A small sample was well crushed and dried in an Abderhalden apparatus over phosphorus pentoxide at 110° for ten hours. The melting point of the anhydrous **dihydrobromide** was 216-220°.

Anal. Calcd. for $C_{13}H_{22}Br_2N_2$: C, 42.64; H, 6.06. Found: C, 42.76; H, 6.31.

We were unable to isolate the monopicrate, m. p. 202°, described by Rupe and Frey,[4] but we obtained a **dipicrate** when the amine in ethanol was treated with a large excess of ethanolic picric acid. Recrystallization from acetone-ethanol gave yellow crystals which softened at 158° and melted at 171-174°.

Anal. Calcd. for $C_{25}H_{26}N_8O_{14}$: C, 45.32; H, 3.96; N, 16.91. Found: C, 45.56; H, 4.18; N, 17.17.

Summary

It has been established that 2-nitronaphthalene is produced from the condensation of 2-methylisoquinolinium iodide with nitromethane in the presence of potassium hydroxide, and a plausible series of reactions has been suggested to account for this unusual transformation. The alkaline condensation of 2-methyliosquinolium iodide with nitromethane also produced some bis-[1-(2-methyl - 1,2 - dihydroisoquinolyl)]-nitromethane, that with nitroethane produced 1,1-bis-[1′-(2′-methyl - 1′,2′ - dihydroisoquinolyl)]-nitroethane, and that with 1-nitropropane gave 1,1-bis-[1′-(2′-methyl-1′,2′-dihydroisoquinolyl)]-1-nitropropane.

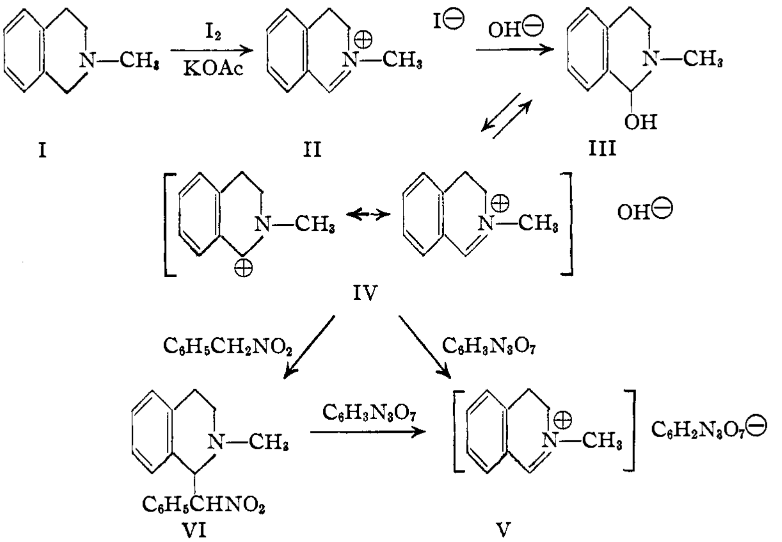
URBANA, ILLINOIS RECEIVED APRIL 28, 1949

[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

Reactions of Nitroparaffins with Pseudo Bases Related to Dihydroisoquinolinium Hydroxide

BY NELSON J. LEONARD AND GERHARD W. LEUBNER[1,2]

In an investigation[3] of the reaction of nitroparaffins with a pseudo base of type III,[4] the attempted characterization of the nitromethane product (analogous to VI) by picrate formation gave an unusual result. The supposed picrate derivative always reverted to the picrate of the pseudo base (V)! This observed elimination of nitromethane prompted a reëxamination of the picrate derivatives of anhydrocotarninenitromethane (VIII) and anhydrohydrastininenitromethane (VIII without methoxyl) reported by Hope and Robinson.[5] It has now been found that these reported derivatives are, in fact, cotarnine picrate (IX) and hydrastinine picrate (IX without methoxyl), both products of nitromethane elimination.



