Competing Hydride Transfer and Ene Reactions in the Aminoalkylation of 1-Alkenes with *N,N*-Dimethylmethyleniminium Ions. A Literature Correction

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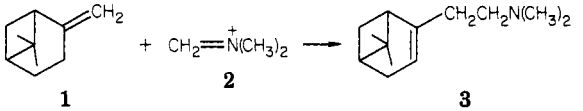
A literature report that *N,N*-dimethylmethyleniminium ion (2) reacts with propylene and styrene to form unsaturated tertiary amines is shown to be incorrect. The major products are the secondary amines 1-(methylamino)butane and 1-(methylamino)-3-phenylpropane in which N-demethylation has occurred along with the saturation of the alkene. Analogous major products are formed with 1-butene, 1-hexene, 1-octene, 1-dodecene, 1-tetradecene, *p*-methylstyrene, and *m*-nitrostyrene as substrates. When the substrates are isobutylene, 2-ethyl-1-hexene, α-methylstyrene, and *p*-methoxystyrene, the major products are tertiary amines, but the secondary amines are also formed in smaller yields. The small yields of tertiary amines obtained in the cases of styrene and *p*-methylstyrene were increased by going from solvent acetic acid to acetonitrile and by increasing the branching of the alkyl groups on nitrogen. The internal olefins 5-decene and cyclohexene were far less reactive, giving only 3–4% of amine products that were mainly tertiary in the former case and secondary in the latter. It is concluded that tertiary amine products are favored by an alkene structure and a solvent that favors the formation of a stable carbenium ion intermediate or a transition state with substantial carbenium ion character upon electrophilic attack of the iminium ion on the alkene. The secondary amine products are favored when a carbenium ion is of low stability and when the β-carbon atom of the olefin and/or the alkyl group attached to nitrogen is sterically unhindered; such hindrance decreases the rate of hydride ion transfer that is believed to occur in the production of secondary amines.

Introduction

The literature contains a number of reports of the reactions of alkenes with the *N,N*-dimethylmethylenimium ion (2) formed by the action of mineral acid on either



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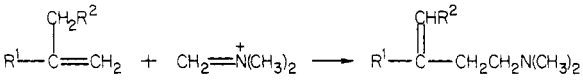

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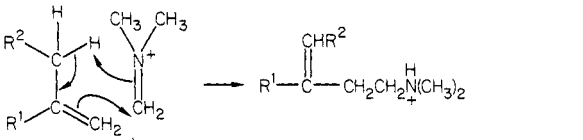
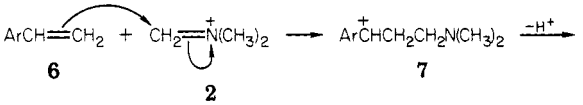
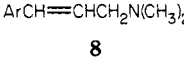


(3)

a, R^1 = Ph; R^2 = H
b, R^1 = CH_3; R^2 = H
c, R^1 = R^2 = H
d, R^1 = H; R^2 = CH_3



6 2 7

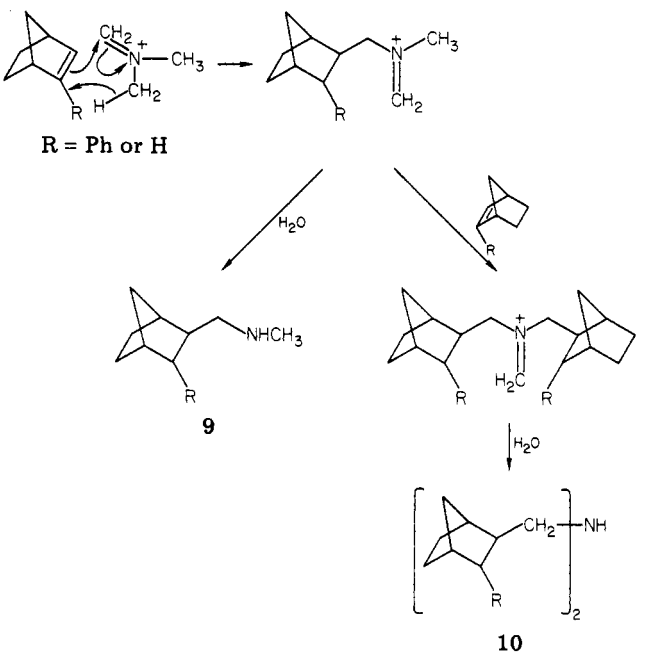


8 (4)

Ar = C_6H_5 or *p*-$CH_3OC_6H_4$

N,N,N',N'-tetramethyldiaminomethane or a mixture of formaldehyde (trioxane) and dimethylamine.[1] For example, β-pinene (1) and terminal olefins **4(a–d)** have been reported to yield, respectively, the unsaturated tertiary amines **3** and **5**.[2,3] Such transformations are examples of

Scheme I



R = Ph or H

9 10

the ene reaction;[4] such a reaction could either be concerted as indicated in eq 3, or could involve a carbenium ion intermediate which, subsequent to its formation, undergoes a proton transfer. Two other olefins (**6**; Ar = C_6H_5[3] or

(1) Bohme, H.; Haake, M. In "Iminium Salts in Organic Chemistry, Part I"; Bohme, H., Viehe, H. G., Eds.; Interscience: New York, 1976; Vol 9, p 107.

(2) (a) Hennion, G. F.; Price, C. C.; Wolff, V. C., Jr. *J. Am. Chem. Soc.* **1955**, *77*, 4633. (b) Schmidle, C. J.; Mansfield, R. C. *Ibid*, **1955**, *77*, 4636. (c) Bohme, H.; Fresenius, W. *Arch. Pharm. (Weinheim, Ger.)* **1972**, *305*, 601. (d) Booth, J. E.; Sharp, A. J.; Noren, G. K. *J. Macromol. Sci., Chem.* **1976**, *310*, 1541.

(3) Schmidle, C. J. U.S. Patent 2778826 (1957); *Chem. Abstr.* **1957**, *51*, 8809e.

(4) Reviews of ene reactions: Hoffmann, H. M. R. *Angew. Chem., Int. Ed. Engl.* **1969**, *8*, 556. Huisgen, R. et al. In "The Chemistry of Alkenes"; Patai, S., Ed.; Interscience: New York, 1964; p 897. Oppolzer, W.; Snieckus, V. *Angew. Chem. Int. Ed. Engl.* **1978**, *17*, 476.

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p-$MeOC_6H_4$[2b]) have also been reported to undergo an apparently related reaction to produce **8** (eq 4); in these cases, the concerted process shown in eq 3 cannot be operative.

