Hydrogenolysis of Carbon–Carbon Bonds in Cyclohexadienones[1]

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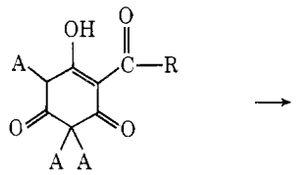
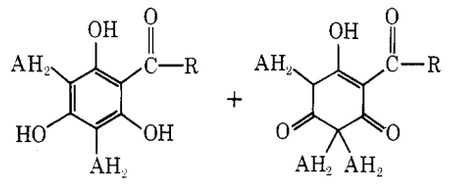
Palladium-catalyzed low-pressure hydrogenation of cross-conjugated and linearly conjugated cyclohexadienones bearing allyl or benzyl groups at the quaternary carbons results in significant hydrogenolysis of the bonds linking the allyl or benzyl groups to the cyclohexadienone rings, as well as reduction of the double bond in the allyl group. The percentage of hydrogenolysis increases with increasing solvent polarity and with increasing hydrogen bonding power of the solvent. No hydrogenolysis occurs with a 2,6-di-*tert*-butylcyclohexadienone. These results are consistent with a hydrogenolysis mechanism involving attack by a hydride ion-like species at the carbon linking the allyl or benzyl group to the ring.

While hydrogenolysis of bonds between carbon and heteroatoms is common, the corresponding cleavage of unstrained carbon–carbon single bonds under mild conditions is quite rare. However, carbon–carbon bond cleavage has been reported to occur during the hydrogenation of cyclic β-diketones bearing highly substituted allyl groups between the two carbonyls.[2-5] For instance, hydrogenation of lupulone[6] and its analogs (**1a**) at room temperature gives appreciable yields of phenol **2**,[3-5] as well as the expected reduction product **3**.[5a] When A is a simple allyl group (**1b**), only reduction to **3** occurs.[4]



1a, A = $-CH_2CH{=}C(CH_3)_2$

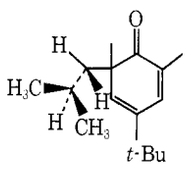
b, A = $-CH_2CH{=}CH_2$



2 **3**

We have now observed that attempted low-pressure reduction of double bonds in allyl groups, even unsubstituted allyl groups, at the quaternary carbons of cyclohexadienones results in appreciable hydrogenolysis of carbon–carbon bonds. The relative rate of hydrogenolysis compared to that of double bond hydrogenation is greatly increased by an increase in the polarity of the solvent employed or by an increase in its hydrogen bonding ability. Our results are summarized in Tables I and II. One run in which the reaction was carried out in the presence of the catalyst (which had previously been hydrogenated) and in polar solvent, but in the absence of hydrogen, gave no reaction. Thus cleavage does not result from a palladium-catalyzed carbenium ion cleavage of the cyclohexadienone, but occurs during the hydrogenation process.

Hydrogenation of the cross-conjugated cyclohexadienone **7** gives, in addition to the hydrogenolysis product 2,4,6-trimethylphenol, a mixture of reduction products which could not be separated. In each solvent, the nmr spectrum of the reduction products suggest that they consist of a mixture of the 4-propylcyclohexadienone and of the corresponding cyclohexenone. Rather surprisingly, no evidence for ring hydrogenation was observed in the hydrogenation of **8** or of the linearly conjugated cyclohexadienones **4** and **5**. The structures of products **10** and **11** were clearly established by their nmr spectra (see Experimental Section). Of interest is the fact that the nmr spectrum of dienone **10** shows two doublets for the methyl groups on the isobutyl side chain at δ 0.76 and 0.88 ppm. This chemical shift difference (0.12 ppm) appears to be the largest such shift recorded for methyl groups in an isopropyl group which is not directly bonded to an asymmetric center.[7] Inspection of molecular models indicates that **11** has a single preferred conformation (**11a**) in which one methyl group (presumably the one



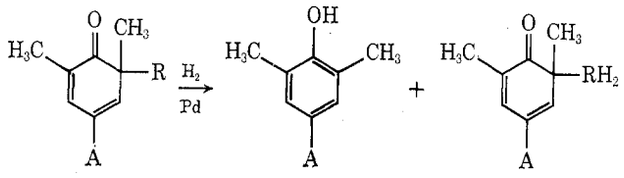
11a

resonating at δ 0.76) is significantly affected by the shielding cone of the C-4–C-5 double bond, while the other methyl group is much less affected by the ring system.

