228° (reported[8] decomposition point 230°). On admixture with an authentic sample of tetramethylammonium iodide, dec. pt. 228°, no depression in decomposition point was observed. A sample of the methiodide was converted to its picrate, melting and mixed melting point 313–314° dec. (reported[9] m.p. 312–313° dec.).

When the reaction was repeated employing 0.12 mole of potassium amide and 10.0 g. (0.04 mole) of *n*-amylcyclohexadieneamines IVa-b in 250 ml. of sodium-dried refluxing xylenes, there was obtained 6.7 g. (89%) of *n*-amylmesitylene (V), b.p. 103–105° at 3 mm., $n^{25}_{\rm D}$ 1.4987 (sulfonamide m.p. and mixed m.p. 102.5–104°), and 6.8 g. (85%) of tetramethylammonium iodide (dec. pt. and mixed dec. pt. 228°). In addition to these products there was recovered 0.63 g. (6%) of crude IVa-b, $n^{25}_{\rm D}$ 1.4629 (picrate m.p. and mixed m.p. 139–140°).

In a similar experiment carried out with 0.08 mole of potassium amide and 10.0 g. (0.04 mole) of *n*-amylcyclohexadieneamines IVa-b in 250 ml. of sodium-dried refluxing benzene (80°) for 24 hr. (pale orange-gray reaction mixture), there was isolated 6.1 g. (80%) of *n*-amylmesitylene (V), b.p. 103–104.5° at 3 mm., $n^{25}_{\rm D}$ 1.4983, and 1.4 g. (14%) of recovered *n*-amylcyclohexadieneamines IVa-b, b.p. 84–88° at 0.3 mm., picrate m.p. and mixed m.p. 139–140.5°.

Reaction of *n*-Amylcyclohexadieneamines IVa-b with Potassium *n*-Pentoxide.—To a solution of 0.12 mole of potassium amide in 200 ml. of liquid ammonia was added dropwise with stirring 250 ml. of dry 1-pentanol, and the ammonia then evaporated (steam-bath) from the resulting suspension of potassium *n*-pentoxide. The mixture was gradually heated to reflux on a heating mantle (solution attained), followed by the dropwise addition of 10.0 g. (0.04 mole) of *n*-amylcyclohexadieneamines IVa-b. The stirred reaction mixture, which rapidly became deep orange in color, was refluxed (137–138°) for 12 hr. (trimethylamine evolved). After cooling to room temperature, water was added slowly and the reaction mixture worked up (as described above) to give 7.1 g. (93%) of *n*-amylmesitylene (V), b.p. 102.5–104° at 3 mm., $n^{25}_{\rm D}$ 1.4984. None of the starting compound was recovered.

When the reaction was carried out similarly with 0.12 mole of sodium ethoxide and 10.0 g. (0.04 mole) of *n*-amylcyclohexadieneamines IVa-b in 250 ml. of refluxing absolute ethanol (24 hr.), there was obtained from the pale orange reaction mixture 0.4 g. (5%) of crude *n*-amylmesitylene, $n^{25}_{\rm D}$ 1.4986. Also, there was recovered 9.1 g. (91%) of amines IVa-b, b.p. 85–87° at 0.3 mm., $n^{25}_{\rm D}$ 1.4822.

***n*-Amylcyclohexadieneamine Methiodides VIa-b.**—This product (m.p. 204–205° dec.) was obtained in 98% yield from 0.127 mole of *n*-amylcyclohexadieneamines (IVa-b) and 0.20 mole of methyl iodide in 50 ml. of absolute ethanol. A sample, recrystallized twice from absolute ethanol–ether and dried *in vacuo*, melted at 205–206° dec.

Anal. Calcd. for $C_{18}H_{34}NI$: C, 55.23; H, 8.75; N, 3.58. Found: C, 55.10; H, 8.74; N, 3.51.

Reaction of *n*-Amylcyclohexadieneamine Methiodides VIa-b with Potassium Amide.—To a stirred solution of 0.25 mole of potassium amide in 600 ml. of liquid ammonia was added rapidly (2 minutes) 48.7 g. (0.125 mole) of mixed methiodides VIa-b. The resulting bright red reaction mixture was allowed to react an additional 8 minutes, followed by the replacement of ammonia by ether (steam-bath) and the cautious addition of 150 ml. of water. The aqueous and ethereal layers were separated, the latter being worked up in the usual manner to give 21.2 g. (89%) of *n*-amylmesitylene (V), b.p. 103–104° at 3 mm., $n^{25}_{\rm D}$ 1.4983 (sulfonamide m.p. and mixed m.p. 102–103°).

