mixture was added to the amalgamated zinc prepared by the addition of 25 g. of mercuric chloride to 390 g. of 80-mesh zinc metal in the presence of 780 ml. of water and 39 ml. of 37% hydrochloric acid.[36] The mixture was refluxed for three hours and then slowly distilled. By the time 1 l. of water had distilled most of the organic material had been removed from the reaction flask. Separation of the organic layer from the water in the distillate gave 165 g. of material. This was washed with several portions of cold, concentrated sulfuric acid. Apparently a considerable portion of the indan was sulfonated by this procedure. The material left (*ca.* 75 g.) was distilled through a small packed column (*ca.* 5 plates) to give indan, b.p. 81° at 31.5–32 mm., n^{20}_D 1.5382, lit.[22] n^{20}_D 1.5382.

The purest available commercial samples of dibenzyl ether, diphenylmethane, methyl phenylacetate, benzyl benzoate, benzyl chloride, phenylacetonitrile, *p*-chlorotoluene, *p*-methoxytoluene, *p*-tolunitrile and chlorobenzene, were distilled through a Vigreux column under reduced pressure. Fluorene, triphenylmethane and *p*-nitrotoluene were recrystallized from ethyl alcohol. The samples used had m.p.'s of 115–116, 92.5 and 52–53°, respectively.

Phenyldimethylsilane was prepared from the reaction of phenyldimethylchlorosilane with lithium aluminum hydride. To 10 g. of lithium aluminum hydride in 200 ml. of ethyl ether 128 g. of phenyldimethylchlorosilane (b.p. 85.5° at 21 mm.) was added over a 3-hour period. The solution was refluxed for three hours and the excess lithium aluminum hydride destroyed by ethyl acetate. The reaction product was poured over ice, the ether layer separated and the aqueous layer extracted twice with 200 ml. of ether. The ethereal solution was dried over sodium sulfate and distilled until a pot temperature of 85° was reached. The residue did not give a qualitative test for chlorine. The residue upon distillation through a small packed column (*ca.* 5 plates) under nitrogen gave 111 g. of phenyldimethylsilane, b.p. 57° at 20 mm., n^{20}_D 1.4988, d^{20}_4 0.876. The molar refraction, 45.62, was in very good agreement with the value of 45.73 as calculated from the data of Warrick.[37]

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[36] J. H. Brewster, This Journal, **76**, 6364 (1954).

[37] E. L. Warrick, *ibid.*, **68**, 2455 (1946).

SCHENECTADY, NEW YORK

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, WESTERN RESERVE UNIVERSITY]

Some Structural and Geometric Isomers of 1-Cyclohexyl-1,3-butadiene[1]

BY OLIVER GRUMMITT AND ZOLTAN MANDEL[2]

RECEIVED JUNE 22, 1955

Four $C_{10}H_{16}$ isomeric conjugated dienes have been prepared and their relative stabilities compared. These are *trans*-1-cyclohexyl-1,3-butadiene (II), 1-cyclohexylidene-2-butene (III), 1-(1-cyclohexenyl)-1-butene (IV) and 1-butylidene-2-cyclohexene (V). *cis*-1-Cyclohexyl-1,3-butadiene (I) could not be obtained. II and III in 4/1 mole ratio are formed by the pyrolysis (475°) of 1-cyclohexyl-3-acetoxy-1-butene (VI). Allylic rearrangement of VI precedes the pyrolysis to III. II does not isomerize to III at 475°. The structure of III (probably the *trans* isomer) was based on oxidative degradation, ultraviolet and infrared absorption, and lack of reactivity with maleic anhydride. II could not be isomerized to I photochemically or thermally, with or without iodine. Thermal isomerization (600°) of II gave III and IV. The structure of IV (probably the *trans* isomer) was elucidated by degradation of the maleic anhydride adduct and by independent synthesis from 1-(1-cyclohexenyl)-1-acetoxybutane (VIII). Pyrolysis of VIII gave IV and V. Calculated heats of hydrogenation indicate the order of increasing stability to be III, I–II and IV. Failure to obtain I by isomerization of II is attributed to hindrance between the ring and side chain which makes the stability difference between the isomers probably greater than 5.5 kcal./mole.

The purpose of this work was to study the preparation and relative stabilities of several $C_{10}H_{16}$ isomeric conjugated dienes: *cis*- and *trans*-1-cyclohexyl-1,3-butadienes (I, II), 1-cyclohexylidene-2-butene (III), 1-(1-cyclohexenyl)-1-butene (IV) and 1-butylidene-2-cyclohexene (V) (Chart 1).

trans-1-Cyclohexyl-1,3-butadiene (II) had been made[3] in 40% yield by the pyrolysis of 1-cyclohexyl-3-acetoxy-1-butene (VI) at 475°. The isomeric 1-cyclohexylidene-2-butene (III) was a coproduct. II does not isomerize to III at 475° under pyrolysis conditions. However, the α-acetoxy group in VI may favor allylic rearrangement to 1-cyclohexyl-1-acetoxy-2-butene (VII) before decomposition. An analogous rearrangement occurs in the conversion of 3-acetoxy-3-cyano-1-butene to 1-acetoxy-3-cyano-3-butene and 2-cyano-1,3-butadiene.[4]

The ease of rearrangement of the isomeric acetates VI and VII was observed at 150, 200 and 240° (Table I). The extent of decomposition was estimated by the acetic acid formed and the extent of isomerization by the refractive index of the recovered reactants.

TABLE I

ALLYLIC REARRANGEMENTS OF ACETATES VI[3] AND VII[5,6]

Temp., °C.	Heat. per., hr.	Frac. decomp., %		n^{20}_D of recovd. acetate[a]		Frac. (%)[b] of iso. acetate from	
		VI	VII	VI	VII	VI	VII
150	2			....	1.4628	..	0
200	3	0.4	0.3	1.4606	1.4622	12	24
200	4.5	..	..	....	1.4620	..	32
240–241[c]	0.5	8	8	1.4607	1.4614	16	56

[a] 1.4603 for pure VI, 1.4628 for pure VII. [b] Accurate to about ±8%. [c] Five grams was distilled in about 0.5 hour.

While both acetates isomerize at 200 and 240°, the ease of isomerization of VII is much greater—over 50% rearranges at 240°. In an anionotropic mechanism,[7] this signifies that the cyclohexyl group has greater electron-releasing effect than the methyl group. Acetic acid formed in these reactions may have catalyzed the isomerization. Acids catalyze allylic rearrangement of alcohols, but their influence on the isomerization of esters is not clear.[7]

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[1] A du Pont postgraduate fellowship granted to Zoltan Mandel in 1953–1954 is gratefully acknowledged.

[2] Textile Fibers Dept., E. I. du Pont de Nemours Co., Wilmington, Del.

[3] O. Grummitt and J. Splitter, This Journal, **74**, 3924 (1952).

