Synthesis and Hydrogenation of the 3,4,5-Trimethylcyclohexenes[1]

BAHRAM H. MAHMOUD[2] AND KENNETH W. GREENLEE

Department of Chemistry, The Ohio State University, Columbus 10, Ohio

Received June 26, 1961

The four 3,4,5-trimethylcyclohexenes were prepared in high purity and identified by their stereospecific genesis as well as by reference to their hydrogenation products, the three 1,2,3-trimethylcyclohexanes, which also were obtained pure.

A mixture of 3,4,5-trimethylcyclohexenes obtained by the Wolff-Kishner reduction of the Diels-Alder adduct of 1,*trans*-3-pentadiene and crotonaldehyde has been reported[3] as having two components, III and IV. Re-examination by gas-liquid chromatography revealed four, equal to the number of possible isomers, prompting the present work in which they were all synthesized and characterized (Table I). Upon hydrogenation, pure 3,*cis*-4,*cis*-5-trimethylcyclohexene (I) yielded pure 1,*cis*-2,*cis*-3-trimethylcyclohexane (V). Both 3,*trans*-4,*trans*-5-trimethylcyclohexene (II) and 3,*cis*-4,*trans*-5-trimethylcyclohexene (III) yielded 1,*cis*-2,*trans*-3-trimethylcyclohexane (VI), while 3,*trans*-4,*cis*-5-trimethylcyclohexene (IV) yielded only 1,*trans*-2,*cis*-3-trimethylcyclohexane (VII). As pure compounds I–IV are new to the literature and the physical properties of VI and VII represent a marked improvement over the best previous data (Table II).

TABLE I
PROPERTIES OF 3,4,5-TRIMETHYLCYCLOHEXENES

Isomer	B.p./760 mm.	n^{20}_D	Purity, mole %
IV	144.36	1.4472	99.5+
II	144.45	1.4481	99+
III	148.30	1.4508	99.5+
I	149.42	1.4524	99+

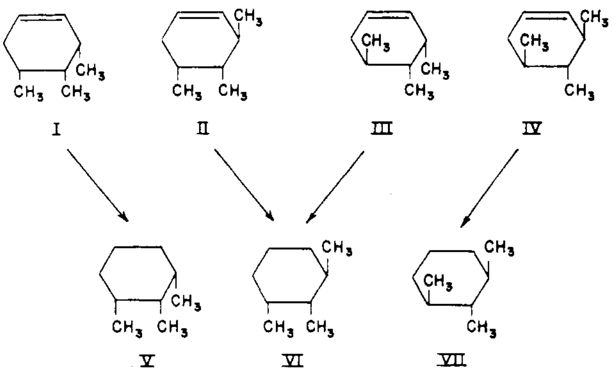

Figure 1

Cycloolefin I was obtained by a series of reactions previously described[3] for the synthesis of cycloparaffin V, except that a double bond present in the first intermediate product was retained (not hydrogenated). The all *cis* adduct[4] of 1,*trans*-3-pentadiene and maleic anhydride was reduced to a glycol which was converted to its ditosylate (di-*p*-toluenesulfonate). This ditosylate was reduced by a combination of lithium aluminum hydride and lithium hydride[5] to the desired cycloolefin which was found to be 99% pure or better by gas-liquid chromatography. A portion of it was hydrogenated over platinum at 30–40°, yielding a cycloparaffin product which was 99.5% pure or better by gas-liquid chromatography. It had the same retention time and infrared spectrum as the major component of the best previous sample of 1,*cis*-2,*cis*-3-trimethylcyclohexane,[3] which was still available for comparison.

TABLE II
PROPERTIES OF 1,2,3-TRIMETHYLCYCLOHEXANES

Isomer	B.p./760 mm.	n^{20}_D	d^{20}_4	F.p.	t_1[b]	A[c]	Purity, mole %
VII	145.60	1.4333	0.7870	−66.94	−66.79	0.033	99.5
	(145.61)[a]	(1.4333)	(0.7870)	(−66.86)	.....	...	(99.8)
VI	151.17	1.4399	0.8031	−85.76	−85.66	.033	99.7
	(151.21)	(1.4401)	(0.8029)	(−86.73)[d]	.....	...	(96.4)
V	151.67	1.4403	0.8027	−85.02	.....	...	99.5+[e]
	(151.43)	(1.4403)	(0.8021)	(glass)	.....	...	(95)[f]

[a] Values in parentheses from literature (ref. 3). [b] Calculated true freezing point (ref. 11). [c] Cryoscopic constant, mole fraction/degree (ref. 11). [d] Misprinted as 85.73° in ref. 3. [e] Estimated from gas-liquid chromatographic chromatogram. Cryoscopic determination was complicated by the appearance of two or more crystalline forms. [f] Estimated value in ref. 3, now corrected to 88% by gas-liquid chromatographic assay.