With certain olefins such as norbornenes, an ene reaction was not expected to occur since it would violate Bredt's rule and secondary amines (**9** and **10**) have been produced instead.[5] Deuterium labeling experiments have been interpreted as indicating the mechanism shown in Scheme I.[5]

Results

Aminomethylations of Nonconjugated Olefins. We were interested in the synthesis of long-chain tertiary amines from α-olefins (possessing the grouping $RCH{=}CH_2$). When propylene (**4c**) was treated with a solution of bis(dimethylamino)methane and concentrated sulfuric acid in acetic acid at 135 °C, as specified in the patent,[3] the major amine product (bp 82–84 °C) was found to possess no unsaturation (^1H, ^{13}C NMR); clearly the product was not the reported **5c**. The ^1H NMR spectrum of the product consisted of peaks at δ 2.51 (t, 2 H, NCH_2, J = 7 Hz), 2.43 (s, 1 H, NH, exchanges with D_2O), 2.03 (s, 3 H, NCH_3), 1.10–1.63 (m, 4 H, CH_2), and 0.92 (distorted t, 3 H, CH_3, J = 5.5 Hz); this spectrum is identical, except for the position of the concentration-dependent NH peak, with that for 1-(methylamino)butane (**11**).[6] The ^{13}C NMR spectrum was completely consistent with this structure: δ 51.53 (t, NCH_2), 35.71 (q, NCH_3), 31.71 (t, NCH_2CH_2), 20.35 (t, $NCH_2CH_2CH_2$), and 13.61 (q, CH_2CH_3). When this amine was treated with carbon disulfide in 2-propanol and the solution titrated with sodium hydroxide,[7] the sample was shown to contain 95% of secondary amine.

The ^1H NMR spectrum of a higher boiling amine fraction (bp 88–145 °C) again showed no vinyl protons. The spectrum was almost identical with that of an authentic sample of di-n-butylamine (**12**) except for (1) the position of the NH peak and (2) the NCH_3 peak due to contamination with 1-(methylamino)butane (19% by GLC). The identity of the NH peak at 0.90 ppm was determined by exchanging with D_2O. This material also caused peak enhancement upon coinjection with di-n-butylamine on two GLC columns. The yields of 1-(methylamino)butane and di-n-butylamine were 30 and 8%, respectively (eq 5).

$$CH_2{=}CHCH_3 + [(CH_3)_2N]_2CH_2 \xrightarrow[HOAc]{H_2SO_4} \underset{\mathbf{11},\ 30\%}{CH_3(CH_2)_3NHCH_3} + \underset{\mathbf{12},\ 8\%}{[CH_3(CH_2)_3]_2NH} \quad (5)$$

The corresponding products were obtained with 1-butene in yields of 20% and 1%, respectively.

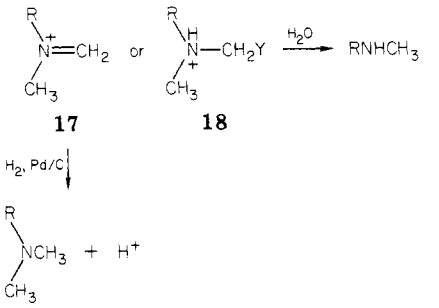
Schmidle[3] reported that accompanying the product believed to be 4-(dimethylamino)-1-butene (**5c**) in the propylene experiment was a higher boiling heptenyldimethylamine, formed by reaction of the iminium ion with a propylene dimer. In his work, both amine products were identified by their neutralization equivalents. It now seems certain that the structures of the products were misassigned, and that the true products are secondary amines as shown above. When the same type of reaction was performed with 1-hexene, 1-octene, 1-dodecene, and 1-tetradecene by using either (tetramethyldiamino)methane and sulfuric acid or a mixture of dimethylamine, trioxane, and sulfuric acid to generate **2**, products analogous to **11** were formed in less than 40% yield (Table I). The recovered olefins in several of the runs examined were isomerized (up to 50%) to internal olefins, which are far less reactive than the terminal olefins (see below). Some of the nonbasic products consisted of olefin dimers and their condensation products with formaldehyde.

The discovery of the literature error revealed above prompted us to reexamine the products of aminomethylation[2d] of isobutylene (**13**) with trioxane and aqueous dimethylamine. Analysis showed that Booth et al.[2d] have correctly identified the major component in the mixture as 2-methyl-4-(dimethylamino)-1-butene (**14**). However, it now becomes evident that two minor amines (**15** and **16**) are also produced (eq 6).

$$\underset{\mathbf{13}}{CH_2{=}C(CH_3)_2} + (CH_2O)_3 + (CH_3)_2NH \xrightarrow[2.\ OH^-]{1.\ H^+} \underset{\mathbf{14},\ 52\%}{CH_2{=}C(CH_3)CH_2CH_2N(CH_3)_2} + \underset{\mathbf{15},\ 8\%}{(CH_3)_2CHCH_2CH_2N(CH_3)_2} + \underset{\mathbf{16},\ 10\%}{(CH_3)_2CHCH_2CH_2NHCH_3} \quad (6)$$

Internal olefins were far less reactive than terminal olefins when treated with dimethylamine, trioxane, and sulfuric acid in acetic acid. 5-Decene and cyclohexene each gave only 3–4% yield of amine product. The distribution of product types obtained from these two olefins differed in a possibly mechanistically significant way. The amines produced from 5-decene consisted of 69% unsaturated tertiary amine and 28% secondary amine, while those from cyclohexene consisted of 84% secondary amine and 16% tertiary amine.

Mechanistic considerations (see below) led us to suspect



Y = OAc or $(CH_3)_2N$

that methyleneiminium ions (**17**) were precursors to the secondary amines. Hydrolysis of such ions or of their reaction products (**18**) with nucleophiles such as acetic acid or dimethylamine would produce secondary amines. In an attempt to detect any free iminium ions of type **17**, the aminomethylation product of 1-dodecene was divided into two portions. One portion was hydrolyzed to provide tertiary and secondary amine in a ratio of 6.6:93.4. The other portion was hydrogenated and then hydrolyzed to give tertiary and secondary amine in a ratio of 33:67. Thus, some free ion **17** is apparently present in the reaction mixture before hydrolysis or is generated during the hydrogenation process.

