Anal. Calcd. for C_7H_8ONBr: N, 6.93. Found: N, 6.87.

In another instance where 0.14 mole of 2,6-dibromoanisole and 0.56 mole of sodium amide reacted over a period of 2.5 hours, a 62% yield of 4-bromo-*m*-anisidine was obtained.

Reaction of 2,5-Dichloroanisole with Sodium Amide in Liquid Ammonia.—A solution of 27.6 g. (0.156 mole) of 2,5-dichloroanisole (m.p. 22°)[11] in 40 cc. of petroleum ether (b.p. 35–40°) was added to 0.624 mole of sodium amide in 500 cc. of liquid ammonia over a period of 40 minutes. Stirring was continued for 3.5 hours. After isolation and two crystallizations from ethanol, 19 g. (78%) of an amine melting at 79–81°[12] was obtained. The acetyl derivative melted at 123–124°.[12] Mixed melting points of the amine and its acetyl derivative with authentic samples of 4-chloro-*m*-anisidine and 4-chloro-*m*-acetaniside, respectively, showed no depression.

Reaction of 2,4-Dichloroanisole with Sodium Amide in Liquid Ammonia.—A solution of 2,4-dichloroanisole (m.p. 24°)[11] in 40 cc. of petroleum ether (b.p. 35–40°) was added to sodium amide in 500 cc. of liquid ammonia. After the desired reaction time, the excess sodium amide was neutralized with ammonium chloride. The amine was isolated and vacuum distilled so as to remove the accompanying tars. The following table summarizes a number of trials.

Trial	2,4-Dichloranisole, moles	Sodium amide, moles	Reaction time, min.	Yield, g.
1	0.1	0.45	30	2
2	.1	.2	45	5
3	.1	.25	75	8
4, 5, 6	.156	.624	250	19 (av.)

The material obtained in trials 4, 5 and 6 was placed in a 25° constant temperature bath and the clear, oily needles (m.p. 40–43°) that formed were filtered off and washed with petroleum ether. The acetyl derivative of the needles melted at 103–104° after two crystallizations from a water-ethanol solution and was identified as 5-chloro-*o*-acetaniside[12] by a mixed melting point with an authentic sample prepared from 4-chloro-2-nitroanisole.

The remaining, liquid portion of the combined products from trials 4, 5 and 6 was distilled with a Todd wire spiral column. A representative fraction (b.p. 136.5–137° at 9 mm., $n^{25.5}_{\mathrm{D}}$ 1.5853) was converted into the benzoyl derivative which melted at 106–107° after repeated crystallizations from ethanol (95%). The benzoyl derivative was identified as 6′-chloro-*m*-benzaniside by a mixed melting point with an authentic sample whose preparation is described below.

The pot residue from the distillation yielded, after extensive purification, a small amount of an amine melting at 68–71°. This amine was converted into its acetyl derivative (m.p. 122–124°)[12] which was identified as 4-chloro-*m*-acetaniside by a mixed melting point with an authentic sample.

4-Chloro-2-nitroanisole.—A mixture of 8.1 g. of nitric acid (70%) and 30 cc. of glacial acetic acid was added to a cooled mixture of 12.8 g. (0.09 mole) of *p*-chloroanisole and 10 cc. of glacial acetic acid. The acid mixture was diluted with water after refluxing for four hours, and the precipitate was collected and crystallized twice from ethanol. The liquor from the crystallizations was diluted with water and steam distilled, yielding more product after the initial distillation of unreacted *p*-chloroanisole. A 16% yield of the desired product was obtained; m.p. 96–98°.[12]

6-Chloro-*m*-anisidine.—Catalytic reduction of 4-chloro-3-nitroanisole (m.p. 43.2–45°)[13] obtained from 2-nitro-*p*-anisidine[14] by means of a Sandmeyer reaction, gave a 92% yield of the amine; b.p. 136–137° (10 mm.), $n^{25.5}_{\mathrm{D}}$ 1.5848.

Anal. Calcd. for C_7H_8ONCl: C, 53.4; H, 5.12. Found: C, 54.01; H, 5.44.

Benzoylation of 6-chloro-*m*-anisidine yielded 6′-chloro-*m*-benzaniside melting at 106–107°.

Anal. Calcd. for $C_{14}H_{12}O_2NCl$: C, 64.3; H, 4.03; N, 5.35. Found: C, 64.22; H, 4.31; N, 5.31.

LAFAYETTE, INDIANA

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[11] A. F. Holleman, *Rec. trav. chim.* **37**, 96 (1917).

[12] F. Reverdin and F. Eckhard, *Ber.*, **32**, 2622 (1899).

[13] H. van Erp, *J. prakt. Chem.*, **127**, 20 (1930).

[14] P. E. Fanta and D. S. Tarbell, *Org. Syntheses*, **25**, 79 (1945).

[CONTRIBUTION FROM THE CHEMICAL LABORATORIES OF HARVARD UNIVERSITY]

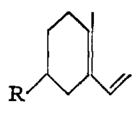
Synthesis and Reactions of 1-Methyl-2-vinyl-4-hydroxycyclohexene

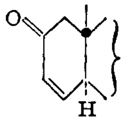
BY GILBERT STORK, S. S. WAGLE AND P. C. MUKHARJI

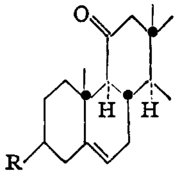
RECEIVED OCTOBER 31, 1952

Pure 1-methyl-2-vinyl-4-hydroxycyclohexene, 1-methyl-2-vinylcyclohexene and 6-methyl-1-vinylcyclohexene have been prepared for the first time. The first two substances do not take part in the Diels–Alder reaction and previously described adducts of the second substance are in reality derived from the third.

One of the attractive synthetic schemes for the elaboration of C-10 methylated steroids of the cortical hormone type consists of the union of two halves of the steroid molecule by means of a Diels–Alder reaction between a suitable derivative of 1-methyl-2-vinylcyclohexene (I) and a dienophile of the general type shown in II.[1] This might be expected to furnish adducts possessing not only the desired structural arrangement, but also presumably the natural steroid stereochemistry shown in III.[2]


