Table VI. Results for Acetophenone and Benzaldehyde Hydrazones[a] Va-r

compd	mp, °C	yield, %	formula[b]
Va	208-209	98	$C_{14}H_{12}N_2O$
Vb	135-136	91	$C_{15}H_{14}N_2O$
Vc	210-211	87	$C_{19}H_{16}N_2O$
Vd	176-177	88	$C_{14}H_{11}ClN_2O$
Ve	175-176	92	$C_{15}H_{13}ClN_2O$
Vf	228-229	95	$C_{19}H_{15}ClN_2O$
Vg	159-160	92	$C_{15}H_{14}N_2O_2$
Vh	170-171	85	$C_{16}H_{16}N_2O_2$
Vi	185-186	88	$C_{20}H_{18}N_2O_2$
Vj	155-156	89	$C_{15}H_{14}N_2O$
Vk	157-158	96	$C_{16}H_{16}N_2O$
Vl	172-173	95	$C_{20}H_{18}N_2O$
Vm	204-205	93	$C_{15}H_{11}ClN_2O$
Vn	164-165	89	$C_{16}H_{13}ClN_2O$
Vo	184-185	92	$C_{20}H_{17}ClN_2O$
Vp	167-168	89	$C_{16}H_{16}N_2O_2$
Vq	167-168	88	$C_{17}H_{18}N_2O_2$
Vr	170-171	97	$C_{21}H_{20}N_2O_3$

[a] Elemental analysis (C, H, N, Cl) in agreement with theoretical values were obtained and submitted for review. [b] Compounds Va-d, k, l were crystallized from benzene-cyclohexane and Ve-j from benzene.

spectra were measured on a Beckman spectrophotometer ACTA MVI using a scan speed of 0.25 nm/s and chart rate of 10 nm/in. (ethanol). The purity of the analytical samples was checked by TLC (silica gel). Microanalyses were determined by Alfred Bernhardt, West Germany.

Reaction of Hydrazide Derivatives IIa-c with Acetylenic Ketones Ia-c, Benzaldehydes IVa-c, and Acetophenones IVd-f. General Procedure. The reported procedure (*5*) for the reaction of acetylenic ketones with hydrazide was used in this work. The compounds ω-aroylacetophenone, benzaldehyde, and acetophenone *N*-(acyl- or benzoyl)hydrazones (IIIa-p, Va-i, and Vk-s, respectively) were obtained by refluxing the hydrazide II (1 mol equiv) with the acetylenic ketones I (1 mol equiv), benzaldehydes IVa-c (1 mol equiv), and acetophenones IVd-f in ethanol for 5 h. The precipitated solid left after evaporation of the solvent was crystallized from a suitable solvent to give the corresponding hydrazone (Tables V and VI).

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Synthesis of Novel Bis(amides) by Means of Triphenyl Phosphite Intermediates

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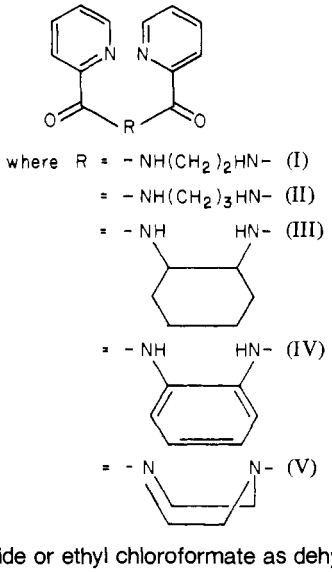
The synthesis, via a triphenyl phosphite intermediate, of a series of bis(amides) of pyridine-2-carboxylic acid and various diamines is reported. Products isolated are of the form $(C_5H_5NCO)_2R$ where R = (I) $-NH(CH_2)_2NH-$, (II) $-NH(CH_2)_3NH-$, (III) $-NHCH(CH_2)_4CHNH-$, (IV) $-NH(o-C_6H_4)NH-$, and (V) $H_2CN(CH_2)_2NCH_2$. The compounds were characterized by microanalysis, melting point, and NMR, IR, and mass spectral data.