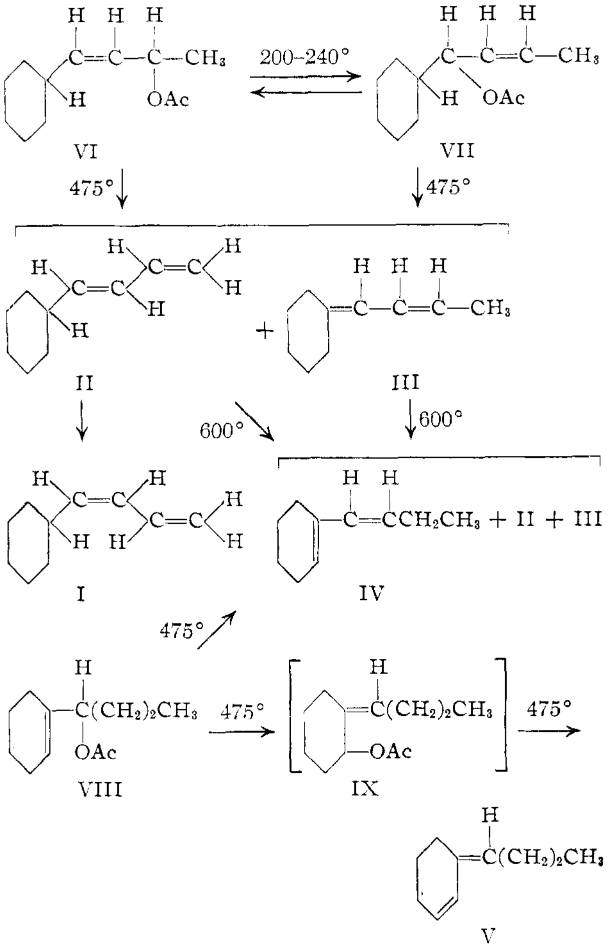
[4] C. S. Marvel and N. O. Brace, *ibid.*, **70**, 3842 (1948).

[5] C. S. Marvel and J. L. R. Williams, *ibid.*, **70**, 3842 (1948).

[6] K. Hess and W. Wustrow, *Ann.*, **437**, 256 (1924).

[7] C. K. Ingold, "Structure and Mechanism of Organic Chemistry," Cornell University Press, Ithaca, N. Y. 1953, pp. 586–601.

CHART 1



When VII was pyrolyzed at 475–480° and the recovered acetates recycled three times, II and III were obtained in yields of 40 and 11–12%, respectively. Recovered acetate consisted of about 70% of VI and 30% of VII, which again shows the greater stability of acetate VI. The isomeric acetate VI gave the same yield of II on pyrolysis.[3]

The 4:1 ratio of II to III in the pyrolysate might be due to a faster rate of formation of II from VI. This elimination removes a primary β-hydrogen, whereas the formation of III from VII removes a tertiary β-hydrogen. The decomposition of acetates to olefins may proceed by a polar mechanism, in which there is intramolecular hydrogen bonding, transfer of a proton and heterolytic splitting of the carbon–oxygen bond in the acetate group,[8-10] or by a free radical mechanism.[11,12] There is no steric hindrance in VI and VII to the formation of the hydrogen-bonded ring, according to molecular models. The energy required for homolytic splitting of carbon–hydrogen bonds is less for a tertiary than for a primary hydrogen. Preferential elimination of a tertiary hydrogen has been observed.[11-13] The behavior of the VI and VII acetates does not favor either mechanism.

The structure of 1-cyclohexyl-1,3-butadiene (II) was elucidated by degradation of its maleic anhydride adduct to diphenyl[3] and by oxidative decomposition of the ozonide to cyclohexanecarboxylic acid. The *trans* configuration was assigned to II on the basis of quantitative addition of maleic anhydride and the formation of a cyclic sulfone.[3] When II was further purified by treatment with silica gel, the physical properties did not change

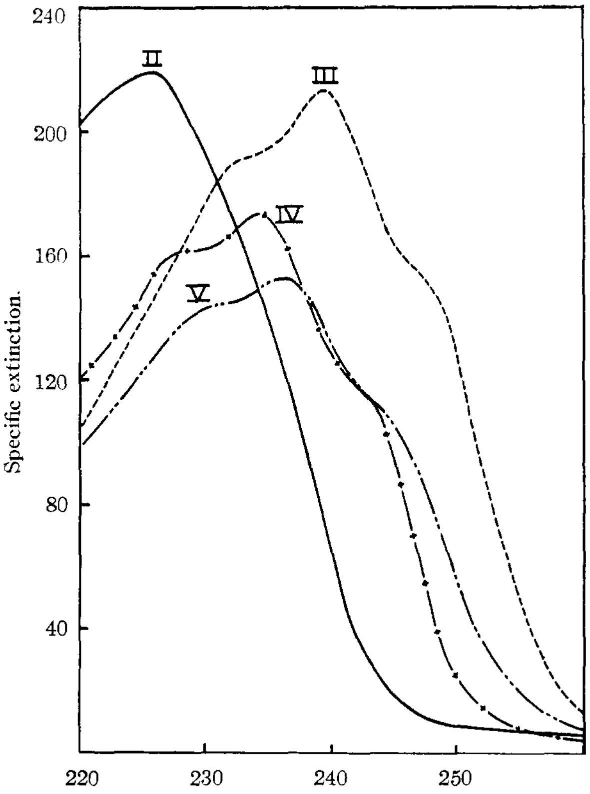


Fig. 1.—Ultraviolet absorption of II, III, IV and V: II, ——; III, - - -; IV, —+—; V, — - - —.

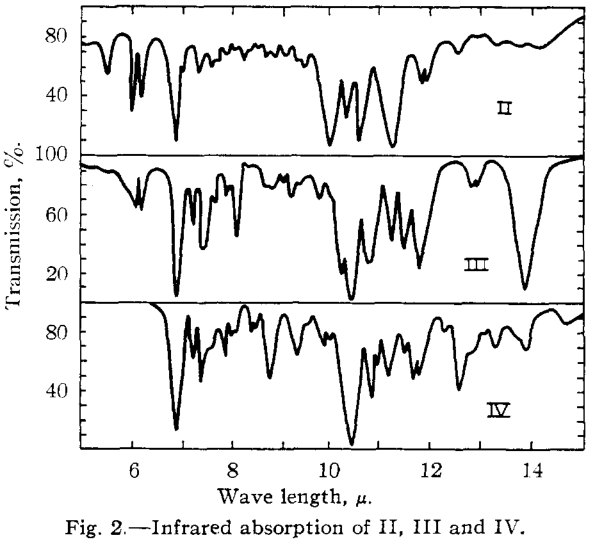


Fig. 2.—Infrared absorption of II, III and IV.

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(8) C. D. Hurd and F. H. Blunck, THIS JOURNAL, **60**, 2419 (1938).

