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PREPARATION OF KETIMINES AND THE CORRESPONDING SECONDARY AMINES

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During a study of the preparation of unsymmetrical aliphatic secondary amines, a three-step process for their preparation from ketones and ammonia has been developed. This method consists of the hydrogenation of a ketone in the presence of ammonia to form the primary amine. The amine may then be condensed with a mole of the same or a different ketone in the presence of an acid catalyst yielding the corresponding ketimine which may be isolated. Hydrogenation of the ketimine yields the secondary amine in high yield.

Preparation of primary amines. As most of the primary amines used for this investigation were prepared by the reductive amination of ketones, a study was made to determine the optimum conditions for their preparation. Although previous investigators have deemed it advisable to use an inert solvent (1–6) or a large excess of ammonia (7) for the hydrogenation of aldehydes or ketones in the presence of ammonia to obtain primary amines, we have not found it necessary to use either the inert solvent or the large excess of ammonia. Hydrogenation of a 1 to 1–1.5 molar mixture of a ketone and ammonia over Raney nickel at 120–150° and 500–1000 p.s.i. in the absence of a solvent has given in many cases primary amines in better than 80% yields. Table I lists the primary amines prepared and their properties.

Preparation of ketimines. Although unsymmetrical aliphatic secondary amines have been prepared by the hydrogenation of ketone in the presence of an amine, little information is available in the literature about the isolation and properties of the intermediate ketimines.[1] Aside from the work of Cope, *et al.* and Blomberg, *et al.* no record of the preparation and isolation of these aliphatic ketimines has been found. Cope, Hancock, *et al.* (8) have prepared a number of condensation products of ketones with alkanolamines by azeotroping the water of reaction with benzene. The majority of these were found to exist as the corresponding oxazolidines. However, the product from diisobutyl ketone did exist as the ketimine. Blomberg and Bruce (9) prepared N-isopropylidenemethylamine using basic catalysts such as sodium hydroxide, calcium oxide, potassium hydroxide, and potassium carbonate. Of these, potassium carbonate was the favored catalyst, giving a 40% conversion to product.

We have found that aliphatic ketimines may be conveniently prepared from ketones and amines with acidic catalysts. After neutralization of the catalyst,

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[1] We are indebted to Mr. Francis L. Schmehl who kindly brought to our attention the excellent work of Campbell, Sommers, and Campbell, *J. Am. Chem. Soc.*, **66**, 82–84 (1944), on the preparation and hydrogenation of aldimines. We were aware of the reference, but decided to restrict our paper to a discussion of ketimines.

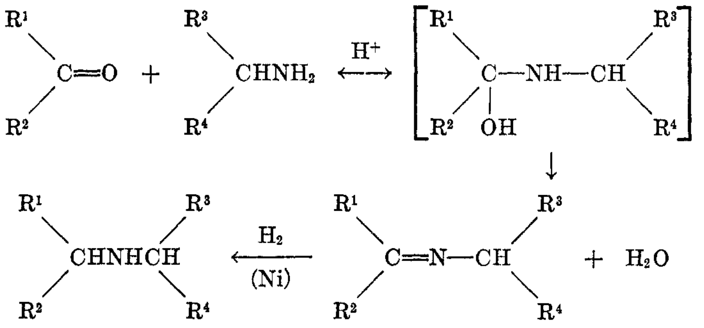
TABLE I

PREPARATION OF PRIMARY AMINES BY HYDROGENATION OF A MIXTURE OF A KETONE AND AMMONIA[a] OVER RANEY NICKEL

STARTING MATERIAL	CONDITIONS		TIME, hrs.	PRODUCT	B.P., °C (MM.)	n_D^{20}	d_4^{20}	CONVERSION TO PRODUCT, %	YIELD,[b] %	NEUT. EQUIV.	
	Temp., °C.	Press., p.s.i.g.								Found	Theory
Acetone	140	740	0.5	Isopropylamine	32.2	1.377 15°	0.694 15°	77	97	60.3	59.1
Methyl ethyl ketone	120	700	—	*sec*-Butylamine	62.6	1.3928	.7225	90	96	73.3	73.1
Methyl isobutyl ketone	120	500	—	1,3-Dimethylbutylamine	108.5	1.4081	.7465	90	—	101.5	101.2
Methyl amyl ketone	130	700	1.5	2-Aminoheptane	141–142	1.4179	.7629	90	—	115.3	115.2
Isophorone	140	500	—	3,3,5-Trimethylcyclohexylamine	179.6	1.4539	.8442	74	—	142.0	141.2
Diisobutyl ketone	150	1000	—	1-Isobutyl-3-methylbutylamine	169	1.4210	.7719	48	85	143.5	143.2

[a] Mole ratio, ketone : NH_3—1 : 1-2. [b] Yield is based on recovery of ketone and alcohol. (Credit is taken for alcohol as equivalent to ketone.)

the ketimines were distilled without decomposition and were stable on storage in a dry inert atmosphere. In the presence of moisture, the lower-boiling ketimines are subject to hydrolysis.