The method of synthesis of the pseudo base III required the initial preparation of 2-methyl-1,2,3,4-tetrahydroisoquinoline (I). The previously described directions for obtaining I by the reduction of 2-methylisoquinolinium iodide with tin and hydrochloric acid[6] or with sodium and ethanol[7] were less convenient than the formaldehyde–formic acid methylation[8] of 1,2,3,4-tetrahydroisoquinoline. 2-Methyl-1,2,3,4-tetrahydroisoquinoline (I) was oxidized to 2-methyl-3,4-dihydroisoquinolinium iodide (II) by means of iodine and potassium acetate. Compound II had been prepared previously, but by a degradation process.[9] The conversion of tetrahydro- to dihydro-compounds by iodine oxidation had been realized previously with several highly substituted tetrahydroisoquinolines,[10,11,12] but Schmidt had reported that iodine oxidation of tetrahydroisoquinoline itself gave iso-

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(1) Eli Lilly and Company Fellow, 1946-1948.

(2) Present address: Eastman Kodak Company, Rochester, N. Y.

(3) For previous paper, see Leonard and Leubner, THIS JOURNAL, **71**, 3405 (1949).

(4) Compound III results from alkali treatment of a 3,4-dihydroisoquinolinium salt (II).

(5) Hope and Robinson, *J. Chem. Soc.*, **99**, 2114 (1911).

(6) Wedekind and Oechslen, *Ber.*, **34**, 3986 (1901).

(7) Emde, *Ann.*, **391**, 88 (1912).

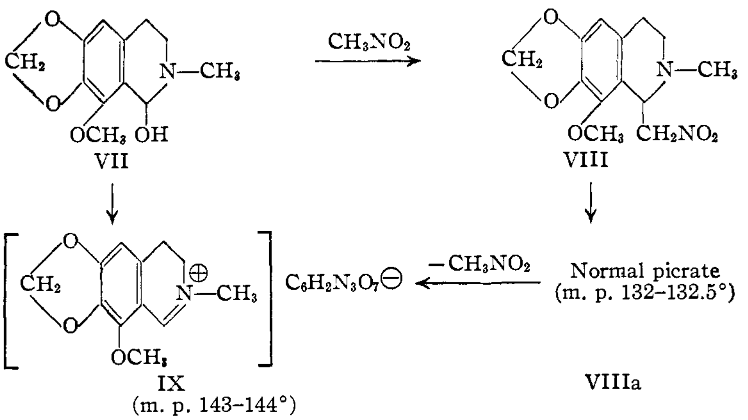
(8) "Organic Syntheses," **25**, 89 (1945).

(9) Pyman, *J. Chem. Soc.*, **95**, 1738 (1909).

(10) Haworth, Perkin and Rankin, *ibid.*, **127**, 1444 (1925).

(11) Haworth and Perkin, *ibid.*, **127**, 1434 (1925).

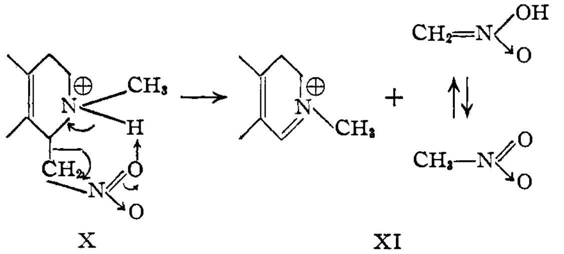
(12) German Patent 267,272, Jan. 19, 1913; *Frdl.*, **11**, 1004 (1912-1914).



quinoline.[13] The conversion of I to II was found to proceed in satisfactory yield. Since the reaction of II with nitromethane in the presence of alkali did not produce any pure chemical individual, attention was turned to the pseudo base III, obtained from II by treatment with sodium hydroxide.

The combination of 1-hydroxy-2-methyl-1,2,3,-4-tetrahydroisoquinoline (III) with nitromethane in methanol led to the liberation of heat, but not to the formation of any crystallizable or distillable condensation product. Although the liberation of heat was indicative at a reaction between III and the nitroparaffin, as was the separation of water when the two were mixed in the absence of a solvent or in benzene, a picrate prepared from the reaction mixture was identified as 2-methyl-3,4-dihydroisoquinolinium picrate (V). The same picrate was prepared directly from the pseudo base (III) without the intervening nitromethane treatment. From these results it appeared that a transient nitromethane condensation product with III was produced, but that this product lost nitromethane readily at some stage. Further information was gained through the reaction of the pseudo base (III) with phenylnitromethane, since this combination produced a readily isolable solid product. The reaction is considered to proceed by combination of the carbonium species IV with the phenylnitromethane carbanion. An eighty-seven per cent. yield of 2-methyl-1-(α-nitrobenzyl)-1,2,3,4-tetrahydroisoquinoline (VI) was obtained merely by bringing the reactants together in methanol at 25°. When a picrate derivative was prepared from crystalline VI, the picrate was non-homogeneous as first precipitated, but heating in ethanol provided pure 2-methyl-3,4-dihydroisoquinolinium picrate (V). Phenylnitromethane must have been eliminated—and as a result of the picric acid.