(9) W. J. Bailey and C. King, *ibid.*, **77**, 75 (1955).

(10) J. P. W. Houtman, J. van Steenis and P. M. Heertjes, *Rec. trav. chim.*, **65**, 781 (1946).

(11) D. H. R. Barton, *J. Chem. Soc.*, 2174 (1949).

(12) W. Hückel, W. Tappe and G. Legutke, *Ann.*, **543**, 191 (1940).

(13) A. J. van Pelt and J. P. Wibaut, *Rec. trav. chim.*, **60**, 55 (1941).

TABLE II

PROPERTIES OF THE ISOMERIC $C_{10}H_{16}$ HYDROCARBONS

	II	III[3]	III[c]	IV[d]	IV[e]	V[d]
Distn. temp.	64° (8 mm.)	59° (4 mm.)	75° (8 mm.)	76° (8 mm.)	76° (8 mm.)	68° (8 mm.)
$n^{20}D$	1.4925	1.5105	1.5145	1.5030	1.5035	1.4973
d^{20}_4	0.8346	0.8554	0.8559	0.8538	....	0.8471
Ultraviolet absorption						
wave length (mμ) at max.	226	239	239	234	234	236
mol. extinction	29,900[b]	27,700	29,100	23,700	23,700	20,800
Diene content, %[a,14]	95.5	10	1	96	....	9.4

[a] By reaction with maleic anhydride at room temperature for 4 days. [b] In 95% ethanol. [c] Made from acetate VII. [d] Made from acetate VIII. [e] Made by isomerization of II.

(Table II, Figs. 1, 2) and only a trace of III was detected.

1-Cyclohexylidene-2-butene (III) was obtained in greater purity than reported earlier[3] (Table II, Figs. 1, 2). The 10% diene content of impure III was probably II. The structure of III was based on its unreactivity with maleic anhydride, which is typical of conjugated dienes containing a semicyclic double bond,[14,15] and the position of maximum absorption in the ultraviolet[3]: calcd., 237 mμ,[16] found, 239 mμ. Ozonolysis of III with oxidative decomposition gave the expected acetic acid but cyclohexanone could not be isolated. When the ozonide was decomposed reductively,[17] no products could be identified. Oxidation of III with aqueous potassium permanganate gave acetic acid and cyclohexanone, which confirms the 1-cyclohexylidene-2-butene structure. The tetrabromide, nitrosochloride and nitrosite addition compounds of III were oils. III coupled with 2,4-dinitrobenzenediazonium chloride gave a solid, $C_{22}H_{20}N_8O_8$, which decomposed on heating. The structure of the latter was not investigated but it is noteworthy that azo derivatives of other dienes contain only one azo group.[18-20]

1-Cyclohexylidene-2-butene (III) may have a *cis* or *trans* configuration. The narrow distillation range and homogeneity of chromatographed samples indicate that III is largely one form. Although the starting compound in the preparation of III was crotonaldehyde, a *trans* isomer,[21] the high temperature (475°) of pyrolysis might give some *cis*-III. Ultraviolet absorption (Fig. 1) points to the *trans* form, because the specific extinction is high (almost equal to that of II), and *cis*-dienes generally show a much lower extinction.[22]

The formation of *cis*-1-cyclohexyl-1,3-butadiene (I) by isomerization of the *trans* isomer II was tried. It is known that dilute solutions of *cis*- or *trans*-1-phenyl-1,3-butadiene exposed to sunlight or to ultraviolet light give a mixture of geometric isomers.[23] Similar irradiation of II in alcohol or cyclohexane, quartz or Pyrex flasks, decreased its ultraviolet absorption but did not shift the maximum wave length. Higher reaction temperatures enhanced the decrease in absorption. Separation of these products gave only unchanged II and polymer. Polymerization was the cause of the decreasing absorption.

The failure of II to isomerize photochemically might be due to a very low quantum efficiency compared to the polymerization reaction. *trans*-Piperylene is not isomerized at ordinary temperatures by ultraviolet light.[24] Photochemical reactions of compounds without phenyl group absorption (or that of several conjugated double bonds), may occur only at very short wave lengths.[25] Shorter wave lengths, however, more likely cause polymerization than isomerization, *e.g.*, the case of 1-phenyl-1,3-butadiene.[26]

With iodine added to the photochemical reaction of II, only decomposition and polymerization occurred. II did not change after 40 hours in refluxing alcoholic iodine solution. Heating at 150–170° for 24 hours gave a product of wide boiling range and altered ultraviolet absorption. About 85% of II and 15% of III–IV were present, as estimated by comparison of the ultraviolet absorption with that of known mixtures of II, III and IV (1-(1-cyclohexenyl)-1-butene).

Thermal isomerization of II to I was tried by heating the vapor of II at 600°. Distillation and separation on silica gel showed 60–65% of II, 21–24% of III and 14–16% of IV.

The structure of IV was elucidated by degradation of the maleic anhydride adduct[27] to 2-ethylnaphthalene. The adduct then is 6-ethyl-3,4-tetramethylene-1,2,3,6-tetrahydro-*o*-phthalic anhydride. Because oxidation of IV by potassium permanganate gave equivocal results, IV was prepared independently. The most suitable inter-

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[14] B. A. Ellis and R. A. Jones, *Analyst*, **61**, 812 (1936).

[15] K. Alder, "Newer Methods of Preparative Organic Chemistry," Interscience Publishing Co., New York, N. Y., 1948, p. 381.

[16] R. B. Woodward, THIS JOURNAL, **64**, 72 (1942).

[17] C. R. Noller and R. Adams, *ibid.*, **48**, 1074 (1926).

[18] G. B. Bachman and R. E. Hatton, *ibid.*, **66**, 1513 (1944).

[19] L. F. Fieser and W. P. Campbell, *ibid.*, **60**, 168 (1938).

[20] K. H. Meyer, *Ber.*, **52**, 1330 (1920).

[21] W. G. Young, THIS JOURNAL, **54**, 2498 (1932).

[22] L. N. Ferguson, *Chem. Revs.*, **43**, 385 (1948).

[23] O. Grummitt and F. J. Christoph, THIS JOURNAL, **73**, 3479 (1951).

[24] R. L. Frank, R. D. Emmick and R. S. Johnson, *ibid.*, **69**, 2313 (1947). At reflux temperatures (41–44°) ultraviolet light affects the course of isomerization (N. I. Shuikin and V. A. Tolupon, *Vestnik Moskow Univ.*, **9**, No. 8, *Ser. Fiz-Mat. i Estestven, Nauk No.* **5**, 91 (1954); *C. A.*, **49**, 3776 (1955)). Refluxing *cis*-piperylene in quartz under ultraviolet light from a quartz mercury lamp for 12–24 hr. gave 73% *cis*, 27% *trans*, according to refractive index. Frank, *et al.*, heated *cis*- or *trans*-piperylene at 50° in the presence of iodine and obtained 87% *trans*, 13% *cis*. In the presence of 5% of precipitated silver and ultraviolet light for 12–28 hr., Shuikin, *et al.*, found 43–49% *cis* and 57–51% *trans* from either pure *cis* or 17% *cis*–83% *trans*. In the dark but with silver *cis*-piperylene was unchanged after 24 hours of reflux.