Cycloolefin II, also, was prepared from the adduct of 1,*trans*-3-pentadiene and maleic anhy-

---

[1] This investigation was performed as a part of American Petroleum Institute Research Projects 45 and 58A.

[2] On leave of absence from the National Petroleum Authority, Cairo, Egypt, U.A.R.

[3] J. F. Bussert, K. W. Greenlee, J. M. Derfer, and C. E. Boord, *J. Am. Chem. Soc.*, **78**, 6076 (1956).

[4] K. Alder, M. Schumacher, and O. Wolff, *Ann.*, **564**, 79 (1949).

[5] H. N. Miller and K. W. Greenlee, *J. Org. Chem.*, **26**, 3734 (1961).

dride. The all *cis* anhydride was changed to its isomer having the methyl group *trans* to the anhydride ring, then was hydrolyzed to the dicarboxylic acid which was purified by crystallization. By successive processes of esterification, reduction with lithium aluminum hydride, tosylation and hydrogenolysis, the pure acid was converted to a pure cycloolefin which must be 3,*trans*-4,*trans*-5-trimethylcyclohexene according to its genesis.

Cycloolefins III and IV were prepared as a mixture by a similar series of reactions, commencing with the adduct of 1,*trans*-3-pentadiene and fumaryl chloride which is known[5,6] to condense in the *trans* configuration. The adduct was converted through diol and ditosylate stages to a mixture (approx. 1:1) of two cycloolefins (Table I) which were easily separated by distillation into pure III and IV. The two were identified on the basis of their genesis, hydrogenation products and relative boiling points. A study of models has shown that the *ctc* isomer can have an all-equatorial configuration, while the *cct* isomer must have one methyl group in the axial position, which generally elevates the boiling point.

Hydrogenation of these two cycloolefins gave cycloparaffins which were shown by gas-liquid chromatography and infrared spectra to be pure and virtually identical with previous[3] samples of VI and VII, respectively. Their physical properties (Table II) also support this conclusion.

Having specimens of each of the 3,4,5-trimethylcyclohexenes, it was possible to show by comparison of gas-liquid chromatographic retention times and infrared spectra that all four were present in the mixture under investigation. In fact, this mixture comprised cycloolefins I (7%), II (37%), III (25%) and IV (31%). Upon hydrogenation, it yielded a mixture of cycloparaffins V (7.5%), VI (61.5%) and VII (31.0%) corresponding closely to what was predicted.

To determine why the 3,4,5-trimethylcyclohexenes derived from the adduct of crotonaldehyde and 1,*trans*-3-pentadiene should include all the possible isomers, the adduct itself was examined by gas-liquid chromatography and found to contain at least six components in significant amount. Moreover, further exposure to the original reaction conditions (250° under autogenous pressure) caused significant changes in the indicated proportions. As for the crotonaldehyde used, it was also examined and found to contain but one major component (97%) which can be assumed to be *trans* isomer.[7] The 1,*trans*-3-pentadiene was admixed with its *cis* isomer, but the latter did not react and would not be expected to do so.[8]

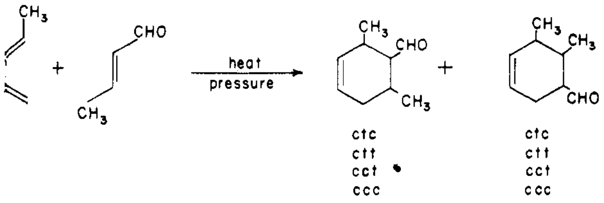

Figure 2

It is likely that all eight of the adduct's possible isomers are present in the mixture, though our chromatogram showed only six. In fact, the largest peak observed (51%) must include two or more isomers since in the derived cycloolefin mixture the most abundant species (II) comprised but 37% of the whole. The several minor components may include all the isomers having the CHO group in the unfavored 5-position.

