dropwise at 45° with an aqueous solution of 1.0 g. of potassium bromide and 0.28 g. of potassium bromate. After the addition, the mixture was warmed for 30 min. on a water bath. The oil which separated solidified on cooling. The product was purified by extraction into methanol twice in the Soxhlet apparatus. It had an infrared spectrum identical with that of the authentic 4,4′,4″-tribromotriphenylamine, and the melting point of the mixture was not depressed. When this bromodesulfonation reaction was carried out at 60°, a substantial part of the product was the hexabromo compound already described.

Nitrogen Analogs of Ketenes. VII.[1] Reactions with Amines

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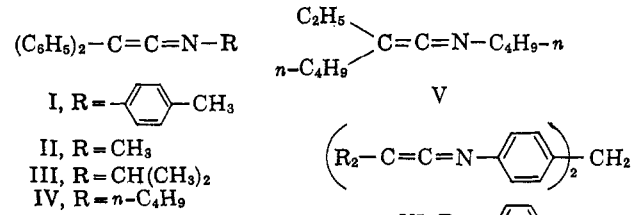
Amidines have been prepared in good yield by treating ammonia, primary and secondary aliphatic amines, and aromatic amines with ketenimines I–VII. Although aromatic amines are less reactive than aliphatic amines, good yields were obtained at elevated temperatures. Ketenimines IV and V were less reactive than other ketenimines, but yields of 84–94% were obtained by employing elevated reaction temperatures and alkali metal catalysts. Structures of amidines are assigned on the basis of both n.m.r. data and on chemical evidence provided by acid hydrolysis of the amidines. Yield data and experimental conditions provide data for discussing the relative reactivities of the amines and ketenimines.

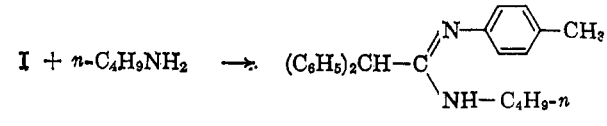
Over the past several years, this laboratory has developed three general and convenient methods for the synthesis of ketenimines.[2] This paper reports a study of the reaction of ketenimines I–VII with amines and the development of a new method for the preparation of amidines.

Amidines, in general, have been prepared most frequently by the reaction of amides, thio amides, imido esters, and nitriles with amines.[3] Amidines have also been prepared by the rearrangement of arylaldehyde hydrazones,[4] and by the reaction of amines with ortho esters,[5] amide acetals,[6] enamines,[7] and ethoxyacetylene.[8] Dijkstra and Backer have studied the reaction of amines with bis-substituted sulfonyl N-methylimines to form amidines.[9]

The scope of our new synthesis includes the reaction of ammonia, primary and secondary aliphatic amines, and aromatic amines with various ketenimines (I–VII) to give amidines in good yields (see Tables I–III). The reactivity of aromatic amines was considerably less than aliphatic amines, but the addition of the aromatic amines to the ketenimines could be successfully carried out at elevated temperatures. In general, amines added smoothly to the ketenimines under mild reaction conditions. The reactivity of ketenimines IV and V toward amines was less than the other ketenimines. However, amidines were isolated in yields of 84–94% from IV and V by using alkali metal catalysts and elevated reaction temperatures.

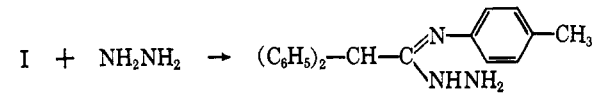


To study the scope of useful amines, ammonia, primary and secondary aliphatic amines, and aromatic amines were added to diphenylketene N-*p*-tolylimine (I) to give amidines in yields ranging from 62 to 97% (see Table I). For example, when *n*-butylamine was added to I, an exothermic reaction occurred and within 3 hr. the amidine, N-*n*-butyl-N′-(*p*-tolyl)diphenylacetamidine (VIII), was obtained in 78% yield after one recrystallization.



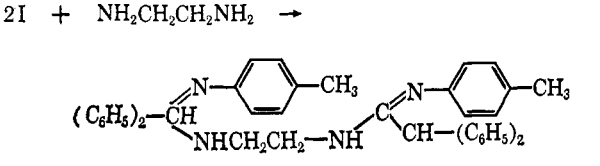
VIII

Amidrazones were isolated from the reaction of I with hydrazines. A 1:1 molar ratio of hydrazine and I gave the stable N³-(*p*-tolyl)diphenylacetamidrazone (IX), in 97% yield.



