

yielded 88% of the diphenylmethane derivative (XII), which was recrystallized from ethanol.

4,4'-Dibromodiphenylmethane and *di-p*-tolylmethane. Method A. These two known compounds were obtained in 95% yield from the corresponding trichloroethanes (XII) and (XIV) (see Table I).

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Terpenoids. XXVII. Base-Catalyzed Reactions with *N*-Lithioethylenediamine

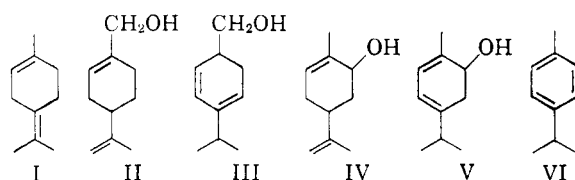
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The application of *N*-lithioethylenediamine previously examined by Reggel, Friedman, and Wender has been extended and its reactions towards several mono- and sesquiterpenoids with or without oxygen functions studied. Some of these underwent facile dehydrogenation, some were isomerized to conjugated products and the rest remained unchanged.

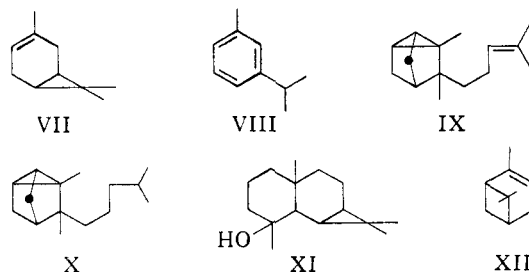
In a recent communication in this journal Reggel has described the use of *N*-lithioethylenediamine for the isomerization of olefins and dehydrogenation of cyclic dienes to aromatic systems.¹ A possible mechanism of the reaction has also been described. This base-catalyzed, low-temperature reaction in homogeneous medium proceeds in high yield. In this respect, it differs from the high temperature conventional dehydrogenation procedures using sulfur, selenium, or palladized charcoal. Because of its possible usefulness in the study of terpenoids in which the dehydrogenation technique is widely used for the elucidation of the carbon skeleton, it was felt that the scope and limitations of this reaction should be further elaborated by examining a number of compounds. The low temperature required in this dehydrogenation procedure is particularly useful in eliminating the possibility of group migration inherent in high temperature dehydrogenation carried out with sulfur or selenium. We have therefore examined several terpenoids and allied products and some of the results are presented in this communication.

*Terpenoids giving *p*-cymene.* Reggel has shown that limonene and phellandrene are converted quantitatively to *p*-cymene (VI).¹ We also found that under the same conditions terpinolene (I),^{2a} perillyl alcohol (II),^{2b} and carveol (IV)^{2c} give *p*-cymene in high yield. The conversion of perillyl alcohol and carveol to *p*-cymene is of particular significance as Reggel has used this reagent only in the case of hydrocarbons. Formation of *p*-cymene from carveol presumably proceeded through the conjugated alcohol (V) followed by dehydration. In case of perillyl alcohol, because of the absence of



an α -hydrogen, the allylic double bond must have migrated to form (III) to facilitate dehydration, followed by rearrangement to give *p*-cymene.

Compounds containing cyclopropane and cyclobutane rings. Because of the presence of cyclopropane and cyclobutane rings in many terpenoids, the behavior of these rings towards the reagent was examined. Δ^3 -Carene (VII)^{2d} gave a quantitative yield of cymenes, which, from comparative infrared analyses, was found to be a mixture of *p*-cymene (VI) and *m*-cymene (VIII)³ in nearly equal proportions, the cyclopropane ring having been opened in two ways in conformity with the reactivity of Δ^3 -carene toward other reagents.⁴ The caged cyclopropane ring systems present in α -santalene (IX)^{2e} and dihydro- α -santalene (X) were, however, stable toward this reagent. The tricyclic alcohol maaliol (XI),⁵ containing a cyclopropane ring as in the case of Δ^3 -carene, was also



(1) L. Reggel, S. Friedman, and I. Wender, *J. Org. Chem.*, **23**, 1136 (1958).

