

Anal. Calcd for $C_{12}H_{27}O_4P$: C, 54.12; H, 10.22. Found: C, 53.42; H, 10.16.

Diisobutyl *t*-Butyl Phosphate (1, R = *i*-Bu).—As above, 22.85 g (0.1 mol) of diisobutyl phosphorochloridate, 12.32 g (0.11 mol) of potassium *t*-butoxide, and 250 ml of petroleum ether were allowed to react, giving after distillation in small batches 18.2 g (69%) of diisobutyl *t*-butyl phosphate (1, R = *i*-Bu): bp 87–89° (0.3 mm); n_D^{25} 1.4171; nmr δ 0.97 [d, 12, J = 6 Hz, $[(CH_3)_2CHCH_2O]_2P(O)$], 1.46 [s, 9, $(CH_3)_3CO$], 1.91 [m, 2, $(>CHCH_2O)_2P(O)$], 3.75 [m, 4, $(>CHCH_2O)_2P(O)$].

Anal. Calcd for $C_{12}H_{27}O_4P$: C, 54.12; H, 10.22. Found: C, 53.63; H, 10.09.

Diphenyl *t*-Butyl Phosphate (1, R = Ph).—As above, 21.3 g (0.08 mol) of diphenyl phosphorochloridate,^{10b} 9.8 g (0.09 mol) of potassium *t*-butoxide, and 250 ml of petroleum ether were allowed to react. The filtrate was concentrated at -20° (0.1 mm) leaving 23.1 g (95%) of diphenyl *t*-butyl phosphate (1, R = Ph) identified by nmr: nmr δ 1.46 [s, 9, $(CH_3)_3CO$], 6.82 [s, 10, $(C_6H_5O)_2P(O)$].

Dibenzyl *t*-Butyl Phosphate (1, R = PhCH₂).—As above 28.33 g (0.096 mol) of dibenzyl phosphorochloridate,^{10b} 12.32 g (0.11 mol) of potassium *t*-butoxide, and 250 ml of petroleum ether were allowed to react. The filtrate was concentrated at -20°

(0.1 mm) giving 22 g (68%) of dibenzyl *t*-butyl phosphate (1, R = PhCH₂) identified by nmr: nmr δ 1.47 [s, 9, $(CH_3)_3CO$], 4.71 [d, 4, $(C_6H_5CH_2O)_2P(O)$], 6.87 [s, 10, $(C_6H_5CH_2O)_2P(O)$].

Registry No.—1 (R = Me), 13232-07-0; 1 (R = Et), 13232-08-1; 1 (R = Pr), 22433-79-0; 1 (R = *i*-Pr), 13232-09-2; 1 (R = Bu), 22433-81-4; 1 (R = *i*-Bu), 22433-82-5; 1 (R = Ph), 22433-83-6; 1 (R = PhCH₂), 22433-84-7; 9 (R = Et), 107-49-3; 9 (R = *i*-Pr), 5836-28-2; 12, 1706-92-9; 13, 1707-03-5; 14 (R = Et), 78-40-0; diisopropyl *t*-butylperoxy phosphate, 10160-46-0.

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Polar Effects on the Formation of Imines from Isobutyraldehyde and Primary Aliphatic Amines¹

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The following dimensionless equilibrium constants for the formation of imines and water from isobutyraldehyde and primary amines were determined in aqueous solution at 35°: MeO(CH₂)₂NH₂, 3600; PhCH₂NH₂, 2500; MeOCH₂CH₂NH₂, 2060; Me₂NCH₂CH₂NH₂, 1700; HC≡CCH₂NH₂, 1400; (MeO)₂CHCH₂NH₂, 1380; H₂NCH₂CONH₂, 621; H₂NCH₂CN, 548; CF₃CH₂NH₂, 238. The equilibrium constants decrease with increasing electron-withdrawing power of the substituents. A plot of log *K* vs. the p*K*_a values of the conjugate acids of the amines gives a satisfactory straight line for amines of the type RNH₂ where R contains an sp²-hybridized β-carbon atom. Deviations from this line in the cases of the imines derived from aminoacetonitrile and propargylamine are attributed to the particular stability of a conformer in which the carbon–nitrogen double bond of the imine is eclipsed by a cyano or ethynyl group. This conclusion is supported by nmr data.