We believe that the results shown in Tables I and II are consistent with a hydrogenolysis mechanism in which a hydride ion-like species displaces a phenoxide ion from an allyl or benzyl group. This mechanism resembles that which Reidl and Nickl have proposed for hydrogenolysis of lupulone.[4] Their mechanism has been supported by Anteunis and Verzele, on the basis of the observation that the ratio of hydrogenolysis to hydrogenation of lupulone increases with increasing hydrogen ion concentration.[5] Reidl and Nickl have proposed, however, that hydride ion attack occurs only following an initial protonation of a carbonyl group of lupulone.[4] The leaving group, according to this mechanism, would be a phenol rather than a phenoxide ion. A similar mechanism seems unlikely for the hydrogenolysis of dienone **5**, at least, since protonation of the carbonyl group would result in a very rapid [3,3] sigmatropic shift of the allyl group to yield **7**.[8] Although protonation therefore does not precede hydrogenolysis, the ability of the solvent to hydrogen bond the developing phenoxide ion is clearly of great importance, as indicated by the sharp increase in the percentage of hydrogenolysis, despite the decrease in dielectric constant, when the solvent is changed from methanol to acetic acid–methanol.

Of particular interest is the absence of any hydrogenolysis in 2,6-di-*tert*-butylcyclohexadienones. In these cases the proposed hydride attack would displace a 2,6-di-*tert*-butylphenoxide anion. These anions are exceptionally strong bases[9] owing to hindrance of solvation at oxygen, and therefore should be very poor leaving groups.

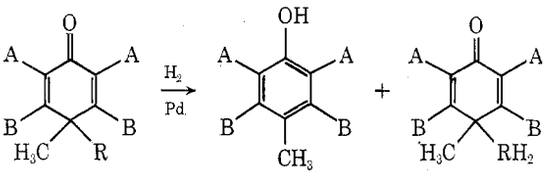
Table I
Hydrogenation of Cyclohexa-2,4-dien-1-ones



4-6 10,11

Dienone	R	A	Solvent	Yield of phenol, %	Other products
4	$-CH_2C(CH_3)=CH_2$	*t*-Bu	Hexane	20	**10**, R = *i*-Bu
5	$-CH_2CH=CH_2$	CH_3	Hexane	13	**11**, R = *n*-Pr; A = Me
5	$-CH_2CH=CH_2$	CH_3	Methanol	49	**11**
5	$-CH_2CH=CH_2$	CH_3	DMF	34	**11**
5	$-CH_2CH=CH_2$	CH_3	Methanol (catalyst only, no hydrogen)	No reaction	
5	$-CH_2CH=CH_2$	CH_3	Acetic acid–methanol (1:3)	85	**11**
6	$-CH_2Ph$	CH_3	Hexane	100	

Table II
Hydrogenation of Cyclohexa-2,5-dien-1-ones



7-9 12

Dienone	R	A	B	Solvent	Yield of phenol, %	Other products
7	$-CH_2CH=CH_2$	CH_3	H	Hexane	0	*a*
7	$-CH_2CH=CH_2$	CH_3	H	Methanol	5	*a*
7	$-CH_2CH=CH_2$	CH_3	H	Acetic acid–methanol (1:3)	63	*a*
8	$-CH_2Ph$	CH_3	CH_3	Hexane	100	
9	$-CH_2CH=CH_2$	*t*-Bu	H	Acetic acid–methanol (1:3)	0	**12**, R = *n*-Pr
9	$-CH_2CH=CH_2$	*t*-Bu	H	Acetic acid	0	**12**, R = *n*-Pr

[a] Apparently a mixture of ketones with zero, one, or two double bonds in the ring (nmr analysis).

Displacement of a phenoxide ion by a hydride-like reagent could conceivably occur at either C-1 or C-3 of the allyl group. A study of the competitive hydrogenations of dienones **4** and **6** in methanol showed that hydrogenolysis of **5** occurred approximately 1.5 times as fast as that of **6**. This rate difference seems too small to require that a mechanism be postulated for the reduction of **4** which is not available to **6**. Thus, a direct SN2-like attack of a hydride ion at the carbon attached to the cyclohexadienone ring seems the best representation of the transition state for hydrogenolysis.

Experimental Section

Preparation of Cyclohexadienones. Cyclohexadienones **5**,[10] **7**,[10] **8**,[11] and **9**[12] were prepared as described in the literature.