The aqueous alkaline layer containing tetramethylammonium hydroxide was neutralized carefully to *p*H 6 with hydrochloric acid with subsequent addition of 30.0 g. (0.13 mole) of picric acid. The resulting suspension was heated to boiling while additional water was put in to attain a clear solution. After cooling to 0°, the precipitated quaternary salt was collected on a funnel and recrystallized twice from a minimum of boiling water to afford 33.2 g. (88%) of tetramethylammonium picrate, m.p. and mixed m.p. 314–315° dec. (reported[9] m.p. 312–313° dec.).

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[8] R. L. Shriner and R. C. Fuson, "The Systematic Identification of Organic Compounds," 4th Ed., John Wiley and Sons, Inc., New York, N. Y., 1956, p. 296.

[9] W. Lossen, *Ann.*, **181**, 364 (1876).

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, DUKE UNIVERSITY]

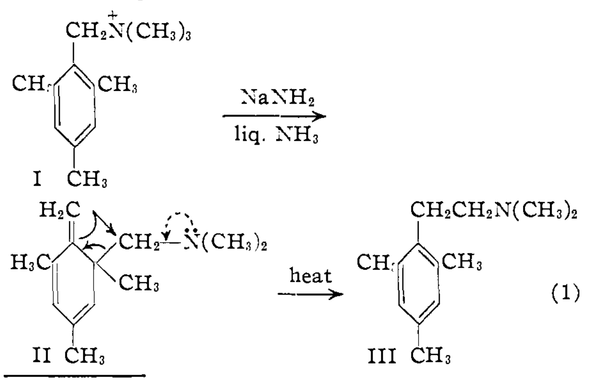
Thermal and Acid Induced Aromatizations of an *exo*-Methylenecyclohexadieneamine with Alcohols. Relation to *ortho* Substitution Rearrangement[1]

BY CHARLES R. HAUSER AND DONALD N. VAN EENAM

RECEIVED JUNE 28, 1957

Two of the characteristic reactions of an *exo*-methylenecyclohexadieneamine, thermal isomerization to a β-arylethylamine and acid induced conversion to isodurene, were realized with certain alcohols and amines. Relatively more of the former reaction and relatively less of the latter occurred as the reactivity of the hydroxyl hydrogen of the alcohols was decreased and/or the temperature raised. These results furnish further evidence for the 1,3-shift mechanism of the thermal isomerization.

Recently[2] aromatic quaternary ammonium ion I was rearranged by sodium amide in liquid ammonia to *exo*-methylenecyclohexadieneamine II which was rearomatized in several ways. One of these processes involved the thermal isomerization of II to form β-arylethylamine III (as shown in eq. 1). Another mode of aromatization of II consisted in its treatment with cold dilute hydrochloric acid which produced isodurene (IV) and dimethylmethyleneiminium chloride (equation 2).



I

II

III

(1)

In the present investigation both of these modes of aromatization were realized simultaneously with certain alcohols and amines. For example, on refluxing *exo*-methylenamine II in ethanol solution there were obtained both β-arylethylamine III and isodurene (IV) in yields of 25 and 71%, respectively. This predominant formation of isodurene was unexpected since amine III is formed exclusively on refluxing II in benzene. Evidently the *exo*-methylene group of II is so reactive toward acids that even ethanol functions largely in this manner

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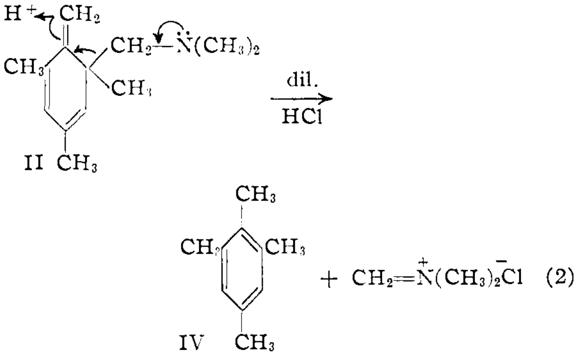
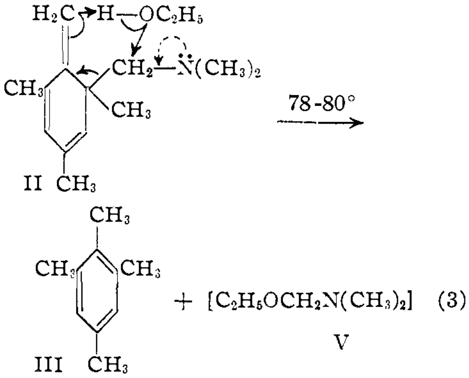
[1] Supported by the National Science Foundation.