We have previously described methods for determining equilibrium constants for the formation of imines from isobutyraldehyde and primary amines by uv measurements at the aldehyde maximum or at the imine maximum or by measurements of the effect of added aldehyde on the pH of amine buffer solutions.² Equilibrium constants were reported for methyl-, ethyl-, isopropyl-, *t*-butyl-, *n*-propyl-, and *n*-butylamine, and the conformational equilibria of the resultant imines were discussed on the basis of their nmr spectra. In these compounds, where polar effects were held relatively constant, differences in ease of formation and in conformational preferences were attributed almost entirely to steric effects. We have now determined the equilibrium constants for the formation of imines from isobutyraldehyde and primary amines of the type RCH₂NH₂, in which steric effects are kept fairly constant and polar effects varied widely.

Results

The equilibrium constant for imine formation is that defined previously²

$$K = IW/AB \quad (1)$$

(1) (a) This investigation was supported in part by Grant DA-ARO-D-31-124-G648 from the U. S. Army Research Office (Durham) and by Public Health Service Grant AM10378 from the National Institute of Arthritis and Metabolic Diseases. (b) Abstracted in part from the Ph.D. thesis of C. Y. Yeh, The Ohio State University, 1968.

where *I*, *W*, *B*, and *A* are the equilibrium concentrations of imine, water, amine, and aldehyde (including both free aldehyde and aldehyde hydrate), respectively. For the ultraviolet method of determining *K*, eq 2 was used when measurements were made at the imine maximum.

$$A_0/[D - A_0\epsilon_A - (B_0 - B')\epsilon_B] = \{1/(\epsilon_I - \epsilon_A - \epsilon_B)\} + \{W/[KB(\epsilon_I - \epsilon_A - \epsilon_B)]\} \quad (2)$$

ϵ_I , ϵ_A , and ϵ_B are the extinction coefficients of the imine, aldehyde, and amine at the wavelength used, *A*₀ and *B*₀ are the initial concentrations (before imine formation) of aldehyde and amine, *B'* is the concentration of amine in the reference cell, and *D* is the absorbance. In order to calculate the real concentrations of amines present (that is, to correct for the amounts present in the protonated forms), it was necessary to know their ionization constants at the ionic strengths and temperatures used. This knowledge was vital in cases where equilibrium constants were determined by pH measurements. The ion-product constant of water was calculated as described previously.² The ionization constants of 2-methoxyethylamine, 3-methoxypropylamine, 2,2-dimethoxyethylamine, 2,2,2-trifluoroethylamine, benzylamine, propargylamine, and 2-dimethylaminoethylamine were determined at 35°. Literature values at 25° were corrected to 35° by the

(2) J. Hine and C. Y. Yeh, *J. Amer. Chem. Soc.*, **89**, 2669 (1967).

method of Perrin³ for aminoacetonitrile⁴ and glycine-amide,⁵ whose equilibrium constants were not determined by the pH method and whose basicities were so low that little ionization occurred. The pK_a values for the conjugate acids of the amines studied (including those studied previously for which no pK_a values were given²) are listed in Table I.