Nevertheless, it seem probable that the bulk of the product *first formed* is the isomer (shown starred here) which would result from condensation in the favored *cis-ortho* fashion.[4,9] Crotonaldehyde, when condensed with butadiene or isoprene under conditions similar to those used in the present work, has yielded 85–90% of the *trans* products.[10] How then can the large yield of the cycloolefin II be explained?

We propose that at least a partial equilibration occurs, with the formyl group swinging from one side of the ring to the other with relative ease. Thus, about half of the starred (*cct*) adduct might rearrange to the *ctt* form since, in either case, the steric hindrance is approximately the same. Isomerization by re-orientation of a methyl group must occur slowly, if at all, else the *ctc* forms of the adduct would surely predominate over the others and 3,-*trans*-4,*cis*-5-trimethylcyclohexene would predominate over its isomers.

Experimental

Analyses.—The gas-liquid chromatographic studies cited herein were all done on a Barber Colman IDS Model 20 gas chromatograph with capillary columns. As used with an argon ionization detector, this system was found to give results not strictly linear with concentration. Thus, the indicated percentage of a minor component of a mixture may be high by 1–2%. However, similar chromatograms should be comparable.

Cryoscopic determinations of purity were made by a somewhat simplified version of the method of Rossini *et al.*[11] The "true freezing points" (t_1) were determined geometrically from the freezing point curves, and the cryoscopic constants (A = mole fraction/degree) were determined from the freezing point lowering caused by measured amounts of added impurity. Purity (P) was then calculated from the equation

$$\log P = 2 - A(t_1 - t)/2.303$$

Diels-Alder Condensation.—The adduct was prepared by treating in an autoclave a mixture of *trans*- and *cis*-1,3-pentadienes (2:1) with an amount of freshly distilled croton-

---

(6) K. Alder, G. Stein, M. Liebmann, and E. Rolland, *Ann.*, **514**, 197 (1934).

(7) W. G. Young, *J. Am. Chem. Soc.*, **54**, 2498 (1932).

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

(9) H. L. Holmes, *Org. Reactions*, **IV**, 60 (1948).

(10) Unpublished work of this laboratory.

(11) B. J. Mair, A. R. Gaslgow, and F. D. Rossini, *J. Research Natl. Bur. Standards*, **26**, 591 (1941).

aldehyde equivalent to the *trans* isomer present, for about 1 hr. at 250 ± 25°. The product (b.p. 90–93°/30 mm., $n^{20}{}_{\mathrm{D}}$ 1.4675–1.4700) was obtained in 56% average yield.

3,4,5-Trimethylcyclohexenes.—The Wolff-Kishner reduction of the cyclic aldehyde was carried out by a modification of the Huang-Minlon[12] procedure, using dihydrazine sulfate as the source of hydrazine. The crude product was steam distilled, washed with 5% sulfuric acid and fractionated at about 15 plates efficiency. The yield of trimethylcyclohexenes (b.p. 144–148°) was 72–75% from the cyclic aldehyde. This mixture was analyzed by gas-liquid chromatography with results given earlier. Using a 200-ft. length of 0.01-in. i.d. copper capillary tube coated with squalane at 80° and 15 p.s.i., only three peaks were obtained (at 74, 84, and 87.5 min.) representing cycloolefins IV + II, III, and I in their order of elution. However, with a longer capillary tube operated at 30° and 25 p.s.i. the first peak was resolved into two (at 414 and 419 min.); the tube included 200-ft of the copper capillary coated with squalane plus 100-ft of stainless steel capillary with a mixture of isooctyl phthalate, 3,3′-oxydipropionitrile and Triton X-100.

A portion of this mixture of trimethylcyclohexenes was mixed with an equal volume of ethanol and hydrogenated over 5% platinum-on-charcoal catalyst at 40–50° and 50 p.s.i.g. in a Burgess-Parr apparatus. The product was shown to comprise a mixture of the 1,2,3-trimethylcyclohexanes, by gas-liquid chromatography analysis using 200-ft of 0.01-in. i.d. stainless steel capillary coated with squalane at 50° and 15 p.s.i. with peaks occurring at 62, 79.5, and 81.5 min. after the injection.

***cis*-3-Methyl-4-cyclohexene-*cis*-1, *cis*-2-dicarboxylic Anhydride.**—This adduct was prepared as previously described.[3,13] The yield of crude adduct was 97%; m.p. 61–63°. One recrystallization from ether raised the m.p. to 63–64°.