[25] W. A. Noyes, Jr., and V. Boekelheide in "Technique of Organic Chemistry," Vol. II, Interscience Publishers, Inc., New York, N. Y., 1948, p. 117.

[26] F. J. Christoph, Ph.D. Thesis, Western Reserve University, 1949.

[27] M. S. Newman and H. V. Zahn, THIS JOURNAL, **65**, 1097 (1943).

mediate, 1-(1-cyclohexenyl)-1-acetoxybutane (VIII), should yield IV on pyrolysis (Chart 1). However, VIII might rearrange to 1-(α-acetoxycyclohexylidene)-butane (IX), which would decompose to 1-butylidene-2-cyclohexene (V), but IX has a semi-cyclic double bond and is therefore less stable than VIII (*v.i.*).

1-(1-Cyclohexenyl)-1-butanone (X), prepared from cyclohexene, *n*-butyryl chloride and aluminum chloride,[28,29] had maximum ultraviolet absorption at 235 mμ (in alcohol), 227.5 mμ (in isoöctane) and a molecular extinction of 10,000, which confirms the α,β-unsaturated carbonyl structure.[30–32] X was reduced[33] to 1-(1-cyclohexenyl)-1-butanol (XI). This was acetylated[5] to VIII and the structures of XI and VIII were checked by hydrogenation to 1-cyclohexyl-1-butanol and 1-cyclohexyl-1-acetoxybutane (XII), respectively, and comparison of the infrared spectra with that of authentic samples.

Pyrolysis of VIII at 475° gave IV and 1-butylidene-2-cyclohexene (V) which were separated by distillation and adsorption. This IV closely resembled IV made by thermal isomerization of II (Table II). The 96% reaction with maleic anhydride[14] indicated IV had the *trans* configuration.[23,34] The absorption maximum at 234 mμ agreed with the calculated value of 232 mμ (Fig. 1).[16]

1-Butylidene-2-cyclohexene (V) (Table II, Figs. 1, 2) the second pyrolysis product of VIII, probably formed *via* allylic rearrangement of VIII to IX. The absorption maximum of V at 236, 237 mμ calculated,[15] eliminates a conjugated cyclohexadiene structure which would absorb at 255–290 mμ. The 9% reaction with maleic anhydride indicated the presence of another compound(s) because the fixed *trans*-butadienoid configuration of V prevents addition.[15] IV was detected by isolation of its maleic anhydride adduct.

The identical carbon skeletons of the $C_{10}H_{16}$ hydrocarbons, II–V, was established by catalytic hydrogenation to 1-cyclohexylbutane. Physical constants and infrared absorption of the four hydrogenation products were identical.

The relative stabilities of I–IV were estimated from heats of hydrogenation. Calculated values for a I–II mixture and IV were obtained from reference olefins.[35] The value for III was calculated by adding 3.7 kcal. to the heat of hydrogenation of the corresponding endocyclic compound[36] (Table III).

Resonance due to conjugation would reduce the actual heats of hydrogenation below the calculated values. On the assumption that the resonance energies for I–IV are equal, 1-(1-cyclohexenyl)-1-butene (IV) is most stable, 1-cyclohexylidene-2-butene (III) is least stable and 1-cyclohexyl-1,3-butadiene is slightly more stable than III.

TABLE III

CALCULATED HEATS OF HYDROGENATION

$C_{10}H_{16}$ Isomer	Calcd. heat of hydrogenation, kcal./mole	Reference compounds
1-Cyclohexyl-1,3-butadiene (I and II)	58.3	1-Butene 2-Pentene
1-Cyclohexylidene-2-butene (III)	58.9	Trimethylethylene 2-Pentene (3.7 kcal.)
1-(1-Cyclohexenyl)-1-butene (IV)	55.2	Trimethylethylene 2-Pentene

The reaction time in the thermal isomerization of II to III and IV, about 0.5 second, was probably too short to give an equilibrium mixture. However, the proportion of III was greater than expected on the basis of its relative stability, which suggests that it was the primary isomerization product. When pure III was thermally isomerized under the same conditions, the product contained 45% of unchanged III, 45% of IV and 10% of II.

cis-1-Cyclohexyl-1,3-butadiene (I) was an expected isomerization product, because the relative stabilities of III and I–II differ only slightly. The absence of I must be due to its lower stability.

Because *cis*- and *trans*-1-phenyl-1,3-butadienes could be prepared under conditions which were unsuccessful for I and II, significant differences must exist here between the cyclohexyl and phenyl groups. The cyclohexyl group is multiplanar and about 20% larger[37] than the coplanar phenyl group. Examination of Fisher–Hirschfelder molecular models and the calculation[38] of distances between non-bonded atoms reveal that both *cis*- and *trans*-1-phenyl-1,3-butadiene are non-coplanar because of hindrance between the ring and side chain. In II, on the other hand, the butadiene chain can be in an unhindered planar state, but I always has steric hindrance between the hydrogen on the γ-carbon atom of the side chain and hydrogen atoms on the 1 or 2 and 6 carbon atoms of the ring. This resulting steric inhibition of resonance in the butadiene side chain of I may make a difference in stability between I and II of 2–8 kcal./mole.[39] If $-\Delta F$ in the I $\rightleftarrows$ II reaction equalled 5.5 kcal./mole, for example, the equilibrium mixture would contain only 0.01% of I ($-\Delta F = RT \ln K$). The stability difference is very probably smaller for the 1-phenyl-1,3-butadienes because there is inhibition of resonance in *both* isomers.

The preparation of I by partial reduction of an acetylenic intermediate will be attempted, as well as the preparation of *cis* and *trans* terminally substituted butadienes with hydrocarbon substituents of intermediate size between methyl and cyclohexyl.

Experimental

Distillations were done in a column of the total condensation, partial take-off type, 5 mm. inside diameter, fitted with a 90 cm. length of Monel metal spiral (Todd Scientific Co.).

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(28) R. E. Christ and R. C. Fuson, THIS JOURNAL, **59**, 893 (1937).

(29) G. Darzens and H. Rost, *Compt. rend.*, **151**, 758 (1910).

(30) H. Mohler, *Helv. Chim. Acta*, **20**, 289 (1937).

(31) G. Scheibe, G. Rossler and F. Backenkohler, *Ber.*, **58**, 586 (1925).

(32) R. B. Woodward, THIS JOURNAL, **63**, 1123 (1941).

(33) R. F. Nystrom and W. G. Brown, *ibid.*, **69**, 1197 (1947).

(34) D. Craig, *ibid.*, **65**, 1006 (1943).

