sisted of a broad multiplet at −4.38 ppm (*H*CBr, 2 H) and a broad multiplet characterisic of the *cis*-decalin framework (14 H).

Methoxymercuration.—A mixture of I (0.80 mmole), methanol (approximately 0.3 ml), and mercury(II) acetate (0.80 mmole) immediately became homogeneous when shaken in an nmr tube. The nmr spectrum consisted of a broad singlet at −5.30 ppm (MeO*H* and AcO*H* exchanging), a broad singlet at −3.30 ppm (OCH_3), a sharp singlet at −1.95 ppm ($OCOCH_3$), and broad, overlapping multiplets at −2.5 to −1.1 ppm (*cis*-decalin framework). The spectrum was devoid of signals for C=CH.

Oxymercuration–Demercuration[27] of I.—When 10 mmoles of I was mixed with a solution of mercury(II) acetate (10 mmoles) in aqueous tetrahydrofuran (10 ml of each solvent), the yellow color of the mixture disappeared within 30 sec. After reduction with sodium borohyride and extraction with ether, the reaction product mixture was shown by gas chromatography (10 ft × $^{1}/_{8}$ in. Carbowax 20 M column, 160°) to consist of two components in proportions 17:83 (minor component, shorter retention time). The major component was isolated (60% yield) by distillation and recrystallization and was identified as *cis,cis*-1-decalol,[28] mp 90–91.5°. Its *p*-toluenesulfonate derivative[28,36] melted at 89–89.5° (lit.[28] mp 88–88.5°), and its 3,5-dinitrobenzoate derivative at 122.5–124° (lit.[37] 123.8°). When a small sample of the alcohol mixture in acetone solution was oxidized with chromic acid,[38] gas chromatography (Carbowax 20 M and silicone SE-30 columns, 160°) of the product mixture revealed that both alcohols had been converted into a single ketone[39] identified as *cis*-1-decalone[40–43] by its 2,4-dinitrophenylhydrazone derivative (mp 170.5–172.5°; lit.[29a] mp 176–177°).

Addition of Methanesulfenyl Chloride.—A solution of methanesulfenyl chloride was prepared by adding chlorine (20 mmoles) to dimethyl disulfide (20 mmoles) in chloroform (1 ml) at −10° and then diluting the mixture to 5.0 ml with chloroform.[44] When a portion of that solution (0.2 ml, 1.6 mmoles) was added to a solution of I (1.4 mmoles) in an equal volume of chloroform in an nmr tube at 25°, an exothermic reaction took place. The nmr spectrum of the mixture was devoid of C=CH signals.

Registry No.—I, 1124-78-3; acetic acid, 64-19-7; carbon tetrachloride, 56-23-5; chloroform, 67-66-3; 1-acetoxy-4-bromo-*cis*-decalin, 13976-54-0; bromo alcohol $C_{10}H_{17}OBr$, 13976-55-1.

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[36] A. C. Cope, R. J. Cotter, and G. G. Roller, *J. Am. Chem. Soc.*, **77**, 3598 (1955).

[37] W. Hückel, D. Mancher, O. Fechtig, J. Kurz, M. Heinzel, and A. Hubele, *Ann.*, **645**, 115 (1961).

[38] K. Bowden, I. M. Heilbron, E. R. H. Jones, and B. C. L. Weedon, *J. Chem. Soc.*, **39** (1946).

[39] *cis*- and *trans*-1-decalones are reported to be separated by gas chromatography on a 1.5-m silicone column at 250°.[29b] We find that the *trans* ketone has a retention time about 1 min shorter than that of the *cis* isomer on a 10 ft × $^{1}/_{8}$ in. Carbowax 20 M column at 160°.