***cis*-3-Methyl-4-cyclohexene-*cis*-1,*cis*-2-dimethanol.**—Lithium aluminum hydride (95 g., 2.5 moles) was dissolved (or suspended) in 2 l. of sodium-dried ether contained in a 5-l., three-necked flask equipped with a motor-driven Hershberg stirrer, dropping funnel, electric heating mantle, and an efficient aluminum coil reflux condenser connected to an overflow trap and a nitrogen reservoir. To this solution was added the cyclic anhydride (332 g., 2 moles) dissolved in dry ether (700 ml.) at such a rate as to maintain a steady, spontaneous reflux. The reaction mixture was stirred under reflux for 12 hr. longer, then hydrolyzed with cold water and 10% hydrochloric acid. The ether and product layer was separated, combined with three ether extracts of the aqueous layer, and washed with cold water and with 5% sodium bicarbonate solution before drying by percolation through a tube of anhydrous magnesium sulfate and magnesium carbonate (7:1). The ether solution was concentrated to 500 ml., and the diol was crystallized by cooling in a Dry Ice–isopropyl alcohol bath. The crude diol was recrystallized from ether as a white solid. Yield, 218 g. or 70%; m.p. 51.5–52°.

Anal. Calcd. for $C_9H_{16}O_2$: C, 69.29; H, 10.25. Found: C, 68.90; H, 10.04.

***cis*-3-Methyl-4-cyclohexene-*cis*-1,*cis*-2-dimethanol-di-*p*-toluenesulfonate.**—The pure diol (312 g., 2.0 moles) and pyridine (949 g., 12 moles) freshly distilled from barium oxide were placed in a 3-l., three-necked flask equipped with a motor-driven Hershberg stirrer and a low temperature thermometer. The solution was cooled to −15° by a Dry Ice–isopropyl alcohol bath and a 10% excess of finely powdered *p*-toluenesulfonyl chloride (838 g., 4.4 moles) was added portionwise at such a rate that the observed temperature never exceeded −5°. After the addition (requiring 1.5–2.0 hr.) the pasty reaction mixture was stirred for 2 hr. longer, then stored overnight in a refrigerator. It was then poured into 2.5 l. of cracked ice and hydrochloric acid, whereupon the ditosylate separated as a viscous oil. The oily product was combined with three ether extracts of the water layer and the whole was washed with water and sodium bicarbonate solution, then dried by percolation through a column of desiccant. The solution was evaporated to about 300 ml. whereupon the ditosylate precipitated as a white solid. It was filtered on a Büchner funnel, washed several times with cold water, air-dried, recrystallized from methanol, filtered again, and vacuum desiccated. There was obtained 840 g. (90.5%) of the ditosylate, m.p. 61–62°. An analytical sample, recrystallized from methanol melted at 62.5–63.0°.

Anal. Calcd. for $C_{23}H_{28}O_6S_2$: C, 59.45; H, 6.07; S, 13.80. Found: C, 59.15; H, 6.06; S, 13.84.

3,*cis*-4,*cis*-5-Trimethylcyclohexene (I).—Lithium aluminum hydride (8 g., 0.2 mole) and 100-mesh lithium hydride (24 g., 3.0 moles) were placed under nitrogen in a three-necked, 5-l. flask equipped with a mechanical stirrer, reflux condenser, and a dropping funnel. Sodium-dried tetrahydrofuran (3.5 l.) was added and the mixture was refluxed for 1 hr. Then, the ditosylate (696 g., 1.5 moles), dissolved in tetrahydrofuran (500 ml.) was slowly added through the funnel, and the mixture was refluxed for 10 hr. after completion of the addition. The tetrahydrofuran was stripped from the reaction mixture under reduced pressure and condensed in Dry Ice-cooled traps. The stripped solvent was replaced with 1.5 l. of ether and the excess hydrides and inorganic residues were decomposed with cold water and 10% hydrochloric acid. The ether–hydrocarbon layer was separated, combined with ether extracts (three, 300 ml. each) of the aqueous layer, washed with 5% sodium bicarbonate solution and dried by percolation through a column of desiccant. The ether was removed, and the product was distilled on a Nester and Faust spinning band fractionating column operated at about 20 plates efficiency. The yield of trimethylcyclohexene was 86.8 g. (0.69 mole) or 46% from ditosylate; b.p. 149.41–149.42°, $n^{20}{}_{\mathrm{D}}$ 1.4524. Gas-liquid chromatographic analysis indicated its purity to to be 99% or better.