In order to determine if the unsaturated tertiary amine can be converted to the saturated secondary amine under the acidic conditions, a mixture containing 77% of 1-(methylamino)tridecane and 21% of 1-(dimethylamino)-

(5) Manninen, K.; Haapalo, J. *Acta Chem. Scand., Ser. B* **1974**, *28*, 433. Manninen, K. *Ibid.* **1978**, *32*, 691 and references cited therein. An earlier and less complete account can be found in Krieger, H.; Manninen, K. *Tetrahedron Lett.* **1966**, 6483. See also: Manninen, K. *Acta Chem. Scand., Ser. B.* **1974**, *28*, 603.

(6) Pouchert, C. J.; Campbell, J. R. "The Aldrich Library of NMR Spectra"; Aldrich Chemical Co.: Milwaukee, 1974; Vol. 2 13D.

(7) Critchfield F. E.; Ruch, J. E. In "Treatise on Analytical Chemistry"; Kolthoff, I. M., Elving, P., Eds.; Wiley-Interscience: New York, 1976; Part II, Vol. 15, p 177.

Table I. Aminomethylation of Olefins (Autoclave Runs)

compd	reagents, mol RH/$Me_4N_2CH_2$/H_2SO_4/HOAc	temp, °C	amine product, % yield[a]	bp, °C	wt % selectivity (GLC) $R(CH_2)_4NHMe$ (titration)[j]	$RCH{=}CHCH_2CH_2NMe_2$ (+ isomers)	Other[k]
H[v]	0.29/0.20/0.33/1.18	e	38	82–84	93 (95)	7	
CH_3[v]	0.29/0.20/0.33/1.18	f	21	118–121	94	6	
n-C_3H_7[v]	0.15/0.10/0.17/1.25	f	36	169–172	94 (91)	4	2
n-C_5H_{11}[v]	0.10/0.07/0.12/0.42	f	15	204–212	95 (92)	5	
n-C_9H_{19}[v]	0.10/0.16/0.16/2.38	g	36	d	88 (87)	5	7
n-$C_{11}H_{23}$[v]	0.09/0.15/0.15/0.15/1.75[b]	h	37	130–134 (0.1 mm)	91 (88)	9	
isobutylene	0.64/0.63/0.60/0.20/1.75[c]	i	70	d	14 (14)[l]	74[m]	12[n]
2-ethyl-1-hexene	0.20/0.20/0.33/1.20	g	60	d	24[o]	76[p]	
5-decene	0.14/0.33/0.32/0.31/2.6[b]	g	~3	d	28[q] (25)	69[r]	3[q]
cyclohexene	0.36/0.32/0.31/0.30/2.16[b]	h	~4	d	84[s] (81)	4[t]	12[u]

[a] Based on limiting reagent, following extraction with acid and distillation. [b] RH/Me_2NH/$(HCHO)_3$/H_2SO_4/HOAc. [c] RH/aq Me_2NH (57%)/$(HCHO)_3$/H_2SO_4/HOAc. [d] Extraction only (GLC). [e] 135 °C (2.5 h). [f] 140 °C (1 h), 180 °C (1 h). [g] 140 °C (1 h), 180 °C (2 h). [h] 200 °C (3 h). [i] 100 °C (17 h). [j] CS_2 method.[7] [k] Saturated tertiary amine. [l] 1-(Methylamino)-3-methylbutane. [m] 2-Methyl-4-(dimethylamino)-1-butene. [n] 2-Methyl-4-(dimethylamino)butane. [o] 1-(Methylamino)-3-ethylheptane. [p] 1-(Dimethylamino)-3-ethylheptenes. [q] Structure unknown. [r] Complex mixture of isomers. [s] Cyclohexyl(methylamino)methane. [t] Cyclohexenyl(dimethylamino)methane. [u] R of $RCH_2CH{=}CH_2$.

tridecenes from the 1-dodecene reaction was heated in the presence of sulfuric acid in acetic acid (180 °C, 1 h). No change occurred in the relative proportions of the two types of amines.

Attempts to increase the yields of amination products by lowering the acid concentration or by adding the olefin incrementally at 180 °C were unsuccessful; in both cases, yields were greatly reduced.

Aminomethylation of Aryl Olefins. The aminomethylation of a series of ring-substituted and unsubstituted styrenes (**6**, Ar = phenyl, *p*-tolyl, *p*-anisyl, and *m*-

$$\underset{\textbf{6, Ar = Ph}}{PhCH{=}CH_2} + (CH_3)_2NCH_2N(CH_3)_2 \xrightarrow{H_2SO_4} PhCH_2CH_2CH_2NHCH_3 \quad (7)$$
$$\textbf{19}$$

nitrophenyl) was studied. The iminium ion **2** was generated by the action of phosphoric or sulfuric acid on (tetramethyldiamino)methane in acetic acid. The results of these experiments are summarized in Table II. The reactions proceeded at a lower temperature (115 °C) than that required in the case of the nonconjugated unbranched olefin and the yields were higher. In the aminomethylation of styrene, the amino fraction (bp 55–60 °C, ~1 mm) exhibited ^1H NMR peaks at δ 0.75 (s, 1 H, NH, exchanges with D_2O), 1.72 (m, 2 H, CH_2), 2.35 (s, 3 H, NCH_3), 2.5 (t, 2 H, NCH_2), 2.62 (t, 2 H, $PhCH_2$) (the last two triplets overlapped and actually appeared as a quartet), and 7.06 (s, 5 H, ring). Titration (CS_2 method)[7] indicated a secondary amine content of 92%. This data is consistent with the major product being 1-(methylamino)-3-phenylpropane (**19**), rather than the unsaturated amine reported.[3]

p-Methylstyrene and *m*-nitrostyrene also gave very predominantly secondary amine. The small quantity of tertiary amine formed in these cases was olefinic with the former and saturated with the latter.