[40] *cis*-1-Decalone is easily converted to *trans*-1-decalone,[29a] and preparation of derivatives certain to be those of the *cis* isomer rather than the trans one is difficult. For example, *cis*-1-decalone 2,4-dinitrophenylhydrazone has been (mistakenly) reported to melt at 225°,[41] approximately the melting point of the *trans* derivative,[42] and two different preparations by us of the 2,4-dinitrophenylhydrazone from the same sample of *cis*-1-decalone (infrared spectral identification[29]) gave material melting after recrystallization at 159.5–162 and 216–219°, respectively. Repeated recrystallizations of the lower melting product did not raise the melting point to 176°, and sometimes led to a lower melting point. The isomerization of the ketone occurs much more easily than we had expected. When an ether solution of *cis*-1-decalone (infrared absorption at 938 cm^{-1} but not at 906 cm^{-1} [29]) extarcted from the chromic acid oxidation mixture was mixed with calcium chloride and neglected for 10 days, the ketone was nearly completely isomerized to *trans*-1-decalone (infrared absorption at 906 cm^{-1} but not at 938 cm^{-1} [29]). The 2,4-dinitrophenylhydrazone derivative of the *trans* ketone melted at 230–231° (lit. 225.2–227.8,[42a] 234–235,[42b] and 238–239°[29a]), and the semicarbazone derivative melted at 224–226.5° (lit.[43] mp 227–229°). Identification of this isomerization product actually reinforces the identification of the initial oxidation product, *cis*-1-decalone.

[41] I. N. Nazarov, L. A. Kazitsyna, and I. I. Zaretskaya, *Zh. Obschch. Khim.*, **27**, 606 (1957); *Chem. Abstr.*, **51**, 1638*h* (1957).

[42] (a) W. G. Dauben and R. C. Tweit, *J. Am. Chem. Soc.*, **76**, 3197 (1954); (b) A. L. Wilds and N. A. Nelson, *ibid.*, **75**, 5360 (1953).

[43] H. Muele and Ch. Tamm, *Helv. Chim. Acta*, **45**, 1475 (1962).

[44] The chlorinolysis of dimethyl disulfide at −78° without solvent was described by I. B. Douglas and D. A. Koop, *J. Org. Chem.*, **27**, 1398 (1962).

Enamines. II. Factors Determining the Structure of Enamines of 2-Substituted Ketones[1]

WILLIAM D. GUROWITZ AND MADELINE A. JOSEPH

Eastern Research Laboratory, The Dow Chemical Company, Wayland, Massachusetts

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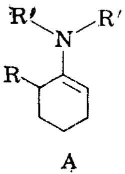
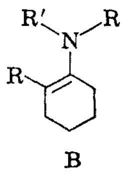
Enamines derived from 2-substituted ketones can and do exist as a mixture of the more and less substituted double-bond isomers. The isomer ratio is determined by various steric and electronic factors which affect the overlap between the nitrogen lone pair and the double bond of the enamine. In general, the greater the overlap, the greater the proportion of less substituted double-bond isomer. In addition, the position of the vinyl proton in the nmr is a reflection of the amount of overlap. Evidence supporting these proposals is presented.

It was previously shown by us[2] that enamines of 2-substituted cyclohexanones do not exist solely as the less substituted double-bond isomer A as was commonly believed,[3] but as a mixture of the two isomers A and B


A


B

with the R groups determining the composition of the mixture. Specifically we proposed that overlap of the lone pair of electrons on nitrogen with the π electrons of the double bond is appreciable with pyrrolidine, but less so with other amines. We further stated that the position of the vinyl hydrogen absorption in the nmr spectrum was an indication of the amount of overlap.

We here offer evidence that the ratio of isomers will be determined by a balance of factors which affect the conjugation between the nitrogen lone pair and the double bond of an enamine. Specifically, within a given series, as the amount of overlap increases, the proportion of less substituted double-bond isomer A increases.

In addition, we give further proof that the position of the vinyl proton reflects the amount of overlap, *i.e.*,

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[1] Presented at the 153rd National Meeting of The American Chemical Society, Miami, Beach, Fla., April 9–14, 1967, Abstracts, p 80-O.

[2] Enamines I: W. D. Gurowitz and M. A. Joseph, *Tetrahedron Letters*, 4422 (1965).

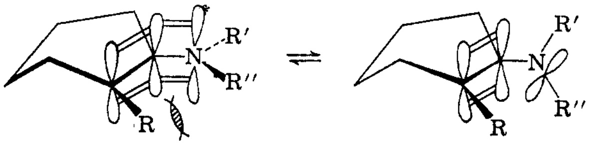
[3] See, for example (a) G. Stork, *et al.*, *J. Am. Chem. Soc.*, **85**, 207 (1963); (b) H. A. P. de Jongh, *J. Org. Chem.*, **30**, 1409 (1965); L. F. Fieser and M. Fieser, "Current Topics in Organic Chemistry," Vol. 1, Reinhold Publishing Corp., New York, N. Y., 1964, p 25; H. O. House, "Modern Synthetic Reactions," W. A. Benjamin, Inc., New York, N. Y., 1965, p 197; J. Szmuszkovicz, *Advan. Org. Chem.*, **4**, 21 (1963); K. Blaha and O. Cervinka, *Advan. Heterocyclic Chem.*, **6**, 167 (1966).

the greater the overlap, the higher the field of the vinyl hydrogen.