The observed probable elimination of nitromethane and certain elimination of phenylnitromethane in these attempts to form picrates of condensation products of type VI suggested a re-examination of analogous derivatives of some of the isoquinoline alkaloids. Cotarnine (VII) forms a picrate (IX), m. p. 143–144°,[14] and a solid condensation product with nitromethane, called anhydrocotarninenitromethane (VIII).[5] The picrate of VIII prepared by Hope and Robinson[5] was described as melting at 136–137°, but no analysis was reported. It appeared from these close melting points that the nitromethane condensation product might have lost some nitromethane upon or after picric acid treatment. Following the procedure of Hope and Robinson, a picrate was prepared from anhydrocotarninenitromethane in aqueous acetic acid. This picrate melted at 134–136° when heated rapidly, and sintered at 140° and melted at 142–144° when heated slowly. The melting point of a mixture with authentic cotarnine picrate (IX) was 143–144°. Recrystallized "anhydrocotarninenitromethane picrate"[5] was definitely cotarnine picrate. When the picrate of VIII was prepared in anhydrous ether solution, a different picrate was obtained, m. p. 132–132.5°. This derivative, which was not recrystallized but was merely washed with ether as a means of purification, had the correct analysis for the normal picrate of anhydrocotarninenitromethane (VIIIa). Picrate VIIIa reverted to cotarnine picrate (IX), with elimination of nitromethane, when heated in acetone for recrystallization. The loss of nitroparaffin is parallel to that observed with 2-methyl-1-nitromethyl-1,2,3,4-tetrahydroisoquinoline and 2-methyl-1-(α-nitrobenzyl)-1,2,3,4-tetrahydroisoquinoline (VI). That the elimination of nitroparaffin is acid-catalyzed (X → XI) follows from the sensitivity of these pseudo base–nitroparaffin condensation products to acetic acid and to picric acid (especially in warm solution)



The alkaloid hydrastinine (VII without methoxyl) forms a picrate, m. p. 173°,[15] and a condensation product with nitromethane, called anhydrohydrastininenitromethane.[5] A picrate of anhydrohydrastininenitromethane was described by Hope and Robinson[5] as melting at 173–174°, but no analysis was reported. Because of the suggestive proximity of these melting points and by

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[13] Schmidt, *Arch. Pharm.*, **237**, 561 (1899).

[14] Heilbron, "Dictionary of Organic Compounds," Vol. I, 1934, p. 356.

[15] Decker, *Ann.*, **395**, 321 (1913).

analogy to the three cases of nitroparaffin elimination described herein, we conclude that the derivative described as "anhydrohydrastinenitromethane picrate" is actually hydrastinine picrate.

Experimental[16]

2-Methyl-1,2,3,4-tetrahydroisoquinoline (I).—Hydrogenation of isoquinoline in absolute ethanol at 200 atm. and 200° over copper chromite catalyst gave a 98% yield of 1,2,3,4-tetrahydroisoquinoline. Methylation of 1,2,3,4-tetrahydroisoquinoline by means of formaldehyde and formic acid[8] gave a 79% yield of 2-methyl-1,2,3,4-tetrahydroisoquinoline,[6,7] b. p. 84-85° (4 mm.), 103-105° (14 mm.), 223-224° (745 mm.); n^{20}D 1.5422.

2-Methyl-3,4-dihydroisoquinolinium Iodide (II).—A solution of 73.5 g. (0.5 mole) of 2-methyl-1,2,3,4-tetrahydroisoquinoline and 54 g. (0.55 mole) of anhydrous potassium acetate (freshly fused) in 500 ml. of absolute ethanol was heated to refluxing, and to the solution was added slowly (four hours) with stirring a solution of 127 g. (0.5 mole) of iodine in 1.2 l. of absolute ethanol. When the addition was complete, the solution was refluxed for three hours. Ethanol (1.5 l.) was distilled from the reaction mixture and the residue was allowed to cool to room temperature. Potassium iodide was removed by filtration and the filtrate and washings were concentrated. After removal of the second crop of potassium iodide, the remaining ethanol and acetic acid were removed under reduced pressure on the steam-bath. The dark viscous residue was dissolved with heating in 125 ml. of acetone and 20 ml. of absolute ethanol. Cooling induced the separation of 54 g. (40%) of yellow prisms which were recrystallized from the same mixed solvent; m. p. 124-125° (reported, 125-128°).[9] Similar runs using smaller amounts (3 g.) invariably gave better yields (65-80%).

