

The Preparation of 2,4- and 2,6-Bis-Triazinyl and Triazoliny Derivatives of Pyridine

Francis H. Case

Department of Chemistry, Temple University, Philadelphia, Pennsylvania 19122

Received June 17, 1971

In previous communications were described the preparation of 1,2,4-triazines and 1,2,4-triazolines from pyridine-carboxamide hydrazones (1,2). In the present work, 2,4- and 2,6-pyridine dicarbonitriles (3,4) have been converted to the dicarboxamide dihydrazones (1). These, on treatment with 2,3-butanedione, benzil and pyridil, afforded the corresponding 2,4- and 2,6-bis(5,6-dimethyl, diphenyl, and dipyridyl-*as*-triazin-3-yl) pyridines (II-VII). Treatment of 1 with benzaldehyde and pyridine-2-carboxaldehyde yielded 2,4- and 2,6-bis[5-phenyl and 5-(2-pyridyl)-1,2,4-triazolin-3-yl] pyridines (VIII-XI).

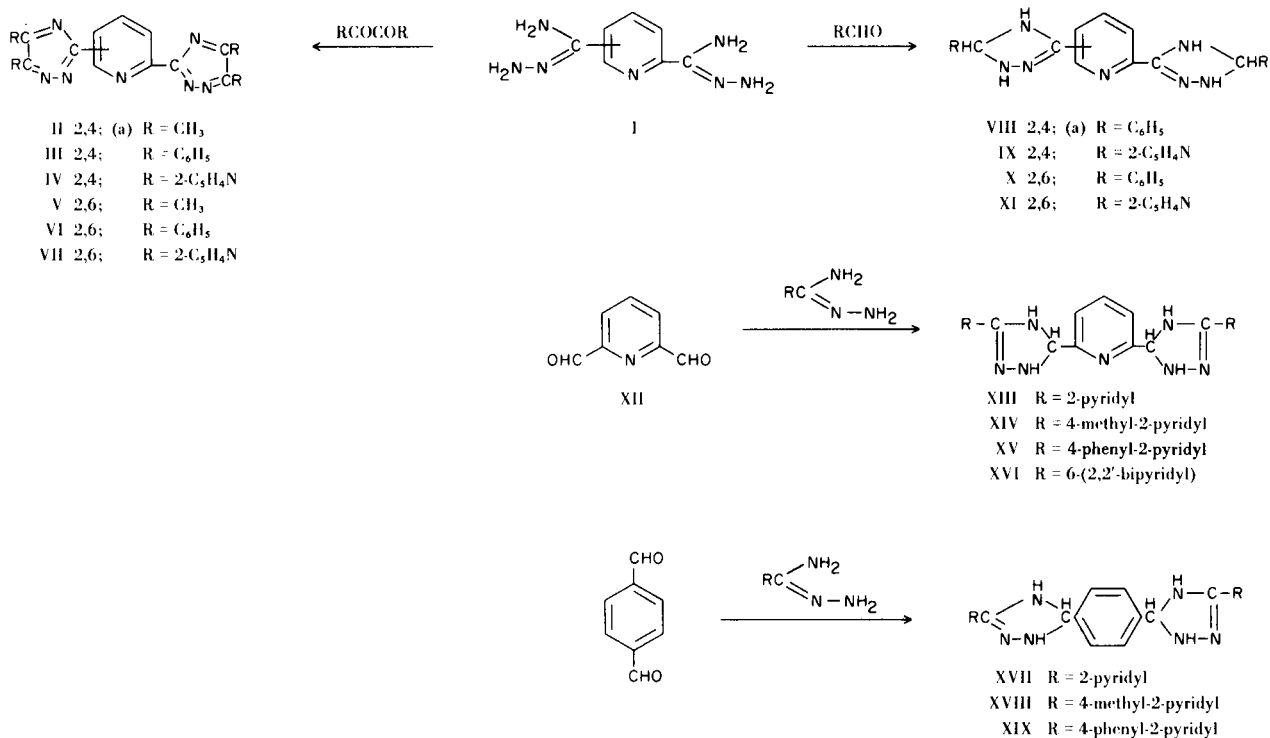
The reaction of pyridine-2,6-dicarboxaldehyde (XII) with picolinamide hydrazone and its 4-methyl and 4-phenyl derivatives (5) afforded 2,6-bis[3-(2-pyridyl)-1,2,4-triazolin-5-yl pyridine (XIII) and 2,6-bis[3-(4-methyl- and 4-phenyl-2-pyridyl)-1,2,4-triazolin-5-yl]pyridine (XIII-XV).

Treatment of XII with 2,2'-bipyridine-6-carboxamide hydrazone yielded 2,6-bis[3-(6-(2,2'-bipyridyl))-1,2,4-triazolin-5-yl] pyridine (XVI).