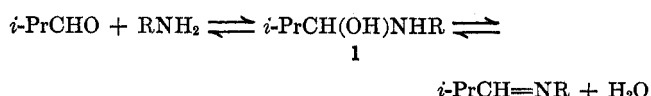
TABLE I
VALUES OF pK_a FOR PRIMARY AMINES IN WATER AT 35°
AND ZERO IONIC STRENGTH^a

Amine	pK_a
Methylamine	10.31 ^b
Ethylamine	10.31 ^b
<i>n</i> -Propylamine	10.21 ^b
Isopropylamine	10.21 ^b
<i>n</i> -Butylamine	10.26 ^b
<i>t</i> -Butylamine	9.72 ^b
3-Methoxypropylamine	9.83
2-Dimethylaminoethylamine	9.45 ^c
2-Methoxyethylamine	9.09
Benzylamine	9.00
2,2-Dimethoxyethylamine	8.35
Propargylamine	7.87
Glycinamide	7.69 ^{d,e}
2,2,2-Trifluoroethylamine	5.52
Aminoacetonitrile	5.16 ^{d,e}

^a pK_a is the negative logarithm of the acidity constant of the conjugate acid of the amine. ^b Determined as described in ref 2. ^c This refers to the acidity of the monoprotonated form of the diamine, which is a mixture of $Me_2NCH_2CH_2NH_3^+$ and $H_2NCH_2CH_2NHMe_2^+$. ^d Calculated from data at 25°. ^e At ionic strengths around 0.01 M.

Equilibrium constants were determined by pH measurements and, in most cases, by measurements at the uv absorption maxima of the imines for all the imines except *N*-isobutylidene-2-dimethylaminoethylamine and those imines for which K is less than 1000. The additional basic functional group in 2-dimethylaminoethylamine made interpretation of the effect of added isobutyraldehyde on the pH of amine buffer solutions excessively complicated. The absorption of 2-dimethylaminoethylamine in the range 2100–2400 Å is so strong as to make equilibrium measurements at the imine maximum relatively unreliable. The addition of isobutyraldehyde to buffers of amines whose equilibrium constants for isobutyraldimine formation were less than about 1000 caused such small changes in the pH that the equilibrium constants could not be determined reliably from them. For these amines the equilibrium constants were determined by measurements at the aldehyde absorption maximum. The values of K obtained are listed in Table II.

As pointed out previously,² the equilibrium constants determined by the present methods are measures of the extent of formation of carbinolamine (1) plus imine.



Stopped-flow kinetic studies of the reaction of isobutyraldehyde with 2,2,2-trifluoroethylamine in water at 35° have shown that the equilibrium constant for

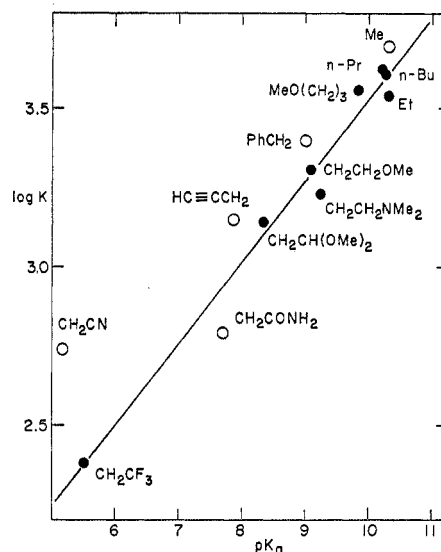


Figure 1.—Plot of $\log K$ for the formation of $i\text{-PrCH=NR}$ from $i\text{-PrCHO}$ and RNH_2 vs. pK_a for RNH_3^+ . For the solid circles, R contains an sp^3 -hybridized β -carbon atom.

TABLE II
EQUILIBRIUM CONSTANTS FOR FORMATION OF IMINES FROM
ISOBUTYRALDEHYDE AND PRIMARY AMINES IN WATER AT 35°

Primary amine	Registry no.	K^a	
		Uv measurements at absorption maximum Imine Aldehyde	pH measurements Av
$MeO(CH_2)_3NH_2$	5332-73-0	3570	3620 3600
$C_6H_5CH_2NH_2$	100-46-9		2500 2500
$MeOCH_2CH_2NH_2$	109-85-3	2090	2020 2060
$Me_2NCH_2CH_2NH_2$	108-00-9	1700	
$HC\equiv CCH_2NH_2$	2450-71-7		1400 1400
$(MeO)_2CHCH_2NH_2$	22483-09-6	1200	1570 1380
$H_2NCOCH_2NH_2$	598-41-4	606 ^b 636	621
$NCCH_2NH_2$	540-61-4	548	548
$CF_3CH_2NH_2$	753-90-2	238	238