IX

Bisamidines were prepared both by the reaction of ethylenediamine with I (eq. 1) and amines with the diketenimines VI and VII. Attempts to isolate an



(1)

X

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TABLE I

PROPERTIES OF AMIDINES PREPARED FROM I

Amidine	M.p., °C.	Yield, %	Recrystn. solvent	Calcd., % C	Calcd., % H	Found, % C	Found, % H
N′-*p*-Tolyldiphenylacetamidine	171–172	76	Acetone	83.96	6.71	84.26	6.81
N-Methyl-	102–103	69	Petr. ether	84.04	7.05	84.05	7.00
N,N-Dimethyl-	120–121	93	2-Propanol	84.10	7.37	84.17	7.35
N-Ethyl-[a]	85	97	Hexane	84.10	7.37	83.82	7.43
N,N-Diethyl-	93–94	95	Ethanol	84.22	7.92	84.51	8.21
N-Isopropyl-[b]	122.5–123.5	73	Hexane	84.16	7.65	84.11	7.88
N-*t*-Butyl-	112–113	62	Petr. ether	84.22	7.92	84.37	7.74
N-*n*-Butyl-	62–63	78	Ethanol	84.22	7.92	83.86	7.61
N,N-Pentamethylene-	119–120	74	Petr. ether	84.74	7.66	84.58	7.50
N,N-(β,β-Diethyl ether)-	128.5–129.5	76	Ethanol	81.04	7.08	81.29	7.00
N-(3-Dimethylaminopropyl)-	68.5–69	93	Petr. ether	81.00	8.11	81.22	8.02
N-Phenyl-	117–118	67	Ethanol	86.13	6.43	86.02	6.72
N-(*p*-Tolyl)-	123–124	94	Ethanol	86.12	6.71	86.44	6.38
N-(*p*-Carboethoxyphenyl)-	125–126	77	Ethanol	80.33	6.29	80.02	6.32
N′,N″-Ethylenebis-	178.5–179.5	80	Acetone	84.31	6.75	83.98	6.92

[a] *Anal.* Calcd.: N, 8.53. Found: N, 8.39. [b] The same amidine was obtained from the reaction of III with *p*-toluidine in 38% yield.

TABLE II

PROPERTIES OF AMIDINES PREPARED FROM II–VII

Amidine	M.p. or b.p., (mm.), °C.	Yield, %	Recrystn. solvent	Calcd., % C	Calcd., % H	Calcd., % N	Found, % C	Found, % H	Found, % N
N-Isopropyl-N′-(methyl)-diphenylacetamidine	85–86	[a]	Hexane	81.16	8.33		81.29	8.26	
N,N-Diethyl-N′-(methyl)-diphenylacetamidine	124 (0.02)	70		81.38	8.63		81.64	8.35	
N,N′-Diisopropyldiphenylacetamidine	68–69	72	Petr. ether	81.58	8.90		81.41	9.05	
N,N′-Di-*n*-butyldiphenylacetamidine	146 (0.02)	84		81.94	9.38		81.92	9.15	
N-(*p*-Tolyl)-N′-(*n*-butyl)-α-ethylcaproamidine	131–132 (0.1)	92		79.10	11.18		78.88	10.97	
N,N-Diethyl-N′-(*n*-butyl)-α-ethylcaproamidine	76 (0.3)	91		75.52	13.47		75.60	13.44	
N,N′-Di-*n*-butyl-α-ethylcaproamidine	91–92 (0.4)	85		75.52	13.47		75.47	13.31	
4,4′-Methylenebis[N′-(diphenylacetamidine)-aniline]	129–130	59	Benzene	84.21	6.20	9.57	84.21	6.45	9.43
4,4′-Methylenebis[N-(ethyl)-N′-(diphenylacetamidine)-aniline]	166.5–168	85	Ethanol	84.34	6.92	8.73	84.33	7.11	8.66
4,4′-Methylenebis[N-(ethyl)-N′-(di-*p*-chlorophenylacetamidine)aniline]	80–82	85	Ethanol	69.41[b]	5.17	7.19	69.60	5.43	7.16

[a] 75% from reaction of II with isopropyl amine; 58% from reaction of III with methyl amine. [b] *Anal.* Calcd.: Cl, 18.21. Found: Cl, 18.41.