I, R = H
Ia, R = OH


II


III

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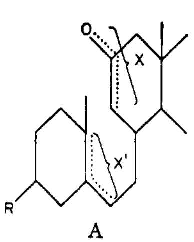
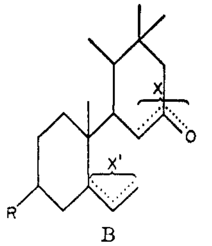
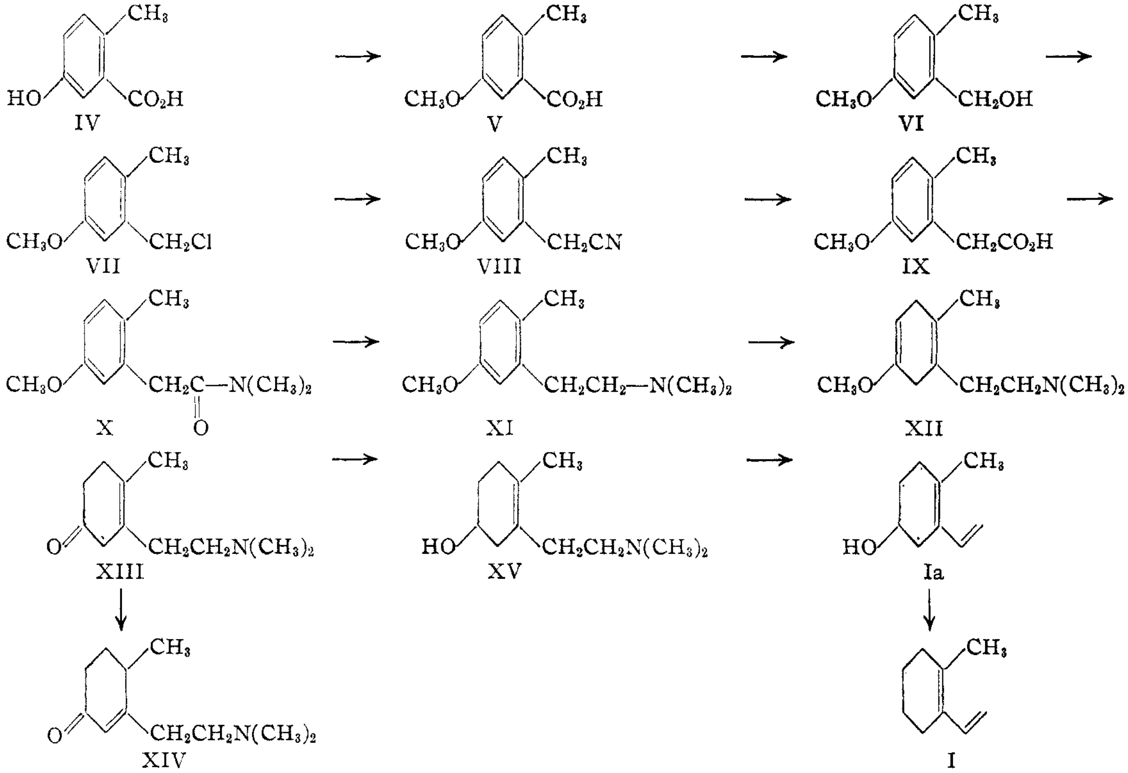
[1] (a) A. B. Meggy and R. Robinson, *Nature*, **140**, 282 (1937); (b) J. W. Cook and C. A. Lawrence, *J. Chem. Soc.*, 58 (1938); (c) P. A. Robins and J. Walker, *ibid.*, 642 (1952). Since this paper was written, a further paper by Robins and Walker has appeared in which they reach conclusions which are to a large extent in agreement with our own (*ibid.*, 1610 (1952)).

[2] After base isomerization at C_9 of the initially *cis* adduct. The structural anticipation follows from a consideration of the four possible formal transition states that can be written for the addition of I to II. The charges associated with the two halves in the transition state are here denoted by x, which in the case under consideration is either one electron or negative, and by x′ which here must be either one electron or positive. Only the two transition states illustrated by A and B need be considered since the alternate mode of addition to the dienophile would result in much less stabilization for x. Of these


A


B

1-METHYL-2-VINYL-4-HYDROXYCYCLOHEXENE AND 1-METHYL-2-VINYLCYCLOHEXENE



It is for these reasons that the synthesis of 1-methyl-2-vinyl-4-hydroxycyclohexene (Ia) was undertaken. The synthetic route finally selected was devised to ensure that the position of the double bonds in the final diene would be that shown in Ia. The starting material, 2-methyl-5-hydroxybenzoic acid (IV), prepared by alkali fusion of 2-naphthol-6,8-disulfonic acid,[3] was methylated with dimethyl sulfate to V which was converted to its ethyl ester and reduced with lithium aluminum hydride to the corresponding benzyl alcohol VI. Transformation of VI into 2-methyl-5-methoxyphenylacetic acid (IX) was carried out in the usual way *via* the chloride VII and nitrile VIII. Treatment of the acid chloride of IX with dimethylamine gave the dimethylamide X which was reduced to the desired N,N-dimethyl-2-methyl-5-methoxy-β-phenylethylamine (XI).[4]

Birch reduction of XI with sodium–methanol in liquid ammonia proceeded readily to give β-N,N-dimethylaminoethyl - 2 - methyl - 5 - methoxy - 1,4-cyclohexadiene (XII) which could be hydrolyzed with dilute hydrochloric acid in the cold, for exactly one minute, to the β,γ-unsaturated ketone XIII. More prolonged treatment with acid resulted in the formation of the α,β-unsaturated isomer XIV. The purity of XIII could be easily ascertained by the absence from its infrared spectrum of the $6.0\ \mu$ band characteristic of the isomeric ketone XIV, and was an essential prerequisite to the successful completion of an unambiguous synthesis of Ia. Reduction of XIII with lithium aluminum hydride gave the expected alcohol XV and the introduction of the extranuclear double bond was then effected by carrying out a Hofmann elimination on the derived methohydroxide which led to the desired hydroxydiene Ia in excellent yield.[5] 1-Methyl-2-vinyl-5-hydroxycyclohexene thus obtained is a liquid, b.p. 82–84° (1.8 mm.), the homo-

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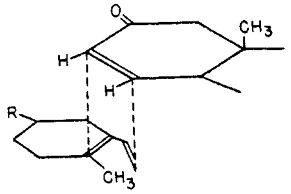
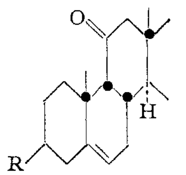
two transition states A is probably of somewhat lower energy as it allows the charge x′ to be distributed between a tertiary and a secondary carbon atom while x′ is distributed between a tertiary and a primary carbon atom in the case illustrated by B. The approach of the diene molecule would be anticipated to take place from the side opposite the *polar* angular methyl group of the dienophile as



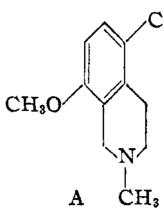
The stereochemical result of such an addition would be



which would obviously be epimerizable to the final structure III.

(3) Th. Zincke and H. Fischer, *Ann.*, **350**, 247 (1906).

(4) An alternate route to this amine, *via* formaldehyde–formic acid methylation of the primary amine obtained in excellent yield by the catalytic hydrogenation of the nitrile VIII failed because the reaction gave the tetrahydroisoquinoline derivative A instead of XI.



A

(5) It is interesting that there was no methylation of the alcoholic hydroxyl group, a fact which must be due to the steric impossibility of internal methylation in the case of XV methohydroxide.

geneity of which was demonstrated by the formation of a crystalline 3,5-dinitrobenzoate, m.p. 88°, in almost quantitative yield, and by the fact that the infrared and ultraviolet spectra of the hydroxydiene regenerated from its dinitrobenzoate were identical with those of the original substance. The positions shown for the two double bonds in Ia follow from the method of synthesis, provided that no rearrangement takes place during the Hofmann elimination.[6] The presence of a terminal methylene grouping in the hydroxydiene is evidenced by the typical infrared absorption bands at 6.1, 10.2 and 11.3 μ (Fig. 1) and is confirmed by the characterization of formaldehyde following the ozonolysis of the pure dinitrobenzoate of Ia. The presence of a conjugated diene system follows from the ultraviolet absorption (λ_{max} 239, ϵ_{max} 18,000), the high intensity of which precludes a *cis*-diene[7] while the lack of reaction of the mesylate of Ia on standing with pyridine makes it clear that the hydroxydiene is not an allylic alcohol. The only structure which is compatible with all these observations is Ia. Two facts, however, seemed to stand in sharp contrast to this conclusion: Neither the free hydroxydiene Ia, nor its dinitrobenzoyl, acetyl or dihydropyran derivatives could be made to take part in the Diels–Alder reaction with maleic anhydride, crotonaldehyde or benzoquinone in spite of the fact that 1-methyl-2-vinylcyclohexene itself had been claimed to lead to normal adducts with these dienophiles.[1,8]

Further, the ultraviolet absorption maximum observed for our pure hydroxydiene was 7 $m\mu$ higher and of much higher intensity than reported[9] for 1-methyl-2-vinylcyclohexene, a difference which is particularly noticeable as the reported position of the absorption maximum agrees with that calculated on the basis of generally reliable rules.[10] The *a priori* unlikely possibility that the peculiarity of the ultraviolet spectrum might be due to the presence of the hydroxyl group in the molecule was ruled out by the observation that the desoxydiene made from Ia by lithium aluminum hydride reduction of its mesylate[11] gave the parent substance I which had an ultraviolet absorption spectrum identical with that of the hydroxydiene, while its infrared spectrum was closely similar to that of Ia except for the absence of the hydroxyl band. The similarity between Ia and I was further underscored by the failure of I to participate in typical Diels–Alder reactions.