(2) E. Guenther, "The Essential Oils," Vol. II, D. Van Nostrand Company, Inc., New York, 1952, (a) p. 31, (b) p. 185, (c) p. 204, (d) p. 50, (e) p. 114, (f) p. 59, (g) p. 398, (h) p. 405, (i) p. 415, (j) p. 504, (k) p. 270, (l) p. 181, and (m) p. 381.

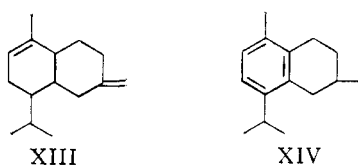
(3) American Petroleum Research Institute Project 44, Serial Nos. 1586 and 1587.

(4) P. P. Pillay and J. L. Simonsen, *J. Chem. Soc.*, 359 (1928).

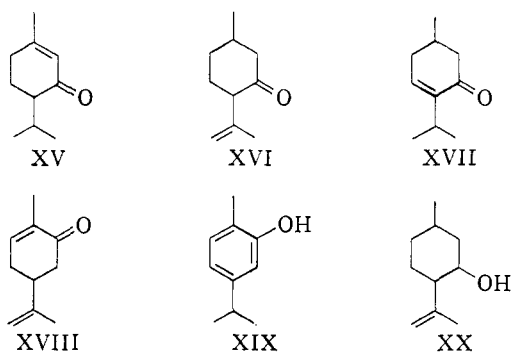
(5) R. B. Bates, G. Büchi, T. Mastura, and R. R. Shaffer, *J. Am. Chem. Soc.*, **82**, 2327 (1960).

similarly stable toward this reagent. α -Pinene (XII)^{2f} containing a cyclobutane ring also remained unaffected.

Sesquiterpene hydrocarbons. We have examined one cadinenic sesquiterpene hydrocarbon, γ_1 -cadinene (XIII),⁶ which was converted to calamenene (XIV)⁷ presumably with migration of the methylenic double bond across a ring followed by aromatization of one of the rings. Aromatization of the other ring could not be effected by repeating the treatment or using excess of the reagent. This partial aromatization may have considerable importance in obtaining fully aromatic substances from many terpenoids which give only poor yields of aromatic systems on conventional dehydrogenation.



Reaction with ketones. In this connection, two aspects were investigated. The possibility of using a monoethenoid ketone through its potential enolic form to give a phenol on dehydrogenation was first examined. The conjugated ketone, *dl*-piperitone (XV),^{2g} on treatment with this reagent remained unaltered and did not form any thymol as might have been anticipated. The unconjugated ketone isopulegone (XVI)^{2h} partly isomerized to the conjugated ketone (XVII). Carvone (XVIII),²ⁱ containing two double bonds, however, gave a quantitative yield of carvacrol (XIX).^{2j} From this it was clear that, for aromatization of a ketonic system of the *p*-menthane series, the presence of two

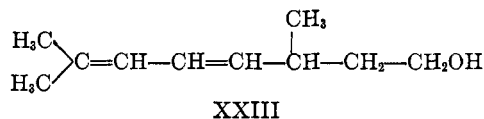
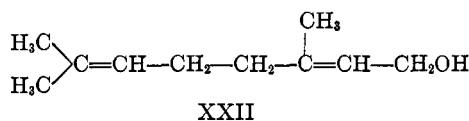
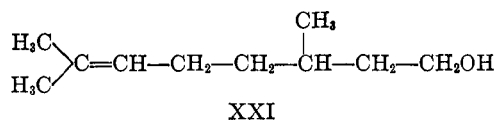


double bonds is essential. It was also noted that, though isopulegone partially isomerized to the conjugated ketone, the double bond in the corresponding alcohol, isopulegol (XX),^{2k} did not migrate; the migration appears to have been prevented by the hydroxyl group.

