tion of 6.0 g (0.035 mol) of 9-fluorenone was added to the suspension of **4**, and the mixture was stirred for 1 hr. The yellow-green suspension was neutralized and worked up as described above to give 7.95 g (93–98%) of white solid, mp 154–156°. Recrystallization from benzene–hexane and then absolute EtOH afforded an analytical sample: mp 155–156°; ir (KBr) 3550 (OH), 3385 cm^{-1} (NH); nmr ($CDCl_3$) δ 2.3 (s, 2, $PhCH_2$), 3.6 (broad s, 0.9, OH), 3.9 (s, 1, NH).

Cyclodehydration of 20 with 20% Sulfuric Acid. Formation of Fluorene-9-spiro-1′-phenylisoindoline (23).—Into a 100-ml round-bottomed flask were placed 4.0 g (0.011 mol) of carbinolamine **20** and 60 ml of 20% sulfuric acid. This mixture was refluxed 4 hr, cooled, and then poured into a sodium hydroxide solution. The resulting white suspension was stirred for 30 min and then filtered, yielding 2.52 g (67%) of white solid. This precipitate was dissolved in absolute ethanol, cooled, and filtered, yielding a white solid, mp 174–176°. Addition of ice to the filtrate afforded a second crop of crystals. Further recrystallization from aqueous ethanol afforded an analytical sample: ir (KBr) no OH or NH; nmr ($CDCl_3$) δ 5.18 (s, 1.9, $PhCH_2$), 6.2–7.9 (m, 17, aromatic).

Condensation of 4 with Acetophenone. Formation of 1,1-[*o*-(*N*-Phenylaminomethyl)diphenyl]methanol (24).—A hexane solution of 3.4 g (0.028 mol) of acetophenone was added to the suspension of **4** precooled in an ice bath for 15 min. After a stirring period of 30–45 min, the yellow-white solution was neutralized and worked up as described above to give 0.9 g (10%) of white solid, mp 139–142°. (Amine **3** was recovered in 65–75%.) Attempts to improve the yield of **24** by condensing lithioamine **4** at −80 were unsuccessful; ir (KBr) 3430 (OH), 3285 cm^{-1} (NH); nmr ($CDCl_3$) δ (1.85 (s, 2.7, $>C(O^-)CH_3$), 3.7 (H_A), 3.9 (H_B) (AB q, 2, $J_{AB_{app}} = 12$ Hz, $PhCH_2$).

Carbonation of Lithioamine 4. Formation of *o*-(*N*-Phenylaminomethyl)benzoic Acid (25).—To the magnetically stirred yellow-white suspension of lithioamine **4** were added small pieces of carbon dioxide over a 15-min period. The resulting milky white slurry was stirred for 30 min and then poured into 50 ml of 10% hydrochloric acid. The acidic solution was stirred for 5 min, 100 ml of ether was added, and stirring was continued another 30 min. The light-red acid layer was separated from the organic layer. The organic fraction was dried ($MgSO_4$) and then concentrated to give 0.3–0.4 g (8%) of 2-phenylphthalimidine (**26**), mp 157–160°. Recrystallization from absolute methanol afforded a white crystalline solid, mp 159–161°.

The acid layer was made basic with sodium hydroxide pellets; when cool, the basic aqueous solution was stirred with an equal volume of ether for 30 min. The ether layer was separated and then washed with 50 ml of 10% sodium hydroxide. The combined basic fractions were carefully acidified to pH 5 with concentrated hydrochloric acid. Cooling and scratching afforded 3.0 g (61%) of green-white solid which was collected by filtration. The solid acid did not melt but decomposed between 103 and 107° to form the lactam, which melted at 158–161°: ir (KBr) 3020–2780 (broad) (OH), 1680 ($>C{=}O$), 1400 and 1252 (OH and C–O), 867 cm^{-1} (OH).

Thermal Cyclization of Amino Acid (25). Formation of 2-Phenylphthalimidine (26).—The solid amino acid **25** was placed in a 250-ml beaker and heated on a hot plate until all the solid had melted. The beaker was cooled and then the solid was dissolved in methanol; the solvent was slowly removed by gentle heating. The resulting solid was again dissolved in methanol, cooled, and filtered, yielding 2.4–2.5 g (90%) of crystalline white solid, mp 160–162°. One recrystallization from absolute methanol gave a white crystalline solid: mp 162–163° (lit.[24] mp 162–163°); ir (KBr) 1690 (five-membered lactam); nmr ($CDCl_3$) δ 4.75 (s, 1.8, $C_6H_5CH_2$–), 6.9–8.3 (m, 9.3, aromatic).