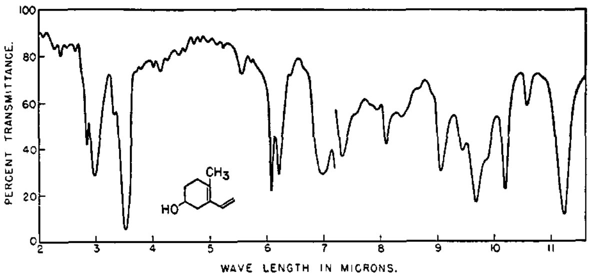
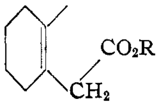


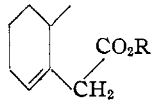
Fig. 1.—Solution in $CHCl_3$ to 7.2 μ; CS from 7.2 μ.

The obvious discrepancies between our results and those of earlier workers led us to investigate the nature of the previously prepared substance to which the structure of 1-methyl-2-vinylcyclohexene (I) had been assigned. It is at once apparent that most of the difficulties would be resolved if that material had in fact been a mixture containing the isomeric diene XVI. The ultraviolet absorption spectrum previously recorded[9] (λ_{max} 233 $m\mu$) would be that of a mixture of I and XVI, and thus lower than that of pure I, while the Diels–Alder adducts, isolated in unspecified yields,[1] would have been produced from XVI, leading to structures of type XVII.

Nothing in the previous work invalidates this hypothesis.[12] Neither Cook and Lawrence[1b] nor Meggy and Robinson[1a] gave any evidence for the structure of their adducts beyond the observation by the latter workers that the analysis of the maleic anhydride adduct gave values tallying with theoretical anticipations. There is in fact good reason to suppose that the dienes used in previous work were mixtures. In the Meggy and Robinson synthesis the double bond is introduced in the cyclohexane ring by the dehydration of the product of the Reformatsky reaction of 2-methylcyclohexanone and ethyl bromoacetate, a dehydration which has been demonstrated in this Laboratory to give a mixture consisting mostly of the unsaturated ester XVIII together with the isomeric ester XIX.[13]



XVIII



XIX

The diene prepared from this mixture of esters *via* the corresponding alcohols should therefore be a mixture of I and XVI.

Cook and Lawrence[1b] prepared their diene by the potassium bisulfate dehydration of the epimeric vinylcarbinols obtained by the partial hydrogenation of the mixture of ethinylcarbinols XX resulting from the addition of sodium acetylide to 2-methylcyclohexanone. Repetition of this work led to a dienic material which had λ_{max} 232 $m\mu$, ϵ 11,000 in agreement with previously reported values.[9] The conclusion that these low figures were the result of the contamination of the 1-methyl-2-vinylcyclohexene prepared in this manner was

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(6) Migration of the double bonds, though unlikely, is not definitely precluded. For instance, 1-methylbutadiene is the product of the Hofmann elimination on the methohydroxide of 5-dimethylaminopentene-1 (*cf.* J. Thiele, *Ann.*, **319**, (1901)). It is of course true that the migration in that case involves the removal of a more acidic proton than would be involved were Ia to rearrange.

(7) *Cf.* R. B. Turner and D. M. Voitle, THIS JOURNAL, **73**, 1403 (1951).

(8) Recently Robins and Walker, ref. 1c, reported results which led them to the conclusion that 1-methyl-2-vinylcyclohexene does not undergo readily the Diels–Alder reaction with benzoquinone.

(9) L. Booker, L. K. Evans and A. E. Gillam, *J. Chem. Soc.*, 1453 (1940). The 1-methyl-2-vinylcyclohexene was identified merely as having been supplied by Drs. G. N. Burkhardt and W. N. Hindley and had λ_{max} 233, ϵ 7200.

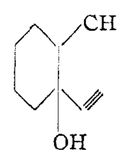
(10) R. B. Woodward, THIS JOURNAL, **64**, 72 (1942).

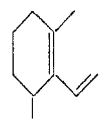
(11) *Cf.* H. Schmid and P. Karrer, *Helv. Chim. Acta*, **32**, 1371 (1949); J. Strating and H. J. Backer, *Rec. trav. chim.*, **69**, 638 (1950).

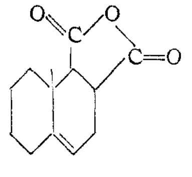
(12) In the recent paper of Robins and Walker, ref. 1c, some evidence is presented that the benzoquinone adduct obtained from a mixture of I and XVI has a structure of type XVII. The *pure* dienes I and XVI, however, were not examined by these authors.

(13) G. Stork and P. C. Dutta, in preparation.

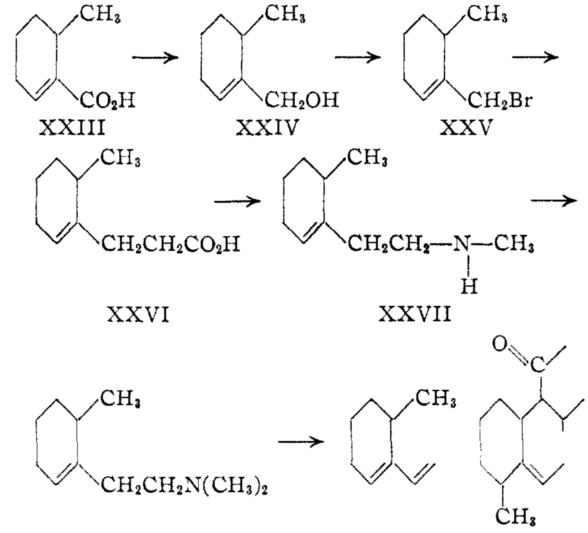
supported by the observation that the dehydration product from 2,6-dimethyl-1-vinylcyclohexanol, a diene XXI which cannot be contaminated by an isomer corresponding to XVI, showed λ_{max} 238 mμ, and like pure I did not react with maleic anhydride.[14]