Anal. Calcd. for C_9H_{16}: C, 87.03°; H, 12.97°. Found: C, 87.06°; H, 13.15.

1,*cis*-2,*cis*-3-Trimethylcyclohexane (V).—The cycloolefin (62.0 g., 0.5 mole), absolute ethanol (50 ml.), and platinum oxide (0.2 g.) were mixed in a magnesia bottle which was connected to a Parr hydrogenation apparatus. At 50 p.s.i.g. absorption was rapid at first, then slowed to a halt at 97% of the theoretical uptake. Some rise in temperature was evident. The product, after filtration, washing with water to remove the ethanol, and percolation through activated silica gel, was found to be saturated by bromine test. It was fractionated on the spinning band column, and the constant-boiling distillate (b.p. 151.83–151.84°/760) amounted to 52 g. or 83% yield from the cycloolefin. Gas-liquid chromatographic analysis indicated this to be a single compound, 99.5% pure or better. Its infrared spectrum was virtually identical with that of the major component (isolated by a gas liquid chromatographic technique) of the previous best sample.[3]

Anal. Calcd. for C_9H_{18}: C, 85.63; H, 14.37. Found: C, 85.56; H, 14.41.

Dimethyl *cis*-3-methyl-4-cyclohexene-*trans*-1,*trans*-2-dicarboxylate.—The all-*cis* adduct of 1,*trans*-3-pentadiene and maleic anhydride (332 g., 2.0 moles) was heated with 10 ml. of diethylaniline in a glass-lined bomb for 4 hr. at 175° to rearrange[14] it to *cis*-3-methyl-4-cyclohexene-*trans*-1,*trans*-2-dicarboxylic anhydride. Vacuum distillation of the reaction mixture gave 289 g. of product (b.p. 125–139°/4 mm.) which was shown by gas-liquid chromatography to contain 70% of the desired isomer.

The anhydride mixture was boiled with 350 ml. of water

---

[12] Huang-Minlon, *J. Am. Chem. Soc.*, **68**, 2487 (1946).

[13] R. Frank, R. Emmick, and R. S. Johnson, *ibid.*, **69**, 2313 (1947).

[14] D. Craig, *ibid.*, **72**, 1678 (1950).

for 25 min. and chilled to 0°. The crystalline product formed was filtered, washed with water, and recrystallized four times from water, yielding 212 g. (1.1 moles) of diacid, m.p. 160–162° (lit.,[14] m.p. 162°).

The diacid was esterified by refluxing it for 3 hr. with methanol (20 moles) containing 3% of dissolved hydrogen chloride. The solution was cooled, diluted with ether (250 ml.), washed thoroughly with water and with dilute sodium bicarbonate solution, and dried by percolation through anhydrous magnesium sulfate. The product was roughly distilled and 200 g. (92%) of the dimethyl ester, b.p. 132–138°/4 mm., was obtained.

3,*trans*-4,*trans*-5-Trimethylcyclohexene (II).—The diester (0.94 mole) was reduced by lithium aluminum hydride to the diol which (as crude) was converted to the ditosylate, by procedures described above. The ditosylate, water-washed and air-dried, was obtained in 98% yield; m.p. 91–93°.

Anal. Calcd. for $C_{23}H_{28}O_6S_2$: C, 59.45; H, 6.07; S, 13.80. Found: C, 59.57; H, 6.15; S, 13.91.

Hydrogenolysis of the ditosylate (358 g., 0.92 mole) was effected by treating with lithium hydride and lithium aluminum hydride (as above) to obtain the corresponding cycloolefin. The product, as a solution in tetrahydrofuran, was filtered from the formed lithium tosylate and distilled. Unfortunately, some lithium compounds remained dissolved and decomposed violently near the end of the distillation. This caused some loss of material, but 39 g. of crude product (b.p. 140–145°) was obtained. By redistilling it at about 20 plate efficiency, 25 g. (20% yield) of nearly constant-boiling material was obtained (b.p. 144.44–144.45°, n^{20}_D 1.4481, d^{20}_4 0.8129).