^a The dimensionless equilibrium constant defined by eq 1. ^b The experimental method used is of diminished reliability for K values this small.

carbinolamine formation is no more than one-tenth as large as that for imine formation.⁶ Equilibrium constants for the formation of carbinolamines have been found to be decreased only slightly by electron-withdrawing substituents.^{7,8} It therefore seems fairly well assured that the equilibrium constants we have measured are very largely for imine formation. Kinetic studies have also shown that equilibrium in reactions of the type studied is reached in a minute or less.⁶ This adds to the evidence that equilibrium had been reached in our measurements, which were made a number of minutes after mixing and in which no drift was noted.

All of the isobutyraldimines except the one derived from glycineamide were isolated and characterized by their ir, nmr, and in most cases uv spectra. All the compounds showed a strong absorption maximum at $1672 \pm 5 \text{ cm}^{-1}$, which we attribute to the $C=N$ stretching vibration. The uv and nmr spectral data are summarized in Tables III and IV.

(3) D. D. Perrin, *Aust. J. Chem.*, **17**, 484 (1964).

(4) G. W. Stevenson and D. Williamson, *J. Amer. Chem. Soc.*, **80**, 5943 (1958).

(5) M. Zief and J. T. Edsall, *ibid.*, **89**, 2245 (1937).

(6) F. A. Via, The Ohio State University, personal communication, 1968.

(7) R. G. Kallen and W. P. Jencks, *J. Biol. Chem.*, **241**, 5884 (1966).

(8) E. G. Sander and W. P. Jencks, *J. Amer. Chem. Soc.*, **90**, 6154 (1968).

TABLE III
 ULTRAVIOLET DATA ON ISOBUTYRALDIMINES

Imine	Registry No.	Me ₃ CCH ₂ CHMe ₂		MeCN		Water	
		λ_{\max} , Å	ϵ , M ⁻¹ cm ⁻¹	λ_{\max} , Å	ϵ , M ⁻¹ cm ⁻¹	λ_{\max} , Å	ϵ , M ⁻¹ cm ⁻¹
<i>i</i> -PrCH=N(CH ₂) ₂ OMe	22483-13-2	2450	90			2300	138
<i>i</i> -PrCH=NCH ₂ CH ₂ OMe	22483-14-3	2360	169	2360	195	2200	118
<i>i</i> -PrCH=NCH ₂ CH ₂ NMe ₂	22483-15-4	2075 ^a	2980 ^a	2175 ^a	1560 ^a		
<i>i</i> -PrCH=NCH ₂ CH(OMe) ₂	22483-16-5	2425	95	2300	199	2275	193
<i>i</i> -PrCH=NCH ₂ CF ₃	22483-17-6	2400	87	2300	130	2300	126
<i>i</i> -PrCH=NCH ₂ CONH ₂	22483-18-7					2350	157
<i>i</i> -PrCH=NCH ₂ CN	22483-19-8	2310	159	2300	177	2250	111
<i>i</i> -PrCH=NCH ₂ C≡CH	22483-20-1	2370	119	2300	181		

^a These results are not very reliable, but they do illustrate the shift in λ_{\max} and increase in ϵ that we have attributed to the tertiary amino group in the molecule.