XX

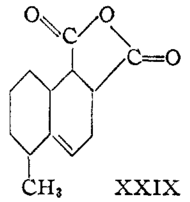

XXI


XXII

6-METHYL-1-VINYLCYCLOHEXENE



The completion of the proof that the adducts obtained from the diene mixtures had structures of type XVII required the unambiguous synthesis of authentic 6-methyl-1-vinylcyclohexene (XVI). This was accomplished by a route designed to ensure that the desired substance would be obtained free from double bond isomers: The known crystalline 6-methyl-1-cyclohexenecarboxylic acid[15] (XXIII) was reduced with lithium aluminum hydride to the alcohol XXIV which was converted to the corresponding bromide XXV with phosphorus tribromide. Reaction of XXV with sodiomalonic ester, followed by base hydrolysis and thermal decarboxylation, produced the propionic acid XXVI which was converted to its acid chloride by reaction of its sodium salt with oxalyl chloride.[16] Reduction of the isocyanate, obtained from the acid chloride *via* the azide, with lithium aluminum hydride[17] led to the N-methyl-β-[6-methylcyclohexenyl]-ethylamine (XXVII). The N-formyl derivative of XXVII was prepared by heating with ethyl formate and was then reduced to N,N-dimethyl-β-[6-methylcyclohexenyl]-ethylamine (XXVIII) with lithium aluminum hydride. The methohydroxide of XXVIII underwent smooth elimination on heating with the formation of the desired diene XVI in high yield. Pure XVI thus obtained had λ_{max} 232 mμ, ε 20,000[18] and reacted with maleic anhydride in boiling benzene with the formation of the expected adduct XXIX, m.p. 113°, in about 80% yield. This adduct was identical with the adduct obtained in very low yield from the diene mixture used by earlier investigators.[1a,b] It is thus convincingly demonstrated that the adducts to which angularly methylated structures, *e.g.*, XXII, have been assigned are in fact of type XVII (*e.g.*, XXIX) and of no value for the elaboration of steroid structures such as III.[19] One further point which deserves emphasis is that the positions of the ultraviolet absorption maxima found for I and XVI are, respectively, 5 and 7 mμ higher than the calculated values. Since the increment due to one alkyl substituent is also about 5 mμ caution is indicated when the empirical rules for the prediction of the absorption maxima of polyenes are used to determine the exact degree of substitution of a given system.


XXIX

Experimental

Ethyl 2-Methyl-5-methoxybenzoate.—A mixture of 2-methyl-5-methoxybenzoic acid (V)[20] (300 g.), absolute ethyl

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[14] It is interesting to note that S. Wang and M. Hu, *J. Chinese Chem. Soc.*, **10**, 1 (1943) separated the mixture which is formed by the addition of sodium acetylide to 2-methylcyclohexanone into the two epimeric alcohols XX. One proved to be a solid, m.p. 60°, and the other was a liquid. This observation was later confirmed by Milas, MacDonald and Black, THIS JOURNAL, **70**, 1829 (1948). The Chinese workers further claimed that the hydrogenation and dehydration of the 60° isomer led to *pure* I while the same procedure applied to the liquid isomer gave *pure* XVI. From *each* of these isomeric dienes it was asserted that crystalline, isomeric maleic anhydride adducts could be obtained. This was so definitely at variance with our experience with what we considered to be pure I that the work of the Chinese authors was repeated: *From either of the epimeric alcohols XX the same diene mixture is eventually obtained that is obtained by starting with the mixture of epimeric ethinylcarbinols.* This was shown by comparison of the ultraviolet and infrared spectra of the various synthetic samples as well as by the fact that all these diene preparations gave the same low yield of maleic anhydride adduct, obviously identical with the adduct made in unspecified yield by previous workers[1a,b] and to which the structure XXII was (erroneously) assigned previously. This result merely means that the process by which the epimeric vinylcarbinols is dehydrated involves the initial formation of a common carbonium ion rather than a concerted elimination of water.

[15] W. S. Rapson and R. G. Shuttleworth, *J. Chem. Soc.*, 636 (1940).

[16] *Cf.* A. L. Wilds and C. H. Shunk, THIS JOURNAL, **70**, 2427 (1948).

[17] *Cf.* H. H. Zeiss and W. B. Martin, Jr., 121st Meeting of the American Chemical Society, Abstracts of Papers, 41K (1952).

[18] The high extinction of the *pure* diene is in marked contrast to the low values recorded for vinylcyclohexene itself for which λ_{max} 230, ε 8500 are given (Booker, Evans and Gillam, ref. 9). It is also worth noting that, by the same token, previously prepared mixtures of I and XVI for which the low value ε 7200 was recorded must have contained considerable amounts of non-absorbing material. The high ε for both I and XVI is of course in agreement with their *s-trans* configurations (see R. B. Turner and D. M. Voitle, ref. 7).

[19] The inability of I to participate in the Diels–Alder reaction is presumably the result of the non-coplanarity of the diene system of I in the *s-cis* form (*cf.* the lack of reaction with *cis*-1-methyl-1,3-butadiene (R. F. Robey, C. E. Morrell and H. K. Wiese, THIS JOURNAL, **63**, 627 (1941)), although it is interesting to note that 1,1,3-trimethyl-1,3-butadiene is reported to react *inter alia* with crotonaldehyde to give the usual adduct (*cf.* J. C. Lunt and F. Sondheimer, *J. Chem. Soc.*, 2957 (1950)).

[20] E. H. Charlesworth, R. P. Lennie, J. E. Sinder and M. M. Yan, *Can. J. Research*, **23B**, 17 (1945).

alcohol (3 liters) and concentrated sulfuric acid (300 cc.) was boiled for 10 hours. Most of the alcohol was removed by distillation; the residue was diluted with water and extracted with ether. The ether extract was washed with sodium bicarbonate solution, with water and dried; the product was isolated by distillation as a colorless oil, b.p. 125–135° (5 mm.), yield 278 g.

Anal. Calcd. for $C_{11}H_{14}O_3$: C, 68.03; H, 7.27. Found: C, 68.13; H, 7.39.

2-Methyl-5-methoxybenzyl Alcohol (VI).—To a solution of lithium aluminum hydride (35 g.) in anhydrous ether (3 liters) in a 5-l. three-necked flask, provided with a stirrer and protected from moisture with a calcium chloride drying tube, the above ester (300 g.) was added dropwise at such a rate as to maintain gentle reflux. After the addition was complete, the solution was refluxed for two hours, then cooled in an ice-bath and very carefully decomposed with a saturated solution of sodium sulfate. The supernatant ether layer was decanted off and the inorganic residue repeatedly extracted with ether. The combined ether extracts were evaporated and the residue left after removal of the ether was isolated by distillation; b.p. 104–106° (0.6 mm.), yield 220 g.

Anal. Calcd. for $C_9H_{12}O_2$: C, 71.01; H, 7.95. Found: C, 70.80; H, 8.01.

2-Methyl-5-methoxybenzyl Chloride (VII).—To a solution of the above alcohol (220 g.) in anhydrous ether (300 cc.) cooled in an ice-bath, thionyl chloride (250 g.) was added dropwise with gentle stirring. After the addition was complete, the mixture was left in the cold for six hours, then poured onto ice and extracted with ether. The ether extract was washed successively with sodium bicarbonate solution and with water, and dried. The chloride was isolated by distillation; b.p. 123–128° (12 mm.), yield 150 g. of an oil which slowly crystallized on standing. Recrystallization from petroleum ether (20–40°) gave the pure chloride, m.p. 44–45°.

Anal. Calcd. for $C_9H_{11}ClO$: C, 63.36; H, 6.50. Found: C, 63.65; H, 6.61.

2-Methyl-5-methoxyphenylacetonitrile (VIII).—A mixture of the above chloride (85 g.), powdered potassium cyanide (56 g., 2 moles) and freshly dried acetonitrile (200 g.) was boiled under reflux for 16 hours. The reaction mixture was then cooled and filtered. The residue on the filter was washed several times with anhydrous ether, and the washings added to the filtrate. The combined solution was then washed with water (four times), dried over drierite and the ether was evaporated. The residual oil, after distillation under reduced pressure, solidified. A portion was recrystallized from cyclohexane and had m.p. 43–45°.

Anal. Calcd. for $C_{10}H_{11}NO$: C, 74.50; H, 6.88. Found: C, 74.49; H, 6.84.

2-Methyl-5-methoxyphenylacetic Acid (IX).—The nitrile (90 g.) was hydrolyzed by boiling under reflux for 16 hours with a solution of potassium hydroxide, prepared from potassium hydroxide (180 g.), water (300 cc.) and ethyl alcohol (300 cc.). The resulting clear solution was cooled, diluted with water and extracted with ether to remove unhydrolyzed nitrile. The aqueous solution was then filtered, cooled in an ice-bath and very carefully acidified with ice-cold dilute hydrochloric acid. The acid separated from the solution in long needles; yield 90 g. After two crystallizations from aqueous methanol it was obtained in white silky needles, m.p. 104°.

