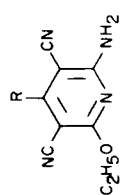


TABLE I

Substituted Pyridines



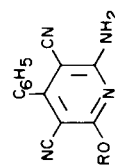
Compound No.	Starting Aldehyde	R	Formula	M.p., °C	Yield, %	Analysis, %		
						C H N		
Ia	Acetaldehyde	Methyl	C ₁₀ H ₁₀ N ₄ O (a)	235-237 (b)	3	Calcd.: 59.39 Found: 59.16	4.98 4.93	27.70 27.68
Ib	Propionaldehyde	Ethyl	C ₁₁ H ₁₂ N ₄ O	203-204 (b)	7	Calcd.: 61.09 Found: 61.42	5.59 5.57	25.91 26.13
Ic	Isobutyraldehyde	Isopropyl	C ₁₂ H ₁₄ N ₄ O	234-235 (b)	32	Calcd.: 62.58 Found: 62.73	6.12 6.28	24.33 24.29
Id	Pivalaldehyde	<i>tert</i> -Butyl	C ₁₃ H ₁₆ N ₄ O	230-231 (b)	5	Calcd.: 63.91 Found: 64.01	6.60 6.43	22.93 23.23
Ie	<i>n</i> -Butyraldehyde	<i>n</i> -Propyl	C ₁₂ H ₁₄ N ₄ O	156-157 (c)	25	Calcd.: 62.58 Found: 62.85	6.12 5.85	24.33 24.15
If	Valeraldehyde	<i>n</i> -Butyl	C ₁₃ H ₁₆ N ₄ O	142-144 (b)	25	Calcd.: 63.91 Found: 63.63	6.60 6.31	22.93 22.77
Ig	Diethylacetaldehyde	1-Ethyl- <i>n</i> -propyl	C ₁₄ H ₁₈ N ₄ O	123-124 (c)	32	Calcd.: 65.09 Found: 64.95	7.02 6.73	21.69 21.54
Ih	<i>n</i> -Heptaldehyde	<i>n</i> -Hexyl	C ₁₅ H ₂₀ N ₄ O	oil	---	Calcd.: 66.15 Found: ----	7.40 ---	20.57 ----
Ii	Phenylacetaldehyde	Benzyl	C ₁₆ H ₁₄ N ₄ O	140-141 (c)	13	Calcd.: 69.04 Found: 68.89	5.07 4.96	20.13 20.12
Ij	Hexahydrobenzaldehyde	Cyclohexyl	C ₁₅ H ₁₈ N ₄ O	159-161 (c)	3	Calcd.: 66.64 Found: 66.68	6.71 6.36	20.72 20.65
Ik	Benzaldehyde	Phenyl	C ₁₅ H ₁₂ N ₄ O (a)	238-239 (d)	50	Calcd.: 68.16 Found: 68.08	4.58 4.62	21.20 21.25
Il	<i>p</i> -Tolualdehyde	<i>p</i> -Tolyl	C ₁₆ H ₁₄ N ₄ O	192-194 (c)	31	Calcd.: 69.05 Found: 68.86	5.07 5.12	20.13 20.13
Im	<i>m</i> -Tolualdehyde	<i>m</i> -Tolyl	C ₁₆ H ₁₄ N ₄ O	230-231 (b)	49	Calcd.: 69.05 Found: 69.33	5.07 5.10	20.13 20.43
In	Anisaldehyde	<i>p</i> -Methoxyphenyl	C ₁₆ H ₁₄ N ₄ O ₂	199-200 (b)	40	Calcd.: 65.29 Found: 65.54	4.79 4.74	19.03 18.95
Io	3,4,5-Trimethoxybenzaldehyde	3,4,5-Trimethoxyphenyl	C ₁₈ H ₁₈ N ₄ O ₄	219-221 (b)	33	Calcd.: 61.01 Found: 60.73	5.12 5.17	15.81 15.74