Ketimines from lower-boiling constituents. In the preparation of the imines from water-soluble ketones and amines where a two-phase azeotrope could not be formed, an acidic catalyst was necessary to attain equilibrium in a reasonable length of time.

Of the variables involved in the preparation of N-isopropylidene-isopropylamine temperature and catalyst concentration were investigated most fully. Refractive indices were found to be satisfactory in the determination of conversion to ketimine by comparison with synthetic mixtures of known composition of the components. Increase of the temperature accelerates the rate of reaction but at the sacrifice of extent of conversion. As can be seen from Figure 1, equilibrium (55% imine) was reached in 30 minutes at 50° using 0.5% m of hydrochloric acid based on the amine as catalyst. At 30°, the equilibrium state was nearly reached after 80 minutes giving 63% imine, whereas, at 20° equi-

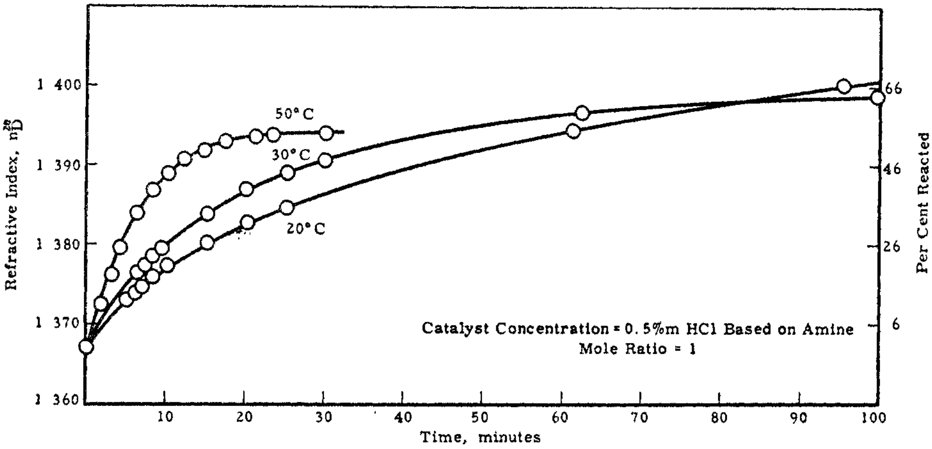


Figure 1. EFFECT OF TEMPERATURE ON REACTION RATE OF ACETONE WITH ISOPROPYLAMINE

FIG. 1

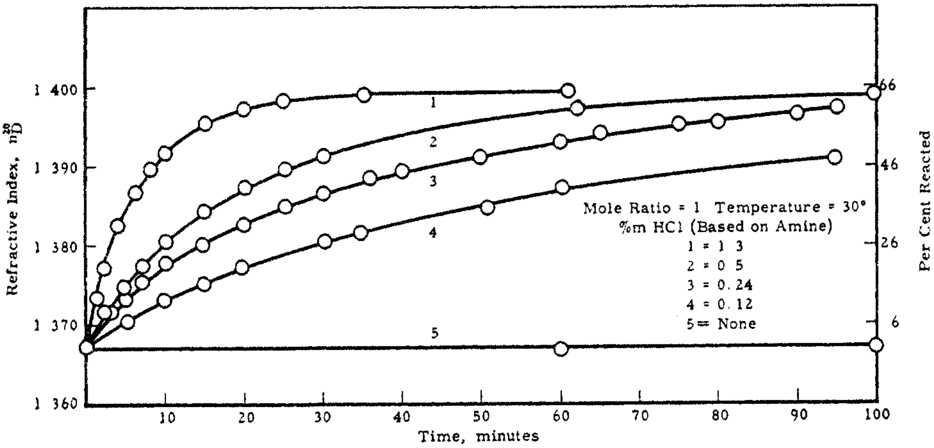


Figure 2. EFFECT OF CATALYST CONCENTRATION ON REACTION RATE OF ACETONE WITH ISOPROPYLAMINE

FIG. 2

librium had not been reached after 100 minutes with a 67% conversion. As expected, increasing the catalyst concentration from 0.12 to 1.3% m hydrochloric acid based on the amine increased the rate of reaction but did not appreciably change the equilibrium state (Figure 2).