Anal. Calcd. for $C_{10}H_{12}O_3$: C, 66.60; H, 6.6. Found: C, 66.61; H, 6.68.

N,N-Dimethyl-2-methyl-5-methoxyphenylacetamide (X).—A mixture of the above phenylacetic acid (90 g.), dry benzene (150 cc.) and thionyl chloride (150 g.) was refluxed on a steam-bath for four hours. The solvent was then removed under reduced pressure. Dry benzene was again added to the residue and removed under reduced pressure. The process was repeated three times to remove the last traces of thionyl chloride, and the resulting crude acid chloride was directly used for the next operation.

To a well-stirred 25% aqueous solution of dimethylamine (75 g., 3 moles), cooled in an ice-bath, the crude acid chloride obtained above was slowly added with efficient stirring. After the addition was complete, the mixture was allowed to come to room temperature and stirred for another 16 hours. The solution was then extracted with ether; the ether extract was washed with water, dried and evaporated to give 82 g. of the crude amide which was directly used for the lithium aluminum hydride reduction. A portion was distilled for analysis: b.p. 142–143° (0.5 mm.).

Anal. Calcd. for $C_{12}H_{17}NO_2$: C, 69.51; H, 8.27. Found: C, 69.29; H, 8.35.

N,N-Dimethyl-2-methyl-5-methoxy-β-phenylethylamine (XI).—The crude amide obtained above (82 g.) was slowly dropped into a stirred suspension of lithium aluminum hydride (16 g.) in anhydrous ether (800 cc.). After the addition was complete, the mixture was refluxed for four hours and then cooled. It was decomposed with a saturated solution of sodium sulfate, the clear supernatant ether layer was decanted off and the inorganic residue was extracted with ether four times. After removal of the ether, the residual amine was purified by distillation, b.p. 90–92° (0.7 mm.).

Anal. Calcd. for $C_{12}H_{19}NO$: C, 74.55; H, 9.91. Found: C, 74.79; H, 10.05.

The picrate, prepared in the usual way, was recrystallized from alcohol, m.p. 162–163.5°.

Anal. Calcd. for $C_{18}H_{22}N_4O_8$: C, 51.19; H, 5.25; N, 13.27. Found: C, 51.39; H, 5.40; N, 13.27.

β-N,N-Dimethylaminoethyl-2-methyl-5-methoxy-1,4-cyclohexadiene (XII).—Metallic sodium (12 g.), cut in small pieces, was added slowly to a solution of the foregoing amine (12 g.) in 250 cc. of liquid ammonia, kept at −50° by means of Dry Ice, and absolute ethyl alcohol (30 cc.), the solution being stirred vigorously throughout the addition. The total amount of sodium was added over a period of about two hours. Stirring was continued until the blue color of the solution disappeared (*ca.* 5 hours), the temperature being maintained throughout between −40 and −50°. The mixture was allowed to evaporate overnight at room temperature. It was then hydrolyzed with distilled water and extracted with ether. The ether extract was washed with water, dried over anhydrous sodium sulfate and evaporated. The residual oil distilled at 98–102° (4 mm.), yield 11 g.

Anal. Calcd. for $C_{12}H_{21}NO$: C, 73.79; H, 10.84. Found: C, 73.78; H, 10.94.

β-N,N-Dimethylaminoethyl-2-methyl-5-hydroxycyclohexene (XV).—The cyclohexadiene prepared above (10 g.) was thoroughly cooled in an ice-bath and an ice-cold 15% solution of hydrochloric acid (10 cc.) was added to it in one portion with rapid stirring. After *exactly one minute* anhydrous sodium carbonate (10 g.) was added to the mixture with vigorous stirring, followed by immediate addition of ether. The ether layer was removed and the residual mass was extracted with ether. The combined ether layer was dried over anhydrous sodium sulfate and the solvent was removed. Without further purification the compound XIII could be directly employed for the next operation, crude yield 9.4 g.

The infrared spectrum showed the compound XIII to be the β,γ-form, with only traces of the α,β-isomer. This was always true when the hydrolysis of the enol ether was carried out exactly under the conditions described above. Contact with the acid for more than one minute invariably resulted in appreciable amounts of the α,β-form XIV.

The crude keto amine XIII obtained above (9.4 g.) was slowly added to a stirred suspension of lithium aluminum hydride (2 g.) in ether (250 cc.). After the addition was complete the solution was stirred at room temperature for another hour and was then decomposed, with vigorous stirring, with a saturated solution of sodium sulfate. An additional quantity of anhydrous sodium sulfate was then added to dry the mixture, the supernatant ether layer was removed and the inorganic mass was repeatedly extracted with anhydrous ether. The combined ether extracts were dried over anhydrous sodium sulfate, the ether was evaporated and the residual hydroxyamine was isolated by distillation as a colorless, mobile liquid, b.p. 149–151° (16 mm.), yield 9.0 g.

Anal. Calcd. for $C_{11}H_{21}NO$: C, 72.06; H, 11.55. Found: C, 71.60; H, 11.64.

N,N,N-Trimethyl-β-(2-methyl-5-hydroxycyclohexenyl)-ethylammonium Iodide.—The hydroxyamine XV (20 g.), dissolved in dry benzene (50 cc.), was cooled in ice-water and methyl iodide (25 g.) in dry benzene (50 cc.) was gradually added to it with gentle stirring. The mixture turned turbid and after some time the quaternary salt separated. After the addition was complete the mixture was heated on a steam-bath for half an hour. This was followed by a fresh addition of methyl iodide (10 g.) in benzene (25 cc.) and the mixture was heated for another 20 minutes. The mixture was then cooled and filtered. The residue was carefully washed several times with dry benzene and dried in the air. The yield of the crude product which was sufficiently pure for the next step was 34 g.

A small portion was recrystallized from methanol and after three crystallizations had m.p. 224° dec.

Anal. Calcd. for $C_{12}H_{24}NIO$: C, 44.31; H, 7.43; N, 4.31. Found: C, 44.49; H, 7.43; N, 4.39.

1-Methyl-2-vinyl-4-hydroxycyclohexene (Ia).—The above methiodide (25 g.) was dissolved in a mixture of methyl alcohol (540 cc.) and water (60 cc.) and stirred vigorously with freshly prepared silver oxide, from silver nitrate (159 g.) and sodium hydroxide (3.8 g.), for 10 hours. The mixture was then filtered, the inorganic residue was washed with methyl alcohol and the combined filtrate was carefully concentrated to a small volume on a steam-bath. The residue was then heated under reduced pressure, when the hydroxydiene distilled between 85 and 110° at 2–4 mm. pressure. The distillate was taken up in ether, washed with water, dried over anhydrous sodium sulfate and the ether was evaporated. The residual oil was then purified by distillation, b.p. 82–84° (1.8 mm.), yield 6.6 g., $\lambda_{\max}^{\text{alc}}$ 240 mμ, $\epsilon_{\max}$ 8,060.

Anal. Calcd. for $C_9H_{14}O$: C, 78.22; H, 10.22. Found: C, 78.30; H, 10.18.

The 3,5-dinitrobenzoate was obtained in the usual way in 86% yield and after three crystallizations from cyclohexane had m.p. 88°.

Anal. Calcd. for $C_{16}H_{16}N_2O_6$: C, 57.8; H, 4.8. Found: C, 57.79; H, 4.97.