Anal. Calcd. for $C_{10}H_{12}IN$: C, 43.97; H, 4.43; N, 5.13. Found: C, 44.10; H, 4.36; N, 5.06.

1-Hydroxy-2-methyl-1,2,3,4-tetrahydroisoquinoline (III).—Fifty-four grams (0.2 mole) of crude 2-methyl-3,4-dihydroisoquinolinium iodide, m. p. 118-124°, was stirred with 90 ml. of water. After removal of the insoluble material (1.2 g.) by filtration, the orange solution was cooled to 0° and a cold solution of 32 g. (0.8 mole) of sodium hydroxide in 50 ml. of water was added slowly with stirring. An orange solid separated. The mixture was extracted with three 250-ml. portions of ether, the ethereal solution was concentrated by distillation and was finally allowed to evaporate at room temperature. The residue, which consisted of a mixture of red oil and beautiful elongated prisms, was stirred and crushed with cold acetone. The insoluble solid was collected and washed with cold acetone; yield, 14.2 g. (45%). Recrystallization from acetone gave colorless prisms, m. p. 101-103° (reported, 110-111°).[9,17]

Anal. Calcd. for $C_{10}H_{13}NO$: C, 73.59; H, 8.03; N, 8.58. Found: C, 73.48; H, 8.28; N, 8.46.

In an infrared spectrum determination no carbonyl absorption was observed, but a band (3093 cm.$^{-1}$) was found at the low frequency characteristic of strongly bonded O-H. Absorption bands at 1607 and 1491 cm.$^{-1}$ were characteristic of the phenyl group and that at 745 cm.$^{-1}$, of *o*-substituted phenyl.

2-Methyl-3,4-dihydroisoquinolinium Picrate (V).—Prepared in absolute ethanol from 1-hydroxy-2-methyl-1,2,3,4-tetrahydroisoquinoline and picric acid and recrystallized from absolute ethanol, the picrate was obtained as yellow elongated prisms, m. p. 147-148° (reported, 145°).[9]

Reaction of 1-Hydroxy-2-methyl-1,2,3,4-tetrahydroisoquinoline with Nitromethane.—The reaction of 2-methyl-3,4-dihydroisoquinolinium iodide with nitromethane in the presence of alkali led to non-homogeneous material from which neither a pure product nor a derivative could be isolated. There was apparently a reaction between nitromethane (0.56 g., 0.09 mole) and 1-hydroxy-2-methyl-1,2,3,4-tetrahydroisoquinoline (0.50 g., 0.03 mole) in methanol (1 ml.) since heat was liberated upon addition of the nitromethane. The solution was allowed to evaporate at room temperature. The light yellow oily residue could not be distilled or induced to crystallize. A picrate prepared in ethanol solution sintered at 103° and melted at 106-145°. Two recrystallizations from absolute ethanol gave yellow elongated prisms, m. p. 147-148°, which gave no depression when mixed with 2-methyl-3,4-dihydroisoquinolinium picrate.

Anal. Calcd. for $C_{16}H_{14}N_4O_7$: C, 51.34; H, 3.77. Found: C, 51.54; H, 3.89.

When the reaction between 1-hydroxy-2-methyl-1,2,3,4-tetrahydroisoquinoline and nitromethane was run in the absence of a solvent or in benzene, water separated from the solution, thus indicating initial condensation before picrate formation. In a run employing 6 g. of pseudo base (III) with excess nitromethane, the theoretical quantity of water was collected by distillation after condensation.

Reaction of 1-Hydroxy-2-methyl-1,2,3,4-tetrahydroisoquinoline with Phenylnitromethane.—A solution of 0.5 g. (0.03 mole) of 1-hydroxy-2-methyl-1,2,3,4-tetrahydroisoquinoline in 1 ml. of methanol was treated with 1.23 g. (0.09 mole) of purified[18] phenylnitromethane. After one-half hour crystals began to separate, and the mixture was allowed to stand at 25° for twelve hours. After cooling, filtering and drying operations, 0.75 g. (87%) of colorless prisms were collected; m. p. 118-119°. Several recrystallizations from methanol did not alter the melting point of the product, 2-methyl-1-(α-nitrobenzyl)-1,2,3,4-tetrahydroisoquinoline (VI).