The water formed in the reaction was removed by three separate means: (a) countercurrent extraction with 48% sodium hydroxide, (b) separation by dilution of the mixture with hydrocarbons, and (c) drying over solid sodium hydroxide. For laboratory preparation the last of these was preferred, but for larger scale preparations one of the other methods may be more economical.

Countercurrent extraction of the water from the equilibrium product with aqueous caustic was accomplished by passing the reaction product up through a column packed with glass beads countercurrent to a stream of 48% aqueous sodium hydroxide. A contact time of 40 seconds was sufficient to remove the water. A minimum concentration of the effluent caustic of 30% was found necessary to give efficient dehydration.

It was found that the water could also be separated by diluting the reaction product with an inert hydrocarbon such as the isodecanes. A ratio of four to five volumes of the hydrocarbon diluent was necessary to remove a major portion of the water. In this case, the water removal was not as complete, the conversion to recovered imine being 45% as compared to 53% for countercurrent extraction. To avoid further condensation during distillation of the ketimine, the acidic catalyst was neutralized by the addition of the appropriate amount of aqueous sodium hydroxide before extraction.

Drying of the product over solid, stick, sodium hydroxide suspended in the organic layer was found to be the simplest for laboratory preparations.

Ketimines from higher-boiling constituents. The imines from the higher-boiling and, in the present cases, water-insoluble ketones and amines were prepared by refluxing the components with an azeotroping agent (*e.g.*, benzene, toluene, xylene, or an excess of the ketone) to remove the water of reaction. Since a catalyst was generally not necessary with this procedure, the product was distilled without further treatment.

Hydrogenation of the ketimines has given the corresponding secondary amines in high yield. The recovery of minor amounts of the original primary amine and ketone, or corresponding alcohol, from hydrogenation of the ketimine product indicates possible incomplete hydrogenation or insufficient drying of the Raney nickel catalyst. The physical properties of the imines prepared are listed in Table II.

It has been found that the size of the alkyl groups on the ketone (R^1, R^2) have a greater effect on the conversion than the size of the alkyl groups (R^3, R^4) of the amine. For example, the reaction of acetone with 1-isobutyl-3-methylbutylamine gave the corresponding imine in 85% conversion, while the reaction of isopropylamine with diisobutyl ketone gave only a 10% conversion to its corresponding imine. This effect is thought to be due to the large alkyl groups (R^1, R^2) on the ketone which hinder the entrance of the amine nitrogen to the carbonyl carbon. On the other hand, although the alkyl groups (R^3, R^4) of the amine may be large, their separation from the point of attachment by the nitrogen atom would lessen their steric effect on the reaction. Consequently, in the preparation of mixed secondary amines with both a large and a small alkyl grouping *via* imines it is advisable to choose the reactants such that the smaller alkyl grouping is derived from the ketone.

EXPERIMENTAL

Preparation of the primary amines. The primary amines were prepared by hydrogenating an equimolar mixture of the ketone and anhydrous ammonia over Raney nickel at 120–150° and 500–1000 p.s.i.g. Distillation of the reaction product without other treatment was suf-