Results and Discussion

In general, an enamine derives its reactivity from the overlap of the nitrogen lone pair with the π electrons of the double bond. This overlap, if complete, requires the substituents on nitrogen and the olefinic groups to be coplanar. However, various steric and electronic factors can arise which either force the groups out of coplanarity or change the overlap requirements.

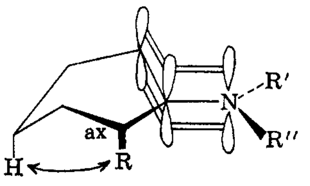
The large steric interactions between the groups on nitrogen (R′ and R″) and the substituent on the cyclohexene ring as B′ in (1) precludes both their coplanarity and a high degree of overlap. Consequently the groups twist out of coplanarity, thereby relieving the steric interactions; however, overlap stabilization is lost as shown by B″ in (1).



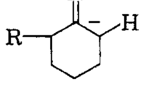
(1)

B′ B″

Isomer A with the R group axial[4,5] is free of this steric interaction and so can maintain the coplanarity and a high degree of overlap. It has, however, gained a 1,3-diaxial R-H steric interaction. Loss of the overlap stabilization makes B a higher energy form than A and so A should predominate. When the amount of overlap in either form is low, "normal" double-bond stabilities should prevail and the more substituted double-bond isomer B should predominate. Furthermore, since the amount of overlap is the amount of double-bond character *exo* to the amine ring, it should be related to the *exo* double-bond stabilities of five- and six-membered rings.[6] As the overlap increases, so does the electron density on the carbon atom bearing the vinyl proton because of the increased contribution of form C. It is known that the greater the electron density on a carbon atom bearing a proton, the further upfield is the proton absorption in the nmr spectrum.[7] Therefore, the greater the overlap, the further upfield should be the vinyl proton absorption. By decreasing the conjugation either sterically or electronically, we should be able to test the above proposals.



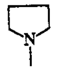
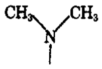
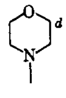
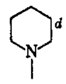
A



C

A. Steric.—In the same series (in this case, the enamines of 2-methylcyclohexanone), one would expect dialkylamines to be intermediate between five- and six-membered ring amines, since in a five-membered ring overlap is favored because of the increase in *exo* double-bond character, while in a six-membered ring overlap is disfavored because of the resistance to any increase in *exo* double-bond character;[6] with a dialkylamine, neither of these factors are operative. Indeed, inspection of Table I clearly shows this intermediacy of dimethylamine enamines whether the parent ketone is substituted or unsubstituted. It is further seen that as we go down the table there is a gradual downfield shift of the vinyl proton absorption with both the unsubstituted and substituted enamines. This we feel reflects a transition to smaller and smaller degrees of overlap with the amount of isomer A decreasing accordingly.

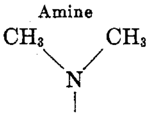
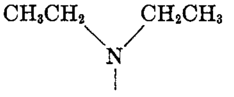
TABLE I[a]

Amine	Cyclohexanone Compd	Cyclohexanone Vinyl H,[b] cps	2-Methylcyclohexanone Compd	A, %	B,[c] %	Vinyl H,[b] cps
	I	250	II	90	10	251
	III	262	IV	60	40	267
 [d]	V	273	VI	52	48	276
 [d]	VII	...	VIII	46	54	277

[a] Values are for neat liquid. [b] Cycles per second downfield from internal tetramethylsilane. [c] Obtained by difference (100 − per cent of A). [d] See ref 1.

At first one would not expect much of a variation between the dimethylamine and diethylamine enamines IV and X. Yet Table II shows a great difference between them. Inspection of XA and XB shows that effective overlap can no longer be achieved by the tautomer with the less substituted double bond and the 2-methyl group axial (isomer A). It is clearly seen that there will be strong steric interactions between the terminal methyl groups of the amine and the cyclohexenyl methyl group, whether it be axial, equatorial, or vinylic. Thus what appears to be, at first glance, an

TABLE II[a]

Amine	Cyclohexanone Compd	Cyclohexanone Vinyl H,[b] cps	2-Methylcyclohexanone Compd	A, %	B,[c] %	Vinyl H,[b] cps
	III	262	IV	60	40	267
	IX	266	X	25	75	273

[a] Values are for neat liquid. [b] Cycles per second downfield from internal tetramethylsilane. [c] Obtained by difference 100 − per cent of A).