Ip	Piperonal	3,4-Methylenedioxyphenyl	C ₁₆ H ₁₂ N ₄ O ₃	174-175 (c)	50	Calcd.: 62.33 Found: 62.60	3.92 4.20	18.17 18.26
Iq	<i>o</i> -Chlorobenzaldehyde	<i>o</i> -Chlorophenyl	C ₁₅ H ₁₁ N ₄ OCl	263-264 (b)	39	Calcd.: 60.31 Found: 60.30	3.71 3.71	18.75 18.86 (f)
Ir	<i>p</i> -Chlorobenzaldehyde	<i>p</i> -Chlorophenyl	C ₁₅ H ₁₁ N ₄ OCl	180-181 (b)	40	Calcd.: 60.31 Found: 60.46	3.71 3.85	18.75 18.74 (g)
Is	<i>p</i> -Dimethylaminobenzaldehyde	<i>p</i> -Dimethylaminophenyl	C ₁₇ H ₁₇ N ₅ O	270-271 (e)	32	Calcd.: 66.43 Found: 66.31	5.56 5.42	22.78 22.57
It	Furfural	2-Furyl	C ₁₃ H ₁₀ N ₄ O ₂	203-204 (b)	10	Calcd.: 61.41 Found: 61.60	3.96 3.97	22.03 21.91
Iu	2-Thiophenylaldehyde	2-Thienyl	C ₁₃ H ₁₀ N ₄ OS	176-178 (c)	21	Calcd.: 57.76 Found: 58.01	3.72 3.59	20.72 20.69 (h)
Iv	3-Pyridinaldehyde	3-Pyridyl	C ₁₄ H ₁₁ N ₅ O	258 dec. (e)	39	Calcd.: 63.38 Found: 63.14	4.18 4.22	26.40 26.57

(a) Previously prepared. (b) Recrystallized from ethanol. (c) Recrystallized from ethanol-water. (d) Recrystallized from chloroform. (e) Recrystallized from dioxane. (f) Calculated chlorine 11.87. Found: 11.67. (g) Calculated chlorine 11.87. Found: 12.22. (h) Calculated sulphur 11.86. Found: 11.66.

TABLE II

Substituted Pyridines



II

Compound No.	Alcohol-alkoxide System	R	Formula	M.p., °C	Yield %	Carbon		Hydrogen		Nitrogen	
						Calcd.	Found	Calcd.	Found	Calcd.	Found
Ila	Methanol-methoxide	Methyl	C ₁₄ H ₁₀ N ₄ O (a)	259-261 (d)	45	67.19	67.12	4.02	4.00	22.38	22.54
Ik	Ethanol-ethoxide	Ethyl	C ₁₅ H ₁₂ N ₄ O (a)	238-239 (d)	50	68.16	68.08	4.58	4.62	21.20	21.25
Ilb	<i>n</i> -Propanol- <i>n</i> -propoxide	<i>n</i> -Propyl	C ₁₆ H ₁₄ N ₄ O	224-225 (b)	45	69.05	69.00	5.07	5.12	20.13	20.42
Ilc	Isopropanol-isopropoxide	Isopropyl	C ₁₆ H ₁₄ N ₄ O	205-207 (c)	20	69.05	69.17	5.07	5.10	20.13	19.88
--	<i>tert</i> -Butanol- <i>tert</i> -butoxide	<i>tert</i> -Butyl	---	----	0	----	----	----	----	----	----

(a) Previously prepared. (b) Recrystallized from ethanol. (c) Recrystallized from ethanol-water. (d) Recrystallized from chloroform.

TABLE III

Infrared and Ultraviolet Spectra of the Pyridines (a)