TABLE II

PREPARATION OF KETIMINES FROM PRIMARY AMINES AND ALIPHATIC KETONES

KETONE	AMINE	IMINE[a]	B.P., °C. (MM.)	n_D^{20}	d_4^{20}	CONVERSION TO PRODUCT, %	YIELD,[b] %
Acetone	*n*-Propylamine	N-Isopropylidenepropylamine[d]	107.2	1.4170	0.7652	67	84
Acetone	Allylamine	N-Isopropylideneallylamine[d]	113–114	1.4638	.7946	70	70
Acetone	Isopropylamine	N-Isopropylideneisopropylamine[d]	93.5	1.4088	.7477	45–53	90–95
Acetone	*sec*-Butylamine	N-Isopropylidene-*sec*-butylamine[d]	115.9	1.4168	.7618	76	97
Acetone	Isobutylamine	N-Isopropylideneisobutylamine[d]	122.0	1.4255	.7772	63	85
Acetone	Methallylamine	N-Isopropylidenemethallylamine[d]	137.5	—	—	63	85
Acetone	Cyclohexylamine	N-Isopropylidenecyclohexylamine[d]	180.6	—	—	73	95
Acetone	1,3-Dimethylbutylamine	N-Isopropylidene-1,3-dimethylbutylamine[c]	150.5	1.4239	.7724	87	95
Acetone	1-Isobutyl-3-methylbutylamine	N-Isopropylidene-1-isobutyl-3-methylbutylamine[d]	127.7 (100)	1.4332	.7868	85	95
Methyl ethyl ketone	*n*-Propylamine	N-*sec*-Butylidenepropylamine[d]	129.2	1.4230	.7743	77	96
Methyl ethyl ketone	Allylamine	N-*sec*-Butylideneallylamine[d]	134.5	—	—	60	86
Methyl ethyl ketone	Isopropylamine	N-*sec*-Butylideneisopropylamine[d]	113.5	1.4146	.7588	68	93
Methyl ethyl ketone	*sec*-Butylamine	N-*sec*-Butylidene-*sec*-butylamine[d]	134.5	1.4202	.7691	42	86
Methyl ethyl ketone	Isobutylamine	N-*sec*-Butylideneisobutylamine[d]	142.0	1.4222	.7723	88	97
Methyl ethyl ketone	Methallylamine	N-*sec*-Butylidenemethallylamine[d]	152.5	—	—	70	95
Methyl ethyl ketone	1,3-Dimethylbutylamine	N-*sec*-Butylidene-1,3-dimethylbutylamine[c]	168.4	1.4267	.7780	80	96
Methyl ethyl ketone	3,3,5-Trimethylcyclohexylamine	N-*sec*-Butylidene-3,3,5-trimethylcyclohexylamine[d]	152.8 (100)	1.4591	.8460	61	99
Methyl ethyl ketone	1-Isobutyl-3-methylbutylamine	N-*sec*-Butylidene-1-isobutyl-3-methylbutylamine[d]	139.8 (100)	1.4344	.7899	76	98
Methyl isobutyl ketone	*n*-Propylamine	N-(1,3-Dimethylbutylidene)propylamine[d]	163.3	1.4282	.7796	82	88
Methyl isobutyl ketone	Allylamine	N-(1,3-Dimethylbutylidene)allylamine[d]	108–112 (140)	—	—	57	99
Methyl isobutyl ketone	Isopropylamine	N-(1,3-Dimethylbutylidene)isopropylamine[d]	148.3	1.4209	.7672	69	93

Methyl isobutyl ketone	*sec*-Butylamine	N - (1,3 - Dimethylbutylidene)*sec* - butylamine^{d}	169.1	1.4272	.7775	66	96
Methyl isobutyl ketone	Isobutylamine	N - (1,3 - Dimethylbutylidene)isobutylamine^{d}	174.8	1.4274	.7788	83	96
Methyl isobutyl ketone	Methallylamine	N - (1,3 - Dimethylbutylidene)methallylamine^{d}	115.6 (100)	—	—	90	95
Methyl isobutyl ketone	1,3 - Dimethylbutylamine	N - (1,3 - Dimethylbutylidene) - 1,3 - dimethylbutylamine^{c}	128.8 (100)	1.4313	.7848	77	85
Methyl isobutyl ketone	3,3,5 - Trimethylcyclohexylamine	N - (1,3 - Dimethylbutylidene) - 3,3,5 - trimethylcyclohexylamine^{c}	152.8 (50)	1.4592	.8414	85	92
Methyl isobutyl ketone	1 - Isobutyl - 3 - methylbutylamine	N - (1,3 - Dimethylbutylidene) - 1 - isobutyl-3-methylbutylamine^{d}	142.9 (50)	1.4332	.7946	70	99
Dihydroisophorone	*n*-Propylamine	N - Propyl - 3,3,5 - trimethylcyclohexanimine^{d}	148.5 (100)	1.4626	.8497	80	96
Dihydroisophorone	Isopropylamine	N - Isopropyl - 3,3,5 - trimethylcyclohexanimine^{d}	136.5 (100)	1.4584	.8438	71	94
Dihydroisophorone	*sec*-Butylamine	N - *sec* - Butyl - 3,3,5 - trimethylcyclohexanimine^{d}	152 (100)	1.4591	.8402	79	88
Dihydroisophorone	Isobutylamine	N - Isobutyl - 3,3,5 - trimethylcyclohexanimine^{d}	98.5 (10)	—	—	82	92
Dihydroisophorone	1,3 - Dimethylbutylamine	N - (1,3 - Dimethylbutyl) - 3,3,5 - trimethylcyclohexanimine^{d}	150.5 (50)	1.4595	.8382	84	90
Dihydroisophorone	3,3,5 - Trimethylcyclohexylamine	N - (3,3,5 - Trimethylcyclohexyl) - 3,3,5-trimethylcyclohexanimine^{c}	133 (6)	1.4775	.8791	80	>95
Dihydroisophorone	1 - Isobutyl - 3 - methylbutylamine	N - (1 - isobutyl - 3 - methylbutyl) - 3,3,5-trimethylcyclohexanimine^{d}	152.9 (20)	1.4598	.8387	73	98
Isophorone	Methallylamine	N - Methallyl - 3,5,5 - trimethyl - 2 - cyclohexenimine^{d}	121 (5)	—	—	8	11
Isophorone	1,3 - Dimethylbutylamine	N - (1,3 - Dimethylbutyl) - 3,5,5 - trimethyl-2-cyclohexenimine^{c}	118 (10)	1.4801	.8535	88	90
Isophorone	3,3,5 - Trimethylcyclohexylamine	N - (3,3,5 - Trimethylcyclohexyl) - 3,5,5-trimethyl-2-cyclohexenimine^{c}	120 (2)	—	—	84	88
Diisobutyl ketone	*n*-Propylamine	N - (1 - isobutyl - 3 - methylbutylidene)propylamine^{d}	133–135 (100)	—	—	30	81