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[4] W. R. N. Williamson, *Tetrahedron*, **3**, 314 (1958).

[5] F. Johnson and A. Whitehead, *Tetrahedron Letters*, 3825 (1964).

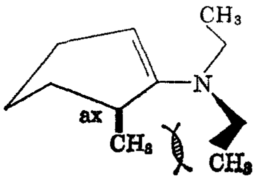
[6] H. C. Brown, J. H. Brewster, and H. Shechter, *J. Am. Chem. Soc.*, **76**, 467 (1954); H. C. Brown, *J. Org. Chem.*, **22**, 439 (1957).

[7] See, for example, J. Feeney, A. Ledwith, and L. H. Sutcliffe, *J. Chem. Soc.*, 2023 (1962).

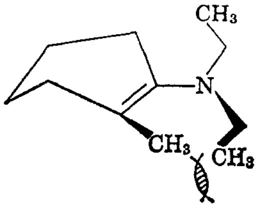
anomalous result actually provides strong support for our proposals. Here isomer XA (in contrast to IVA) is no longer a lower energy form because of this severe methyl–methyl interaction even with the cyclohexene methyl group axial.

The amine therefore is twisted out of coplanarity to relieve these interactions which are large in either form and the factors which determine normal (nonconjugated) double-bond stabilities manifest themselves; the more substituted double bond predominates.

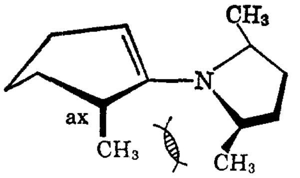
The chemical shift of the vinyl proton of the diethylamine enamine of cyclohexanone (IX) is downfield relative to the dimethylamine enamine (III); we feel this reflects the steric interference between the methyl groups of the diethylamine moiety and the vinyl and methylene protons on the 2,6-carbon atoms of the cyclohexene ring. If this reasoning is extended, an even greater shift should be seen with the 2,5-dimethylpyrrolidine enamine of 2-methylcyclohexanone (XII). Here the pseudo diethylamine grouping[8] would be tied back by the ethylene bridge and thereby lack the flexibility and rotational freedom of the diethylamine.



XA



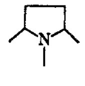
XB



XIIA

This fixes the amine methyl groups so that the strong steric interactions with the cyclohexenyl methyl can not be at least partially relieved by rotation. That this is so is shown in Table III. Here we see a dramatic reversal of the isomer ratio, with the predominant isomer changing from almost exclusively the less substituted to almost entirely the more substituted double-bond isomer. Furthermore, the vinyl proton absorption has shifted downfield from 251 to 272 cps!

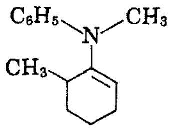
TABLE III[a]

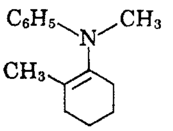
	Cyclohexanone		2-Methylcyclohexanone			
Amine	Compd	Vinyl H,[b] cps	Compd	A, %	B,[c] %	Vinyl H,[b] cps
	I	250	II	90	10	251
	XI	259	XII	$\leqslant 10$	$\geqslant 90$	272

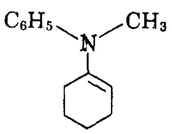
[a] Values are for neat liquid. [b] Cycles per second downfield from internal tetramethylsilane. [c] Obtained by difference (100 − per cent of A).