Treatment of terephthalaldehyde with the first three above-mentioned carboxamide hydrazones yielded 5,5'-*p*-phenylenebis[3-(2-pyridyl)-1,2,4-triazoline] (XVII) and 5,5'-*p*-phenylenebis[3-(4-methyl and 4-phenyl-2-pyridyl)-1,2,4-triazolines (XVIII, XIX).

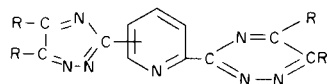
It is of interest that XVII is the tetrahydro derivative of 5,5'-*p*-phenylenebis[3-(2-pyridyl)-1,2,4-triazol] prepared by Ried and Schomann (6) from picolinamide hydrazone and *p*-phenylene diimido ether. Dehydrogenation of XVII by Pd-C in decalin yielded the latter compound.

The compounds described in this paper will be tested for their chelating ability for Fe(II) and Cu(I) by Dr. Alfred Schilt.



(a) The numbers indicate the positions of the triazinyl or triazoliny groups in the pyridine ring.

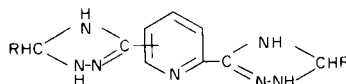
TABLE I

Bis(5,6-Disubstituted-*as*-triazin-3-yl)pyridines

R	Position of triazinyl groups in pyridine ring	Yield %	M.p. °C	Crystallization solvent	Formula	Analysis						
						Calcd. % C	Calcd. % H	Calcd. % N	Found % C	Found % H	Found % N	
II	CH ₃	2,4	72.4	193-194	ethanol	C ₁₅ H ₁₅ N ₇	61.42	5.15	33.43	61.24	5.14	33.93
III	C ₆ H ₅	2,4	71.4	292-293	dimethyl formamide	C ₃₅ H ₂₃ N ₇	77.62	4.28	18.10	77.53	4.47	18.35
IV	2-C ₅ H ₄ N	2,4	50.0	287-288	dimethyl formamide	C ₃₁ H ₁₉ N ₁₁	68.25	3.51	28.24	68.02	3.65	28.49
V	CH ₃	2,6	50.0	245-246	ethanol	C ₁₅ H ₁₅ N ₇	61.42	5.15	33.43	61.40	5.21	33.64
VI	C ₆ H ₅	2,6	46.4	300-301	dimethyl formamide	C ₃₅ H ₂₃ N ₇	77.62	4.28	18.10	77.47	4.26	18.14
VII	2-C ₅ H ₄ N	2,6	35.7	264-265	dimethyl formamide	C ₃₁ H ₁₉ N ₁₁	68.25	3.51	28.24	67.93	3.71	28.52

TABLE II

Bis(5-Substituted triazolyl-3-yl)pyridines



R	Position of triazolyl groups in pyridine ring	Yield %	M.p. °C	Crystallization solvent	Formula	Analysis						
						Calcd. % C	Calcd. % H	Calcd. % N	Found % C	Found % H	Found % N	
VIII	C ₆ H ₅	2,4	79.0	155-156	ethanol	C ₂₁ H ₁₉ N ₇	68.27	5.18	26.54	68.29	5.07	26.80
IX	2-C ₅ H ₄ N	2,4	68.4	230-231	methyl cellosolve	C ₁₉ H ₁₇ N ₉	61.44	4.61	33.94	61.23	4.64	34.04
X	C ₆ H ₅	2,6	68.4	172-173	ethanol	C ₂₁ H ₁₉ N ₇	68.27	5.18	26.54	68.13	5.14	26.83
XI	2-C ₅ H ₄ N	2,6	84.2	250-251	ethanol	C ₁₉ H ₁₇ N ₉	61.44	4.61	33.94	61.09	4.59	34.22

EXPERIMENTAL

2,4-Pyridinedicarboxamide Dihydrazone.

A mixture of 4 g. of pyridine-2,4-dicarbonitrile (3) and 11 ml. of 95% hydrazine was allowed to stand overnight. The resulting solid was separated by filtration, dried and crystallized from ethanol to which water was added to effect solution. The yield of pure product melting at 190-191° was 3.3 g. (55%).

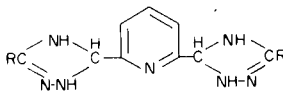
Anal. Calcd. for C₇H₁₁N₇: C, 43.51; H, 5.74; N, 50.74. Found: C, 43.19; H, 5.69; N, 50.83.

2,6-Pyridinedicarboxamide Dihydrazone.

To 1.5 g. of pyridine-2,6-dicarbonitrile (4) was added 7 ml. of 95% hydrazine and the mixture allowed to stand overnight. The resulting solid was removed by filtration, and crystallized from water. The yield of pure product, melting at 228° dec., (lit. (7) 230-231° dec.), was 2 g. (87.0%).