Table II—*Continued*

KETONE	AMINE	IMINE[a]	B.P., °C. (MM.)	n_D^{20}	d_4^{20}	CONVERSION TO PRODUCT, %	YIELD,[b] %
Diisobutyl ketone	Isopropylamine	N-(1-isobutyl-3-methylbutylidene)isopropylamine[d]	125–127 (100)	—	—	10	62
Diisobutyl ketone	*sec*-Butylamine	N-(1-Isobutyl-3-methylbutylidene)-*sec*-butylamine[d]	145 (100)	1.4317	.7929	11	75
Diisobutyl ketone	1,3-Dimethylbutylamine	N-(1-Isobutyl-3-methylbutylidene)-1,3-dimethylbutylamine[c]	145.2 (50)	1.4341	.7961	17	97
Diisobutyl ketone	1-Isobutyl-3-methylbutylamine	N-(1-Isobutyl-3-methylbutylidene)-1-isobutyl-3-methylbutylamine[d]	122–128 (10)	—	—	52	99
Mesityl oxide	1,3-Dimethylbutylamine	N-(1,3-Dimethyl-2-butenylidene)-1,3-dimethylbutylamine[c]	113.7	1.4520	.8076	14	—

[a] The dried imines were all distilled through a 30-plate Oldershaw column at a 20:1 reflux ratio. The major portion of each of the products distilled on a plateau and there was very little residue in most cases. Although analyses of all the ketimines were not obtained, analysis of representative compounds indicated high purity. (Table III) [b]Based on recovery of primary amine. [c]Analysis of these ketimines is given in Table III. [d]Not analyzed, but analysis of secondary amine isolated in high yield is given in Table V.

ficient to isolate isopropylamine and *sec*-butylamine. The other amines thus produced were isolated and purified in the following manner. The reaction product was acidified with dilute sulfuric acid and the acid-insoluble material, largely alcohol derived from the ketone, was separated by steam-distillation. The amine was liberated from its salt by the addition of an excess of sodium hydroxide. After separation of the aqueous phase, the amine was dried and fractionated. The following example will serve to describe the process.

Isopropylamine. A mixture of 696 g. (12 moles) of acetone and 204 g. (12 moles) of ammonia was hydrogenated in a stirred autoclave over 50 g. of Raney nickel at 140° and 740 p.s.i.g. Upon distillation, 545 g., 77% yield of isopropylamine, b.p. 31.5–32.5°, n_D^{15} 1.377, d_4^{15} 0.694, was obtained.

Anal. Calc'd for C_3H_9N: C, 60.95; H, 15.34; Neut. equiv., 59.1.

Found: C, 60.68, 60.53; H, 15.25, 15.19; Neut. equiv., 60.3, 60.8.

Preparation of the ketimines. Generally the imines from the lower-boiling, water-soluble amines and ketones were prepared by adding 3 g. of concentrated hydrochloric acid to a mixture of 5 moles of each component. After the reaction mixture had stood at room temperature for 24 hours, sodium hydroxide sticks were suspended from wires in the organic phase to neutralize the catalyst and to separate the water formed. The product was distilled directly after removal of the aqueous layer.

The imines from the higher-boiling, water-insoluble amines and ketones were made by refluxing the components with an azeotroping agent such as benzene, toluene, or an excess of the ketone to remove the water of reaction. The product was distilled directly. The following examples serve to illustrate the processes.

N-Isopropylideneisopropylamine. Conc'd hydrochloric acid (3 g.) was added to a mixture of 5 moles (290 g.) of acetone and 5 moles (295 g.) of isopropylamine. The temperature rose to 50° over a period of five minutes and then slowly subsided. The mixture was set aside overnight. Several pieces of stick sodium hydroxide were added and the mixture was occasionally shaken. When the water removal was complete, the product was distilled and gave 125 g. of isopropylamine, 128 g. of acetone, and 262 g. of N-isopropylideneisopropylamine b.p. 93.5°, n_D^{20} 1.4088, d_4^{20} 0.7477. For analysis see Table III.