This paper reports the synthesis of some new bis(amides) by means of a triphenyl phosphite intermediate. The following compounds have been prepared: *N,N'*-bis(2-pyridinecarboxamide)-1,2-ethane (I); *N,N'*-bis(2-pyridinecarboxamide)-1,3-propane (II); *N,N'*-bis(2-pyridinecarboxamide)-1,2-cyclohexane (III); *N,N'*-bis(2-pyridinecarboxamide)-1,2-benzene (IV); *N,N'*-bis(2-pyridylcarboxamide)piperazine (V).

Gardiner et al. (*1*) synthesized the 4-pyridyl analogue of I for possible chemotherapeutic use in the treatment of tuberculosis. Castle (*2*) reported the same compound as a reaction product from the attempted synthesis of 2-(4'-pyridyl)imidazoline. Ojima (*3*) condensed methyl picolinate with the corresponding diamines to produce both I and II. Compounds III-V have not appeared in the literature. The synthetic method used here was first reported by Mitin and Glinskaya (*4*) and has been discussed in detail by Yamazaki and Higashi (5, 6). Several other methods, including the use of acid chloride intermediates and dicyclohexylcarbodiimide or ethyl chloroformate as dehydrating agents, were attempted initially. In all cases yields were found to be considerably lower than for that reported here. Physical and spectroscopic data for the compounds are given in Table I.



Experimental Section

General Methods. Melting points were recorded on a Gallenkamp melting point apparatus and are uncorrected.

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Table I. Physical and Spectroscopic Data for Bis(amide) Products

compd	empirical formula	mp, °C	IR, cm^{-1}	NMR,[a] ppm	mass spectrum (*m/e*, parent)
I	$C_{14}H_{14}N_4O_2$	192–193	3330, 3060, 2980, 2949, 1655, 1520	8.4 (m) 8.3 (br),[b] 8.1 (m) (combined: 6 H), 7.7 (m, 2 H), 7.3 (m, 2 H), 3.7 (t, 4 H)	270
II	$C_{15}H_{16}N_4O_2$	94–95	3300, 3050, 2960–2840 m, 1635, 1525	8.6 (d), 8.3 (d), 8.5 (br)[b] (combined: 6 H), 7.9 (m, 2 H), 7.4 (m, 2 H), 3.6 (m, 4 H)	284
III	$C_{18}H_{20}N_4O_2$	201–202	3300, 3050, 2940, 2850, 1655, 1535	8.6 (m), 8.4 (br),[b] 8.1 (m) (combined: 8 H), 7.8 (m, 2 H), 7.4 (m, 2 H), 4.1 (br, 2 H), 2.3 (br), 1.6 (br) (combined: 6 H)	324
IV	$C_{18}H_{14}N_4O_2$	175	3330, 3060, 1680, 1670, 1520	10.2 (br, 2 H), 8.2 (m, 4 H), 7.7 (m, 4 H), 7.2 (m, 4 H)	318
V	$C_{16}H_{16}N_4O_2$	134–135	3060, 3000, 2920, 1625	9.1 (d, 2 H), 7.8 (m, 4 H), 7.4 (m, 2 H), 3.9 (s, 8 H)	296

[a] Key: br = broad; s = singlet; d = doublet; t = triplet; m = multiplet. [b] Partly obscured.

Infrared spectra were recorded in KBr disks using a Perkin-Elmer 621 I.R. spectrophotometer. NMR spectra were recorded using a Varian A-60D CW ^1H spectrometer with $CDCl_3$ as solvent and are reported in parts per million downfield from an internal standard of tetramethylsilane. Mass spectra were recorded on an AEI MS12 electron impact source mass spectrometer. Elemental analyses were carried out by the Australian Microanalytical Service, and satisfactory microanalysis results (C, H, and N) were obtained for all products. All starting materials were AR grade chemicals used as obtained.