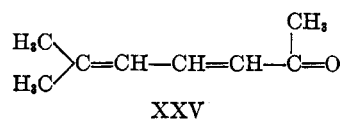
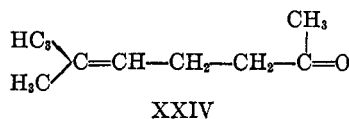
(6) B. B. Ghatge, R. K. Razdan, K. K. Chakravarti, and S. C. Bhattacharyya, *Perf. & Ess. Oil Rec.*, **46**, 365 (1955); **47**, 157 (1956).

(7) W. Treibs, *Ber.*, **82**, 530 (1949); F. Sorm, K. Veress, and V. Herout, *Collection Czech. Chem. Commun.*, **18**, 106 (1953).

Acyclic systems. In this group, several compounds have been examined. The monoethenoid alcohol, citronellol (XXI),^{2l} remained unaltered; no migration of the double bond to give rise to an allylic alcohol was noticed. In the case of geraniol (XXII) the allylic double bond actually migrated away from the alcoholic group to furnish the conjugated diene alcohol (XXIII). Because of its interesting features, the structure of this alcohol was carefully examined. It showed the presence of two double bonds, gave acetone on ozonolysis, did not react with manganese dioxide, and in conformity with the structure showed characteristic ultraviolet absorption, λ_{\max} 237 $m\mu$, ϵ 15620. In this reaction, the presence of no triene conjugated alcohol was indicated. Dihydromyrcene,⁸ the hydrocarbon corresponding to geraniol remained unaltered under similar conditions. Neither the formation of a conjugated diene through migration of one of the trisubstituted double bonds nor formation of a conjugated triene by dehydrogenation was observed. Dehydrogenation in the case of hydrocarbons would thus appear to be characteristic only for cyclic dienes.



We have examined only one acyclic ketone, methylheptenone (XXIV),^{2m} which gave the fully conjugated dienone (XXV), evidently formed through dehydrogenation; but because of its somewhat unstable nature, it could not be isolated in pure form. The impure specimen gave characteristic color reactions⁹ and also showed the expected ultraviolet absorption, λ_{\max} 223 $m\mu$, ϵ 4385 and 266 $m\mu$, ϵ 557.



(8) J. L. Simonsen and W. C. J. Ross, "The Terpenes," Vol. I, The Cambridge University Press, Bentley House, London, N.W.1, 1953, p. 9.

(9) F. G. Fischer and K. Lowenberg, *Ber.*, **66B**, 669 (1933).

EXPERIMENTAL

Lithium, obtained from Riedel (Germany), was used in the form of thin wires. Anhydrous ethylenediamine (b.p. 114–115°) was prepared by azeotropic distillation of ethylenediamine monohydrate with thiophene-free benzene followed by refluxing and distilling over potassium hydroxide pellets and finally several times over metallic sodium. We found that, by this procedure, using azeotropic distillation at the initial stages, practical quantities of anhydrous ethylenediamine could be conveniently prepared. The entire operation during the present investigation was carried out in an atmosphere of nitrogen which was purified by passing successively through three towers of alkaline pyrogallol, three towers of anhydrous sulfuric acid, and finally, if required, through a furnace containing heated (700°) copper turnings.

Apparatus and procedure. On a mantle, a 3-necked flask with a suitable multiple adaptor was fitted with a mercury sealed stirrer, a thermometer nearly touching the bottom, a nitrogen inlet, a dropping funnel, and an efficient vertical condenser connected from the top to a mercury sealed outlet. A steady current of pure anhydrous nitrogen prepared according to the procedure described earlier was passed through the apparatus and, when the entire system was flushed with nitrogen, ethylenediamine (over sodium) was directly distilled into the flask in order to avoid exposure to air. When the requisite amount of ethylenediamine was collected, the distilling apparatus was disconnected.

The internal temperature of the contents of the flask was raised to 100°. Lithium, in the form of freshly drawn wire and preserved under carefully dried liquid paraffin, was then added through one arm of the multiple adaptor in small installments during about 0.5 hr. under stirring. The blue color formed after the addition of each lot of lithium wires faded in a few minutes. The rate of addition of lithium was controlled by the evolution of hydrogen and by the disappearance of the blue color. After the addition of lithium was complete, the contents of the flask were heated for another hour to ensure the completion of the formation of the lithio derivative. The reaction mixture usually developed a light yellowish color with little or no suspended white turbidity.