[2] C. R. Hauser and D. N. Van Eenam, THIS JOURNAL, **79**, 5512 (1957).

giving up its hydroxyl hydrogen as a proton to this group. Possibly a cyclic mechanism operates (equation 3). Although the amino ether by-product V was not isolated, its hydrolysis products, formaldehyde and dimethylamine were obtained.



(2)



(3)

That this reaction was brought about by the ethanol and not by traces of a stronger acid was shown by the observation that approximately the same relative yields of amine III and isodurene (IV) were obtained when the reaction was carried out in refluxing ethanol in the presence of an equivalent of sodium ethoxide.

Since the thermal isomerization is unimolecular[3] whereas the acidic type of aromatization with ethanol is bimolecular, *exo*-methyleneamine II should undergo relatively more of the former reaction and relatively less of the latter in the presence of only one equivalent of the alcohol than with the large excess employed in the experiment described above. In agreement with this, the yields of amine III and isodurene (IV) were 73 and 22%, respectively; these yields are practically the reverse of those obtained when ethanol alone was employed as solvent.

It was anticipated that the relative yields of isodurene (IV) would be decreased and that of amine III increased on heating *exo*-methyleneamine II at 78–80° in solutions of a series of alcohols in which the presumed acidities of the hydroxyl hydrogens decrease in the following order: ethanol > 1-pentanol > *t*-butyl alcohol > triethylcarbinol. This was verified, the yields of the products being given in Table I. Thus, in this series of alcohols the yields of isodurene decreased from 71 to 31% while those of amine III increased from 25 to 62%.

TABLE I

INFLUENCE OF SOLVENT ON YIELDS OF III AND IV FROM II AT 78–80°

Solvent	Amine III yield, %	Isodurene (IV) yield, %	Total yield, %
C_2H_5OH	25	71	96
n-$C_5H_{11}OH$	27	66	93
$(CH_3)_3COH$	45	51	96
$(C_2H_5)_3COH$	62	31	93
$[(CH_3)_2CH]_2NH$	84	11	95
C_6H_6	91	..	91

Also in Table I are given the yields of products in diisopropylamine and benzene as solvents. Even this amine, which is an extremely weak acid, produced some isodurene, although the thermal isomerization product, amine III, was mainly obtained. Benzene gave exclusively the latter product.

In Table II are given the yields of the two products resulting on heating *exo*-methyleneamine II in solutions of 1-pentanol and triethylcarbinol at two different temperatures. As was expected, each alcohol produced relatively less isodurene and relatively more amine III as the temperature was raised.

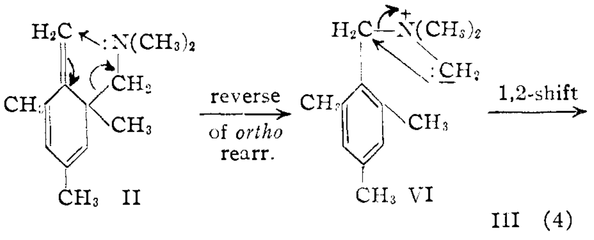
TABLE II

INFLUENCE OF TEMPERATURE ON YIELDS OF III AND IV FROM II

Solvent	Temp., °C.	Amine III yield, %	Isodurene (IV) yield, %
n-$C_5H_{11}OH$	78–80	27	66
n-$C_5H_{11}OH$	136–137	40	54
$(C_2H_5)_3COH$	78–80	62	31
$(C_2H_5)_3COH$	136–137	90	5

In view of the great reactivity of the *exo*-methylene group of II toward acids, it was of interest to determine whether the thermal isomerization could be realized in the presence of phenol or acetic acid. However, even though II was added to these acids at their refluxing temperatures, only isodurene (93–94%) was obtained.

Bearing of Results on Mechanism of Thermal Isomerization of II.—Although the thermal isomerization of II to form β-mesitylethyldimethylamine (III) has been considered to involve the 1,3-shift of the dimethylaminomethyl group from a ring carbon to the *exo*-methylene carbon (equation 2),[2] there was a possibility that the mechanism involved the reversal of the process by which II was formed from quaternary ion I, accompanied by a 1,2-shift within the resulting carbanion VI (equation 4).