***N,N'-Bis(2-pyridinecarboxamide)-1,2-ethane* (I).** To a solution of 2-pyridinecarboxylic acid (73.8 g, 0.6 mol) in pyridine (240 mL) was added 1,2-diaminoethane (18.3 g, 0.3 mol) in pyridine (60 mL). The mixture was stirred gently for 10 min, during which time a white precipitate formed. The mixture was heated on a steam bath and triphenyl phosphite (186 g, 0.6 mol) was added slowly over a period of 15 min. The resultant solution was then heated with stirring on the steam bath for 4 h. On cooling of the mixture, a pale yellow crystalline solid resulted, 73 g (90%). An analytical sample was twice recrystallized from chloroform to give white needles.

***N,N'-Bis(2-pyridinecarboxamide)-1,3-propane* (II).** To a solution of 2-pyridinecarboxylic acid (12.3 g, 0.1 mol) in pyridine (40 mL) was added 1,3-diaminopropane (3.71 g, 0.05 mol) in pyridine (20 mL). The solution was stirred gently for 15 min and heated on a steam bath and triphenyl phosphite (31.0 g, 0.1 mol) was added slowly. The temperature was maintained for 4 h. A brown solution resulted, which after volume reduction yielded a brown oil. This was taken up in chloroform, washed three times with water, four times with saturated sodium bicarbonate solution, and then again three times with water. The resulting solution was dried over magnesium sulfate and filtered and the solvent removed. The resultant light brown oil was taken up in a small amount of chloroform and added dropwise to ice-cold diethyl ether with vigorous stirring. The mixture was stirred in an ice bath for 1 h. A white solid, II, resulted, 6.9 g (49%). An analytical sample was recrystallized from chloroform to yield white crystals.

***N,N'-Bis(2-pyridinecarboxamide)-1,2-cyclohexane* (III).** To a solution of 2-pyridinecarboxylic acid (12.3 g, 0.1 mol) in pyridine (40 mL) was added 1,2-diaminocyclohexane (5.7 g, 0.05 mol) in pyridine (20 mL). After triphenyl phosphite addition (31.0 g, 0.1 mol) the reaction solution has heated on a steam bath with occasional stirring for 12 h. The brown oil resulting was taken up in chloroform, washed twice with both sodium bicarbonate solution and water, and then dried over magnesium sulfate. After volume reduction the solution was allowed to stand overnight at room temperature. Pale brown crystals of III resulted, 7.6 g (47%). An analytical sample was recrystallized from chloroform to give white crystals.

***N,N'-Bis(2-pyridinecarboxamide)-1,2-benzene* (IV).** To a solution of 2-pyridinecarboxylic acid (73.8 g, 0.6 mol) in pyridine (240 mL) was added 1,2-diaminobenzene (32.4 g, 0.3 mol) in pyridine (60 mL). After triphenyl phosphite (186 g, 0.6 mol) addition the reaction solution was heated for 4 h on a steam bath and allowed to stand at room temperature overnight. A pale brown crystalline solid resulted, IV, 91 g (96%). An analytical sample was recrystallized twice from chloroform to give long white needles.

***N,N'-Bis(2-pyridinecarboxamide)piperazine* (V).** To a solution of 2-pyridinecarboxylic acid (12.3 g, 0.1 mol) in pyridine (40 mL) was added piperazine (4.31 g, 0.05 mol) in pyridine (20 mL). After triphenyl phosphite (31 g, 0.1 mol) addition the mixture was heated on a steam bath for 5 h. The solution was reduced in volume and allowed to stand overnight at room temperature. The resultant red-brown oil was twice subjected to a workup procedure identical with that of II above. White crystals resulted, V, 5.9 g (40%). An analytical sample was recrystallized from 95% ethanol to give white needles.

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