(35) J. B. Conant and G. B. Kistiakowsky, *Chem. Revs.*, **20**, 181 (1937).

(36) W. A. Roth and K. von Auwers, "Landolt-Bornstein," Hauptw., Vol. II, p. 1591.

(37) The molecular volume (20°) of cyclohexane is 108.093 ml., of benzene, 88.857 ml. F. D. Rossini, *et al.*, "Selected Values of Properties of Hydrocarbons," National Bureau of Standards, Washington, D. C., 1947, p. 93.

(38) L. Pauling, "The Nature of the Chemical Bond," Cornell University Press, Ithaca, N. Y., 1939, pp. 84, 176.

(39) Reference 38, p. 202.

The column efficiency measured at 10 mm. pressure with *n*-decane–*trans*-decalin was 29 theoretical plates.[40]

Ultraviolet spectra were determined with a Beckman model DU quartz spectrophotometer, and infrared spectra with a Perkin-Elmer model 12-C IR spectrophotometer (rock salt blank).

Isomerization of Acetates VI and VII.—VI was made as before,[3] 42% yield. 1-Cyclohexyl-2-buten-1-ol[3] was made in 57% yield, b.p. 89–90.5° (4 mm.), $n^{20}\text{D}$ 1.4808; reported[6] 98–100° (13 mm.), $n^{16}\text{D}$ 1.47987. Acetylation with acetic anhydride and pyridine[5] gave 90% of VII, b.p. 100–101° (5 mm.), $n^{20}\text{D}$ 1.4628; reported[41] 87° (1 mm.), $n^{25}\text{D}$ 1.4607. Infrared spectral data for VI and VII are given in Table IV. Samples of VI and VII, 3–10 g., heated under nitrogen at 150 or 200° for 3–4.5 hours or distilled at 240–241°, were titrated for acetic acid, the organic layer was separated, dried and distilled. The composition as VI and VII was estimated by refractive index (Table I).

TABLE IV

INFRARED ABSORPTION OF ACETATES VI, VII AND XII

VI		VII		XII	
Wave length, μ	Trans-mission, %	Wave length, μ	Trans-mission, %	Wave length, μ	Trans-mission, %
5.80	3.5	5.80	3.5	5.75	4.5
6.95	5	6.95	5	6.90	7
7.35	3.5	7.35	3.5	7.30	4.5
7.70	41i[a]	7.78	26i		
8.12	1.5	8.12	1.5	8.00	4.5
		8.43	20.5	8.38	28.5
8.80	17.5			8.82	31.5
				8.91	31
9.15	33.5i	9.08	36.5i	9.14	23
		9.24	26	9.34	30i
		9.40	25	9.50	19
9.62	2.5	9.60	18		
9.87	10i	9.86	3	9.75	4.5
10.35	5	10.33	3	10.25	8
10.60	6	10.64	6	10.63	25
10.88	46i	11.05	43i	10.92	66i
11.25	49	11.30	29	11.12	62i
		11.41	30	11.20	49
		11.65	60i		
11.88	38.5	11.88	53	11.81	66
12.28	68	12.39	74.5	12.14	47

[a] i means inflection on a larger and stronger band.

Pyrolysis of Acetate VII.—VII (160 g., 0.817 mole) was distilled under nitrogen at 30 mm. pressure through a 20 mm. glass tube packed for 33 cm. with glass beads and heated electrically to 475–480°. The pyrolysate was collected in an ice-cooled receiver at 1 drop/3 seconds. The calculated contact time[42] was 0.6 second. Product boiling below 82° (4 mm.) was removed by distillation and the residue recycled. Repeating this operation twice gave 132.5 g. boiling below 82° (4 mm.) and 15.5 g. of residue. The crude product was washed with water, dried with potassium carbonate, and fractionally distilled under nitrogen at a reflux ratio of 25/1. *trans*-1-Cyclohexyl-1,3-butadiene (II), 41 g. (36.9%), was collected at 59.5–61.5° (7 mm.), $n^{20}\text{D}$ 1.4907–1.4925. 1-Cyclohexylidene-2-butene (III), 8 g. (7.2%), distilled at 72–73.5° (7 mm.), $n^{20}\text{D}$ 1.5140. The residue (20.5 g.) plus the 15.5 g. of high-boiling pyrolysate was distilled to give 28 g. (17.5%) of acetates, $n^{20}\text{D}$ 1.4610. Refractive index and infrared absorption indicated 30% of VII and 70% of VI.

***trans*-1-Cyclohexyl-1,3-butadiene (II).**—II obtained by pyrolysis of VII was redistilled at a reflux ratio of 50/1; the main fraction boiled at 64° (8 mm.), $n^{20}\text{D}$ 1.4925 (Table II). A solution of 20 g. of redistilled II in 100 ml. of Skellysolve A (28–38° boiling petroleum ether, Skelly Oil Co.) was passed through a 78 × 0.9 cm. column packed with activated silica gel (28–200 mesh, commercial grade, Davidson Chemical Corp.). The column was washed with 200 ml. of Skellysolve A, then with 50 ml. of anhydrous ether. Five fractions were collected and the recovery of II was 80%. The first four fractions had identical physical properties; the fifth consisted of II and about 2% of III.

Four grams (0.03 mole) of II in 60 ml. of methylene chloride was cooled in Dry Ice and ozonized (9% ozone in oxygen)[43] until the effluent gas oxidized starch–potassium iodide solution. The ozonized solution was allowed to warm to 20° and 13.6 g. of 30% hydrogen peroxide was added. After refluxing at 40° for two hours, the methylene chloride was evaporated and the residue heated on a steam-bath for 15 hours. Extraction with ether gave 2.5 g. (65%) of cyclohexanecarboxylic acid. The anilide[44] melted at 139–141°; an authentic sample melted 144°; the mixed m.p. was 141–143°.

1-Cyclohexylidene-2-butene (III).—III from the pyrolysis of VII was redistilled at a reflux ratio of 50/1 to give a main fraction at 75° (8 mm.) (Table II).

Anal. Calcd. for $C_{10}H_{16}$: C, 88.16; H, 11.84. Found: C, 88.13; H, 11.93.

III (4 g., 0.03 mole) was ozonized and cleaved as for II. The crude product, neutralized with sodium carbonate and distilled, gave no test in the distillate or solid residue for ketones with 2,4-dinitrophenylhydrazine.[45] The residue mixed with 15 ml. of 85% phosphoric acid was distilled to give 0.0186 equivalent (62% of theory) of acetic acid; the *p*-nitrobenzyl ester melted 71–73.5°. A mixed m.p. with authentic *p*-nitrobenzyl acetate showed no depression.