TABLE III

PROPERTIES OF AMIDRAZONES

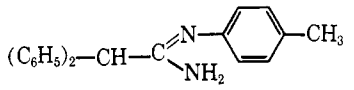
Diphenylacetamidrazones	M.p., °C.	Yield, %	Recrystn. solvent	Calcd., % C	Calcd., % H	Found % C	Found % H
N^1-Phenyl-N^3-(*p*-tolyl)-	95–97	75	Petr. ether	82.62	6.68	82.49	6.60
N^3-(*p*-Tolyl)-	97.5–98	97	Hexane	79.97	6.71	79.96	6.79

amidine from a 1:1 molar ratio of I to ethylenediamine were unsuccessful.

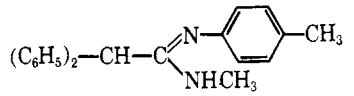
Chemical evidence for the gross structure of the amidines prepared in this work was obtained by degradation of amidine adduct, N,N′-di-(*p*-tolyl)diphenylacetamidine. This amidine was hydrolyzed to diphenylacetic acid and *p*-toluidine with aqueous sulfuric acid. Diphenylacetic acid was isolated in 96% yield and *p*-toluidine in 64% yield (as *p*-tolylacetamide). From a phosphoric acid hydrolysis of the amidine, N-(*p*-tolyl)diphenylacetamide was isolated along with diphenylacetic acid and *p*-toluidine.

An n.m.r. analysis of N-*p*-tolyldiphenylacetamidine (XI) and N-methyl-N′-*p*-tolyldiphenylacetamidine (XII) confirmed the amidine structure as shown and ruled out a possible enamine-type structure.

The benzhydryl protons appeared as sharp singlets in both spectra showing at τ 4.40 in the case of XI and at τ 4.70 in the case of XII. The aromatic C-methyl protons were singlets at τ 7.67 and 7.81 for



XI



XII

XI and XII, respectively. The N-methyl protons of XII appeared at τ 7.17 as a much broadened singlet which suggested coupling with an adjacent hydrogen atom or a single bond restricted rotation phenomenon similar to that found in amides. The N-proton appeared as a broadened singlet at τ 5.81. With the aromatic protons of the N-*p*-tolyl group sharply defined, the n.m.r. indicated that the amidine XII was best represented by the structure shown. Integration of peak areas was consistent with the amidine formulation.

By examination of experimental conditions and yields obtained in the amidine preparations, one can ascertain the relative reactivities of both amines and ketenimines. In general, secondary amines required shorter reaction times with I than primary amines to give comparable yields of amidines. The reaction of *t*-butylamine with I required a longer reaction time (17 hr. at room temperature plus an additional 3 hr. at reflux) and gave a lower yield of amidine (62%) than all other reactions of aliphatic amines with I studied. Addition of aromatic amines to I occurred readily only at elevated temperatures. The reaction of I and *p*-toluidine did occur slowly at room temperature, but ethyl *p*-aminobenzoate and aniline failed to react with I under similar conditions. Thus, the more basic the amine is, the faster the reaction with a particular ketenimine occurs. However, steric hindrance can be a retarding rate factor as evidenced by the slow reaction of I with *t*-butylamine.

Interesting differences in the reactivities of the various ketenimines were observed. The addition of isopropylamine to diphenylketene N-methylimine (II) gave an exothermic reaction and, after standing 34 hr., resulted in a 75% yield of amidine. However, the reaction of methylamine and diphenylketene N-isopropylimine (III) to give the same amidine occurred in only 56% yield after 3 days at room temperature. The reactivities of diphenylketene N-*n*-butylimine (IV) and ethylbutylketene N-*n*-butylimine were still less toward amines and required alkali metal catalyts and elevated temperatures before good yields of amidines were obtained. It appears that the electron-withdrawing effect of the N-aromatic substituent increased the likelihood of attack by amine at the imine carbon in comparison to N-alkyl-substituted ketenimines. Perhaps a combination of steric and inductive effects of the alkyl groups of N-alkyl-substituted ketenimines results in a concomitant decrease in the rates of reaction toward amines.

It is apparent that one must consider both the nature of the amine and ketenimine before predicting the ease of amidine formation. The amidine, once formed, is quite stable as indicated by the vigorous conditions required for hydrolysis by sulfuric and phosphoric acids.[10]

Experimental Section

Preparation of Ketenimines.—Ketenimines I, II, and IV–VI have been previously prepared.[2] Ketenimine III was prepared according to the procedure of Stevens and French[2a] from the corresponding α-chloroimino chloride in 54% yield, m.p. 45–46°.

