaction occurred in 4 days at 25°. Dry dioxan (10 ml) was added and the temperature was kept at 45—55° for 46 h. Evaporation of the dioxan at 12 mmHg, then treatment with 15% hydrochloric acid (50 ml) for 2 days at 25°, then for 45 min at 100°, extraction with ether, and drying and evaporation of the extract gave the cyclohexenone (544 mg, 13%), identical with the sample obtained by method B.

Method B. Isobutyraldehyde (60·0 g) and isopropenyl methyl ketone (56·0 g), condensed by the method of Eliel and Lukach [41] (as used by Dauben and his co-workers [22]), gave the cyclohexenone (37·12 g, 40%), b.p. 60—70° at 15 mmHg (75—96% pure), of which the best fractions, b.p. 67—70° at 15 mmHg were >96% pure (lit.,[22] b.p. 44·5—45·5° at 2·5—3·0 mmHg; lit.,[59] 55—57° at 2 mmHg). The n.m.r. (Table 2) and i.r. data agree well with those in ref. 22, but the n.m.r. data differ from those reported in ref. 59.

2,4,4-*Trimethylcyclohexa*-2,5-*dienone* (6).—The foregoing cyclohexenone (2·36 g) was heated 13 days at reflux in dry benzene with DDQ (5·42 g), under nitrogen, until >90% had reacted. Work-up as in the preparation of the 3,4,4-trimethyl-dienone (method C) gave the cyclohexadienone (1·36 g, 56%), >90% pure (g.l.c. on NGS at 150°). Chromatography on alumina, and molecular distillation gave material >99% pure (NGS at 110°), $\nu_{max.}$ (film) 1666, 1641, and 1635 cm^{-1}, $\nu_{max.}$ (CCl_4) 1665br (with fine structure), 1642, 1635sh, and 1618 cm^{-1}, $\lambda_{max.}$ (H_2O) 242 nm (log ε 4·19), $\lambda_{max.}$ (iso-octane) 229·5 nm (log ε 4·094) [lit.,[23] $\lambda_{max.}$ (EtOH) 237 nm (log ε 4·10)], n.m.r. data in Table 1 (Found: C, 79·2; H, 9·0%; *M*, 136. Calc. for $C_9H_{12}O$: C, 79·4; H, 8·9%; *M*, 136). The 2,4-dinitrophenylhydrazone had m.p. 185—185·5° (from ethyl acetate) (lit.,[23,60] 179—181°) (Found: C, 57·0; H, 5·4; N, 17·8. Calc. for $C_{15}H_{16}N_4O_4$: C, 57·0; H, 5·1; N, 17·7%).

2,4,4,5-*Tetramethylcyclohexanone*.—Methylation of 4,4,6-trimethylcyclohex-2-enone (4·38 g) with lithium dimethylcuprate gave the tetramethylcyclohexanone (4·52 g, 87%), b.p. 84—89° at 12 mmHg, *ca.* 90% pure (lit.,[61] b.p. 80—85° at 14 mmHg), $\nu_{max.}$ (film) 1713 cm^{-1} (lit.,[61] 1712 cm^{-1}). The 2,4-*dinitrophenylhydrazone* had m.p. 133·5—134° (Found: C, 57·6; H, 6·7; N, 17·0. $C_{16}H_{22}N_4O_4$ requires C, 57·5; H, 6·6; N, 16·8%).

2,4,4,5-*Tetramethylcyclohexa*-2,5-*dienone* (7).—The preceding ketone (714 mg) was treated with DDQ (2·50 g) and toluene-*p*-sulphonic acid monohydrate (*ca.* 2 mg) in refluxing benzene for 57 h. The usual work-up gave crude dienone (173 mg, 24%, *ca.* 70% pure). Chromatography of this and further samples on alumina, and molecular distillation gave material >98% pure; $\nu_{max.}$ (film) 1673, 1667, 1640sh, 1633, 1626sh, 1622sh, and 1613 cm^{-1}, $\lambda_{max.}$ (H_2O) 246·5 nm (log ε 4·18), n.m.r. data in Table 1, *m/e* 150 (M^+). Lack of material after physical measurements [1] precluded microanalysis. The 2,4-*dinitrophenylhydrazone* had m.p. 170—172° (from ethyl acetate) (Found: C, 57·9; H, 5·6; N, 17·3. $C_{16}H_{18}N_4O_4$ requires C, 58·2; H, 5·5; N, 17·0%).

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