(4)

However, this mechanism is now untenable since *exo*-methyleneamine (II) is converted partly to β-arylethylamine III in alcohols (Table I), and in

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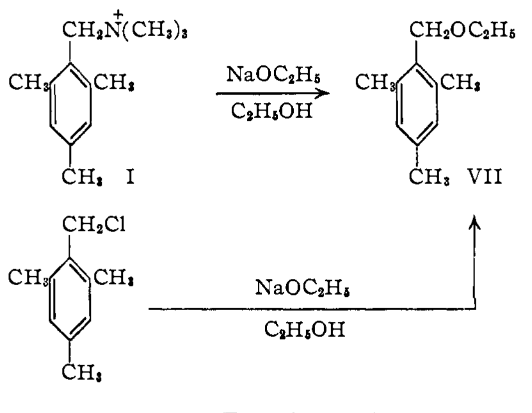
[3] This should be largely independent of solvent, although a slight influence of solvent has been observed; see ref. 2.

these solvents such a carbanion as VI should have acquired a proton to form quaternary ion I and alkoxide ion. Had these products been formed they would have given the corresponding ether VII which was not obtained. Thus, under similar conditions quaternary ion I and sodium ethoxide were shown to be converted almost quantitatively to ether VII, the structure of which was established by an independent synthesis from α^2-isoduryl chloride (equation 5).



(5)

Experimental[4]

Reactions of *exo*-Methyleneamine (II) with Ethanol. (A) with Ethanol Alone.—To 250 ml. of refluxing absolute ethanol contained in a 500-ml. 3-necked flask equipped with sealed stirrer, dropping funnel and a reflux condenser fitted with a Drierite drying tube was added 19.1 g. (0.10 mole) of *exo*-methyleneamine (II) (prepared[2] from the rearrangement of 2,4,6-trimethylbenzyltrimethylammonium chloride (I)). The resulting reaction mixture was refluxed and stirred for 24 hours, cooled, and poured onto 1 l. of water. After taking up the reaction products in ether, 100 ml. of 6 *N* hydrochloric acid was added and the mixture shaken in a separatory funnel. The ethereal layer was washed with water, dried over magnesium sulfate, filtered and the solvent removed. Distillation of the residue afforded 9.5 g. (71%) of isodurene (IV), b.p. 85–86° at 18 mm., $n^{25}\text{D}$ 1.5108 (reported[5] b.p. 84.6–84.7° at 17 mm., $n^{25}\text{D}$ 1.5107). The dinitro derivative of this hydrocarbon, after two crystallizations from 95% ethanol, melted at 180–181° (reported[6] m.p. 181°).

The aqueous acidified layer was made alkaline (*p*H 9–10) with 50% sodium hydroxide and the resulting liberated amine extracted with ether, washed with water, dried, and the solvent evaporated. The residual oil was distilled *in vacuo* to give 4.8 g. (25%) of β-mesitylethyldimethylamine (III), b.p. 111–112° at 5 mm., $n^{25}\text{D}$ 1.5088 (reported[2] b.p. 111.5–112° at 5 mm., $n^{25}\text{D}$ 1.5088). The picrate, after three crystallizations from 95% ethanol, melted at 169–170° (reported[2] m.p. 169.5–170.5°). The melting point was not depressed on admixture with an authentic sample of β-mesitylethyldimethylamine picrate, m.p. 169.5–170.5°.

The aqueous alkaline solution, which contained formaldehyde and dimethylamine (resulting from the acid-catalyzed hydrolysis of amino ether V), smelled strongly of the former. On the addition of phenyl isothiocyanate, a precipitate of N,N-dimethylphenylthiourea was obtained after shaking for several minutes. Following crystallization from 95% ethanol, the derivative melted at 134–135° (reported[7] m.p. 135°). The melting point was not depressed on admixture with an authentic sample of N,N-dimethylphenylthiourea, m.p. 134–135°.

(B) **With an Equivalent of Sodium Ethoxide.**—When the reaction was repeated using one equivalent of sodium ethoxide (prepared *in situ* from 2.30 g. (0.10 g. atom) of sodium in 250 ml. of refluxing absolute ethanol) and 19.1 g. (0.10 mole) of *exo*-methyleneamine II, there was obtained on work-up (as described above) 10.0 g. (75%) of isodurene (IV), b.p. 85–87° at 18 mm., $n^{25}\text{D}$ 1.5109, and 3.8 g. (20%) of β-mesitylethyldimethylamine (III), b.p. 111–113° at 5 mm., $n^{25}\text{D}$ 1.5089.