Under the same conditions, *p*-methoxystyrene gave a very different result. The product was very predominantly tertiary amine and this contained 40% of the olefinic component **20** and 53% of the acetate **21** (eq 8). Tertiary

$$p\text{-}CH_3OC_6H_4CH{=}CH_2 \xrightarrow[H_3PO_4\text{–}HOAc]{[(CH_3)_2N]_2CH_2} \underset{\textbf{20}}{p\text{-}CH_3OC_6H_4CH{=}CHCH_2N(CH_3)_2} + \underset{\textbf{21}}{p\text{-}CH_3OC_6H_4CH(OAc)(CH_2)_2N(CH_3)_2} \quad (8)$$

amines were also the major products when 2-phenylpropene (**22**) was subjected to the same aminomethylation conditions with phosphoric acid. The amine was shown (GLC, titration, ^1H NMR) to consist of 88% tertiary amine and 12% secondary amine. The former consisted of 92% 1-(dimethylamino)-3-phenyl-3-butene (**23**) and 8% of 1-(dimethylamino)-3-phenyl-2-butene (**24**) (eq 9). Thus, the

$$\underset{\textbf{22}}{C_6H_5C(CH_3){=}CH_2} \xrightarrow[H_3PO_4\text{–}HOAc]{[(CH_3)_2N]_2CH_2} \underset{\textbf{23}}{C_6H_5C(=CH_2)CH_2CH_2N(CH_3)_2} + \underset{\textbf{24}}{C_6H_5C(CH_3){=}CHCH_2N(CH_3)_2} + \underset{\textbf{25}}{C_6H_5C(CH_3)HCH_2CH_2NHCH_3} \quad (9)$$

report by Schmidle[3] that the products are those of the ene reaction is largely substantiated. When sulfuric acid was used in place of phosphoric acid, the ratio of the less stable olefin (**23**) to the more stable one (**24**) decreased to 48:52. When the amine product of this reaction was heated at reflux in the presence of sulfuric acid in acetic acid, the

Table II. Aminoalkylation of Styrenes

Ar of ArCH=CH$_2$	reagents	solvent	temp, °C	amine product, % yield	wt % selectivity (GLC) ArCH=CHCH$_2$NR$_2$	ArCH$_2$CH$_2$CH$_2$NHR
Ph	$Me_4N_2CH_2/H_3PO_4$	HOAc	115	70	2	98
	$Me_4N_2CH_2/H_2SO_4$	HOAc	115	63	8	92
	Me_2NCH_2I	CH_3CN	75	67	24	76
	CH_2O/H_3PO_4 + n-$C_6H_{13}NHCH_3$	HOAc	115	40	4	96[a,j]
	CH_2O/H_3PO_4 + n-$C_4H_9NHCH_3$	HOAc	115	47	1	99[b,j]
	CH_2O/H_3PO_4 + 2-$C_3H_7NHCH_3$	HOAc	115	38	4	96[c,j]
	CH_2O/H_3PO_4 + $(C_2H_5)_2NH$	HOAc	115	42	8	92
	CH_2O/H_3PO_4 + $(2\text{-}C_3H_7)_2NH$	HOAc	115	10	8	37
					55[d]	
p-$CH_3C_6H_4$	$Me_4N_2CH_2/H_3PO_4$	HOAc	115	68	10	90
	Me_2NCH_2I	CH_3CN	70	59	68	32
	Me_2NCH_2I	HOAc	70	44	31	69
	Me_2NCH_3I	HOAc	115	26	67	33
p-$CH_3OC_6H_4$	$Me_4N_2CH_2/H_3PO_4$	HOAc	115	70	40	7
					53[e]	
	$Me_4N_2CH_2/H_3PO_4$	HOAc	75	60	11	18
					71[e]	
m-$O_2NC_6H_4$	$Me_4N_2CH_2/H_3PO_4$	HOAc	115	5	14[f]	86
α-methylstyrene	$Me_4N_2CH_2/H_3PO_4$	HOAc	115	72	79[g]	13[i]
					8[h]	
	$Me_4N_2CH_2/H_2SO_4$	HOAc	115	82	46[g]	11[i]
					43[h]	

[a] 38% R = C_4H_7, 58% R = CH_3. [b] 41% R = C_4H_9, 58% R = CH_3. [c] 86% R = C_3H_7, 10% R = CH_3. [d] $PhCH_2CH_2CH_2N(2\text{-}C_3H_7)_2$. [e] p-$CH_3OC_6H_4CH(OAc)CH_2CH_2NR_2$. [f] m-$O_2NC_6H_4(CH_2)_3NR_2$. [g] $PhC(=CH_2)(CH_2)_2NR_2$. [h] $PhC(CH_3)=CHCH_2NR_2$. [i] $PhCH(CH_3)(CH_2)_2NHR$. [j] Molar % rather than wt % selectivity.

unsaturated amine was isomerized mainly to **24** and a small quantity of a substance believed to be the enamine, 1-(dimethylamino)-3-phenyl-1-butene; the proportion of amine **25** remained constant. It is reasonable to conclude that the proximate products of the aminomethylation reaction of 2-phenyl-1-propene are **23** and **25**, and that the former is isomerized to **24** under acid conditions. Bohme and Fresenius[2c] treated a number of activated styrenes including *p*-methoxystyrene and 2-phenyl-1-propene with *N,N*-dimethylmethyleneiminium chloride (the chloride salt of **2**) in acetonitrile and identified the corresponding unsaturated tertiary amines (50–70% yield); several of these products exhibited the expected ^1H NMR spectra and gave satisfactory elemental analyses. In order to examine the nature of the products of this type of reaction with less activated styrenes, styrene itself and *p*-methylstyrene were treated with the corresponding iodide salt of **2** (Eschenmoser's salt, $(CH_3)_2NCH_2I$) in acetonitrile at reflux. In the case of styrene, the secondary amine **19** was the major product, but the ratio of tertiary to secondary amine, 24:76, was significantly higher than in the aminomethylation in acetic acid described above. The trend was still more pronounced in the case of *p*-methylstyrene which gave tertiary amine as the major product (ratio of tertiary to secondary amine, 68:32) in acetonitrile and secondary amine as the major product (ratio 31:69) in acetic acid.

The effect of the nature of the alkyl groups of the aminomethylating agent was briefly examined. When diethylamine, trioxane, and phosphoric acid reacted with styrene, the ratio of generated secondary amine, 1-(ethylamino)-3-phenylpropane, to the unsaturated tertiary amine was 92:8. When diisopropylamine was used instead, the ratio of secondary amine to tertiary amine product was 37:63; the tertiary amine in this case consisted largely of the saturated amine, 1-(diisopropylamino)-3-phenylpropane. Finally, when the amine component was 1-methylaminooctane or 2-methylaminopropane, two secondary amines were produced in each case: 1-(*n*-octylamino)-3-phenylpropane, (58%) and 1-(methylamino)-3-phenylpropane (38%) in the first, and 1-(isopropylamino)-3-phenylpropane (88%), and 1-(methylamino)-3-phenylpropane (8%) in the second. Only small amounts of the corresponding tertiary amines were formed.