 TABLE IV
 NMR SPECTRA OF N-ISOBUTYLIDENEALKYLAMINES^a

Chemical shifts, τ , and types of protons							Coupling constants, cps					
A	B ^b	C	D	E	F	G	J _{AB}	J _{BC}	J _{CD}	J _{DE}	J _{EF}	J _{BD}
(CH ₃) ₂ CH—CH=N—CH ₂ —CH ₂ —CH ₂ —O—CH ₃							6.9	4.0	1.3	6.8	6.3	
8.99	2.49		6.7	8.27	6.7	6.79						
(CH ₃) ₂ CH—CH=N—CH ₂ —C ₆ H ₅ ^c							7.0	4.2	1.4			
8.99	2.34		5.45	2.70								
(CH ₃) ₂ CH—CH=N—CH ₂ —CH ₂ —O—CH ₃							7.0	4.3				
8.96	2.52		6.55	6.55	6.75							
(CH ₃) ₂ CH—CH=N—CH ₂ —CH ₂ —N(CH ₃) ₂							6.7	4.0	1.3	6.8		1.0
8.98	2.56		6.62	7.63	7.84							
(CH ₃) ₂ CH—CH=N—CH ₂ C≡CH							7.2	4.3	1.8	2.5		1.3
8.95	1.95		5.70	7.45								
(CH ₃) ₂ CH—CH=N—CH ₂ —CH(OCH ₃) ₂							6.8	4.1	1.3	5.3		
8.99	2.54		6.57	5.54	6.75							
(CH ₃) ₂ CH—CH=N—CH ₂ —CF ₃ ^d							7.0	4.3	1.3	9.4		1.0
8.93	2.34		6.17									
(CH ₃) ₂ CH—CH=N—CH ₂ —CN ^e							6.8	4.3	1.8			1.3
9.01	2.23		5.71									

^a Run neat, using internal tetramethylsilane unless otherwise indicated. ^b Absorption by type B protons was too broad and weak to permit a reliable determination of the chemical shift, but this shift corresponded to a τ of about 7.7 ppm in all cases except those of N-isobutylidene-2,2,2-trifluoroethylamine, N-isobutylidenebenzylamine, N-isobutylidenepropargylamine, and N-isobutylideneaminoacetonitrile, where it was about 7.6 ppm. ^c Registry no.: 22483-21-2. ^d The hydrogen-fluorine coupling constant J_{CF} was 1.2 cps. ^e Using external tetramethylsilane as reference.

Discussion

From the results shown in Table II it may be seen that electron-withdrawing substituents tend to decrease the equilibrium constants for the formation of isobutyraldimines from primary amines. One might examine this tendency quantitatively by making a Taft equation plot, but most of the required σ^* values do not appear to be directly available. We have therefore plotted $\log K$ vs. the pK_a values of the conjugate acids of the amines studied. To the extent to which the amine basicities follow the Taft equation⁹ this procedure constitutes a test of the applicability of the Taft equation to our equilibrium constants. In the plot (Figure 1) all of the equilibrium constants determined in the present investigation were used; in addition, data on all the amines of the type RNH₂, where R is primary, that were previously studied² are included. (The equilibrium constants for isopropylamine and *t*-butylamine are relatively small because of greater steric hindrance.) The appropriate K_a value that should be used for the case of 2-dimethylaminoethylamine is

$$K_a = [H^+][Me_2NCH_2CH_2NH_2]/[Me_2NCH_2CH_2NH_3^+]$$

That is, the denominator should contain the concentration of only that monoprotinated species that is pro-

tonated at the primary amino group. This species has been found to comprise 62% of the total monoprotinated form of 2-dimethylaminoethylamine.⁶ Therefore the K_a value given in Table I was divided by 0.62 and the resultant pK_a value (9.24) used in plotting Figure 1. The slope of the line shown in the figure was calculated by the method of least squares, using all of the solid circles, which refer to amines of the type RNH₂ where R contains an sp³-hybridized β -carbon atom. This value, 0.256, may be multiplied by the ρ^* value for the acidity of primary ammonium ions (-3.14)⁹ to give -0.80 as an estimate of ρ^* for the formation of isobutyraldimines from primary amines. The ρ^* value has the expected algebraic sign. Electron-withdrawing substituents would be expected to discourage the transformation of the amino group, in which the nitrogen is probably approximately sp³ hybridized, to an imino group, in which the nitrogen is sp² hybridized and hence more electron withdrawing. The situation is somewhat similar to that found in the case of olefins, aldehydes, and ketones, whose enthalpies and free energies of hydrogenation are made more negative by electron-withdrawing substituents.¹⁰