Registry No.—TMEDA, 110-18-9; *n*-butyllithium, 109-72-8; **1**, 103-67-3; **3**, 103-32-2; **6**, 28504-92-9; **7**, 15496-39-6; **7** (dibenzoylated derivative), 28504-94-1; **8**, 28504-95-2; **9**, 28504-96-3; **10**, 28504-97-4; **12**, 28504-98-5; **13**, 28504-99-6; **14**, 28505-00-2; **15**, 28505-01-3; **16**, 28505-02-4; *cis*-**17**, 28505-03-5; *trans*-**17**, 28505-04-6; **18**, 28505-05-7; **19**, 28505-06-8; **19** diacetate, 28505-07-9; **20**, 28519-58-6; **21**, 28607-62-7; **22**, 28519-59-7; **23**, 28519-60-0; **24**, 28519-61-1; **25**, 28519-62-2; **26**, 5388-42-1.

[24] J. R. A. Pollock and R. Stevens, Ed., "Dictionary of Organic Compounds," 4th ed, Oxford University Press, New York, N. Y., 1965, p 2711.

A Direct Preparation of Amidines. The Reaction of Tetrakis(dimethylamino)titanium with N–H Carboxamides

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Received September 4, 1970

Tetrakis(dimethylamino)titanium reacts with N-monosubstituted carboxamides to give free trisubstituted amidines. Benzamide is converted to a mixture of benzonitrile and *N*,*N*-dimethylbenzamidine, and 1*H*-2-pyridones yield 2-dimethylaminopyridines. This reaction appears to be the first direct conversion of amides to trisubstituted amidines. Nmr spectral data are presented for the amidines prepared.

Although we know of many reactions which lead to amidinium salts,[1] conversion to their conjugate bases, amidines, cannot always be achieved in good yield.[2] Previous reports from this laboratory have described the reactions of various carboxylic acid derivatives with tetrakis(dimethylamino)titanium (**1**) by which reaction carboxylic anhydrides, *N*,*N*-dialkylamides, and esters are all converted to alkylidene bis(dialkylamines).[5] Thus it was of interest to study the reactions of **1** with a series of N–H amides to see (1) whether carbon and titanium can undergo nitrogen–nitrogen ligand exchange reactions similar to the carbon-bound oxygen for titanium-bound nitrogen exchanges previously observed,[5] and (2) if amidines can be directly prepared this way. We report our results here.

Results and Discussion

The reactions of several N-monosubstituted amides with tetrakis(dimethylamino)titanium were observed; the products and their physical properties are presented in Table I. In general, the reactions appear to follow eq 1 although no quantitative reactions were observed. The conditions employed were generally similar to those previously employed:[5] the reagents were mixed, either

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[1] (a) P. A. S. Smith, "Open-Chain Nitrogen Compounds," Vol. 1, W. A. Benjamin, New York, N. Y., 1965, pp 182–194.

[2] This is particularly true for the smaller, aliphatic amidines. Thus Short and his coworkers consistently obtained lower yields of aliphatic than aromatic amidines in their extensive research in the area.[3] Similar results were reported by Pettit and Garson.[4]

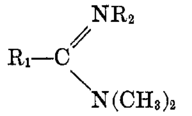
[3] P. Oxley and W. F. Short, *J. Chem. Soc.*, 147 (1946), 382 (1947), and subsequent publications.

[4] G. R. Pettit and L. R. Garson, *Can. J. Chem.*, **43**, 2640 (1965).

[5] H. Weingarten and W. A. White, *J. Amer. Chem. Soc.*, **88**, 850 (1966); H. Weingarten and W. A. White, *J. Org. Chem.*, **31**, 2874 (1966).

TABLE I

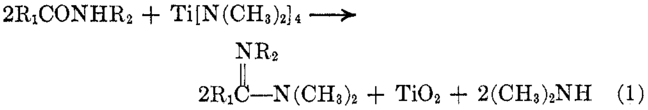
PHYSICAL PROPERTIES OF AMIDINES PREPARED