The compound to be treated was then gradually added at 100–110° from the dropping funnel. The rate of addition depended upon the rate of evolution of hydrogen or formation of froth in the reaction medium. The reaction mixture was then stirred and heated for 3 to 12 hr. depending on the nature of the compound. After the reaction was complete, the product was allowed to cool and the mantle was replaced by an ice bath. An adequate quantity of water was gradually added to dissolve the solid material which was formed. The reaction product was then extracted with a suitable solvent, processed in the usual way, and purified by distillation, crystallization, or chromatography (alternatively, it has been found possible to recover part of the ethylenediamine under vacuum before addition of water for decomposition).

Purity of all chemicals used and products formed was determined by elemental analysis, ultraviolet and infrared absorption, and other physico-chemical properties.

Reactions resulting in *p*-cymene. a) Lithium (1.5 g., 0.216 g.-atom), ethylenediamine (100 ml.), and terpinolene (2.5 g., 0.02 mole) on refluxing for 4 hr., b) lithium (2 g., 0.3 g.-atom), ethylenediamine (100 ml.), and carveol (8 g., 0.053 mole, prepared by reduction of pure carvone with lithium aluminum hydride, b.p. 71°/5 mm., $[\alpha]_D -31.36^\circ$, $n_D^{25} 1.4970$) on refluxing for 7 hr.; or c) lithium (1.5 g., 0.216 g.-atom), ethylenediamine (150 ml.), and perillyl alcohol (10 g., 0.066 mole), isolated by careful fractionation of palmarosa oil "sofia," b.p. 120°/13 mm., $n_D^{25} 1.4950$, $[\alpha]_D +28.8^\circ$.

Anal. Calcd. for $C_{10}H_{16}O$: C, 78.89; H, 10.59. Found: C, 78.4; H, 10.7 on refluxing for 6 hr. gave nearly quantitative yields of *p*-cymene purified by distillation over sodium, b.p. 175.5°/700 mm., $n_D^{25} 1.4860$, $[\alpha]_D \pm 0^\circ$.

Anal. Calcd. for $C_{10}H_{14}$: C, 89.49; H, 10.51. Found: C, 89.5; H, 10.7.

Infrared spectrum was identical with an authentic sample.³

Reaction with Δ^3 -carene. The material was isolated by careful fractionation of Indian turpentine oil (*Pinus longifolia*), b.p. 167.5°/700 mm., $n_D^{25} 1.4680$, $[\alpha]_D +11^\circ$. Lithium (8.5 g., 1.23 g.-atom), ethylenediamine (190 ml.), and Δ^3 -carene (27.5 g., 0.2 mole) on refluxing for 12 hr. gave a mixture of *m*- and *p*-cymene purified by distillation over sodium, b.p. 175.5°/700 mm., $n_D^{25} 1.4860$.

Anal. Calcd. for $C_{10}H_{14}$: C, 89.49; H, 10.51. Found: C, 89.72; H, 10.72.

Infrared peaks at 703, 784, 880, 1088, 1050, 1460, and 1606 cm^{-1} (*m*-cymene) and 722, 816, 1021, 1059, 1112, 1186, 1211, 1467, 1648, 1792, and 1900 cm^{-1} (*p*-cymene).

Reaction with γ_1 -cadinene. Lithium (5 g., 0.72 g.-atom), ethylenediamine (150 ml.), and γ_1 -cadinene (5.8 g., 0.028 mole, obtained from our laboratory stock, b.p. 94°/0.9 mm., $n_D^{25} 1.5120$, $[\alpha]_D -17.25^\circ$) on refluxing for 12 hr. gave calamenene, b.p. 111°/2 mm., $n_D^{25} 1.5204$, $[\alpha]_D +4^\circ$.