Anal. Calcd. for C_9H_{16}; C, 87.03; H, 12.97. Found: C, 86.92; H, 13.07.

1,*cis*-2,*trans*-3-Trimethylcyclohexane (VI).—The cycloolefin of the preceding section (5 g.) was hydrogenated to saturation (as before) and examined by gas-liquid chromatography. This revealed it as a single compound, 99% pure or better, with the same retention time as previous samples of the *cct* cycloparaffin.

***cis*-3-Methyl-4-cyclohexene-*cis*-1,*trans*-2-dicarbonyl Chloride and *cis*-3-Methyl-4-cyclohexene-*trans*-1,*cis*-2-dicarbonyl Chloride.**—In a 3-l., three-necked flask fitted with stirrer, reflux condenser, and dropping funnel was placed an amount of pentadienes mixture (136 g.) estimated to contain 1.2 moles of 1,*trans*-3-pentadiene. Fumaryl chloride (153 g. or 1.0 mole) was then added dropwise at such a rate so as to maintain a gentle reflux (2 hr.). The reaction mixture was stirred another hour, then fractionally distilled at about 3 plates efficiency. The product (b.p. 89–93°/3 mm., n^{20}_D 1.5035–1.5039) was a liquid; yield 100.5 g. or 90%.

Anal. Calcd. for $C_9H_{10}O_2Cl_2$: C, 49.00; H, 4.54; Cl, 31.81. Found: C, 49.33; H, 4.68; Cl, 31.80.

***cis*-3-Methyl-4-cyclohexene-*cis*-1,*trans*-2-dicarbinol and *cis*-3-Methyl-4-cyclohexene-*trans*-1,*cis*-2-dicarbinol.**—To a 5-l., three-necked flask fitted with stirrer, reflux condenser, and separatory funnel were added lithium aluminum hydride (65 g. or 1.7 moles) and 2 l. of ether. After these were stirred at reflux for 3 hr., the dicarbonyl chloride (330 g. or 1.5 moles in 600 ml. of ether) was added slowly. The reaction mixture was refluxed for 12 hr. longer, then hydrolyzed with 15% sulfuric acid. The ether and product layer was separated, combined with three ether extracts (250 ml. each) of the aqueous layer, washed with water, washed with 5% sodium bicarbonate solution, and dried over anhydrous magnesium sulfate. The ether solution was then evaporated to a volume of about 1 l. and cooled, whereupon the diol mixture separated in a semicrystalline state; yield, 187 g. or 80%. It was used in the next step without further purification.

3,*trans*-4,*cis*-5-Trimethylcyclohexene (IV) and 3,*cis*-4,-*trans*-5-Trimethylcyclohexene (III).—The crude diol mixture (0.86 mole) was converted to crude mixed ditosylates in 87% yield by the procedure used on *cis*-3-methyl-4-cyclohexene-*cis*-1,*cis*-2-dimethanol (above). The hydrogenolysis was carried out as before, and 352 g. of ditosylate gave 74.5 g. of trimethylcyclohexenes or 60% yield. Gas-liquid chromatographic analysis showed the mixture to consist almost entirely of two components occurring in 1:1 ratio and separable by distillation. The separation was done at about 30 plates efficiency on the spinning band column and 90% of the distillate occurred on two flats, center cuts of which boiled at 144.36° and 148.30°, respectively. Both of these appeared to be 99.5% pure by gas-liquid chromatography and were used for other properties (Table I) and for hydrogenation. Their infrared spectra were consistent with the assigned structures.

Anal. Calcd. for C_9H_{16}: C, 87.03; H, 12.97. Found for the *ctc* isomer: C, 87.28; H, 12.79. Found for the *cct* isomer: C, 86.86; H, 13.17.

1,*trans*-2,*cis*-3-Trimethylcyclohexane (VII) and 1,*cis*-2,*trans*-3-Trimethylcyclohexane (VI).—The two cycloolefins (25 g. each) were hydrogenated over platinum oxide in ethanol at 50 p.s.i.g. The product in each case was saturated and sufficient for distillation, about 15 g. of pure material being recovered in each case.

Acknowledgment.—The authors are indebted to Mr. Vincent G. Wiley for assistance in physical studies and gas-liquid chromatographic analyses and to Dr. Jack F. Bussert (present address, American Oil Co., Whiting, Ind.) for helpful suggestions.