Product[a] R₁	Product[a] R₂	Registry no.	Bp, °C (Torr)	Mol wt[f]	Nmr,[h] τ	% C[n]	% H	% N
H	C_6H_5	1783-25-1	85 (1.0)	148	7.3 s (6 H), 3.0 m (5 H), 2.5 s (1 H)		j	
H	*tert*-C_4H_9	23314-06-9	28 (17)	128	8.9 s (9 H), 7.2 s (6 H), 2.7 s (1 H)		128.1305[k] (128.1313)	
CH_3	CH_3	28504-67-8	72 (75)	100	7.1 s (3 H), 7.2 s (6 H), 8.2 s (3 H)	59.95 (60.00)	12.02 (12.00)	28.00 (28.00)
C_6H_5	CH_3	25092-88-0	42 (0.2)	162	2.5 m (5 H), 7.2 s (3 H), 7.3 s (6 H)	73.31 (74.04)	9.34 (8.70)	17.32 (17.27)
tert-C_4H_9	CH_3	28504-69-0	75 (55)	142	7.2 s (3 H), 7.4 s (6 H), 8.9 s (9 H)[i]			
$-(CH_2)_3-$		1003-55-0	80 (30)	112	6.6 t (2 H), 7.2 s (6 H), 7.6 m (4 H)	64.56 (64.25)	10.86 (10.80)	24.32 (24.06)
$-CH_2OCH_2CH_2-$[b]		28504-71-4	125 (35)	128	5.8 s (2 H), 6.6 m (4 H)	55.49 (56.22)	9.43 (9.45)	21.96[l] (21.84)
$-CH{=}CHCH{=}CH-$[c]		5683-33-0	90 (40)	122	1.7 m (1 H), 2.5 m (1 H), 3.3 m (2 H), 6.9 s (6 H)			
$-CH{=}\underset{\displaystyle CH_3}{\underset{\vert}{C}}N{=}\underset{\displaystyle CH_3}{\underset{\vert}{C}}-$[d]		5177-09-3	61 (0.8)	139	3.8 s (1 H), 7.0 s (6 H), 7.6 s (3 H), 7.8 s (3 H)			
CH_3	$C(NMe_2){=}CH_2$[e]	28504-74-7	58 (0.55)	g	6.3 s (2 H), 7.2 s (12 H), 7.9 s (3 H)			
C_6H_5	H[m]	20548-18-9	115 (0.25)	148	2.7 m (5 H), 7.2 s (6 H)			

[a] In each case the starting material was the amide R_1CONHR_2. [b] Starting material, 3-ketomorpholine. [c] Product, 2-(dimethylamino)pyridine. [d] Product, 4-(dimethylamino)-2,6-dimethylpyrimidine. [e] Starting material, diacetamide. [f] Mass number of parent ions. [g] Parent ion not observed. [h] CD_3CN solution, internal TMS reference. [i] Dioxane solution. [j] Mass and ir spectra compared with those of authentic sample. [k] Molecular weight from high-resolution mass spectrum. [l] Oxygen: 13.44% found; 12.47% calculated. [m] Benzonitrile is also produced in this reaction. See Experimental Section. [n] Calculated values in parentheses.

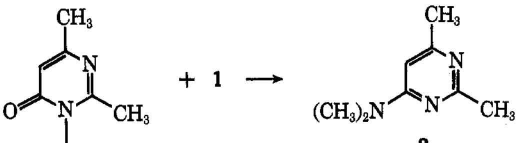
neat or in an unreactive solvent (ether, benzene, THF), and heated if necessary, and the product was recovered by distillation.



$$2R_1CONHR_2 + Ti[N(CH_3)_2]_4 \longrightarrow 2R_1\overset{\displaystyle NR_2}{\overset{\|}{C}}{-}N(CH_3)_2 + TiO_2 + 2(CH_3)_2NH \qquad (1)$$

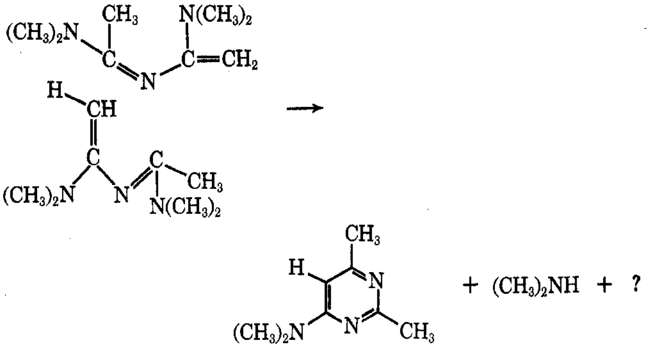
The only products observed in this work were those derived by amination of the carbonyl function.[6] From this we conclude that, at least in these simple systems, amide ligand exchange occurs much more slowly than amination. This presumably reflects the relatively greater strength of Ti–O than Ti–N bonds.