Anal. Calcd. for $C_{15}H_{22}$: C, 89.04; H, 10.96. Found: C, 88.9; H, 11.2.

Infrared peaks at 810, 878, 1035, 1166, 1179, 1369, 1380, 1492, 1572, 1600 cm^{-1} ; ultraviolet absorption λ_{max} 269 $m\mu$, ϵ 1263 and 277.5 $m\mu$, ϵ 1095.

Reaction with carvone. The carvone used was isolated from American spearmint oil by the neutral sulfite method, b.p. 66°/0.9 mm., $n_D^{25} 1.4971$, $[\alpha]_D +54^\circ.9$. Lithium (3 g., 0.432 g.-atom), ethylenediamine (80 ml.), and carvone (7.5 g., 0.05 mole) were refluxed for 12 hr. After decomposition with water in the usual way, the reaction mixture was carefully acidified to Congo Red and extracted thoroughly with ether and processed in the usual way to isolate carvacrol, b.p. 73°/0.3 mm., $n_D^{25} 1.5228$.

Anal. Calcd. for $C_{10}H_{14}O$: C, 79.95; H, 9.39. Found: C, 80.16; H, 9.23.

The naphthylurethane was prepared in the usual way, m.p. 115° (lit.² m.p. 116°).

Reaction with isopulegone. Lithium (2 g., 0.3 g.-atom), ethylenediamine (100 ml.), and isopulegone (8 g., 0.053 mole, purified by distillation and chromatography, b.p. 80°/3 mm., $n_D^{25} 1.4680$, $[\alpha]_D +14.9^\circ$, no specific ultraviolet absorption) on refluxing for 10 hr. gave the partially conjugated ketone (XVII), which was washed in ethereal solution with aqueous alkali or chromatographed to remove traces of phenolic impurities, dried, and distilled, b.p. 65°/0.9 mm., $n_D^{25} 1.4750$.

Anal. Calcd. for $C_{10}H_{16}O$: C, 78.89; H, 10.59. Found: C, 79.1; H, 10.4.

Infrared peaks at 815, 846, 1027, 1666 cm^{-1} ultraviolet spectrum, λ_{max} 239 $m\mu$, ϵ 1859.

Reaction with geraniol. Lithium (1.5 g., 0.216 g.-atom), ethylenediamine (100 ml.), and geraniol (10 g., 0.065 mole; $n_D^{25} 1.4780$) on refluxing for 8 hr. gave the conjugated alcohol (XXIII) purified by distillation, b.p. 88°/3 mm., $n_D^{25} 1.4900$.

Anal. Calcd. for $C_{10}H_{18}O$: C, 77.86; H, 11.76. Found: C, 78.2; H, 11.8.

Ultraviolet absorption, λ_{max} 237 $m\mu$, ϵ 15,620; infrared peaks at 816, 842, 919, 968, 1047, 1627, 1666, 3400 cm^{-1} . On hydrogenation (platinum oxide and acetic acid) XXIII it showed the presence of two double bonds, gave acetone on ozonolysis, and failed to react with freshly prepared manganese dioxide.

Reaction with methylheptenone. As the properties of the reaction product obtained in this case varied, no representative experiment will be described. The properties were approximately as follows: b.p. 40°/4 mm., $n_D^{25} 1.6070$; gave characteristic color tests as described for this compound in the literature,⁹ developed a red color on exposure to air and

light, showed ultraviolet absorption for a dienone, λ_{\max} 223 $m\mu$, ϵ 4385 and 266 $m\mu$, ϵ 600.

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permitting one of them (B. S. Tyagi) to work as a guest worker. They are indebted to Mr. V. S. Pansare and his colleagues for microanalyses and to Miss Vasanti Prabhu and Mr. Gopinath for ultraviolet and infrared spectra, respectively.