III (5 g., 0.037 mole) in 100 ml. of dry acetic acid was ozonized and decomposed reductively with zinc dust and water.[17] The ether extract of the reaction mixture added to saturated sodium bisulfite solution did not give the bisulfite adduct of cyclohexanone after 12 hours of stirring. The ether layer was separated, dried with potassium carbonate and distilled. A few drops boiled at 68° (80 mm.); the residue was 4 g. The distillate gave a test for ketones with 2,4-dinitrophenylhydrazine and for esters with hydroxylamine.[45]

To a suspension of 2.7 g. (0.02 mole) of III in 100 ml. of ice-water was added slowly with stirring a 3% aqueous solution of 14.7 g. of potassium permanganate. After filtering, the filtrate was continuously extracted with ether. The residue from the evaporated ether with 2,4-dinitrophenylhydrazine[45] gave 0.36 g. (13%) of cyclohexanone 2,4-dinitrophenylhydrazone, melting 159–161°. A mixed m.p. with an authentic sample gave no depression. The residue from the distillation and the aqueous layer from the ether extraction were combined, concentrated, acidified with hydrochloric acid and then continuously extracted with ether. The 80–104° fraction of the distilled extract contained 0.015 equivalent (75% yield) of acetic acid, as determined by the *p*-nitrobenzyl acetate derivative and titration.

Addition Compounds of III.—A solution of 0.77 g. (0.00565 mole) of III in 8 ml. of 1/1 ethanol–ether was cooled to −34° and a solution of bromine in ethanol–ether (2.7 *N*) was added until the bromine color persisted. The absorption of bromine was 83% of the amount calculated for two double bonds. Evaporating the solvent and cooling the oily residue in Dry Ice, gave no crystals in two months. At room temperature the oil evolved hydrogen bromide.

The nitrosochloride and nitrosite of III[46] were dark brown oils which could not be crystallized.

To 1.2 g. of diazotized 2,4-dinitroaniline solution was added 1.36 g. (0.01 mole) of III.[18] The greenish-yellow solid was separated, dissolved in ethyl acetate, precipitated by addition of Skellysolve B to give 0.2 g. of finely divided greenish-yellow solid which darkened on heating and decomposed at 170°.

Anal. Calcd. for $C_{16}H_{18}N_4O_4$: N, 16.96; for $C_{22}H_{20}N_8O_8$: N, 21.36. Found: N, 21.04.

Photochemical Isomerizations of *trans*-1-Cyclohexyl-1,3-butadiene (II).—Dilute solutions of II (4–8 mg./liter) in

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(42) C. D. Hurd and H. T. Bollman, THIS JOURNAL, **55**, 699 (1933).

(43) A. L. Henne, *ibid.*, **51**, 2676 (1929); A. L. Henne and W. L. Perilstein, *ibid.*, **65**, 2183 (1943).

(44) J. S. Lumsden, *J. Chem. Soc.*, 92 (1905).

(45) N. D. Cheronis and J. B. Entrikin, "Semimicro Qualitative Organic Analysis," Thos. Y. Crowell Co., New York, N. Y., 1947, pp. 121–122

(46) W. J. Hickinbottom, "Reactions of Organic Compounds," 2nd edition, Longmans, London, 1948, p. 27.

95% ethanol or cyclohexane (Phillips Spectro Grade) in quartz and Pyrex flasks were exposed to summer sunshine. No change in the ultraviolet absorption of the solutions was noted after one hour. Irradiation with ultraviolet light (Hanovia SH lamp) of the alcohol solutions at 50–55° decreased their ultraviolet absorption. Similar results were obtained when solutions of II in cyclohexane (stirred by a magnetic stirrer), held at 27–32° by a stream of cold air on the flask, were exposed to the ultraviolet lamp.

On a larger scale, 5 g. (0.037 mole) of II in 95 ml. of alcohol in a quartz flask was irradiated with the ultraviolet lamp at 10 cm. from the flask while the solution temperature was kept at 31–36°. After 150 hours the solution was added to 150 ml. of water, extracted with Skellysolve A, and the extract dried (calcium chloride) and distilled under nitrogen to give 1 g. (20% recovery) of II and 2.8 g. of viscous polymer. Additional polymer remained on the walls of the flask.

The presence of iodine in these solutions did not alter the results. Alcoholic solutions of II (1–5%) containing 1% of iodine with respect to II were exposed in Pyrex to sunlight. The iodine color disappeared in 15 minutes and 1% of iodine was added. After 3 hours there was no change in the ultraviolet absorption of the solutions. The solutions were irradiated at room temperature with tungsten bulbs (700 watts). After 20 hours, half of the solution was added to water, shaken with sodium thiosulfate until the iodine color disappeared and extracted with Skellysolve A. The extract, dried and distilled under nitrogen, gave only II. The remainder of the alcoholic solution was irradiated for 70 hours more while the iodine content was gradually raised to 16%. The product was dark, non-volatile and contained iodine.[47]

Thermal Isomerizations of II.—A solution of 10 g. (0.073 mole) of II, 0.5 g. of picric acid, 0.1 g. of iodine and 100 ml. of alcohol was refluxed for 40 hours. After removal of the iodine with aqueous sodium thiosulfate, 6.5 g. (65%) of unchanged II was recovered by distillation.

A solution of 4.2 g. (0.031 mole) of II, 0.4 g. of picric acid, 0.04 g. of iodine and 38 ml. of Skellysolve A was heated in a 110-ml. stainless steel bomb (American Instrument Co.) at 150–170° for 24 hours. After treatment with sodium thiosulfate, etc., distillation under nitrogen gave three fractions, 0.3, 1.2 and 0.8 g., boiling up to 62° (7 mm.), n^{20}_{D} 1.4915–1.4980. Ultraviolet absorption spectra of the distillates indicated about 85% of II and 15% of a mixture of III and IV.

II (70 g., 0.514 mole) was distilled at 40 mm. nitrogen pressure through a Pyrex tube 20 mm. i.d. and 33 cm. long, packed with glass beads and heated at 600–602°. The contact time was 0.5 second. Fractionally distilling the crude product (65 g.) under nitrogen at a reflux ratio of 50/1 gave six fractions (2.5, 16.7, 14.7, 14.7, 4.2 and 13.7 g.) boiling up to 73.2° (7 mm.), n^{20}_{D} 1.4924–1.5103. The yield of isomerization products was 83%.

A mixture of 11.5 g. (0.085 mole) of fraction 6 (73.2° (7 mm.), n^{20}_{D} 1.5100) and 3.6 g. (0.037 mole) of maleic anhydride was heated on a steam-bath for 5 minutes, cooled at 0° overnight, and diluted with Skellysolve A to precipitate the product. This was filtered, washed with water and crystallized from Skellysolve B, 2.8 g. (28%), m.p. 61.0–61.5°. This adduct forms from 1-(1-cyclohexenyl)-1-butene (IV) (*vide infra*).

Anal. Calcd. for $C_{14}H_{18}O_3$: C, 71.77; H, 7.74. Found: C, 71.50; H, 7.95.