Three products require further comment. The conversion of 2-pyridone and 2,4-dimethyl-6-pyrimidone into respectively 2-(dimethylamino)pyridine and 4-(dimethylamino)-2,6-dimethylpyrimidine (**2**) represents a new kind of entry into aminoheterocyclic systems. This reaction should be applicable in most heterocyclic series.



2

Diacetamide, $(CH_3CO)_2NH$, reacts with **1** to give $CH_3C(NMe_2){=}NC(NMe_3){=}CH_2$ (**3**) which is formally an amidine but which is perhaps best regarded as an aza derivative of the 1,3-bis(dimethylamino)butadienes.[7] Pyrolysis of **3** at about 100° unexpectedly gives a product identified as **2** by comparison of its mass and nmr spectra with those of the compound pre-



pared from 2,4-dimethyl-6-pyrimidone. This condensation parallels the base-catalyzed cyclotrimerization of acetonitrile to 6-amino-2,4-dimethylpyridimine.[8] The stoichiometry of the pyrolysis requires the disposition of another fragment (or fragments) corresponding to $C_2H_2(NMe_2)_2$ but no evidence was seen for one logical compound of that formula, vinylidenebis(dimethylamine). A sample of **3** was pyrolyzed during introduction into a mass spectrometer, but there was no significant peak at *m/e* 114, which there would have been if any quantity of vinylidenebis(dimethylamine) were present in the pyrolysate.

Benzamide, unsubstituted on nitrogen, reacts with **1** to give a 53% yield of benzonitrile and 26% of *N,N*-

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(6) Except, of course, the benzonitrile from benzamide (see below).

(7) H. Weingarten and M. G. Miles, *J. Org. Chem.*, **33**, 1506 (1968); H. Weingarten, M. G. Miles, S. R. Byrn, and C. F. Hobbs, *J. Amer. Chem. Soc.*, **89**, 5974 (1967).

(8) R. Schwarze, *J. Prakt. Chem.*, **42**, 1 (1890).

dimethylbenzamidine,[9] indicating that competition exists between dehydration and substitution in this reaction. Although this was not studied, it seems likely that conditions could be chosen so as to achieve good yields of either amidine or nitrile.

N,N'-Dimethyloxamide reacts with 1 to give an insoluble, involatile product which strongly resembles brick dust. This may be a high molecular weight coordination polymer,[10] but it has not been characterized.

Experimental Section

Chemicals and solvents used in this work were obtained from Fisher Scientific or Aldrich Chemical Corp. unless otherwise noted. Solvents were the driest commercially available and not further treated. Tetrakis(dimethylamino)titanium was obtained from Alfa Inorganics. Nmr spectra were determined using a Varian A-60, in CD_3CN solvent with TMS reference. Mass spectra were obtained on a CEC-104 spectrometer and ir spectra on a Beckman IR-4. Boiling points are uncorrected.

***N,N*-Dimethyl-*N'*-butylformamidine.**—To a stirred solution of 8.08 g (0.08 mol) of *tert*-butylformamide in 200 ml of dry THF was added dropwise 10.75 g (0.048 mol) of tetrakis(dimethylamino)titanium. The reaction was allowed to reflux for 48 hr. The titanium dioxide precipitate was then removed by filtration and washed with pentane. The solvent was removed from the combined filtrate and washings under reduced pressure and the liquid residue distilled at reduced pressure to give 5.0 g (51%) of a colorless liquid, bp 28° (17 Torr). The structure was confirmed by nmr and low and high resolution mass spectrometry. (Table I. The high resolution mass spectrum was obtained on a CEC-110 instrument.)

The following compounds were obtained from reaction virtually identical with that described above; only differences from it and additional relevant data will be presented here.

***N,N*-Dimethyl-*N'*-phenylformamidine.**—From 12.1 g (0.10 mol) of formanilide and 11.2 g (0.05 mol) of 1, 7.90 g (72%) of the product was obtained after 3 days reaction at 25°. Its structure was proved by comparison of its ir, nmr, and mass spectra with those of an authentic sample from Frinton Laboratories.

***N,N,N'*-Trimethylacetamidine.**—From 7.3 g (0.10 mol) of *N*-methylacetamide and 12.5 g (0.056 mol) of 1, 3.14 g (31%) of the product was obtained. It was characterized from the data given in Table I.