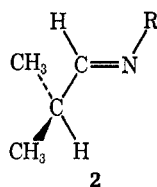
The fact that the equilibrium constant for formation of the N-methylimine is somewhat larger than those for the ethyl-, propyl-, and butylimines has already been

(9) Cf. H. K. Hall, Jr., *J. Amer. Chem. Soc.*, **79**, 5441 (1957).

(10) R. W. Taft, Jr., and M. M. Kreevoy, *ibid.*, **79**, 4011 (1957).

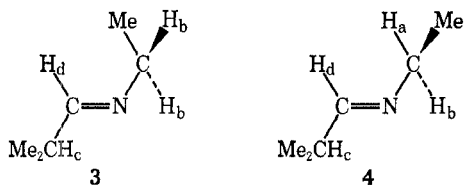
explained in terms of the three stable conformations with respect to rotation around the carbon–nitrogen single bond that exist for this imine compared with only two for the other imines.² If the equilibrium constant for the methyl compound were only two-thirds as large as it is, the point for methyl in Figure 1 would lie slightly below the line. The deviations of the other open circles from the line are also best discussed in terms of conformational equilibria.

All of the values of J_{BC} fall in the range 4.1 ± 0.2 cps previously observed.² We had estimated that this indicates that $32 \pm 3\%$ of these imines exist in conformation 2, with the two hydrogens *trans* to each



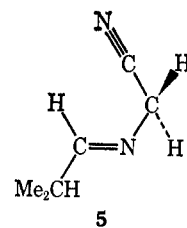
other. A more reliable estimate is now available from the work of Karabatsos and Lande, who made measurements at several temperatures using imines derived from a number of aldehydes.¹¹ From their values of J_{trans} and J_{gauche} and their alkyl correction factor, a coupling constant of 4.1 ± 0.2 cps may be calculated to correspond to $35 \pm 3\%$ conformation 2.

In our previous analysis of conformational isomerization due to rotation around the carbon–nitrogen single bond,² we described evidence that conformation 3, in which the carbon–nitrogen double bond is eclipsed by a carbon–methyl bond, is about 2.0 kcal/mol less stable than 4, in which the carbon–nitrogen double bond is



eclipsed by a carbon–hydrogen bond. Inasmuch as the previously undetectable J_{CD} for N-isobutylideneisopropylamine has subsequently been found to be 0.7 cps, our previous estimates of the H_a-H_d and H_b-H_d (see 3 and 4) coupling constants have been revised to 0.5 and 2.1 cps, respectively. From the values of J_{CD} in Table IV it follows that the 3-methoxypropyl-, 2-dimethyl-aminoethyl-, 2,2-dimethoxyethyl-, and 2,2,2-trifluoroethylimines, like the ethyl-, propyl-, and butylimines studied previously, all exist almost entirely in conformations analogous to 4, in which the carbon–nitrogen double bond is not eclipsed by a carbon–carbon bond in the amine part of the molecule. From the considerably larger coupling constant found for the imines derived from propargylamine and aminoacetonitrile, it may be calculated that these imines exist to an extent of about 63% in conformations like 5. This conclusion is supported qualitatively by the facts that J_{BD} is larger for these imines than for any others and

that the hydrogen atom attached to sp^2 carbon, which, in a conformation like 5, would lie in a deshielding region



with respect to the triple bond, absorbs at lower field in the cases of these two imines than in any others. If it were not possible for these two imines to exist in the particularly stable conformers like 5, the equilibrium constants for their formation would be only about 37% as large as they are. If the equilibrium constants were only 37% as large, the agreement with the straight line in Figure 1 would be better.