Anal. Calcd. for $C_{17}H_{18}N_2O_2$: C, 72.32; H, 6.42; N, 9.92. Found: C, 72.02; H, 6.75; N, 9.81.

The picrate prepared in ether solution melted over a range 135-145°. When this derivative was heated in ethanol solution for recrystallization, it was converted to a pure compound, isolated as yellow elongated prisms, m. p. 147-148°, and identified as 2-methyl-3,4-dihydroisoquinolinium picrate.

Cotarnine Picrate (IX).—Prepared in and recrystallized from absolute ethanol, cotarnine picrate was obtained as delicate yellow needles, m. p. 143-144°.[14]

Anhydrocotarninenitromethane (VIII).—To a hot solution of 1.0 g. (0.004 mole) of cotarnine chloride (Merck Stypticin) and 0.72 g. (0.012 mole) of nitromethane in 3 ml. of absolute ethanol was added a hot solution of 0.52 g. (0.008 mole) of potassium hydroxide in ethanol. The mixture was filtered hot to remove the by-product potassium chloride. From the cooled filtrate, 0.76 g. (69%) of anhydrocotarninenitromethane separated as colorless prisms, m. p. 125-126° (reported, 129°).[5]

The infrared absorption spectrum showed strong bands at 1549 and 1321 cm.$^{-1}$, characteristic of the nitro group. The strong band observed at 1620 cm.$^{-1}$ was due partially, at least, to the phenyl group, which also accounted for the band at 1498 cm.$^{-1}$. The strong absorption bands at 1123, 1095, 1077, 1061, 1050, 1033 and 1026 cm.$^{-1}$ were in the C-O vibration region.

Anhydrocotarninenitromethane Picrate (VIIIa).—The picrate was made by treating a saturated solution of anhydrocotarninenitromethane in ether with anhydrous picric acid in ether. The precipitated yellow prisms were collected and washed with ether; m. p. 132-132.5°.

Anal. Calcd. for $C_{19}H_{19}N_5O_{12}$: C, 44.80; H, 3.76; N, 13.75. Found: C, 45.19; H, 3.90; N, 13.52.

When heated in ethanol or acetone for recrystallization, this picrate was converted to cotarnine picrate, yellow needles, m. p. 143-144°, as established by mixed melting point,

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(16) All melting points are corrected. The authors are indebted to Mr. Roger E. Beyler for assistance and to Mrs. James L. Johnson for determination of the infrared absorption spectra.

(17) Avenarius and Pschorr, *Ber.*, **62**, 321 (1929).

(18) Fieser and Gates, THIS JOURNAL, **68**, 2249 (1946).

Following Hope and Robinson's directions[5] for the preparation of anhydrocotarninenitromethane picrate, anhydrocotarninenitromethane was dissolved in aqueous acetic acid and an aqueous solution of picric acid was added. A solid picrate resulted which melted at 134–136°, when the melting point was taken with rapid heating, and sintered at 140° with melting at 142–144°, when the temperature was raised slowly. When mixed with cotarnine picrate, the melting point was 143–144°. A sample was submitted for analysis after two recrystallizations from absolute ethanol; yellow needles, m. p. 143–144°.

Anal. Calcd. for cotarnine picrate, $C_{18}H_{16}N_4O_{10}$: C, 48.22; H, 3.60; N, 12.50. Found: C, 48.35; H, 3.66; N, 12.14.

Summary

The elimination of nitromethane from 2-methyl-1-nitromethyl-1,2,3,4-tetrahydroisoquinoline and anhydrocotarninenitromethane and of phenylnitromethane from 2-methyl-1-(α-nitrobenzyl)-1,2,3,4-tetrahydroisoquinoline has been observed in the presence of picric acid.