Interestingly the chemical shift of the vinyl proton of enamine XI is also downfield relative to I and II. This we feel reflects the steric interference between the methyl groups and the vinyl and methylene protons on the 2,6-carbon atoms of the cyclohexene ring, which forces the amine ring out of coplanarity with the double bond and its substituents. It is meaningful that XI falls between I (or II), where there is no deviation from coplanarity and XII, where the steric interference should be greatest and therefore so should the deviation from coplanarity.[9]

B. Electronic.—The electronic evidence in support of the proposals is also based on diminishing the conjugation between the lone pair on nitrogen and the double bond, not by forcing anything to twist out of coplanarity, but by putting in a group which will conjugate more effectively with the nitrogen lone pair than does the double bond. To this end, we have made the N-methylaniline enamine of 2-methylcyclohexanone (XIII). Here, the lone pair on nitrogen should conjugate predominantly if not entirely with the phenyl ring and not with the enamine double bond. If so, there would be no requirements for coplanarity between the olefinic substituents and the groups attached to nitrogen. Indeed steric interactions between the 2-methyl group and the nitrogen substituents would be minimal if the amine moiety and the cyclohexene were not coplanar. As a result, the more substituted double-bond isomer (XIIIB) should predominate.







	XIIIA	XIIIB	XV
Vinyl H	319 cps	. . .	316 cps
%	0	100	. . .

We have found *only* the more substituted double bond isomer (XIIIB) present! If one heats the enamine at 150° overnight, a peak which could be the vinyl proton of the other isomer (XIIIA) is observed. This amounts to 2–3%. No further change is observed.

C. General.—It would be useful to be able to derive some generalities relating the isomer ratio with the vinyl proton absorption and the way in which various factors will affect the isomer ratio. For those we call simple enamines, in which R is methyl and R′ and R″ are methyl or together form a ring system, approximate predictions of the ratio of isomers can be made on the basis of the position of the vinyl proton absorption. Furthermore, valid relationships can be made within a family of enamines such as the dialkylamines and the pyrrolidine enamines. However, the data from the simple enamines cannot be directly correlated with the data from the diethylamine enamines and pseudo diethylamine enamines.[8]

An example of the difficulty in trying to do this is to compare the isomer ratio obtained with VI (See Table I) with that of X or XII. It is seen that, while they all have very similar vinyl proton absorptions, they have different isomer ratios. The reasons for this are essen-

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[8] The pseudo diethylamine enamines are those having alkyl substitution on the carbon adjacent to nitrogen, *e.g.*, 2,5-dimethylpyrrolidine. This type of compound presents a diethylamine-type grouping to the substituted cyclohexene ring.

[9] The downfield shift of IX (4 cps) is smaller than that of XI (9 cps) and is probably due to the greater flexibility of the diethyl groups; *i.e.*, the diethyl can relieve some of the steric interaction by twisting out of coplanarity *and* by rotation of the ethyl groups, whereas the 2,5-dimethylpyrrolidine can only twist out of coplanarity.

TABLE IV

CONSTANTS AND ANALYTICAL DATA[a] FOR ENAMINES OF 2-METHYLCYCLOHEXANONE

Enamine	Bp (mm), °C	$n^{25}\mathrm{D}$	Calcd, % C	Calcd, % H	Calcd, % N	Found, % C	Found, % H	Found, % N
II	54 (1.4)	1.5136	79.9	11.6	8.5	79.6	11.5	9.0
IV	*b*	*b*	77.6	12.3	10.1	77.8	12.2	10.2
VI	52 (1.5)	1.5001	72.9	10.6	7.7	72.9	10.6	7.6
VIII	48 (1.7)	1.5000	80.4	11.8	7.8	80.2	11.9	7.8
X	72 (9)	1.4677	79.0	12.6	8.4	78.9	12.7	8.5
XII	*b*	*b*	80.8	12.0	7.3	80.7	11.9	7.3
XIII	*b*	*b*	83.5	9.5	6.7	83.4	9.5	7.1

[a] Analyses were done by Dr. C. K. Fitz, Needham, Mass., and Galbraith Laboratories, Knoxville, Tenn. [b] Purified by preparative glpc on an F & M 770.

tially the same as those already advanced for the 2,5-dimethylpyrrolidine and diethylamine, wherein the methyls on the amine portion interfere with the substituent on the cyclohexene ring even when it is axial. We feel that the position of the vinyl proton is still a reflection of the degree of overlap and that the difference in the ratio of isomers results from the severe steric interactions engendered by the diethyl grouping. These interactions can now no longer be relieved by further twisting (with resulting loss of overlap) because this leads to an *increase* in steric interactions due to the other methyl group on the amine interfering with the cyclohexene methyl group.