Anal. Calcd. for $C_{17}H_{17}N$: C, 86.80; H, 7.29. Found: C, 86.77; H, 7.36.

Ketenimine VII could be prepared in 23% yield by dehydrochlorination of the imino chloride or better by a new procedure which involved shaking the α-chloroimino chloride with excess lithium amalgam in ether for 36 hr. This latter procedure gave III, m.p. 109–110°, in 61% yield.

Anal. Calcd. for $C_{41}H_{26}Cl_4N_2$: C, 71.52; H, 3.80; Cl, 20.59; N, 4.08. Found: C, 71.74; H, 3.88; Cl, 20.78; N, 4.22.

Preparation of Amidines and Amidrazones.—The preparation of N,N-diethyl-N′-(*p*-tolyl)diphenylacetamidine represents a general procedure for the preparation of amidines and amidrazones. Disappearance of the characteristic yellow color of ketenimine was used to follow the course of the reaction. Modifications, where used, are noted.

N,N-Diethyl-N′-(*p*-tolyl)diphenylacetamidine.—An ethereal solution (3 ml.) of 500 mg. (1.77 mmoles) of diphenylketene *p*-tolylimine (I) and 130 mg. (1.77 mmoles) of diethylamine was allowed to stand at room temperature for 8.25 hr. The ether was then removed *in vacuo* and the residual oil was crystallized from petroleum ether (b.p. 30–60°). There was obtained 600 mg. (95.2%) of the amidine, m.p. 91–92°. The analytical sample melted at 93–94° after one recrystallization from ethanol.

Anal. Calcd. for $C_{25}H_{28}N_2$: C, 84.22; H, 7.92. Found: C, 84.51; H, 8.21.

All reactions of ketenimines with aromatic amines required heating at reflux temperatures in anhydrous toluene or xylene. The reaction of I with ammonium hydroxide was carried out in acetone solvent. Reaction of ketenimine V with amines required lithium or sodium metal catalysts and reflux temperatures in toluene and xylene. The reaction of I with phenylhydrazine required a short reflux period in dry benzene solvent.

Acid Hydrolysis of N,N′-Di-*p*-tolyldiphenylacetamidine. Method A.—A mixture of 0.5 g. (1.28 mmoles) of N,N′-di-*p*-tolyldiphenylacetamidine, 10 ml. of concentrated sulfuric acid, and 12 ml. of water was refluxed 60 hr. and then allowed to cool to room temperature. About 20 ml. of water was added and the aqueous solution was extracted three times with 75-ml. portions of ethyl ether. The ethereal extract was dried with calcium chloride and subsequently evaporated to dryness *in vacuo*. There was obtained 0.26 g. (96%) of diphenylacetic acid, as was shown by mixture melting point (m.p. 144–145°) determination with an authentic sample. The aqueous layer was made basic with sodium hydroxide pellets followed by three extractions with 50-ml. portions of ethyl ether. The ethereal solution was treated with an excess of acetic anhydride (5 ml.). There was obtained 0.235 g. (64%) of *p*-toluidineacetamide, m.p. 146–147°. A mixture melting point determination with an authentic sample was undepressed.

Method B.—A solution of 1 g. (2.56 mmoles) of N,N′-di-*p*-tolyldiphenylacetamidine and 25 ml. of concentrated phosphoric acid was refluxed 14 hr. The white solid which resulted was filtered off and dried: m.p. 171–172 and 179–180° (two isomorphic forms). A mixture melting point determination with both isomorphic forms of N-*p*-tolyldiphenylacetamide was not depressed. The filtrate was poured into 100 ml. of water which was extracted three times with 100-ml. portions of ethyl ether. The ether was distilled *in vacuo* and the residue was dissolved in 50 ml. of a saturated solution of sodium bicarbonate. Acidification of the sodium bicarbonate solution with *ca.* 6 *N* hydrochloric acid followed by extraction with three 50-ml. portions of ethyl ether and subsequent evaporation yielded 0.11 g. (20.2%) of the diphenylacetic acid, m.p. 141–144°. A mixture melting point with an authentic sample of diphenylacetic acid was not depressed: m.p. 144–145°. The aqueous phosphoric acid layer was made basic and the amine fraction was extracted with ether. The ethereal amine solution was then treated with 3 g. of *p*-toluenesulfonyl chloride. There was obtained 0.51 g. of the N-*p*-tolyl-*p*-toluenesulfonamide, as was demonstrated by a mixture melting point determination with an authentic sample, m.p. 116–118°.

(10) See Experimental Section.