(C) **With an Equivalent of Ethanol in Benzene.**—The reaction was again repeated in 250 ml. of refluxing sodium-dried benzene solution containing 4.61 g. (0.10 mole) of absolute ethanol and 19.1 g. (0.10 mole) of *exo*-methyleneamine (II). The reaction mixture afforded 2.9 g. (22%) of isodurene (IV), b.p. 85–87° at 18 mm., $n^{25}\text{D}$ 1.5109, and 13.9 g. (73%) of amine III, b.p. 111–113° at 5 mm., $n^{25}\text{D}$ 1.5090.

Reactions of *exo*-Methyleneamine (II) in Various Solvents (Tables I and II).—These reactions were carried out essentially as described above for ethanol (procedure A) using solvents that were carefully dried over Drierite and purified by distillation to a boiling range of 1°. To 250 ml. of the appropriate solvent maintained at the desired temperature was added with continued stirring 19.1 g. (0.10 mole) of *exo*-methyleneamine (II). After completion of the reaction,[8] the resulting reaction mixture was cooled and poured onto water. In the case of water-soluble solvents the reaction products were taken up in ether and worked-up as described above. With water-insoluble solvents the organic layer was treated with excess 6 *N* hydrochloric acid, diluted with 250 ml. of ether, shaken in a separatory funnel, and the layers separated. The ether–solvent solution of isodurene was dried over magnesium sulfate, filtered, and the solvent carefully distilled through a 40-cm. Podbielniak type column. The remaining residual oil was then distilled *in vacuo* to give essentially pure isodurene (IV), b.p. 85–87° at 18 mm. After making the aqueous acidified layer alkaline with 50% sodium hydroxide, the resulting liberated amine was processed in the usual manner and distilled *in vacuo* to give β-mesitylethyldimethylamine (III), b.p. 111–113° at 5 mm.

In the experiment carried out with refluxing phenol (m.p. 40–41°, b.p. 180°) there was a copious evolution of dimethylamine and the reaction mixture became dark reddish-brown by the end of the 5-hour reaction period. During the work-up of the reaction mixture none of the usual strong odor of formaldehyde was detected. The yield of isodurene, the sole product, was 93%.

With refluxing glacial acetic acid (b.p. 117°) the sole product after 5 hours was again isodurene (94%).

Reaction of 2,4,6-Trimethylbenzyltrimethylammonium Chloride (I) with Sodium Ethoxide.—To a stirred solution of sodium ethoxide in ethanol (prepared *in situ* from 2.30 g. (0.10 g. atom) of freshly cut sodium and 250 ml. of absolute ethanol) was added rapidly 22.8 g. (0.10 mole) of quaternary ammonium chloride I. The resulting reaction mixture was heated under reflux with stirring for 12 hours, during which time trimethylamine was evolved readily. After cooling to room temperature, the mixture was poured onto 1 l. of water followed by the addition of 100 ml. of 6 *N* hydrochloric acid. The organic product was taken up in ether, washed with water, dried, and the solvent evaporated. Distillation of the residual oil *in vacuo* gave 16.9 g. (94%) of 2,4,6-trimethylbenzyl ethyl ether (VII), b.p. 115–116° at 14 mm., $n^{25}\text{D}$ 1.5003 (reported[9] b.p. 114–115° at 14 mm.).

There was no isolable amine liberated from the aqueous acidified solution on addition of excess 50% sodium hydroxide.

Independent Synthesis of Ether VII.—This reaction was carried out in a similar manner to that described above for quaternary halide I with equimolar amounts (0.10 mole) of α^2-isoduryl chloride and sodium ethoxide in 250 ml. of absolute ethanol. There was obtained 16.2 g. (91%) of 2,4,6-trimethylbenzyl ethyl ether (VII), b.p. 115–116° at 14 mm., $n^{25}\text{D}$ 1.5003.

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[4] Melting and boiling points are uncorrected.

[5] L. I. Smith and F. H. MacDougall, THIS JOURNAL, **51**, 3004 (1929).

[6] L. I. Smith and L. C. Moyle, *ibid.*, **55**, 1680 (1933).

[7] R. L. Shriner and R. C. Fuson, "The Systematic Identification of Organic Compounds," Fourth ed., John Wiley and Sons, Inc., New York, N. Y., 1956, p. 288.

[8] The experiments in Table I were allowed to proceed for 24 hours and those in Table II for 18 hours. A preliminary experiment showed that at least in refluxing ethanol the reaction was essentially complete after only 8 hours.

[9] W. Th. Nauta and J. W. Dienske, *Rec. trav. chim.*, **55**, 1000 (1936).