The tendency of the cyano group to eclipse the carbon–nitrogen double bond is analogous to (but stronger than) its tendency to eclipse a carbon–carbon double bond. Allyl cyanide exists to the extent of about 44% in the conformation analogous to 5 and only about 28% in each of the other two conformations.¹² It seems possible that the particular stability of conformations like 5 for the imines derived from propargylamine and aminoacetonitrile should be attributed to stabilizing van der Waals interactions; the cyano and ethynyl groups are smaller (in the relevant direction) than alkyl groups. If this explanation is correct, then it would seem possible that stabilizing van der Waals interactions would also be found in N-isobutylidenebenzylamine and N-isobutylidene-glycinamide if they existed in conformations analogous to 5 with the phenyl or carbamido group oriented in a plane perpendicular to the plane of the aldimino group. However, it is known that the phenyl group in allylbenzene has a smaller tendency to eclipse the carbon–carbon double bond than does the cyano group in allyl cyanide.¹² To freeze a phenyl or a carbamido group perpendicular to the plane of the aldimino group would result in unfavorable entropy effects that have no analogs in the cases of the cyano and ethynyl compounds. Furthermore, in such an orientation the carbon–oxygen double bond of the carbamido group would not be eclipsed by any of the bonds of the adjacent carbon atom, as would be required for maximum stability. Finally, there is, of course, no reason to believe that the van der Waals forces due to the π electrons would be the same for the phenyl, carbamido, ethynyl, and cyano groups. Therefore, it is not surprising that the N-isobutylidene-glycinamide compound shows no tendency to exist in a conformation like 5, and the tendency of N-isobutylidenebenzylamine to exist in such a conformation is small at best ($J_{CD} = 1.4$ cps).

The preceding interpretation of part of our results in terms of conformational stabilities may be complicated by the fact that most of our information concerning conformational stabilities comes from nmr measurements on neat imines rather than on imines in aqueous solution where the equilibrium constants for imine formation were determined.

(11) G. J. Karabatsos and S. S. Lande, *Tetrahedron*, **24**, 3907 (1968).

(12) A. A. Bothner-By and H. Günther, *Discussions Faraday Soc.*, **34**, 127 (1962).

TABLE V
 PROPERTIES OF ISOBUTYRALDIMINES

Imine	Bp, °C	d^{25}_4	t_1 , °C	n^{25}_D	t_2 , °C	Calcd, %			Found, %		
						C	H	N	C	H	N
<i>i</i> -PrCH=N(CH ₂) ₃ OMe	160	0.820	35	1.4245	25	67.09	11.82	9.93	67.07	11.97	9.79
<i>i</i> -PrCH=NCH ₂ CH ₂ OMe	142	0.839	35	1.4139	25	65.07	11.70	10.84	64.93	11.80	10.67
<i>i</i> -PrCH=NCH ₂ CH ₂ NMe ₂	110 ^a	0.796	25	1.4283	27	67.54	12.76	19.70	67.67	12.88	19.48
<i>i</i> -PrCH=NCH ₂ CH(OMe) ₂	127 ^b	0.899	25	1.4237	27	60.34	10.76	8.80	60.52	10.93	8.64
<i>i</i> -PrCH=NCH ₂ CF ₃ ^c	102	1.036	26	1.3632	27.5	47.07	6.58	9.14	47.28	6.67	9.17
<i>i</i> -PrCH=NCH ₂ CN	35 ^d			1.4326	28	65.43	9.15	25.42	65.34	9.42	25.40
<i>i</i> -PrCH=NCH ₂ C≡CH	132	0.841	26	1.4443	26	77.01	10.16	12.83	76.92	10.23	12.97
<i>i</i> -PrCH=NCH ₂ C ₆ H ₅	66 ^e	0.856	26	1.5079	26	81.94	9.38	8.69	81.84	9.32	8.74

^a At 138 mm. ^b At 143 mm. ^c Calcd: F, 37.23. Found: F, 37.12. ^d At 2.5 mm. ^e At 0.26 mm.