6-(2-Methylallyl)-4-*tert*-butyl-2,6-dimethylcyclohexa-2,4-dien-1-one (4) was prepared by Claisen alkylation of sodium 4-*tert*-butyl-2,6-dimethylphenoxide with methallyl bromide in the usual manner.[10] It was obtained in 49% yield as a pale yellow oil after chromatography on Florisil. Its nmr spectrum in CCl_4 showed a multiplet (1 H) at δ 6.99 ppm (hydrogen at C-3), a doublet (1 H, J = 3 Hz) at δ 5.94 (hydrogen at C-5), a broad doublet (2 H) around δ 4.54 (terminal vinyl protons), a doublet (3 H, J = 1.5 Hz) at δ 1.84 (methyl at C-2), a singlet (9 H) at δ 1.13 (*tert*-butyl at C-4), a singlet (3 H) at δ 1.08 (methyl at C-6), a pair of doublets (2 H, J = 14 Hz) at δ 2.11 and 2.76 (methylene at C-6), and a doublet (3 H, J = 1.5 Hz) at δ 1.85.

6-Benzyl-2,4-6-trimethylcyclohexa-2,4-dien-1-one (6) was similarly prepared by Claisen alkylation of sodium 2,4-6-trimethylphenoxide with benzyl bromide, and isolated as a pale yellow oil in 22% yield by chromatography on Florisil. Its nmr spectrum in CCl_4 showed a multiplet (5 H) around δ 6.93 (phenyl group), a quartet (1 H, J = 1.5 Hz) at δ 6.35 (hydrogen at C-3), a singlet (1 H) at δ 5.83 (hydrogen at C-5), a pair of doublets (1 H each, J = 12.5 Hz) at δ 2.60 and 3.04 (methylene at C-6), a doublet (3 H, J = 1.5 Hz) at δ 1.79 (methyl at C-2), a singlet (3 H) at δ 1.71 (methyl at C-4), and a singlet (3 H) at δ 1.16 (methyl at C-6).

Hydrogenation Procedures. All hydrogenations were carried out in a conventional small-scale hydrogenation apparatus, at essentially atmospheric pressure. The cyclohexadienones (10^{-3} mol) were dissolved in 5–10 ml of solvent and *ca.* 5 mg of 5% Pd on charcoal catalyst (obtained from Matheson Coleman and Bell) was added. The mixture was stirred by a magnetic stirrer until uptake of hydrogen essentially ceased and was then filtered to remove the catalyst. Hexane and methanol solutions were evaporated on a steam bath. Acetic acid and acetic acid–methanol solutions were neutralized with sodium bicarbonate solution, and the mixtures were extracted with methylene chloride. The organic layers were washed with water, dried over magnesium sulfate, filtered, and evaporated. Dimethylformamide solutions were diluted with 25 ml of distilled water and extracted with two 10-ml portions of pentane, which were combined and washed with five 20-ml portions of

water. The organic layers were dried over magnesium sulfate, filtered, and evaporated.

Nmr analysis showed the absence of peaks attributable to allyl groups at C-6 of the cyclohexadienones, indicating complete reaction of the starting dienones **4** and **5**. The relative yields of phenols and reduction products from the hydrogenation of compounds **4** and **5** were determined by the relative areas of the aromatic methyl absorptions due to the phenols and the allylic methyl absorptions due to the hydrogenated dienones **10** and **11**. The yield of phenol from hydrogenation of dienone **7** was determined by vpc analysis on a 6 ft × 0.25 in., 3% SE-30 on Chromosorb W column.

Isolation of Products of Hydrogenation. With the exception of the product from reduction of cyclohexadienone **9**, the reaction products from each hydrogenation, after work-up as described above, were dissolved in 10 ml of pentane and extracted with three 10-ml portions of Claisen alkali. The organic fractions were washed with water, dried, and evaporated to give the reduced cyclohexadienones. Pure samples of the previously unreported **10** and **11** were obtained by vpc on a 1 ft × 0.375 in., 30% SE-30 on Chromosorb W column.

The nmr spectrum of **6-isobutyl-4-*tert*-butyl-2,6-dimethylcyclohexa-2,4-dien-1-one (10)** in $CDCl_3$ showed a multiplet (1 H) at δ 7.0 (hydrogen at C-3), a doublet (1 H, J = 2.5 Hz) at δ 5.93 (hydrogen at C-5), a broad singlet (3 H) at δ 1.90 (methyl at C-2), singlets at δ 1.15 (9 H) and 1.08 (3 H) for the *tert*-butyl at C-4 and the methyl at C-6, and doublets (3 H, J = 6 Hz) at δ 0.76 and 0.88 (methyl groups on isobutyl side chain), as well as a multiplet (*ca.* 3 H) at δ 2.30–1.15 (methylene and methine of isobutyl group).