The diene regenerated from the crystalline dinitrobenzoate had infrared and ultraviolet spectra identical with those of the original diene. On ozonolysis formaldehyde was isolated as its crystalline dimedon compound, m.p. 187–189°, in *ca.* 28% yield.

All attempts to induce the above diene to take part in the Diels–Alder reaction with various dienophiles like maleic anhydride, crotonaldehyde, benzoquinone failed (refluxing in benzene solution in the case of the anhydride and quinone, up to 180°, in sealed tube with crotonaldehyde gave only polymers and no adducts).

1-Methyl-2-vinyl-5-hydroxycyclohexene Acetate.—The hydroxydiene Ia (3 g.) dissolved in pyridine (5 cc.) was treated with acetic anhydride (3 g.) in pyridine (5 cc.) and kept at room temperature for eight hours. The mixture was then poured onto crushed ice and extracted with ether. The ether extract was washed with water, dilute ice-cold hydrochloric acid, dilute ice-cold sodium carbonate solution, again with water and finally dried over anhydrous sodium sulfate. The residue after removal of the ether distilled at 79–81° (0.7 mm.) as a colorless mobile liquid; yield 2 g.

Anal. Calcd. for $C_{11}H_{16}O_2$: C, 73.33; H, 8.88. Found: C, 73.44; H, 9.02.

The acetoxy diene did not react normally in attempted Diels–Alder condensations with maleic anhydride or crotonaldehyde.

Tetrahydropyran Ether of 1-Methyl-2-vinyl-5-hydroxycyclohexene.—The hydroxyamine (XV, 6 g.) was added slowly to a solution of anhydrous hydrogen chloride in ether, with ice cooling. The resulting white solid was quickly filtered off, washed with dry ether and then dissolved in chloroform (15 cc.). To this solution was added concentrated hydrochloric acid (5 drops) and dihydropyran (15 cc.), and the mixture was left at room temperature for five hours. It was then washed twice with 10% sodium hydroxide solution and finally with water until free from alkali. After drying over anhydrous sodium sulfate, the solvent was removed and the resulting oil was distilled, the fraction boiling at 130–140° (4 mm.) was collected (3.6 g.).

The above oil dissolved in dry benzene (15 cc.) was treated with an excess of methyl iodide (5 g.). Heat was evolved; after about 20 minutes another portion of methyl iodide (5 g.) was added, the mixture was heated on a steam-bath for about 20 minutes and was then cooled in an ice-bath. As no crystals separated, the solvent was removed under reduced pressure and the residual oil was treated with freshly prepared silver oxide in methyl alcohol solution in the usual way. The resulting methohydroxide was decomposed by heating in an oil-bath under diminished pressure and the distillate coming over between 80 and 120° at 6 mm. was collected. On redistillation in a current of nitrogen most of the oil boiled at 95–105° (3 mm.); yield 1.5 g. Before analysis the oil was distilled once more and the fraction distilling at 95–98° (3 mm.) was collected.

Anal. Calcd. for $C_{14}H_{22}O_2$: C, 75.64; H, 9.98. Found: C, 75.74; H, 10.19.

1-Methyl-2-vinylcyclohexene (I).—To a solution of the hydroxydiene (6.9 g., 1 mol) in pyridine (30 cc.), mesyl chloride (7.0 g., 1.2 mols) was added with cooling under the tap. After the initial vigorous reaction subsided, the mixture was left at room temperature for *ca.* 45 minutes. It was then poured onto crushed ice, extracted with ether and the ether extract washed with water, ice-cold dilute hydrochloric acid, ice-cold dilute sodium carbonate solution and finally with water. After drying over anhydrous sodium sulfate, the solvent was distilled off and the residual oil directly employed for the next step. The oil had a distinct sulfonic ester band in the infrared spectrum at 7.5 and 8.6 μ.

The above crude mesylate dissolved in ether was added dropwise to a stirred suspension of lithium aluminum hydride (4 g.) in anhydrous ether (250 cc.). After the addition was complete, the solution was refluxed for two hours, cooled and then decomposed with a saturated solution of sodium sulfate. After the decomposition was complete a fresh amount of anhydrous sodium sulfate was added, the ether layer was removed by decantation and the residue was extracted several times with ether. The combined ether extracts were again dried and the solvent was distilled off in a current of nitrogen. The residual oil was then distilled at atmospheric pressure when the diene was obtained as a colorless liquid with a characteristic odor, b.p. 154–158°, yield 4.5 g. For analysis this was redistilled and a middle cut was collected; $\lambda_{\max}^{C_2H_5OH}$ 240 mμ, $\epsilon_{\max}$ 16,000.

Anal. Calcd. for C_9H_{14}: C, 88.52; H, 11.4. Found: C, 88.56; H, 11.23.

2,6-Dimethyl-1-ethinylcyclohexanol.—2,6-Dimethylcyclohexanone (48 g.) and potassium *t*-amylate prepared from potassium (18 g.) and *t*-amyl alcohol (340 cc.) were added simultaneously during one hour to ether (600 cc.) which had been saturated with acetylene for *ca.* two hours. The solution was vigorously stirred during the addition, the passage of acetylene being continued during the addition and for a further four hours after the addition was complete. After standing overnight at room temperature, the mixture was decomposed with a saturated solution of ammonium chloride, the ether layer was separated, washed with water, dried and the ether was removed. The ethinyl carbinol was isolated by distillation as a colorless liquid, b.p. 92–95° (25 mm.), yield 27 g. The distillate solidified on cooling. A small portion was dissolved in petroleum ether (30–60°), and crystallization was allowed to proceed in the cold. After a second crystallization, the compound had m.p. 55°.

Anal. Calcd. for $C_{10}H_{16}O$: C, 78.9; H, 10.5. Found: C, 78.56; H, 10.67.

2,6-Dimethyl-1-vinylcyclohexene (XXI).—The ethinyl carbinol (16 g.) obtained above was reduced in the presence of 2% Pd/SrCO$_3$ catalyst. After absorption of one mole of hydrogen, the hydrogenation was stopped and the reduced product was isolated in the usual way, b.p. 82–83° (25 mm.).

The vinylcarbinol (10 g.) was heated with potassium bisulfate (12 g.) at 195–200° in an atmosphere of nitrogen as in the case of the monomethyl compound below. The distillate was dried and distilled. The fraction boiling at 164–168° was redistilled and a constant boiling fraction was collected at 165–166°. It had $\lambda_{\max}^{C_2H_5OH}$ 238 mμ, $\epsilon_{\max}$ 10,530. A satisfactory analysis could not be obtained on this diene, possibly because of oxidation.

This diene did not form any adduct with maleic anhydride after prolonged refluxing in benzene solution in the presence of hydroquinone and was instead polymerized.

2-Methyl-1-ethinylcyclohexanol (XX).—Acetylene was bubbled through ether (1000 cc.) for two hours and to the solution was added simultaneously with efficient stirring 2-methylcyclohexanone (80 g.) and potassium *t*-amylate (prepared from potassium metal (32 g.) and *t*-amyl alcohol (600 cc.)) during a period of *ca.* 1.5 hours. The current of acetylene was continued during the addition and for another five hours after the addition was complete. The mixture was left overnight, then was decomposed with a saturated solution of ammonium chloride, the ether layer was removed, washed with water, dried and distilled. After a small forerun of the unreacted ketone, the carbinol distilled at 82–86° (25 mm.) as a colorless liquid which immediately solidified; yield 45 g.

The solid distillate was dissolved with gentle warming in petroleum ether (30–60°) containing a little ether and filtered. The filtrate on cooling deposited silky needles which were collected by filtration. The mother liquor deposited a small second crop on standing for two days in a cold room. The product was recrystallized from ether–petroleum ether mixture and had m.p. 59°, reported m.p. 60°, yield 24 g.