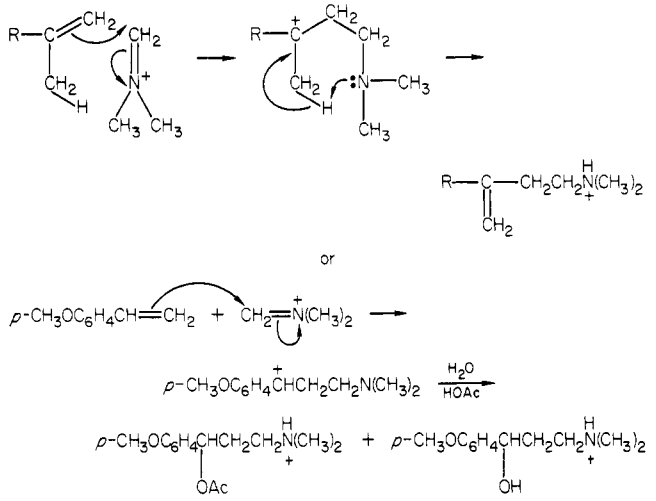
In a number of cases, it was found that the ratios of products were invariant with time. Since product ratios were our major interest, in most experiments attempts to maximize yields were not made.

Discussion

It is clear that Schmidle[3] had misassigned the structures of the products of reaction of *N,N*-dimethylmethyleneiminium ion **2** with propylene and styrene as unsaturated tertiary amines, whereas the actual structures in these cases as well as the reactions of the same ion with other unbranched aliphatic 1-alkenes, *p*-methylstyrene and *m*-nitrostyrene, are saturated amines. Furthermore, such secondary amines are also formed, albeit as the minor basic product, when the substrate is a 2-alkyl-1-alkene or *p*-methoxystyrene. The cases in which secondary amines are produced from aliphatic 1-alkene substrates are apparently the first examples of such a reaction in the case of alkenes which are capable of undergoing the more usual ene type reaction to produce unsaturated tertiary amines. The hydride transfer mechanism[5] (see Introduction) is eminently reasonable for production of the secondary amines.

Since our work indicates that, in general, this type of process can compete with the ene reaction (eq 3 and/or 4), it is appropriate to define the circumstances which favor one or the other type of reaction. One major influence is

Scheme II

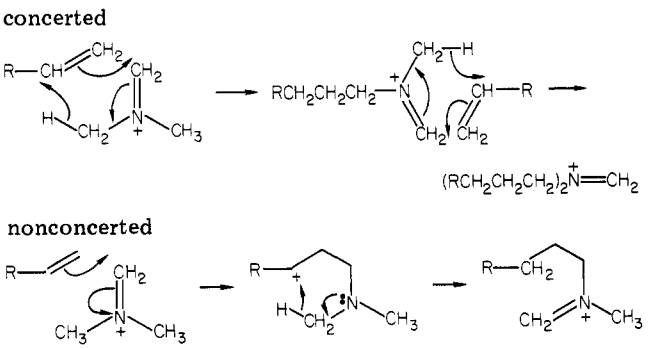


that factors which favor the formation of a stable carbenium ion upon attack of the olefin on the iminium ion favor the production of tertiary amines which are unsaturated or substituted by an acetoxy group. Thus, 2-alkyl-1-alkenes, which would yield tertiary carbenium ions, yield mainly unsaturated tertiary amines, whereas unbranched 1-alkenes, which would yield secondary carbenium ions, lead mainly to saturated secondary amines. Likewise, *p*-methoxystyrene yields mainly tertiary amine, while styrene, *p*-methylstyrene, and *m*-nitrostyrene give mainly secondary amines.[8] Tertiary amines are also formed from 2-phenylpropene. When Eschenmoser's salt is used with *p*-methylstyrene, a 2:1 ratio of secondary to tertiary amine is produced in acetic acid (dielectric constant $\mu = 0.83$), while the ratio is reversed in the more polar solvent acetonitrile ($\mu = 3.37$).

There is evidence that steric effects may play a role in determining which reaction course is followed with a high degree of congestion at the hydride ion donor or acceptor termini disfavoring production of secondary amine. Although solvolysis data[9] indicate that $(CH_3)_3C^+$ is about equal in stability to PhC^+HCH_3, isobutylene upon aminomethylation gave mainly unsaturated tertiary amine, while styrene gave mainly secondary amine. Finally, the aminomethylation of cyclohexene and 5-decene should give carbenium ions of approximately equal stability and yet the former gave predominantly secondary amine and the latter tertiary amine; the cyclohexyl cation should be less hindered toward acceptance of a hydride ion than the corresponding linear secondary cation because in the former case the two alkyl substituents are "tied back."

All of our results and those in the literature can be rationalized by assuming that the unsaturated tertiary amines and the 3-hydroxy- and 3-acetoxy-1-(dimethylamino)alkanes are produced via an intermediate or transition state possessing a high degree of carbenium ion character. The carbenium ion can transfer a proton to the amine or to another proton acceptor and/or it can be attacked in a nucleophilic manner by water or acetic acid to form the alcohol and acetate. These latter products may also be formed in some cases by acid-catalyzed additions to the first formed unsaturated tertiary amines. The carbenium ion process is depicted in Scheme II. On the other hand, it seems likely that the alkylative demethylation reaction proceeds by a more concerted process, thus avoiding the high-energy carbenium species which would be an intermediate in the nonconcerted mechanism (Scheme III). Because of considerable steric congestion in the transition state which is depicted in the concerted process of Scheme III, substitution at either the carbon atom donating the hydride ion, or the one accepting it, raises the activation energy and favors the competing process of Scheme II. Hydrolysis of the methyleneiminium intermediate in Scheme III produces the secondary amine products.[1] A small amount of reduction of these ions by formaldehyde, or perhaps formic acid produced in situ, leads to production of some saturated tertiary amine; this process has been discussed.[5]

Scheme III



Experimental Section

The aminoalkylation reactions under pressure were carried out in a 300-mL Hastalloy B autoclave (The Autoclave Engineers, Inc.) equipped with cooling coils and heaters. The aminoalkylation reactions at atmospheric pressure were carried out by heating the reactants under reflux in standard laboratory glassware under nitrogen. The chromatographic analyses were performed on a Hewlett-Packard 5710A (TC) or 5880A (FID) chromatograph. The columns used for most work included a 3 m × 0.32 cm column packed with 10% Carbowax 20M plus 2% KOH on 80–100 mesh Supelcoport, programmed from 150 to 225 °C at 2 °C/min; a 10-m, 2% OV-101, fused silica capillary column, programmed from 50 to 280 °C at 8 °C/min; and a 3 m × 0.05 cm column packed with 10% UC 980 on Chromasorb W, programmed from 80 to 200 °C at 30 °C/min. The ^1H NMR spectra were obtained in carbon tetrachloride on a Varian T-60 spectrometer. The ^{13}C NMR spectra were run on a Varian FT 80A spectrometer (C_6H_6 or $CDCl_3$). Chemical shifts are in δ units (ppm) relative to Me_4Si (s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, and m = multiplet). The IR spectra were recorded on a Perkin-Elmer Infracord or a Model 237B spectrometer. Mass spectra were run on Kratos MS-50 high resolution mass spectrometer with an electron impact source at 70 eV.