Compound No.	Infrared Spectra, ν max, cm^{-1} , (nujol)						U.V. (ethanol)		
	N-H stretching		C \equiv N	N-H bending and C=C, C=N stretching			λ max (log ϵ), $\text{m}\mu$		
Ib	3430s	3350s	3250s	2240s	1660s	1600s	1560s	274 (4.33)	317 (4.14)
Ic	3440s	3350s	3250s	2250s	1660s	1600s	1560s	274 (4.35)	317 (4.08)
Id	3400s	3300s	3220s	2210s	1650s	1590s	1560s	274 (4.34)	316 (4.17)
Ie	3400s	3300s	3200s	2210s	1640s	1575s	1540s	275 (4.27)	317 (4.04)
If	3400s	3320s	3220s	2220s	1650s	1595s	1560s	274 (4.27)	317 (4.10)
Ig	3400s	3320s	3220s	2220s	1655s	1595s	1555s	275 (4.24)	318 (4.09)
Ih	3400s	3300s	3200s	2210s	1670s	1600s	1550m	---	---
Ii	3450m	3320s	3200m	2215s	1640s	1600s	1560s	275 (4.36)	318 (4.09)
Ij	3500w	3350s	3200m	2220s	1640s	1590s	1550s	275 (4.28)	317 (4.09)
Ik	3450w	3300s	3200m	2215s	1640s	1595s	1550s	273 (4.32)	326 (4.05)
Il	3500w	3320s	3210m	2220m	1640s	1600s	1560s	268 (4.39)	328 (3.98)
Im	3450w	3300s	3200m	2220s	1645s	1585s	1550s	268 (4.29)	327 (4.00)
In	3400s	3330s	3230s	2215s	1655s	1595s	1555s	275 (4.56)	324 (4.05)
Io	3500m	3350s	3240m	2215s	1645s	1570s	1550s	275 (4.46)	332 (4.09)
Ip	3450w	3350s	3210w	2220s	1650s	1570s	1555s	275 (4.51)	328 (4.07)
Iq	3400w	3300m	---	2210m	1650s	1615s	1540s	268 (4.15)	327 (3.90)
Ir	3530w	3400s	3210s	2215s	1665s	1595s	1550s	268 (4.28)	328 (3.89)
Is	3400w	3320s	3210s	2210s	1650s	1580s	1540s	275 (4.60)	326 (4.10)
It	3480w	3320s	3210m	2215s	1640s	1575s	1550s	275 (4.42)	318 (4.18) 347 (3.96)
Iu	3500w	3350s	3210w	2220s	1640s	1600s	1550s	275 (4.37)	333 (4.05)
Iv	3390s	3310m	3200s	2215s	1660s	1600s	1570s	275 (4.30)	330 (4.06)
Ila	3400w	3250s	3140m	2200s	1610s	1565s	1540s	---	---
Ilb	3460m	3310s	3210m	2220s	1620s	1580s	1540s	272 (4.59)	328 (4.32)
Ilc	3460m	3310s	3210m	2220s	1620s	1580s	1560s	272 (4.60)	327 (4.20)

(a) s = strong, m = medium, w = weak.

TABLE IV

Nuclear Magnetic Resonance Spectra of some Substituted Pyridines (a)

Compound No.	Solvent	Chemical Shift (Multiplicity) Number of Protons						
Ib	Pyridine	8.75 (t) 6;	7.15 (q) 2;	5.65 (q) 2.				
Ic	Pyridine	8.65 (m) 9;	6.45 (m) 1;	5.65 (q) 2.				
Ie	CCl ₃ D	8.95 (t) 3;	8.60 (t) 3;	8.25 (m) 2;	7.15 (t) 2;	5.58 (q) 2;	4.38 (b) 2.	
If	CCl ₃ D	9.05 (t) 3;	8.60 (t) 3;	8.40 (m) 4;	7.15 (t) 2;	5.55 (q) 2;	4.40 (b) 2.	
Ig	CCl ₃ D	9.12 (t) 6;	8.60 (t) 3;	8.10 (m) 4;	7.06 (m) 1;	5.55 (q) 2;	4.35 (b) 2.	
Ii	CCl ₃ D	8.63 (t) 3;	5.82 (s) 2;	5.60 (q) 2;	4.40 (b) 2;	2.65 (m) 5.		
In	CCl ₃ D	8.60 (t) 3;	6.15 (s) 3;	5.52 (q) 2;	4.35 (b) 2;	2.98 (d) 2;	2.46 (d) 2.	
Is	Pyridine	8.70 (t) 3;	7.23 (s) 6;	5.58 (q) 2.				

(a) The chemical shift values are reported in tau (τ) units. s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, b = broad singlet.

The first stage (a) consists in a Knövenagel type condensation between the aldehyde used and the malononitrile to give the alkylidenemalononitrile (III). In agreement with this hypothesis is the fact that a good yield of the corresponding pyridine derivative is obtained when III is used instead of the aldehyde (6).

Furthermore, the low yields obtained when using aliphatic aldehydes (see Table I) are to be expected because it is well known (7-11) that in the Knövenagel condensation of these aldehydes several side reactions are operative.

The second step (b) should consist of a Michael addition of the intermediate III to another molecule of malononitrile (sodium salt), to produce the corresponding 1,1,3,3-tetracyanopropene salt (IV). This addition has been previously observed in the cases of different alkylidenemalononitriles (6,8,11).