The residue after removal of the crystalline carbinol distilled at 78–80° (25 mm.), yield 18 g.

Diene from the Solid Carbinol (XX).—The solid ethinyl carbinol (40 g.) was reduced with 2% Pd–$SrCO_3$ catalyst with initial cooling and the hydrogenation was stopped as soon as one mole of hydrogen had been absorbed. The product, 2-methyl-1-vinylcyclohexanol, was isolated by distillation, b.p. 76–77° (30 mm.), yield 36 g.

The vinyl carbinol (16 g.) was heated with powdered potassium bisulfate (18 g.) at 190° in an atmosphere of nitrogen. The diene was distilled off as soon as it was formed. The distillate was dried over anhydrous sodium sulfate and distilled twice under nitrogen; b.p. 156–157°, $\lambda_{\max}^{C_2H_5OH}$ 233 mμ, $\epsilon_{\max}$ 12,310.

The above diene (6 g.) and maleic anhydride (8 g.) dissolved in dry benzene (50 cc.) were refluxed overnight in an atmosphere of nitrogen. An amorphous precipitate was formed. The solution was concentrated, diluted with ether and filtered. The filtrate was washed several times with water, dried and evaporated, leaving a residue which soon solidified. The adduct was crystallized three times from ether–petroleum ether mixture and had m.p. 113°, yield 0.6 g.

Anal. Calcd. for $C_{13}H_{16}O_3$: C, 70.90; H, 7.2. Found: C, 70.90; H, 7.52.

Diene from the Liquid Carbinol (XX).—The liquid ethinylcarbinol was reduced to the vinylcarbinol which was then dehydrated with potassium bisulfate under the conditions described above to yield a diene distilling at 154–156°, $\lambda_{\max}^{C_2H_5OH}$ 233 mμ, $\epsilon_{\max}$ 10,000. The infrared spectrum of this material was identical with that of the product from the solid carbinol. The diene (12 g.) and maleic anhydride (16 g.) in dry benzene (120 cc.) were refluxed overnight under nitrogen. After working up in the usual manner, a crystalline adduct was obtained which after three crystallizations from ether–petroleum ether mixture had m.p. 113°, yield 1.2 g. The mixed melting point with the adduct of the diene from the solid carbinol was 113°.

6-Methylcyclohexenylcarbinol (XXIV).—6-Methyl-1-cyclohexenecarboxylic acid (62 g.) dissolved in a mixture of ether (450 cc.) and tetrahydrofuran (50 cc.) was added to lithium aluminum hydride (18 g.) in ether (600 cc.) at a rate such as to maintain gentle reflux. After the initial vigorous reaction had subsided, the solution was refluxed for one hour, then cooled, the excess lithium aluminum hydride was destroyed with ethyl acetate and the mixture was finally decomposed with ice-cold dilute hydrochloric acid. The ether extract was washed with water, dilute sodium bicarbonate solution, dried and distilled. The alcohol distilled at 110–112° (20 mm.) as a colorless mobile liquid, yield 42 g.

6-Methyl-1-(β-bromoethyl)-cyclohexene (XXV).—A solution of the above alcohol (56 g.) in petroleum ether (230 cc.) containing pyridine (5 cc.) was cooled in an ice–salt-bath and phosphorus tribromide (99 g.) dissolved in petroleum ether (180 cc.) was added dropwise with efficient stirring, the addition being carried out over a period of three hours. The mixture was then allowed to come slowly to room temperature and left overnight. It was then poured onto crushed ice, extracted with ether and the ether extract washed with water, dilute sodium carbonate solution, again with water and finally dried over anhydrous calcium chloride. The bromide was isolated by distillation, b.p. 102–104° (30 mm.), yield 60 g.

Ethyl α-Carbethoxy-β-(6-methylcyclohexenyl)-propionate.—Diethyl malonate (102 g.) was added to sodium hydride (8.0 g.) under dry benzene (400 cc.), with ice cooling. After two hours at room temperature the mixture was heated on a steam-bath for two hours to complete the salt formation. The mixture was then cooled in ice and the bromide (60 g.) was added dropwise with shaking. After standing overnight at room temperature, it was heated on a steam-bath for 10 hours and finally refluxed in an oil-bath for a further three hours. After cooling to room temperature, the mixture was poured into water, the benzene layer was removed, washed with water and evaporated. The residue was distilled, and the fraction boiling at 120–125° (0.9 mm.) was collected. On redistillation it came over at 122–123° (0.9 mm.), as a colorless, mobile liquid, yield 78 g.

Anal. Calcd. for $C_{15}H_{24}O_4$: C, 67.16; H, 8.95. Found: C, 66.63; H, 9.07.

β-(6-Methylcyclohexenyl)-propionic Acid (XXVI).—The diester (75 g.) described above was added dropwise to a well stirred solution of potassium hydroxide (80 g.) in water (50 cc.) heated to 80°. The addition was carried out over a period of 1.5 hours, after which the mixture was heated for another hour. The solution was evaporated to dryness, the residue was dissolved in water (50 cc.) and extracted once with ether to remove any unhydrolyzed ester. The aqueous solution was then cooled in an ice–salt-bath and decomposed with the calculated amount of ice-cold dilute hydrochloric acid, taking care that the temperature of the mixture did not rise above 5°. The oil that separated was extracted with ether; the ether extract was carefully washed with water, dried and evaporated. The residual viscous liquid was then dried under reduced pressure for *ca.* 30 minutes and then decarboxylated by heating at 180° until the evolution of carbon dioxide ceased (*ca.* 25 minutes). The residue was purified by distillation, b.p. 114–116° (0.5 mm.), yield 43 g.

Anal. Calcd. for $C_{10}H_{16}O_2$: C, 71.42; H, 9.52. Found: C, 70.88; H, 9.60.

The benzylthiuronium salt after two crystallizations from alcohol had m.p. 162°.

Anal. Calcd. for $C_{18}H_{26}N_2O_2S$: C, 64.67; H, 7.78. Found: C, 64.56; H, 7.89.

N-Methyl-β-(6-methylcyclohexenyl)-ethylamine (XXVII).—The propionic acid described above was carefully neutralized with the calculated quantity of sodium bicarbonate and the resulting sodium salt was thoroughly dried at 120° overnight. The finely powdered sodium salt (19 g.) suspended in dry benzene (200 cc.) was cooled in an ice-bath, a drop of pyridine was added, followed by oxalyl chloride (20 g.). A vigorous reaction set in; after one hour at 0°, and two hours at room temperature, the benzene solution was filtered and the benzene was evaporated under reduced pressure at room temperature. After a fresh addition of benzene (100 cc.) the process was repeated and the resulting crude acid chloride was immediately used for the next step.

A solution of sodium azide (9 g.) in water (24 cc.) was cooled in an ice–salt-bath and to that solution was added, with efficient stirring, the above acid chloride dissolved in acetone (60 cc.); the addition was done at such a rate that the temperature did not rise above 5°. After the addition was complete, the mixture was stirred for one more hour. The acetone upper layer was then carefully removed and the solvent was removed under reduced pressure at ordinary temperature. The residue was dissolved in dry benzene (100 cc.) and gently heated on a steam-bath, when a vigorous evolution of nitrogen started, which was over in *ca.* 30 minutes. After refluxing for another 15 minutes, the benzene was removed under reduced pressure and the residual oil, which had the strong band at 4.5 μ characteristic of isocyanates, was immediately reduced with lithium aluminum hydride.