Analysis for Secondary Amines.[7] Secondary amines were converted to their dithiocarbamic acids by reaction with CS_2, followed by titration with caustic.

Aminomethylation of Propylene. To 20 g (0.2 mol) of cooled *N,N,N',N'*-tetramethyldiaminomethane was incrementally added 71 g of acetic acid, followed by 98% sulfuric acid (33.2 g, 0.33 mol). The reaction mixture was transferred to the autoclave, and purged with nitrogen. After addition of 12 g (0.29 mol) of propylene, the autoclave was heated at 135 °C for 2.5 h. The reaction mixture was cooled, withdrawn from the autoclave, and most of the acetic acid was removed on a rotary evaporator. The residue was treated with 160 g of water, made basic with 50% aqueous sodium hydroxide, and extracted with ether. The residue (11 g) from evaporation of the dried (K_2CO_3) ether extract was distilled by using a 1.27 cm × 25 cm column packed with 0.63 cm Burl saddles. The major amine fraction, bp 82–84 °C, corresponded to a 30% yield of 1-(methylamino)butane. The heavier cut, bp 88–145 °C, contained largely di-*n*-butylamine (8% yield). Evidence for these structures is presented in the text.

(8) For a discussion of the stabilities of variously substituted benzylic cations see: Deno, N. C.; Jaruzelski, J. J.; Schriesheim, A. *J. Am. Chem. Soc.* **1955**, *77*, 3044.

(9) Brown, R. F. "Organic Chemistry"; Wadsworth: Belmont, CA, 1975; p 424.

Aminomethylation of 1-Butene. The reaction of 1-butene as above afforded a 20% yield of 1-(methylamino)pentane: bp 118–121 °C; NMR ($CDCl_3$) δ 2.58 (t, high-field member obscured by NCH_3, 2 H, NCH_2), 2.42 (s, 3 H, NCH_3), 1.03–1.67 (m, 6 H, CH_2), 1.0 (s, 1 H, NH, exchanges with D_2O), 0.87 (distorted t, 3 H, CH_3). This spectrum is similar to that of 1-methylaminopentane[10] (solvent not specified), except that the position of the NH peak is at 0.6 ppm; its position is greatly dependent on the exact state of the sample. A small amount of di-*n*-pentylamine (1% yield) in the residue was identified on the basis of a coinjection–peak enhancement GLC method on two columns with an authentic sample.

Aminomethylation of 1-Hexene. The reaction of 1-hexene as above gave a 36% yield of amines, bp 169–172 °C. Titration of the sample for secondary amine[7] gave a value of 91%. ^1H NMR (neat) δ 2.5 (t, partially resolved with high field member obscured by NCH_3, 2 H, NCH_2), 2.36 (s, 3 H, NCH_3), 2.03 (s, 1 H, NH, exchanges with D_2O), 1.07–1.53 (m, 10 H, CH_2), 0.9 (distorted t, 3 H, CH_3); ^{13}C NMR (C_6D_6) 52.65 (t, NCH_2), 36.56 (q, NCH_3), 32.48 (t, NCH_2CH_2), 30.46 (t, $N(CH_2)_2CH_2$), 29.90 (t, $N(CH_2)_3CH_2$) 27.90 (t, $N(CH_2)_4CH_2$), 23.13 (t, $N(CH_2)_5CH_2$), and 14.25 (q, CH_3). Examination of amine fraction by GLC (capillary) showed several components. The first peak (2%) was identified as 1-(dimethylamino)heptane by coinjection with an authentic sample. Several peaks (4%) before the major component were assumed to be isomeric, unsaturated, tertiary amines which disappeared after hydrogenation (10% Pd/C, 25 °C, EtOH, 3 atm H_2) and enhanced the first peak. The major product in the mixture is therefore 1-(methylamino)heptane.

Aminomethylation of 1-Octene. The aminomethylation of 1-octene as above gave a 15% yield of 1-(methylamino)nonane: bp 204–212 °C; ^1H NMR (neat) δ 2.5 (t, distorted with high field member obscured by NCH_3, 2 H, NCH_2), 2.35 (s, 3 H, NCH_3), 1.09–1.73 (m, 14 H CH_2), 1.08 (s, 1 H, NH), 0.89 (distorted t, 3 H, CH_3); ^{13}C NMR (C_6D_6) 52.61 (t, NCH_2), 36.58 (q, NCH_3) 32.49 (t, NCH_2CH_2), 30.44 (t, $N(CH_2)_2CH_2$), 30.25 (t, intensity about twice that of the other peaks, $N(CH_2)_3CH_2CH_2$), 29.92 (t, $N(CH_2)_5CH_2$), 27.95 (t, $N(CH_2)_6CH_2$), 23.17 (t, CH_2CH_3), 14.29 (q, CH_2CH_3). A small impurity peak appeared at 45.46 ppm (q), identifying it as an NCH_3 group.

Aminomethylation of 1-Dodecene. The aminomethylation of 1-dodecene was carried out as above to give a 37% yield of amine fraction. Analysis by GLC showed 1-(methylamino)tridecane (87.5%), 1-(dimethylamino)tridecane (7.7%), and 1-(methylamino)tridecenes (4.8%) to be in the mixture.

Treatment of the Aminomethylation Product of 1-Dodecene with Sulfuric Acid. An aminomethylation product (7.5 g) containing 1-(methylamino)tridecane (76.8%) and 1-(dimethylamino)tridecenes (21.2%) was treated with 5 g of sulfuric acid in 125 g of acetic (180 °C, 1 h. The recovered product showed no change.

Aminomethylation of 1-Dodecene and Hydrogenation. A typical aminomethylation run was carried out as above. A sample was taken, treated with 50% sodium hydroxide, and extracted with ether. Analysis by GLC showed 1-(methylamino)tridecane and 1-(dimethylamino)tridecenes to be in a ratio of 93.4 to 6.6%. The remaining product was transferred to a Parr shaker and hydrogenated (1 g 10% Pd/C, 25 °C, 3 atm H_2). On workup, a 43% yield of amines were obtained. The ratio of 1-(methylamino)tridecane to 1-(dimethylamino)tridecane in the hydrogenated sample was 68 to 32%.