It may be that some of the deviations from linearity in the plot in Figure 1 arise from complications that affect only the pK_a values.

Experimental Section

Unless otherwise stated, the experimental methods were the same as those used previously.²

Aminoacetonitrile bisulfate and glycinamide hydrochloride were recrystallized from 95% ethanol and dried in a desiccator. All the other amines used were tested by gas-liquid partition chromatography and found to contain less than 0.5% impurity, except for 2,2,2-trifluoroethylamine, which contained about 1.5% impurity.

Imines.—The various imines were prepared from isobutyraldehyde and the appropriate primary amine by methods like that described previously,² except in the cases of the 2,2-dimethoxy-

ethyl and the 2,2,2-trifluoroethyl compounds, where magnesium sulfate was used as the drying agent instead of potassium hydroxide, and the case of N-isobutylideneaminoacetonitrile, which was prepared as follows. A mixture of 15.4 g (0.1 mol) of aminoacetonitrile bisulfate and 18 g (0.18 mol) of triethylamine was stirred at 0° while 7.2 g (0.1 mol) of isobutyraldehyde was added. After 2 hr the reaction mixture was dried over molecular sieves, Type 5A, and distilled under vacuum. Data on the imines prepared are listed in Table V. Attempts to isolate N-isobutylidene-glycinamide were unsuccessful.

Registry No.—Isobutyraldehyde, 78-84-2.

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A New Addition Reaction of Chloromethyl Methyl Sulfide to Olefins in Sulfuric Acid. A New Synthesis of 3-(Methylthio)propionaldehyde

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Chloromethyl methyl sulfide (10) has been found to add to vinyl chloride in sulfuric acid to give 3-(methylthio)propionaldehyde. The addition reaction of 10 with other olefins was investigated, but similar reactions did not occur in the case of cyclohexene, acrylonitrile, or 1-chlorocyclohexene.

Presently, *dl*-methionine, an essential amino acid, is produced from acrolein and methanethiol.¹ The present study has been undertaken to find a new synthetic route from dimethyl sulfide and vinyl chloride (11). The chlorination of dimethyl sulfide is known to give chloromethyl methyl sulfide (10)² in good yields. The electrophilic addition of α -chloro ethers to olefins has been widely investigated³ but the analogous reaction of α -chloro sulfides seems not to have been, presumably because of the weak reactivities of the sulfides compared with the ethers.⁴ The Markovnikov addition of 10 to 11 would give rise to 1,1-dichloro-3-(methylthio)propane (1), which might in turn be converted into *dl*-methionine.

On exploring this possibility, it has been found that 10 adds to 11 in the presence of aluminum chloride yielding 1 in low yield. This result has led to the

investigation of other Lewis acids as catalysts for this reaction, and to success with sulfuric acid.

Reaction of Chloromethyl Methyl Sulfide with Vinyl Chloride in Sulfuric Acid.—When the sulfide 10 was treated with sulfuric acid, it gradually dissolved with the evolution of hydrogen chloride to give a clear solution. The solution was allowed to react with 11 in a pressure vessel, and 3-(methylthio)propionaldehyde (4) was found in the ether extract of the hydrolysate of the reaction mixture and was isolated as its 2,4-dinitrophenylhydrazone (13a). A part of unreacted 10 was recovered as the methylthiomethyl derivatives of the hydrazine (15a), one of which was isolated and identified as 1-(2,4-dinitrophenyl)-1,2-bis(methylthio-methyl)hydrazine (15b). There were also found some by-products, among which formaldehyde and acetaldehyde were isolated as 13b and 13c, respectively. From the ether extract of the original hydrolysate, bis(methylthio)methane (5),⁵ *cis*- and *trans*-1,3-bis(methylthio)propene (6a and b), and 3-(methylthio)propionaldehyde dimethyl mercaptal (9) were separated

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