The filtrate was washed well with water, dried and distilled under nitrogen to give 6.7 g. (58% recovery), n^{20}_{D} 1.511. This was allowed to stand with maleic anhydride at 0° for 28 days to remove all maleic anhydride-reactive material. Distilling the filtrate from this mixture gave 2.3 g. at 75° (8 mm.), n^{20}_{D} 1.5128. Ultraviolet absorption showed 1-cyclohexylidene-2-butene (III).

Fifty grams (0.367 mole, n^{20}_{D} 1.5098) of distillate similar to fraction 6 was dissolved in 250 ml. of Skellysolve A and passed through a 35 × 3.5 cm. column of activated silica gel. The column was washed with Skellysolve A until no more product was being removed. Ten fractions were collected, each was passed through a 78 × 0.9 cm. column of silica gel and the separation measured by ultraviolet spectra. Fractions with similar spectra were combined and rechromatographed. After 25 passes, 11 g. (22%) of the less strongly adsorbed component was obtained. This distilled under nitrogen to give 7.6 g. (15%) at 76–77° (8 mm.), n^{20}_{D} 1.5034, and 3 g. of viscous residue. The maleic anhydride adduct of the distillate melted 61.0–61.5° and gave no depression when mixed with the adduct described above. This distillate is 1-(1-cyclohexenyl)-1-butene (IV). The more strongly adsorbed material was distilled to give 21 g. (42%) of III contaminated with IV.

Thermal Isomerization of III.—Fifteen grams (0.11 mole) of III was distilled at 40 mm. pressure through the apparatus used to isomerize II. Temperature was 600–602°, contact time 0.6 second. Distilling the crude product (12.5 g.) at a reflux ratio of 50/1 gave four fractions (2.5, 1.7, 2.1 and 5.2 g., 76.5% yield) boiling up to 74° (8 mm.), n^{20}_{D} 1.4978–1.5088. The over-all composition based on refractive index and ultraviolet absorption was 45% of III, 10% of II and 45% of IV.

1-Cyclohexenyl-1-butene (IV).—IV obtained by thermal isomerization of II (fraction 6) was oxidized with potassium permanganate (*vide supra*). IV (2.7 g., 0.02 mole) gave 0.5 g. (3%) of cyclohexanone 2,4-dinitrophenylhydrazone and 0.0275 equivalent of acids distilling up to 146°. The *p*-bromophenacyl and *p*-nitrobenzyl derivatives[47] of the acids had wide melting ranges and could not be purified.

The maleic anhydride adduct of IV, m.p. 61.0–61.5° (*vide supra*), was degraded[27] to 2-ethylnaphthalene. In a 50-ml. Claisen flask with a cold-finger condenser in the bent tube was placed 0.3 g. of 10% palladium-on-charcoal and 1 g. of adduct. A 50-ml. distilling flask was used as the receiver and the side arm of this flask led to a gas buret. With nitrogen passing through the mixture was heated to 200° (oil-bath), the nitrogen inlet was removed, a thermometer was placed in the reaction mixture, which was then gradually heated to 320°. When the gas evolution stopped, the mixture was cooled to 150° and distilled at 130 mm. The distillate (0.3 g.) was dissolved in 5 ml. of methanol and mixed with 10 ml. of a saturated methanolic solution of picric acid. The picrate, 0.1 g. (7%), melted at 75–76°, reported[48] 76–77°. A mixed melting point with authentic 2-ethylnaphthalene picrate showed no depression.

IV was synthesized independently. 1-(1-Cyclohexenyl)-1-butanone (X) was made by a modification of the method of Darzens and Rost.[28,29] A mixture of 140 g. (1.71 moles) of cyclohexene, 175 g. (1.65 moles) of *n*-butyryl chloride and 800 g. of carbon disulfide was placed in a 2-l. three-necked flask, fitted with a stirrer, reflux condenser and inlet for aluminum chloride. The mixture was cooled to 0°, 200 g. (1.65 moles) of anhydrous aluminum chloride was added, the ice-bath was removed and the mixture stirred for two more hours. After cooling, hydrolyzing with 600 ml. of 5% hydrochloric acid, the carbon disulfide layer was separated, washed with water, dried with calcium chloride and distilled. From the crude product (154 g.), distilled under nitrogen at a reflux ratio of 10/1, the main fraction (112.5 g.) boiled 99–102° (10 mm.), n^{14}_{D} 1.486. The residue distilled from sodium carbonate gave an additional 16 g., 54.5% yield, n^{14}_{D} 1.486. X thus obtained was yellow and irritating in odor. Refluxing with dimethylaniline and distilling from potassium acid sulfate failed to purify it. The semicarbazone was prepared from 39 g. (0.257 mole) of X, 28.7 g. (0.257 mole) of semicarbazide hydrochloride and 43 g. (0.525 mole) of sodium acetate. Two crystallizations from aqueous ethanol and two from methanol gave 29 g. (54%) of semicarbazone, m.p. 169–71°, reported[29] 171°. This was hydrolyzed by adding 500 ml. of 5% sulfuric acid and steam distilling. Separation of the distillate and ether extraction, drying (calcium chloride) and distilling under nitrogen gave: 18.5 g. (47% recovery) of X, 91.5–93.5° (7 mm.), n^{14}_{D} 1.4875, n^{20}_{D} 1.4847; reported[29] 113–114° (7 mm.), also[49] 100–102° (8 mm.), n^{14}_{D} 1.4885. Ultraviolet absorption of X was determined on ethanol (95%) and isooctane solutions.

1-(1-Cyclohexenyl)-1-butanol (XI) was prepared by reduction of X.[33] From 2.85 g. (0.075 mole) of lithium aluminum hydride in 120 ml. of anhydrous ether and 18.5 g. (0.122 mole) of X in 30 ml. of ether there was obtained 15.3 g. (81.5%) of XI, b.p. 86.5–87.5° (1.5 mm.), n^{20}_{D} 1.4792.

Anal. Calcd. for $C_{10}H_{18}O$: C, 77.87; H, 11.76. Found: C, 77.87; H, 11.62.

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[47] R. L. Shriner and R. C. Fuson, "Identification of Organic Compounds," 3rd ed., John Wiley and Sons, Inc., New York, N. Y., 1948, p. 55.

[48] G. Levy, *Compt. rend.*, **192**, 1397 (1931).

[49] J. Colonge and E. Duroux, *Bull. soc. chim.*, **7**, 459 (1940).

XI was hydrogenated with platinum oxide catalyst at 30 pounds pressure to 1-cyclohexyl-1-butanol, b.p. 80–81° (3 mm.), $n^{20}\mathrm{D}$ 1.4655; reported[50] 115° (40 mm.), $n^{20}\mathrm{D}$ 1.4652. Infrared absorption of this was identical with that of 1-cyclohexyl-1-butanol made by hydrogenation of 1-cyclohexyl-2-buten-1-ol.