Aminomethylation of 1-Tetradecene. The aminomethylation of 1-tetradecene as above gave a 37% yield of amines, bp 130–134 °C (~0.1 mm). Titration for the secondary amine gave a value of 83%, in agreement with the chromatographic purity of 84%. On standing, 1-(methylamino)pentadecane crystllized to form white flakes: mp 39–41 °C; NMR δ 2.43 (m, 2 H, NCH_2), 2.3 (s, 3 H, NCH_3), 1.23 (s, 26 H, CH_2), 1.03 (s, 1 H, NH, exchanges with D_2O), 0.9 (distorted t, 3 H, CH_3). Anal. Calcd for $C_{16}H_{35}N$: C, 79.59; H, 14.16. Found: C, 79.42; H, 14.35.

Aminomethylation of Isobutylene. The aminomethylation of isobutylene was carried out with dimethylamine and trioxane (100 °C, 17 h) as reported.[2d] On workup, a 70% yield of amines was obtained, bp 115–117 °C. Capillary GLC analysis indicated three components in 12%, 74%, and 14%, respectively, in order of increasing retention time. The most diagnositc peaks in the ^1H NMR spectrum consisted of vinyl protons at 4.6 ppm (singlet) and a methyl group doublet of an isopropyl group at 0.89 ppm (J = 7 Hz). Titration for the secondary amine gave a value of 14.2%; this titration procedure was found to be invaluable in detecting small amounts of secondary amine mixed with tertiary amine, a mixture which could not be resolved by noncapillary GLC methods. The first component was identified as dimethylisopentylamine by coinjection with an authentic sample. The largest component was identified by ^1H NMR as 2-methyl-4-(dimethylamino)-1-butene. This result was confirmed by hydrogenation of the mixture which led to a two-component mixture in the proportion 87:13. The last peak appearing on the chromatogram must be attributed to the secondary amine, 1-(methylamino)-3-methylbutane.

Aminomethylation of Styrene. A mixture of tetramethyldiaminomethane (12.8 g, 0.12 mol), sulfuric acid (23 g, 0.23 mol), and styrene (12.2 g, 0.12 mol) was heated at reflux (N_2) in acetic acid (150 g) for 5 h. On workup as before, 16.4 g of product was obtained, from which a 63% yield of amines was obtained by extraction with hydrochloric acid and distillation, bp 55–60 °C (~1 mm). The NMR spectrum of the product is described in the text. Titration for the secondary amine gave a value of 92%. Mass spectrum, m/e calcd for $C_{10}H_{15}N$, 149.1204; m/e found, 149.1209. The major product is therefore 1-(methylamino)-3-phenylpropane.

Aminomethylation of *p*-Methylstyrene. The aminomethylation of *p*-methylstyrene was carried out as above in the presence of phosphoric acid to give a 68% yield of amines, bp 80–85 °C (~0.2 mm). The ratio of secondary to tertiary amine in the product, determined by both titration and GLC, corresponded to about 90:10. ^1H NMR δ 1.0 (s, 1 H, NH, exchanges with D_2O), 1.65 (p, 2 H, $CH_2CH_2CH_2$), 2.2 (s, 3 H, CH_3), 2.3 (s, 3 H, NCH_3), 2.4–2.8 (m, 4 H, $ArCH_2$, NCH_2), 6.95 (s, 4 H, ring); mass spectrum, m/e calcd for $C_{11}H_{17}N$, 163.1361; m/e found, 163.1366. A small peak at 2.15 ppm was attributed to the NMe_2 group of the small quantity of tertiary amine. The major product is 1-(methylamino)-3-(*p*-tolyl)propane.

Aminomethylation of *p*-Methylstyrene with Eschenmoser's Salt. A mixture of *p*-methylstyrene (6.3 g, 0.053 mol) and Eschenmoser's salt (Me_2NCH_2I, 10 g, 0.05 mol) was heated at reflux for 12 h in acetonitrile. Upon workup, an amine fraction (59%) was isolated. Analysis by GLC showed 1-(methylamino)-3-(*p*-tolyl)propane (27%) and a tertiary amine believed on the basis of NMR to be 1-(dimethylamino)-3-(*p*-tolyl)-2-propene (56%). The most diagnostic peaks in the ^1H NMR spectrum were at 1.7 ppm (p, $CH_2CH_2CH_2$) for the secondary amine, and peaks at 2.9 (d, $C{=}CHCH_2N$) and 6.0–6.3 ppm (m, vinyl) for the unsaturated tertiary amine.[2c] The mass spectrum of the tertiary amine in the mixture showed no parent ion, but contained strong peaks at m/e 130 (65%) $(M\text{-}Me_2NH)^+$ and at 132 (26%) $(M\text{-}MeN{=}CH_2)^+$.

Aminomethylation of *p*-Methylstyrene with Eschenmoser's Salt in Acetic Acid. When the above experiment was repeated in acetic acid at 70 °C, a 44% yield of amines was obtained. The ratio of tertiary to secondary amine was 31:69. When the same reaction was performed at 115 °C, a 26% yield of amines was obtained, with the ratio of tertiary to secondary amine increasing to 67:33.

Aminomethylation of *p*-Methoxystyrene. The aminomethylation of *p*-methoxystyrene with tetramethyldiaminomethane as above gave a 70% yield of amine product. Chromatographic analysis showed three components in relative quantities of 7%, 53%, and 40%, respectively. Titration of the sample for secondary amine established the smallest component as 1-(methylamino)-3-(*p*-methoxyphenyl)propane (9.4%). The major products were characterized spectroscopically as 1-(dimethylamino)-3-(*p*-methoxyphenyl)propane (40%) and 1-(dimethylamino)-3-acetoxy-3-(*p*-methoxyphenyl)propane (53%). The IR spectrum of the mixture showed the carbonyl band at 1722 cm^{-1}, and the NMR spectrum showed a strong singlet at 1.95 ppm (CH_3COO) and a triplet at 4.65 ppm ($PhCH(OAc)CH_2$) for the methine proton. The NMR spectrum also showed the required unsaturation (5.6–6.4 ppm), and a doublet at 2.9 ppm for the CH_2

(10) Abatoglou, A. G.; Eliel, E. L. *J. Org. Chem.* **1974**, *39*, 3042.

group of unsaturated amine. Integration of the NMR peaks gave composition of products similar to the GLC analysis. Mass spectrum, m/e calcd for $C_{11}H_{17}NO$, 179.1303; m/e found, 179.1310. No parent ion was detected for the tertiary amine.