The lack of reaction of the α,β unsaturated aldehydes suggests that, either in this step or in the previous one, the above addition involves an attack at the end of the conjugation and the sodium salt of 1,1,3,3-tetracyanopropene is not produced. This is what happened with the acrolein, and the tiglic, cinnamic and 3-indene aldehydes.

The above two steps also offered an explanation why the negatively substituted benzaldehydes (COOH, NO₂) do not react to form the pyridines, since the electron withdrawing effect of these groups prevents the Michael addition.

On the other hand, the lack of reaction of the *o*- and *p*-aminobenzaldehydes seems to be due to the formation of trimers and polymers of these aldehydes. In some cases it was possible to isolate polymeric compounds identical to those described in the literature (12).

Final conversion of IV into the corresponding pyridine involves cyclization, addition of a molecule of the alcohol used, and dehydrogenation. The order of these steps is not known. Since the aliphatic polycyano compounds are strong acidic compounds (13), the step preceding the formation of VI proceeds probably through the intermediate V which undergoes oxidation (giving up a hydride ion) to give the corresponding salt of 1,1,3,3-tetracyanopropene (VI).

The hydride ion acceptor must be the unreacted aldehyde. In the case of the benzaldehyde the isolation of benzyl alcohol from the reaction mixture seemed to prove it. Nevertheless, this has not been considered a conclusive proof since benzyl alcohol may be formed from the benzaldehyde by the Cannizzaro reaction.

The conversion of VI into the pyridine I (d), as it is

known (1) proceeds without difficulty in about quantitative yield.

EXPERIMENTAL

Melting points are uncorrected. Infrared spectra were obtained on Perkin-Elmer 137 and 257 spectrometers. Ultraviolet spectra were obtained with a Perkin-Elmer 350 spectrophotometer in ethanol solutions. NMR spectra were determined on a Perkin-Elmer R-10 spectrometer using TMS as an internal standard.

General Procedure for the Preparation of the Pyridines.

To a solution of 0.06 mole of the appropriate sodium alkoxide in 50 ml. of the corresponding absolute alcohol was added 0.04 mole of malononitrile in 20 ml. of the alcohol, and then 0.02 mole of the appropriate aldehyde was added at once. The mixture was heated under reflux for 3 hours and then allowed to stand for 12 hours at room temperature. The reaction mixture was poured into 300 ml. of cool water. Finally, the crude product was separated by filtration and recrystallized as indicated in each case (see Table I).

The physical properties and analytical data for the compounds synthesized are shown in Tables I and II. Data concerning the infrared and ultraviolet absorption of the new compounds prepared are shown in Table III. The nuclear magnetic resonance spectral data for some substituted pyridine derivatives are recorded in Table IV.

REFERENCES

- (1) E. L. Little, W. J. Middleton, D. D. Coffman, V. A. Englehardt and G. N. Sausen, *J. Am. Chem. Soc.*, **80**, 2832 (1958).
- (2) S. G. Cottis and H. Tieckelmann, *J. Org. Chem.*, **26**, 79 (1961).
- (3) A. P. Krapcho and P. S. Huyffer, *ibid.*, **28**, 2461 (1963).
- (4) A. Alberola, M^a A. Günther, M. Lora-Tamayo and J. L. Soto, *Anal. Quim. (Madrid)*, **63**, 691 (1967).
- (5) A. S. Alvarez-Insúa, D. Dissertation, University of Madrid, 1970.
- (6) M. R. S. Weir, K. E. Helmer and J. B. Hyne, *Can. J. Chem.*, **41**, 1042 (1963).
- (7) B. B. Corson and R. W. Stoughton, *J. Am. Chem. Soc.*, **50**, 2825 (1928).
- (8) R. P. Mariella and A. J. Roth, *J. Org. Chem.*, **22**, 1130 (1957).
- (9) M. R. S. Weir and J. B. Hyne, *Can. J. Chem.*, **43**, 772 (1965).
- (10) O. Diels, H. Gärtner and R. Kaack, *Ber.*, **55**, 3439 (1922).
- (11) J. C. Westfahl and T. L. Gresham, *J. Org. Chem.*, **21**, 319 (1956).
- (12) A. Albert and N. Yamamoto, *J. Chem. Soc. (B)*, 956 (1966).
- (13) W. J. Middleton, E. L. Little, D. D. Coffman and V. A. Englehardt, *J. Am. Chem. Soc.*, **80**, 2795 (1958).

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