TABLE III

ANALYSES OF KETIMINES

IMINE	C		H		N	
	Theory	Found	Theory	Found	Theory	Found
N-Isopropylideneisopropylamine	72.62	72.33	13.21	13.20	14.2	13.6
N-Isopropylidene-1,3-dimethylbutylamine	76.52	76.39	13.56	15.58	9.92	9.81
N-*sec*-Butylidene-1,3-dimethylbutylamine	77.35	77.05	13.63	13.53	9.02	8.78
N-(1,3-Dimethylbutylidene)-1,3-dimethylbutylamine	78.61	78.12	13.75	13.65	7.64	7.52
N-(1,3-Dimethyl-2-butenylidene)-1,3-dimethylbutylamine	79.49	78.82	12.78	12.75	7.73	7.53
N-(1-Isobutyl-3-methylbutylidene)-1,3-dimethylbutylamine	79.92	79.92	13.86	13.88	6.22	6.25
N-(1,3-Dimethylbutyl)-3,5,5-trimethyl-2-cyclohexenimine	81.38	81.30	12.29	12.26	6.33	6.32
N-(1,3-Dimethylbutylidene)-3,3,5-trimethylcyclohexylamine	80.64	80.54	13.08	13.05	6.27	6.27
N-(3,3,5-Trimethylcyclohexyl)-3,5,5-trimethyl-2-cyclohexenimine	82.69	82.09	11.95	11.95	5.36	5.41
N-(3,3,5-Trimethylcyclohexyl)-3,3,5-trimethylcyclohexanimine	82.06	81.99	12.62	12.62	5.32	5.24

TABLE IV

Hydrogenation of Aliphatic Ketimines to Secondary Amines over Raney Nickel

IMINE	AMINE PRODUCT	B.P., °C. (MM.)	n_D^{20}	d_4^{20}	CONVERSION TO PRODUCT, %	YIELD,[a] %	pK$_b$
N-Isopropylideneisopropylamine	Diisopropylamine	83.9	1.3918	0.7163	89	98	2.93
N-Isopropylideneallylamine	N-Isopropylpropylamine	98.3	1.3988	.7278	75	75	3.04
N-Isopropylidenemethallylamine	N-Isopropylisobutylamine	113.8	1.4018	.7322	73	73	3.45
N-Isopropylidene-*sec*-butylamine	N-Isopropyl-*sec*-butylamine	110.6	1.4027	.7359	92	92	3.00
N-*sec*-Butylideneisopropylamine	N-Isopropyl-*sec*-butylamine	110.6	1.4027	.7359	92	97	—
N-*sec*-Butylidenepropylamine	N-Propyl-*sec*-butylamine	123.6	1.4093	.7466	88	92	—
N-*sec*-Butylideneallylamine	N-Propyl-*sec*-butylamine	123.6	1.4093	.7466	75	75	—
N-*sec*-Butylidenemethallylamine	N-Isobutyl-*sec*-butylamine	138.1	1.4100	.7486	88	94	3.23
N-*sec*-Butylidene-*sec*-butylamine	Di-*sec*-butylamine	135.8	1.4110	.7525	81	93	3.06
N-Isopropylidene-1,3-dimethylbutylamine	N-Isopropyl-1,3-dimethylbutylamine	148.0	1.4210	.7511	95	97	2.96
N-(1,3-Dimethylbutylidene)isopropylamine	N-Isopropyl-1,3-dimethylbutylamine	148.0	1.4210	.7511	87	95	—
N-(1,3-Dimethylbutylidene)allylamine	N-Propyl-1,3-dimethylbutylamine	161.1	1.4180	.7597	81	95	3.02
N-(1,3-Dimethylbutylidene)methallylamine	N-Isobutyl-1,3-dimethylbutylamine	172.8	1.4180	.7605	94	95	3.17
N-*sec*-Butylidene-1,3-dimethylbutylamine	N-*sec*-Butyl-1,3-dimethylbutylamine	170.1	1.4186	.7638	95	98	2.98
N-(1,3-Dimethylbutylidene)-1,3-dimethylbutylamine	Bis-(1,3-dimethylbutyl)amine	199.8	1.4242	.7718	88	92	—
N-Isopropyl-3,3,5-trimethylcyclohexanimine	N-Isopropyl-3,3,5-trimethylcyclohexylamine	134.6 (100)	1.4471	.8268	78	81	—
N-Isobutyl-3,3,5-trimethylcyclohexanimine	N-Isobutyl-3,3,5-trimethylcyclohexylamine	152.1 (100)	1.4501	.8297	83	84	—
N-*sec*-Butylidene-3,3,5-trimethylcyclohexylamine	N-*sec*-Butyl-3,3,5-trimethylcyclohexylamine	150.7 (100)	1.4489	.8312	82	85	—
N-(1,3-Dimethylbutyl)-3,5,5-trimethyl-2-cyclohexenimine	N-(1,3-Dimethylbutyl)-3,3,5-trimethylcyclohexylamine	126.8–127 (20)	1.4519	.8317	88	95	—
N-(3,3,5-Trimethylcyclohexyl)-3,5,5-trimethyl-2-cyclohexenimine	Bis(3,3,5-trimethylcyclohexyl)amine	131.6 (5)	1.4718	.8742	80	88	—