From 33.5 g. (0.217 mole) of XI and 52 ml. (0.575 mole) of acetic anhydride there was obtained 33 g. (77.5%) of 1-(1-cyclohexenyl)-1-acetoxybutane (VIII), b.p. 78–79° (1 mm.), $n^{20}\mathrm{D}$ 1.4602.

Anal. Calcd. for $C_{12}H_{20}O_2$: C, 73.43; H, 10.27. Found: C, 73.54; H, 10.21.

Catalytic hydrogenation of VIII (as for XI) gave 1-cyclohexyl-1-acetoxybutane (XII), b.p. 85–86.5° (2 mm.), $n^{20}\mathrm{D}$ 1.4494. Infrared absorption of XII (Table IV) was identical with XII made from 1-cyclohexyl-1-butanol and acetic anhydride.

Anal. Calcd. for VIII, $C_{12}H_{22}O_2$: C, 72.68; H, 11.18. Found: C, 72.97; H, 11.12.

When 40 g. of VIII was pyrolyzed at 475° as described above, 35 g. of pyrolysate was collected. Washing with water, drying with sodium carbonate and fractionally distilling under nitrogen at a reflux ratio of 120/1 gave 16.4 g. (59%) in three fractions. Fraction 1 consisted of 3.7 g. (13.3%) of 1-butylidene-2-cyclohexene (V) distilling at 63–66° (7 mm.), $n^{20}\mathrm{D}$ 1.4961. Fraction 3 (5.3 g., 19%) was 1-(1-cyclohexenyl)-1-butene (IV) 73° (7 mm.), $n^{20}\mathrm{D}$ 1.5028. Fraction 2, 7.4 g., was a mixture of IV and V.

Fraction 3 in 70 ml. of Skellysolve A was passed through an 18 × 1.8 cm. column of activated silica gel, followed by 100 ml. of solvent. Distillation of the solution gave IV, 3.7 g. (70% recovery), b.p. 76° (8 mm.), $n^{20}\mathrm{D}$ 1.5030, $d^{20}{}_4$ 0.8538 (Table II). The maleic anhydride adduct melted at 61.0–61.5°, and there was no depression in a mixed m.p. with the adduct of IV from the thermal isomerization of II.

Anal. Calcd. for IV, $C_{10}H_{16}$: C, 88.16; H, 11.84. Found: C, 88.48; H, 11.60.

Chromatography of fraction 1 gave 2 g. (54% recovery) of 1-butylidene-2-cyclohexene (V), b.p. 68° (8 mm.), $n^{20}\mathrm{D}$ 1.4973, $d^{20}{}_4$ 0.8471 (Table II). The maleic anhydride determination showed 8.5–9.4% reaction.

Anal. Calcd. for V, $C_{10}H_{16}$: C, 88.16; H, 11.84. Found: C, 87.96; H, 12.04.

Catalytic Hydrogenation of II-V.—A sample of each diene (2–4 g.) in 25 ml. of absolute methanol with 0.1 g. of 10% palladium-on-charcoal catalyst was hydrogenated at about 30 pounds pressure. The catalyst was filtered, the product extracted with Skellysolve A, the extract then washed with concentrated sulfuric acid, dried and distilled. Each product distilled at 178–180°, $n^{20}\mathrm{D}$ 1.4415–1.4430; reported[51] for 1-cyclohexylbutane, b.p. 180.5°, $n^{20}\mathrm{D}$ 1.4410. The infrared spectra of the four products were identical and similar to the A.P.I. spectrogram of 1-cyclohexylbutane.

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[CONTRIBUTION FROM THE WELLCOME RESEARCH LABORATORIES]

Phenylcyclohexylcarbinols with Antispasmodic Activity[1]

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RECEIVED JULY 27, 1955

New methods of preparation of the antispasmodics (I) proceed *via* the product of a Reformatski reaction of phenyl cyclohexyl ketone. One route involves conversion of the Reformatski ester IV *via* its methylamide to the methylamine Va, and simultaneous alkylation-cyclization of that with 1,4-dibromobutane to II. Other routes go through reduction of IV to the glycol VI and reaction of VI 1-tosylate with secondary and tertiary amines. Some limitations and advantages of these routes are discussed, as well as exploratory attempts to make compounds related to I from phenylcyclohexylethinylcarbinol.

Among the compounds with the formula I are a number which have shown high atropine-like antispasmodic activity in laboratory tests by the acetylcholine-stimulated guinea pig ileum method. The compound II, in particular, is used clinically under the generic name tricyclamol,[2] by which it will be referred to below. The methods previously reported for the preparation of the compounds I have involved quaternization of the corresponding phenylcyclohexyldialkylaminoethylcarbinols, III. These amines have been prepared either by the action of a cyclohexyl Grignard reagent on the Mannich base prepared from acetophenone, formaldehyde and a secondary amine,[3] or by partial reduction of the diphenyldialkylaminoethylcarbinols[4] (III, for C_6H_{11} put C_6H_5). Since the Mannich reaction is limited notably with respect to the amine and aldehyde components, and the partial reduction would be expected to be limited especially by steric factors, synthetic procedures were sought which might be broader in scope or more readily applicable.

The methods reported here go by way of the product IVa and b[5] of a Reformatski reaction on phenyl cyclohexyl ketone, the ketone being best prepared by the Friedel–Crafts reaction of cyclohexanoyl chloride and benzene. The Reformatski reaction went readily in excellent yield with ethyl bromoacetate or ethyl α-bromopropionate, provided that moisture was excluded rigorously. The two synthetic schemes using the esters IV are illustrated in the chart.

When the ester IVa[5] was treated with two equivalents of methylamine in methanol, a quantitative uptake of amine was found by titration, and an excellent yield of recrystallized amide could be obtained readily. This gave only a fair yield of secondary amine V when it was heated with ethereal lithium aluminum hydride solution for 5.5 hours under reflux, but substantially all of the unreduced amide could be recovered. When the reflux time was increased to 41 hours an 85% yield of analytically pure amine was isolated as hydrochloride.

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(1) Presented in part before the Division of Organic Chemistry, American Chemical Society, at New York, N. Y., Sept., 1954.

(2) Tricylamol is sold by Burroughs Wellcome & Co. (U.S.A.) Inc. under the trademark Tricoloid.

(3) J. J. Denton and V. A. Lawson, THIS JOURNAL, **72**, 3279 (1950); A. W. Ruddy and J. S. Buckley, Jr., *ibid.*, **72**, 718 (1950), and references given in these.

(4) D. W. Adamson, P. A. Barrett and S. Wilkinson, *J. Chem. Soc.*, 52 (1951).

(5) The final "a" in compounds numbered in this paper indicates that the compounds so numbered bear two hydrogens on the center carbon of the straight chain, *e.g.*, in IVa, Z = H. The "b" series have one methyl group on the same carbon, *e.g.*, IVb, where Z = CH_3.