Notes

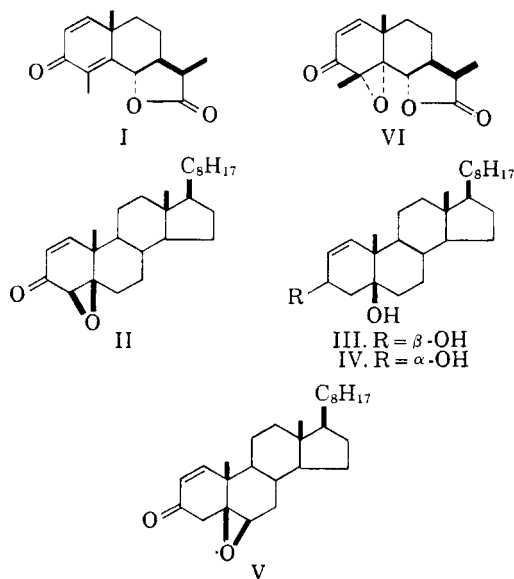
4,5 β -Epoxycholest-1-en-3-one

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In connection with another problem it became desirable to synthesize a 1,2 α -epoxide of a steroid 1,4-dien-3-one. It has been reported that the cross-conjugated dienone, santonin (I), yields a mixture of stereoisomeric 1,2-epoxides² upon treatment with perbenzoic acid or hydrogen peroxide in acetic acid.³ Consequently we investigated the analogous epoxidation of the readily available cholest-1,4-dien-3-one and now wish to record our observations.

Prolonged treatment of cholest-1,4-dien-3-one with perbenzoic acid in refluxing benzene solution resulted in a low yield of a mono epoxide II, m.p.



123–124°, exhibiting infrared absorption at 1690 ($-\text{CO}-$) and 1610 ($-\text{C}=\text{C}-$) cm^{-1} . Ultraviolet absorption occurred at 232 $m\mu$, but no definitive structure assignment was possible based on these observations only. Lithium aluminum hydride reduction of this product proceeded smoothly and gave two unsaturated diols in a ratio of 1:4. The major diol III, m.p. 173.5–174.5°, possessed infrared absorption at 1650 ($-\text{C}=\text{C}-$) and 3550 (intermolecular hydrogen bonded $-\text{OH}$) cm^{-1} while the minor diol IV, m.p. 135–136°, exhibited an additional absorption at 3600 (nonbonded $-\text{OH}$) cm^{-1} .

Hydrogenation of III yielded cholestan-5 β -ol⁴ (50%), m.p. 80°, and cholestan-3,5 β -diol⁵ (50%), m.p. 129–130/149°, while IV under the same conditions gave cholestan-5 β -ol and cholestan-3 α ,5 β -diol,⁵ m.p. 188.5–189° in a ratio of 1:2. Further verification of the position of the 1,3-diol system was obtained by oxidation of cholestan-3,5 β -diol to cholestan-3-one-5 β -ol, m.p. 158–159°, and subsequent dehydration to cholest-4-en-3-one identified by mixed melting point determination with an authentic sample.

The preceding evidence can be rationalized if it is assumed that the initial epoxide possesses the 4,5 β - (II) or 5,6 β - (V) configuration. *trans*-Diaxial oxirane ring opening and carbonyl reduction by hydride affords the pair of unsaturated diols epimeric at C-3 since on catalytic hydrogenation both give the same hydrogenolysis product.

A 60 mc./sec. NMR spectrum of the original epoxide in carbon tetrachloride solution showed two vinylic hydrogens at low field. Spin-spin coupling⁶ ($J = 10$ c.p.s.) between these *cis* hydrogens is responsible for the β -hydrogen doublet centered at 3.61 τ while the α -hydrogen quartet at 4.31 τ indicated additional transannular cou-

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(5) Pl. A. Plattner, H. Heusser, and A. B. Kulkarni, *Helv. Chim. Acta*, **31**, 1885 (1948).

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(1) National Science Foundation predoctoral fellow, 1960–1961.

(2) John Simonsen and D. H. R. Barton, *The Terpenes*, Vol. III, Cambridge University Press, Cambridge, 1952, pp. 260, 277, 279.

(3) G. Cusmano, *Gazz. chim. ital.*, **48**, I, 248 (1918).