N - Isopropylidene - 1 - isobutyl - 3 - methylbutylamine	N - Isopropyl - 1 - isobutyl - 3 - methylbutylamine	126.0 (100)	1.4231	.7693	75	94	—
N - (1 - Isobutyl - 3 - methylbutylidene)isopropylamine	N - Isopropyl - 1 - isobutyl - 3 - methylbutylamine	126.0 (100)	1.4231	.7693	95	95	—
N - (1 - Isobutyl - 3 - methylbutylidene)propylamine	N - Propyl - 1 - isobutyl - 3 - methylbutylamine	136.5 (100)	1.4271	.7766	79	93	—
N - *sec* - Butylidene - 1 - isobutyl - 3-methylbutylamine	N - *sec* - Butyl - 1 - isobutyl - 3 - methylbutylamine	141.2 (100)	1.4282	.7990	87	95	—
N - (1 - Isobutyl - 3 - methylbutylidene)-*sec*-butylamine	N - *sec* - Butyl - 1 - isobutyl - 3 - methylbutylamine	141.2 (100)	1.4282	.7990	98	98	—
N - (1,3 - Dimethylbutylidene) - 1 - isobutyl-3-methylbutylamine	N - (1,3 - Dimethylbutyl) - 1 - isobutyl-3-methylbutylamine	142.6 (50)	1.4311	.7830	89	97	—
N - (1 - Isobutyl - 3 - methylbutylidene)-1,3-dimethylbutylamine	N - (1,3 - Dimethylbutyl) - 1 - isobutyl-3-methylbutylamine	142.6 (50)	1.4311	.7830	94	94	—
N - (1 - Isobutyl - 3 - methylbutyl) - 3,3,5-trimethylcyclohexanimine	N - (3,3,5 - Trimethylcyclohexyl) - 1-isobutyl-3-methylbutylamine	154.1 (20)	1.4537	.8323	90	94	—
N - (1 - isobutyl - 3 - methylbutylidene)-1-isobutyl-3-methylbutylamine	Bis - (1 - isobutyl - 3 - methylbutyl)amine	143.6 (20)	1.4358	.7917	88	88	—
N-Isopropylidenecyclohexylamine	N-Isopropylcyclohexylamine	174.8	1.4460	.8353	79	86	—
N-Cyclopentylcyclopentanimine	Dicyclopentylamine	123.1 (50)	1.4781	.9087	95	95	—

[a] Based on recovery of primary amine.