***N,N,N'*-Trimethylbenzamidine.**—Reaction of 13.5 g (0.10 mol) of *N*-methylbenzamide with 11.2 g (0.05 mol) of 1 for 18 hr at 25° yielded 6.30 g (90%) of a colorless liquid characterized as above.

***N,N,N'*-Trimethylpivalamidine.**—The reaction of 5.75 g (0.05 mol) of *N*-methylpivalamide (Frinton Laboratories) with 6.75 g (0.03 mol) of 1 for 48 hr at reflux in dioxane solvent gave 1.0 g (14%) of a colorless liquid characterized by its mass and nmr spectra.

***N,N*-Dimethyl-2-(1-pyrrolinyl)amine.**—The reaction of 8.95 g (0.04 mol) of 1 with 6.35 g (0.075 mol) of 2-pyrrolidone, neat, for 24 hr at 100°, yielded 3.72 g (37%) of a colorless liquid characterized by elemental and spectral analyses.

3-Dimethylamino-5,6-dihydrooxazine.—From 5.05 g (0.05 mol) of 3-ketomorpholine and 8.96 g (0.04 mol) of 1, reaction for 48 hr, neat, at 80°, 2.60 g (40%) of product was obtained. It was characterized as above.

2-(Dimethylamino)pyridine.—From a reaction of 4.75 g (0.05 mol) of 2-pyridone with 6.75 g (0.03 mol) of 1 for 3 days at reflux (in THF solution), 1.0 g (16%) of a colorless product was obtained which was characterized as above. The picrate (from ethanol) exhibited mp 182–183° (lit.[11] 181–182°).

4-(Dimethylamino)-2,6-dimethylpyrimidine.—The reaction of 2.48 g (0.02 mol) of 2,4-dimethyl-6-hydroxypyrimidine with 2.30 g (0.012 mol) of 1, for 3 days at reflux, gave 0.50 g (17%) of a colorless liquid, characterized as above. The picrate (from ethanol) exhibited mp 177–179° (lit.[12] 177°).

Reaction of Benzamide with 1.—To a solution of 6.5 g (0.05 mol) of benzamide in 25 ml of dry benzene was added, dropwise with stirring, 5.60 g (0.025 mol) of 1. The mixture was refluxed for 4 hr, after which time it was colorless. The precipitated TiO_2 was removed by filtration, and the benzene solvent was removed from the filtrate by distillation at atmospheric pressure. The remaining yellow liquid was distilled under reduced pressure, giving fractions boiling at 90° (2 Torr) (2.37 g) and 115° (25 Torr) (2.30 g). The first was identified as benzonitrile by comparison of the glpc retention times (on a column made up of OV-17 on high-performance Chromosorb G) and infrared spectra of it and an authentic sample. The second was characterized by its mass and nmr spectra. From the nmr spectrum it appeared that the sample contained about 15% benzonitrile; the phenyl hydrogen adsorptions of the two compounds are separated well enough for approximate integral areas of the two peaks to be measured. From these data the yields of the two compounds were benzonitrile (53%) and *N,N*-dimethylbenzamide (26%).

Reaction of Diacetamide with 1.—To a stirred solution of 4.04 g (0.04 mol) of diacetamide in 30 ml of acetonitrile was added 9.0 g (0.042 mol) of 1, dropwise with stirring, giving a two-phase reaction mixture (1 is only slightly soluble in CH_3CN). This mixture was allowed to reflux for 2 days, the precipitated TiO_2 was then filtered off, and the acetonitrile removed from the filtrate by reduced-pressure evaporation. The yellow liquid residue was distilled under reduced pressure at 58–83° (1.0 Torr) giving a mixture of two compounds which were identified as 4-(dimethylamino)-2,6-dimethylpyrimidine and 2,4-bis(dimethylamino)-3-aza-1,3-pentadiene by their mass and nmr spectra. The pyrimidine was confirmed by independent synthesis (above); the azapentadiene spectra were then deduced by substraction of the peaks arising from the pyrimidine.

Registry No.—Tetrakis(dimethylamino)titanium, 7229-79-0.

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[9] Glpc results imply that the conversion of benzamide was not complete under these conditions.

[10] Polymeric coordination complexes of N,N'-disubstituted dithioöxamides with various transition metals are well known. See F. G. A. Stone and W. A. Graham, "Inorganic Polymers," Academic Press, New York, N. Y., 1962.

[11] L. Pentimalli, *Gazz. Chim. Ital.*, **94**, 458 (1964).

[12] D. J. Brown, B. T. England, and J. M. Lyall, *J. Chem. Soc. C*, 226 (1966).