The nmr spectrum of **2,4,6-trimethyl-6-propylcyclohexa-2,4-dien-1-one (11)** in CCl_4 showed a multiplet (1 H) at δ 6.90 (hydrogen at C-3), a broad singlet (1 H) at δ 6.10 (hydrogen at C-5), a doublet (3 H, J = 1.5 Hz) at δ 1.99 (methyl at C-2), singlets (3 H each) at δ 1.93 and 1.11 (methyls at C-4 and C-6), and a multiplet (*ca.* 7 H) at δ 0.73–1.46 (propyl at C-6).

The neutral fraction from hydrogenation of dienone **7** showed a complex spectrum indicating that appreciable hydrogenation of double bonds in the ring had occurred. No pure product could be obtained from this mixture.

The aqueous layers from extraction with Claisen alkalie were acidified with 6 *N* hydrochloric acid and extracted with methylene chloride. The organic layers were washed with water, dried, and evaporated to give essentially pure phenols, which were identified by comparison with samples of known structure.

The hydrogenation product of dienone **9** was shown by vpc to contain a single product, which was identified by its nmr and ir spectrum as the known **2,6-di-*tert*-butyl-4-methyl-4-propylcyclohexa-2,5-dien-1-one.**[13]

Competitive Hydrogenolysis of Benzyl and 2-Methylallyl Groups. A solution of dienones **4** and **6** (3.0×10^{-4} mol of each) in 5 ml of methanol was hydrogenated as usual until *ca.* 20% of the starting materials had reacted. The mixture was filtered free of catalyst, the solvent was evaporated on a steam bath, and the residue was dissolved in 15 ml of pentane and extracted with Claisen alkali. The nmr spectrum of the neutral fraction showed it to consist largely of unreacted starting dienones. The alkaline fraction was acidified and extracted with methylene chloride. The methylene chloride layer was washed with water, dried over magnesium sulfate, and evaporated. The phenols obtained in this manner were analyzed by vpc on a 6 ft × 0.25 in., 5% SE-30 on Chromosorb W column at 170°. Comparison with synthetic mixtures showed the product to be 4-*tert*-butyl-2,6-dimethylphenol and 2,4,6-trimethylphenol in the molar ratio 1.5:1.

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Registry No.—**4,** 51869-07-9; **5,** 4278-92-6; **6,** 41388-92-5; **7,** 4278-95-9; **8,** 31040-77-4; **9,** 2756-79-8; **10,** 51869-08-0; **11,** 51869-09-1.

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Cis–Trans Isomerization of Allylic Radicals

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A series of cis and trans allylic halides has been reduced with triphenyltin hydride in a chain reaction which involves allylic radicals. Varying degrees of cis–trans isomerization of the intermediate allylic radicals have been observed and it has been shown that the variation is concentration dependent and also dependent on structure. Attempts to study allylic radicals where there is delocalization of the free electron onto CN, CO_2CH_3, and $CON(CH_3)_2$ by the same technique led to isomerization of starting material or product and thus no conclusion concerning the interconvertibility of the isomeric radicals could be reached. Chlorination of crotonitrile, isocrotonitrile, methyl crotonate, and methyl isocrotonate with *tert*-butyl hypochlorite led to varying amounts of cis–trans isomerization in the intermediate radicals as reflected by the composition of the chloro-substituted products. The factors which control these isomerizations are discussed.

In 1961 Walling and Thaler studied the chlorination of a variety of olefins by *tert*-butyl hypochlorite.[1] They found that in general cis and trans olefins gave cis and trans allylic chlorides, respectively. A notable exception was *cis*-4,4-dimethyl-2-pentene, which at 40° gave *trans*-1-chloro-4,4-dimethyl-2-pentene. It was suggested that the *tert*-butyl group destabilized the intermediate cis allylic radical by introducing steric effects which were not present in the other allylic radicals, and that the rate of conversion of the cis to trans allylic radical was thus enhanced.

Subsequently other workers have investigated the cis–trans isomerization of allylic radicals,[2] and isomerization has been observed under a variety of conditions.[2a-d] In the work being reported here cis and trans allylic radicals have