TABLE V

HYDROGENATION OF ALIPHATIC KETIMINES TO SECONDARY AMINES OVER RANEY NICKEL

AMINE	C		H		N		NEUT. EQUIV.	
	Found	Theory	Found	Theory	Found	Theory	Found	Theory
Diisopropylamine	71.17	71.21	14.96	14.95	13.62	13.84	101.4	101.2
N-Isopropylpropylamine	71.02	71.21	14.89	14.95	13.83	13.84	101.3	101.2
N-Isopropylisobutylamine	73.12	72.96	14.85	14.88	12.12	12.16	115.7	115.2
N-Isopropyl-*sec*-butylamine	72.72	72.96	14.72	14.88	12.12	12.16	115.8	115.2
N-Propyl-*sec*-butylamine	72.87	72.96	14.67	14.88	12.12	12.16	115.6	115.2
N-Isobutyl-*sec*-butylamine	74.31	74.35	14.67	14.66	10.80	10.65	130.7	129.2
Di-*sec*-butylamine	—	—	—	—	—	—	130.7	129.2
N-Isopropyl-1,3-dimethylbutylamine	75.27	75.44	14.72	14.78	9.72	9.78	143.8	143.3
N-Propyl-1,3-dimethylbutylamine	75.39	75.44	14.76	14.78	9.77	9.78	144.1	143.3
N-Isobutyl-1,3-dimethylbutylamine	76.43	76.36	14.74	14.74	8.89	8.91	157.8	157.3
N-*sec*-Butyl-1,3-dimethylbutylamine	76.22	76.36	14.74	14.74	8.91	8.91	157.8	157.3
Bis(1,3-dimethylbutyl)amine	77.73	77.75	14.72	14.68	7.34	7.55	186.0	185.4
N-Isopropyl-3,3,5-trimethylcyclohexylamine	78.59	78.69	13.70	13.75	7.56	7.64	182.5	183.3
N-Isobutyl-3,3,5-trimethylcyclohexylamine	79.32	79.11	13.75	13.79	7.04	7.10	197.2	197.4
N-*sec*-Butyl-3,3,5-trimethylcyclohexylamine	79.17	79.11	13.74	13.79	7.14	7.10	196.8	197.4
N-(1,3-Dimethylbutyl)-3,3,5-trimethylcyclohexylamine	—	—	—	—	—	—	225.5	225.4
Bis(3,3,5-trimethylcyclohexyl)amine	—	—	—	—	—	—	265.5	265.5
N-Isopropyl-1-isobutyl-3-methylbutylamine	77.62	77.75	14.53	14.68	7.52	7.55	—	—
N-Propyl-1-isobutyl-3-methylbutylamine	77.74	77.75	14.64	14.68	7.54	7.55	—	—
N-*sec*-Butyl-1-isobutyl-3-methylbutylamine	78.42	78.31	14.64	14.66	7.02	7.03	—	—
N-(1,3-Dimethylbutyl)-1-isobutyl-3-methylbutylamine	79.37	79.21	14.59	14.62	6.17	6.16	228.6	227.4
N-(3,3,5-Trimethylcyclohexyl)-1-isobutyl-3-methylbutylamine	80.61	80.82	13.75	13.94	5.17	5.24	272.1	267.5
Bis(1-isobutyl-3-methylbutyl)amine	80.14	80.22	14.49	14.59	5.31	5.20	—	—
N-Isopropylcyclohexylamine	76.18	76.52	13.40	13.56	9.94	9.92	—	—

The above corresponds to a 53% conversion to product in a 95% yield.

N-(1,3-Dimethylbutylidene)-1,3-dimethylbutylamine. A mixture of 1000 g. (10 moles) of methyl isobutyl ketone, 1010 g. (10 moles) of 1,3-dimethylbutylamine, and 100 ml. of benzene was refluxed through a column with a phase-separating head. During about 24 hours 150 g. of water had separated. Upon distillation after removal of the benzene, 197 g. of 1,3-dimethylbutylamine, 190 g. of methyl isobutyl ketone, and 1412 g. of N-(1,3-dimethylbutylidene)-1,3-dimethylbutylamine, b.p. 74–76° (10 mm.), n_D^{20} 1.4313, d_4^{20} 0.7848 were obtained. This corresponds to a 77% conversion to product in a 96% yield. For analysis see Table III.

Hydrogenation of the ketimines. The imines were hydrogenated over Raney nickel at 100–150° and 200–1000 p.s.i.g. Copper chromite catalyst at 170–200° and 1000 p.s.i.g. was used in a few instances, but it showed no advantage over the Raney nickel catalyst. N-Isopropylideneisopropylamine has also been hydrogenated in vapor phase in 91% yield over a copper on activated alumina catalyst. The physical properties and analyses of the secondary amines prepared here are recorded in Tables IV and V. The following example will serve to demonstrate the reaction.

Diisopropylamine. A 970-g. sample of N-isopropylideneisopropylamine was hydrogenated over about 50 g. of Raney nickel at 100° and 200 p.s.i.g. After separation from the catalyst the product was acidified with dilute sulfuric acid and the acid-insoluble material was separated by steam-distillation. Approximately 60 g. of a mixture of isopropyl alcohol and acetone was recovered from the steam-distillation. The amines were liberated from the acid solution with sodium hydroxide, separated, and dried over solid NaOH. Distillation gave 58 g. of isopropylamine and 880 g. of diisopropylamine boiling at 82–84°, n_D^{20} 1.3918, d_4^{20} 0.7063. The above corresponds to an 89% conversion to product in better than 95% yield based on recovery of isopropylamine. For analysis see Table V.

SUMMARY

A study has been made of the reaction of aliphatic ketones with ammonia and amines. Primary amines have been prepared in excellent yield by the hydrogenation of ketones in the presence of anhydrous ammonia, without the use of an inert solvent or excess ammonia.

A number of novel aliphatic ketimines have been prepared and isolated in high yield by the reaction of ketones with primary amines in the presence of an acidic catalyst.

These ketimines can be hydrogenated to the corresponding secondary amines which provides a convenient means for preparing secondary amines with different alkyl groups in the same molecule.

A study of the reaction variables in the above reactions has led to both a better understanding of the reaction conditions and to increased yields.

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