Aminomethylation of *m*-Nitrostyrene. The aminomethylation of *m*-nitrostyrene as above gave only a 5% yield of amine (3 h). Analysis by GLC showed only two components in 86% and 14%, respectively. Titration for the secondary amine indicated the largest component to be 1-(methylamino)-3-(*m*-nitrophenyl)propane (81%): NMR δ 0.80 (s, 1 H, NH, exchanges with D_2O, 1.75 (p, 2 H, CH_2), 2.2 (s, 3 H, NCH_3), 2.22–2.8 (m, 4 H, $PhCH_2$, NCH_2), 7.35 (m, 2 H, ring), 7.9 (m, 2 H, ring); mass spectrum, m/e calcd for $C_{10}H_{14}N_2O_2$, 194.1055; m/e found, 194.1053. The minor component is the saturated tertiary amine; mass spectrum, m/e calcd for $C_{11}H_{16}N_2O_2$, 208.1212; m/e found, 208.1221.

Aminomethylation of α-Methylstyrene. The aminomethylation of α-methylstyrene as above gave a 72% yield of amine fraction. Analysis by GLC showed 1-(methylamino)-3-phenylbutane (13%), 1-(dimethylamino)-3-phenyl-3-butene (79%), and 1-(dimethylamino)-3-phenyl-2-butene (8%) to be in the mixture. The presence of the secondary amine was supported by titration (13.8%) as well as by the NMR peak at 1.2 ppm (d, $PhCHCH_3$). The remainder of the spectrum was identical to that reported for the same compounds.[2c]

Aminoethylation of Styrene. The aminoethylation of styrene with diethylamine and trioxane gave a 42% yield of amines, bp 90–105 °C (2.5 mm). Titration for the secondary amine (95%) and NMR established the major product as 1-(ethylamino)-3-phenylpropane: NMR δ 0.72 (s, 1 H, NH, exchanges with D_2O), 1.03 (t, 3 H, CH_3), 1.7 (p, 2 H, CH_2), 2.36–2.8 (m, 6 H, $ArCH_2$, NCH_2), and 7.03 (s, 5 H, ring); mass spectrum m/e calcd for $C_{11}H_{17}N$, 163.1360; m/e found, 163.1353.

Aminoisopropylation of Styrene. The aminoisopropylation of styrene with diisopropylamine and trioxane gave a 10% yield of amine product. Analysis by GLC showed three components in relative quantities of 37%, 8%, and 55%, respectively. Titration for the secondary amine (42%) and mass spectrometry established the first peak as 1-(isopropylamine)-3-phenylpropane: mass spectrum, m/e calcd for $C_{12}H_{19}N$, 177.1517; m/e found, 177.1513. The smallest components was identified as 1-(diisopropylamino)-3-phenyl-2-propene on the basis of hydrogenation to the saturated tertiary amine, but no parent ion was detected by mass spectrometry. The major product is believed to be the saturated teritary amine, 1-(diisopropylamino)-3-phenylpropane (GLC, ^1H NMR, hydrogenation).

Aminoalkylation of Styrene with 1-(Methylamino)octane. The aminoalkylation of styrene with 1-(methylamino)octane and trioxane gave a 40% yield of amines. Two secondary amines, 1-(*n*-octylamino)-3-phenylpropane and 1-(methylamino)-3-phenylpropane, were obtained in a molar ratio of 58:38: mass spectrum, m/e calcd for $C_{17}H_{19}N$, 247.2300; m/e found, 247.2311; m/e calcd for $C_{10}H_{15}N$, 149.1204; m/e found, 149.1202.

Aminoalkylation of Styrene with 2-(Methylamino)propane. The aminoalkylation of styrene with 2-(methylamino)propane and trioxane gave a 38% yield of amines. Analysis showed two secondary amines, 1-(methylamino)-3-phenylpropane and 1-(isopropylamino)-3-phenylpropane, to be in the mixture in a molar ratio of 86% and 10%, respectively. Both amines were characterized earlier.

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Registry No. **2**, 28149-27-1; **4a**, 98-83-9; **4b**, 115-11-7; **4c**, 115-07-1; **4d**, 106-98-9; **6** (Ar = C_6H_5), 100-42-5; **19**, 23580-89-4; **21**, 87462-08-6; $[(CH_3)_2N]_2CH_2$, 51-80-9; Me_2NH, 124-40-3; *n*-$C_3H_7CH_2CH{=}CH_2$, 592-41-6; *n*-$C_5H_{11}CH_2CH{=}CH_2$, 111-66-0; *n*-$C_9H_{19}CH_2CH{=}CH_2$, 112-41-4; *n*-$C_{11}H_{23}CH_2CH{=}CH_2$, 1120-36-1; *p*-$CH_3C_6H_4CH{=}CH_2$, 622-97-9; *p*-$CH_3OC_6H_4CH{=}CH_2$, 637-69-4; *m*-$O_2NC_6H_4CH{=}CH_2$, 586-39-0; Me_2NCH_2I, 36627-00-6; CH_2O, 50-00-0; *n*-$C_6H_{17}NHCH_3$, 2439-54-5; *n*-$C_4H_9NHCH_3$, 110-68-9; 2-$C_3H_7NHCH_3$, 4747-21-1; $(C_2H_5)_2NH$, 109-89-7; $(2\text{-}C_3H_7)_2NH$, 108-18-9; 1-(diisopropylamino)-3-phenyl-2-propene, 87462-12-2; 2-ethyl-1-hexene, 1632-16-2; 5-decene, 19689-19-1; cyclohexene, 110-83-8; 1-(methylamino)nonane, 39093-27-1; 1-(methylamino)pentadecane, 29664-53-7; 1-(*n*-octylamino)-3-phenylpropane, 87462-13-3; 1-(methylamino)-3-(*p*-tolyl)propane, 87462-06-4; 1-(dimethyl)amino-3-(*p*-tolyl)-2-propene, 87462-07-5; 1-(methylamino)-3-(*p*-methoxyphenyl)propane, 83986-67-8; 1-(dimethylamino)-3-(*p*-methoxyphenyl)propane, 59907-34-5; trioxane, 110-88-3; 1-(methylamino)-3-(*m*-nitrophenyl)propane, 87462-09-7; 1-(dimethylamino)-3-(*m*-nitrophenyl)propane, 87462-10-0; 1-(ethylamino)-3-phenylpropane, 13125-62-7; 1-(isopropylamino)-3-phenylpropane, 87462-11-1.