URBANA, ILLINOIS RECEIVED MAY 6, 1949

[CONTRIBUTION FROM THE CHEMICAL LABORATORY, FACULTY OF SCIENCE, TOKYO UNIVERSITY]

Equilibrium Ratio of Rotational Isomers of *n*-Pentane: with Special Reference to its Difference from that of 1,2-Dichloroethane

BY SAN-ICHIRO MIZUSHIMA AND HIROATSU OKAZAKI

As shown in our preceding papers on the Raman effect, infrared absorption, dipole moment, and electron diffraction,[1] the molecules of 1,2-dichloroethane $ClH_2C–CH_2Cl$ in the gaseous and liquid states consist of the *trans* and the gauche forms, where the former is the configuration in which the two chlorine atoms are at the farthest distance apart and the latter differs from the former in an internal rotation by ±120° about the C–C bond as axis.

We determined also the equilibrium ratio of these two "rotational isomers" in the gaseous state by the measurement of dielectric constant and of the intensity ratio of two Raman lines or of two infrared absorption lines, one assigned to the *trans* form and the other to the gauche form.[1] From this equilibrium ratio the energy of the gauche molecule was found to be greater than that of the *trans* molecule by an amount of $\Delta E = 1.20$ kcal./mole. The intensity measurement made for the liquid spectra tells us that the situation is quite different in the liquid state. The relative number of molecules in the gauche form was found much larger than was expected from the value of ΔE stated above.[1a] This was explained[2] as due to the electrostatic interaction between the molecules in the liquid state: *i. e.*—while the *trans* molecule has no dipole moment, the gauche molecule has a considerable one and in consequence the energy of the gauche molecule is lowered by the electrostatic interaction to approach to that of the *trans* molecule.[3] If this explanation be appropriate, we expect for a non-polar substance that the value of ΔE in the liquid state will not be much different from that in the gaseous state. It would, therefore, be very interesting to measure the intensity change of the Raman spectrum of a non-polar liquid with temperature. With this object in view we have measured the Raman spectrum of *n*-pentane at 32° and at −72°.

For *n*-pentane there can be considered three rotational isomers of skeleton: the first one corresponding to the planar, zigzag form (four consecutive carbon atoms forming the *trans* configuration), the second one containing one gauche structure, and the third one containing two gauche structures. Of these three forms the first one is the most stable and the third one the most unstable, since in the first form all the movable groups (*i. e.*, CH_3– or CH_2–groups) are at the farthest distance apart.

The identification of the Raman lines to be assigned to the first form can at once be made from

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(1) The former part of this series of researches is summarized in: Mizushima and Morino, *Bull. Chem. Soc. Japan*, **17**, 94 (1942), (see also Mizushima, Morino and Takeda, *J. Chem. Phys.*, **9**, 826 (1941)) and the latter part is published in Mizushima, Morino, Watanabe, Simanouti, Yamaguchi, *etc.*, *Sci. Papers Inst. Phys. Chem. Research, Tokyo*, **39**, 387, 396, 401 (1942), **40**, 87, 100, 417, 425, 467 (1943), **42**, *Chem.*, 1, 5, 27 (1944), **42**, *Chem.*, 51 (1946).

(1a) *Cf.* Gerding and Meerman, *Rec. trav. chim. pays-bas*, **61**, 523 (1942). This paper is not available to the authors.

(2) Watanabe, Mizushima, and Masiko, *Sci. Papers Inst. Phys. Chem. Research, Tokyo*, **40**, 425 (1943).

(3) If we assume the same model of dielectrics as that of Onsager (THIS JOURNAL, **58**, 1486 (1936)) and consider a small cavity of radius a in the continuous medium of dielectric constant ϵ, a dipole of moment μ situated at the center of this spherical cavity will cause dielectric polarization in the continuous medium, which in turn exerts a field R (reaction field) upon the original dipole.

$$R = \frac{2(\epsilon - 1)}{2\epsilon + 1}\frac{\mu}{a^3}$$

Let us further assume that the gauche molecule can be represented by a sphere of radius a, at whose center the total permanent moment is located. The gauche molecule in the liquid state will then acquire an excess of electrostatic energy by an amount of

$$\Delta E' = \int_0^{\mu} -R\mathrm{d}\mu = -\frac{(\epsilon - 1)}{2\epsilon + 1}\frac{\mu^2}{a^3}$$

as compared with that in the gaseous state (*i. e.*, of the free molecule). The corresponding energy change of the *trans* molecule with no moment is negligible. Introducing the moment value of the gauche molecule (2.55 D) into μ of the above equation, we see that the value of $\Delta E'$ is almost equal to the value of ΔE, and therefore, the energy of the gauche molecule approaches to that of the *trans* molecule in the liquid state (see footnote (2)).