The crude isocyanate (15 g.) was added to lithium aluminum hydride (15 g.) in dry ether (900 cc.) and the mixture was stirred overnight at room temperature and then refluxed for four to five hours. After cooling in ice, the mixture was decomposed with a saturated solution of sodium sulfate and isolated in the usual way. The amine was purified by distillation; the fraction boiling at 65–80° (1.5 mm.) was redistilled and the constant boiling fraction, b.p. 70° (1.5 mm.), was collected. It was obtained as a colorless liquid with a characteristic smell. It turned yellow on standing.

Anal. Calcd. for $C_{10}H_{19}N$: C, 78.43; H, 12.41. Found: C, 78.05; H, 12.59.

The phenylthiourea derivative, prepared in the usual way, after two crystallizations from benzene–petroleum ether mixture had m.p. 78°.

Anal. Calcd. for $C_{17}H_{24}N_2S$: C, 70.83; H, 8.33. Found: C, 70.63; H, 8.52.

N,N - Dimethyl - β - (6 - methylcyclohexenyl) - ethylamine (XXVIII).—A mixture of the above secondary amine (5 g.) and ethyl formate (7.5 g.) was heated in a sealed tube at 150° for nine hours. The resulting liquid was heated on a steam-bath under reduced pressure for *ca.* one hour to remove low boiling substances. The residual oil XXVII had a very intense amide band in the infrared at 6 μ.

The crude N-formyl derivative (10 g.) was reduced with lithium aluminum hydride (5.2 g.) in ether (600 cc.). After stirring for three hours at room temperature the mixture was refluxed for one hour. It was then cooled, decomposed with a saturated solution of sodium sulfate and worked up in the usual way. The oil left after removal of the benzene distilled at 72–74° (2.5 mm.) as a colorless mobile liquid. It was redistilled and the constant boiling fraction was collected at 70° (2.5 mm.).

Anal. Calcd. for $C_{11}H_{21}N$: C, 79.04; H, 12.57. Found: C, 78.77; H, 12.73.

The picrate, prepared in the usual way, was crystallized three times from dilute alcohol and had m.p. 118°.

Anal. Calcd. for $C_{17}H_{24}N_4O_7$: C, 51.51; H, 6.06. Found: C, 51.10; H, 6.03.

6-Methyl-1-vinylcyclohexene (XVI).—The tertiary amine XXVIII (11 g.) dissolved in benzene (30 cc.) was cooled in ice-water and to this was added with stirring methyl iodide (15 g.) dissolved in benzene (20 cc.). After the addition was complete, the flask was heated on a steam-bath for about 30 minutes; a fresh quantity of methyl iodide (7.5 g.) in benzene (20 cc.) was added and heating was continued for another 20 minutes. After cooling, the mixture was diluted with petroleum ether and filtered. The crude methiodide was washed three times with petroleum ether and then dried in the air; crude yield 20.5 g.

The crude methiodide (20 g.) was dissolved in methanol containing 10% water (480 cc.) and treated with vigorous stirring with freshly prepared silver oxide (from silver nitrate (13 g.) and sodium hydroxide (3.3 g.)). Stirring was continued overnight. The solution was filtered and the inorganic residue was washed three times with methanol. The filtrate was then carefully concentrated on the steam-bath. The residual viscous liquid was then heated in an oil-bath when decomposition started around 150°; water and an oily liquid distilled over. The cloudy distillate was extracted with ether, the ether extract was washed with water, dried, and the ether was evaporated in a current of nitrogen. The residual oil was distilled in a nitrogen atmosphere, b.p. 155–158°, yield 4.5 g. On redistillation the constant boiling fraction, b.p. 156°, was collected as a colorless, mobile liquid with a characteristic smell; $\lambda_{\max}^{C_2H_5OH}$ 232 mμ, $\epsilon_{\max}$ 20,000.

Anal. Calcd. for C_9H_{14}: C, 88.52; H, 11.47. Found: C, 88.70; H, 11.46.

5-Methyl-1,2,3,5,6,7,8,9-octahydronaphthalene-1,2-dicarboxylic Acid Anhydride (XXIX).—The diene XVI (2.5 g.) and maleic anhydride (4 g.) dissolved in benzene (25 cc.) were heated on a steam-bath for *ca.* 8 hours in an atmosphere of nitrogen. The clear solution was then concentrated, diluted with ether, and the ether solution was washed several times with water, dried, concentrated and cooled. The crystals (2.5 g.) were removed by filtration; the mother liquor on concentration gave a second crop of crystals (0.5 g.), making the total yield 3.0 g. After one recrystallization the adduct had m.p. 113° and gave no depression in melting point on admixture with the adducts obtained previously from the diene mixtures prepared from XX. The infrared spectra of the adducts were also identical in all respects.

CAMBRIDGE 38, MASS.

[CONTRIBUTION FROM THE NATIONAL INSTITUTE OF ARTHRITIS AND METABOLIC DISEASES, NATIONAL INSTITUTES OF HEALTH]

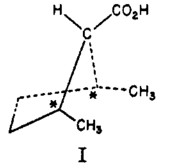
Stereoisomeric Quaternary Ammonium Derivatives of Tropine Having a Pseudoasymmetric Nitrogen Atom

BY STEPHEN P. FINDLAY

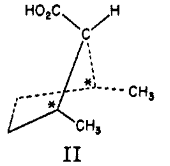
RECEIVED NOVEMBER 28, 1952

Tropine reacts with ethyl iodide to give tropine ethiodide which is identical with N-ethylnortropine methiodide obtained from N-ethylnortropine and methyl iodide. On the other hand N-ethylnortropine *n*-propiodide obtained from N-ethylnortropine and *n*-propyl iodide is different from N-*n*-propylnortropine ethiodide got from N-*n*-propylnortropine and ethyl iodide. This pair of isomeric iodides is convertible to the corresponding pair of bromides. The significance of these results is discussed. The nitrogen atom in these pairs of stereoisomeric halides is *pseudoasymmetric*.

Regarding optical activity in terms of asymmetric carbon atoms rather than in terms of asymmetry of the molecule as a whole has well known shortcomings.[1] One of these is that some symmetrically constituted, and hence optically inactive, molecules contain two or more asymmetric carbon atoms. A special case is the type of inactive compound in which a centrally located carbon atom is attached to four different groups: CXY(+)Z(−)Z. Such carbon atoms have been called *pseudoasymmetric*[2] which term may be applied to any atom attached tetrahedrally to four different groups two of which are the same except in being non-superposable and, therefore, optical opposites.[3] The α-carbon atom of the two inactive or *meso* forms of 2,5-dimethylcyclopentane-1-carboxylic acid (I and II) and C_3 of ribitol and xylitol are examples of pseudoasymmetric carbon atoms. Heretofore no examples of other atoms of this description appear to have been reported, although mention has been made of pseudoasymmetry of the nitrogen atom.[4]



I



II

In connection with a study of the stereochemistry of the tropane alkaloids it was noticed that certain of the symmetrically constituted derivatives of this class should furnish compounds in which the nitro-

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(1) *Cf.* G. Wittig, "Stereochemie," Akademische Verlagsgesellschaft, Leipzig, 1930, pp. 87-90.

(2) A. Werner originated this word to describe those central carbon atoms which possess certain of the properties of an asymmetric carbon atom without in effect being one. K. Freudenberg, "Stereochemie," Franz Deuticke, Leipzig and Vienna, 1933, p. 599.

(3) It will be necessary to modify this definition if examples of the type C(+)X(−)X(+)Y(−)Y also prove to be optically inactive.

(4) H. Gilman, "Organic Chemistry," Second Edition, John Wiley and Sons, Inc., New York, N. Y., 1943, p. 417.