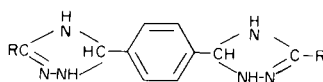
TABLE III

2,6-Bis(3-Substituted-1,2,4-triazolin-5-yl pyridines)



R	Yield %	M.p. °C	Crystal- lization solvent	Formula	Analysis						
					Calcd. %		Found %		Found %		
					C	H	N	C	H	N	
XIII	2-pyridyl	40.0	210	ethanol	C ₁₉ H ₁₇ N ₉	61.44	4.61	33.94	61.38	4.59	33.99
XIV	4-methyl- 2-pyridyl	53.1	185	ethanol	C ₂₁ H ₂₁ N ₉	63.14	5.30	31.56	63.06	5.33	31.65
XV	4-phenyl- 2-pyridyl	55.6	275	dimethyl formamide	C ₃₁ H ₂₅ N ₉	71.11	4.81	24.08	70.71	4.99	24.30
XVI	6-(2,2'-bipyridyl)	31.3	251	methyl cellosolve	C ₂₉ H ₂₃ N ₁₁	66.27	4.41	29.31	66.15	4.68	28.87

TABLE IV

5,5'-*p*-Phenylenebis(3-substituted-1,2,4-triazolines)

R	Yield %	M.p. °C	Crystal- lization solvent	Formula	Analysis						
					Calcd. %		Found %		Found %		
					C	H	N	C	H	N	
XVII	2-pyridyl	74.1	250	methyl cellosolve	C ₂₀ H ₁₈ N ₈	64.85	4.90	30.25	64.80	4.89	30.30
XVIII	4-methyl- 2-pyridyl	55.2	227-228	methyl cellosolve	C ₂₂ H ₂₂ N ₈	66.31	5.57	28.12	66.27	5.66	27.96
XIX	4-phenyl- 2-pyridyl	36.5	271	dimethyl formamide	C ₃₂ H ₂₆ N ₈	73.54	5.01	21.44	72.96	5.12	21.75

Preparation of 2,4- and 2,6-Bis(5,6-disubstituted as triazin-3-yl)pyridines.

A mixture of 0.02 mole of diketone (pyridil, benzil, or 2,3-butanedione), 0.01 mole of 2,4- or 2,6-pyridinedicarboxamide dihydrazone and 25 ml. of ethanol was heated at reflux for 2.5 hours. The precipitate obtained after cooling and filtration was then crystallized from the solvent indicated in Table I.

Preparation of 2,4- and 2,6-Bis[5-Phenyl and (2-Pyridyl)-1,2,4-triazolin-3-yl]pyridines.

A solution of 0.02 mole of benzaldehyde or pyridine-2-carboxaldehyde and 0.01 mole of 2,4- or 2,6-pyridine-dicarboxamide dihydrazone in 25 ml. of ethanol was refluxed for 2.5 hours. The solid precipitating after cooling was removed by filtration and crystallized from the solvent indicated in Table II.

Preparation of 2,6-Bis[3-(Substituted 2-pyridyl)-1,2,4-triazolin-5-yl]pyridines.

A mixture of 0.01 mole of pyridine-2,6-dicarboxaldehyde, 0.02 mole of picolinamide hydrazone, its 4-methyl or 4-phenyl derivative or 2,2'-bipyridyl-6-carboxamide hydrazone, and 25 ml. of ethanol was heated at reflux for 2.5 hours. The precipitate separating on cooling was separated by filtration and crystallized from the solvent indicated in Table III.

Preparation of 5,5'-*p*-Phenylenebis[3-(substituted-2-pyridyl)-1,2,4-triazolines].

The procedure was the same as for the preceding preparation except that terephthalaldehyde was substituted for pyridine-2,6-dicarboxaldehyde and only the first three reactants were used. The crystallizing solvents are indicated in Table IV.

REFERENCES

- (1) F. H. Case, *J. Heterocyclic Chem.*, **7**, 1001 (1970).
- (2) F. H. Case, *ibid.*, **8**, 173 (1971).
- (3) W. E. Feely and E. M. Beavers, *J. Am. Chem. Soc.*, **81**, 4004 (1959).
- (4) H. Tani, *Yakugaku Zasshi*, **80**, 1418 (1960); *Chem. Abstr.*, **55**, 6478d (1961).
- (5) F. H. Case, *J. Org. Chem.*, **30**, 931 (1965).
- (6) W. Ried and P. Schomann, *Ann. Chem.*, **714**, 122 (1968).
- (7) P. M. Hergenrother, *J. Polymer Sci. A-1*, **7**, 945 (1969).