Conclusions

The ratio of isomers of enamines of 2-substituted ketones is determined by the way various steric and electronic factors affect the overlap between the nitrogen lone pair and the double bond. In general, the greater the overlap the larger the amount of less substituted double-bond isomer present. Furthermore, the amount of overlap is reflected by the position of the vinyl proton in the nmr spectrum; the greater the overlap, the further upfield will be the vinyl proton absorption. Application to ketones with different size rings (and open chain) and different substituents is currently underway.

Experimental Section

Preparation of Enamines.—All enamines except for the dimethylamine and diethylamine were prepared in the usual manner by refluxing the amine, ketone, and toluene containing a small amount of *p*-toluenesulfonic acid with removal of the water by means of a Dean–Stark apparatus or Linde 4A Molecular Sieves. The dimethylamine enamine of cyclohexanone (III) was prepared by letting a dimethyl sulfoxide solution of dimethylamine and cyclohexanone stand over Linde 4A Molecular Sieves at room temperature for 1 week.

The dimethylamine enamine of 2-methylcyclohexanone (IV) was prepared in the same manner as III except acetonitrile was used as solvent. The diethylamine enamines IX and X were prepared by dissolving the ketone in a large excess of amine as solvent and refluxing the solution over Linde 4A Molecular Sieves. Constants and analytical data for all 2-methylcyclohexanone enamines are listed in Table IV. Since we were interested in the position of the vinyl proton and not exact percentages with the enamines of cyclohexanone, we did not feel it necessary to carry out extensive purification. However all enamines were at least 95% pure as shown by glpc. The nmr spectra were obtained on a Varian A56-60 at 60 Mc and were calibrated with an audio frequency side-band oscillator. The amount of isomer A was determined by mixing an accurately weighed amount of enamine with an accurately weighed amount of triphenylmethane in a drybox under nitrogen. The nmr spectrum was then run. The vinyl proton and the triphenylmethane absorptions were run on a 100-cycle sweep and the areas determined by use of a planimeter. The values are a result of at least three determinations taken at different times, often using enamines prepared separately. All enamines were measured after long standing; in addition, determinations were also made on samples which had a small amount of dry methanol[10,11] added to ensure that the thermodynamic composition had been achieved. The values are accurate to ±4% and probably less.

Compound XIIA is listed as a maximum of 10% because of the difficulty in measuring a small area. The true value is most likely somewhat less than 10%. XIII is listed as 100% isomer B as no absorption for vinyl hydrogen (or alternately CH_3 on saturated carbon) could be found even at high spectrum amplitudes. To ascertain that we indeed had XIII, it was quantitatively hydrolyzed to N-methylaniline and 2-methylcyclohexanone with aqueous acid. However, by heating overnight at 150°, a very small peak was observed at 319 cps. This amounted to 2–3% and was presumed to be due to the vinyl proton.

Hydrolysis of the N-Methylaniline Enamine of 2-Methylcyclohexanone (XIII).—The enamine (1.00 g) was added to 50 ml of 10% aqueous HCl and stirred at 85° for 2 hr. It was then cooled and extracted with four 25-ml portions of ether. The combined ether extracts were dried over sodium sulfate. The sodium sulfate was filtered off and the ether removed by distillation, leaving 0.45 g of a pale yellow liquid (theoretical yield, 0.56 g, 80%). Glpc showed a single peak identical in retention time with 2-methylcyclohexanone. The infrared and nmr spectra were also identical with those of 2-methylcyclohexanone.

The aqueous layer was made basic with a saturated solution of sodium bicarbonate. This was then extracted with four 25-ml portions of ether; the combined ether extracts were washed with two 10-ml portions of water, and dried over sodium sulfate. The sodium sulfate was filtered off; the ether was removed *in vacuo*, leaving 0.57 g (theoretical yield, 0.53 g, 108%) of a pale yellow liquid. Glpc showed a very small peak before the main peak. The main peak was identical in retention time with N-methylaniline. The infrared and nmr spectra were identical with those of N-methylaniline.

Registry No.—I, 1125-99-1; IIa, 13815-44-6; IIb, 5049-40-1; III, 13815-46-8, IVa, 13815-47-9; IVb, 13952-46-0; V, 670-80-4; VIa, 13815-49-1; VIb, 6127-98-6; VII, 2981-10-4; VIIIa, 13815-51-5; VIIIb, 6128-00-3, IX, 10468-24-3; Xa, 13952-48-2; Xb, 6128-02-5; XI, 13815-58-2; XIIa, 13815-55-9; XIIb, 13815-56-0; XIIIb, 13815-57-1.

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