when the group left behind is *p*-anisyl (in Ib) is 7.0 times as fast as interconversion of IIIb and IVb ($k_2/k_1 = 7.0$). Again assuming that the remote *para* substituent has no effect on rates of rotation (*i.e.*, the value of k_1 is the same for each reactant), we conclude that phenyl migration, leaving behind a carbonium ion stabilized by a hydroxyl group and a *p*-anisyl group, is faster by 10% than the migration of phenyl in a system in which the developing carbonium ion center is stabilized by the hydroxyl group and an unsubstituted phenyl group.

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[CONTRIBUTION FROM EASTERN RESEARCH LABORATORY, THE DOW CHEMICAL COMPANY]

Addition of Hydrogen Cyanide to Aromatic Schiff Bases

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Details are presented on the synthesis of *N,N'*-alkylenebis[(2-substituted) glycinonitriles] by the addition of hydrogen cyanide to aromatic bis-Schiff bases. Where thermally stable, the nitriles may be hydrolyzed to the *N,N'*-alkylenebis-2-arylglycines.

In previous publications[2] we have reported on the properties of a novel chelating agent, *N,N'*-ethylenebis[2-(*o*-hydroxyphenyl)] glycine[3] and we wish now to report the synthesis of this and of related compounds. In essence, our method consists of the addition of 2 mol. of anhydrous hydrogen cyanide to a bis-Schiff base derived from an aromatic aldehyde and a diamine, and subsequent hydrolysis of the resulting glycinonitrile to an *N,N'*-alkylenebis-2-arylglycine. Though bis-glycinonitriles have been prepared from diamine dihydrochlorides, carbonyl compounds and potassium cyanide in aqueous solution,[4,5] little data is available on the addition of anhydrous hydrogen cyanide to Schiff bases, a reaction originally discovered by Plöchl.[6]

Inasmuch as the aromatic Schiff bases are readily prepared and purified, this method offers an alternate to the usual processes for the preparation of 2-substituted amino acids. However, the reaction sequence is limited severely by the lack of reactivity of certain of the aromatic Schiff bases with hydrogen cyanide and the thermal instability of the bis-glycinonitriles. Thus, of the twenty-seven Schiff bases reported in Table I, seven (19–27) did not react at all with hydrogen cyanide and a number of the others yielded intractable oils. Attempts to catalyze the cyanide addition were not successful and the use of solvents of varied polarity, other than liquid hydrogen cyanide, offered little advantage in the case of the non-reactive Schiff bases, but was of some advantage in moderating the reaction for the more reactive compounds. The electronic nature of the substituent on the aromatic ring seems to have little or no effect on the formation of these adducts. Thus, while the *ortho*-hydroxyphenyl derivative affords product in almost quantitative yield, the corresponding 2,4-dihydroxyphenyl counterpart yields no glycinonitrile whatsoever, and is recovered unchanged.

A characteristic property of the glycinonitriles listed in Table II is their thermal instability. This undesirable feature greatly limited the number of compounds which were successfully hydrolyzed to the corresponding amino acids. Even those nitriles which could be successfully hydrolyzed had a limited stability; *N,N'*-ethylenebis[2-(*o*-hydroxyphenyl)]glycinonitrile though almost white when stored in the cold, slowly decomposed at room temperatures to give an orange brown solid which could not be characterized. A second mode of decomposition, which was typical of the heterocyclic derived Schiff bases, was their reversion to starting compounds with evolution of hydrogen cyanide. Thus, it is not surprising that only the most stable of the glycinonitriles were successfully hydrolyzed whereas the majority afforded only intractable highly colored tars. The *N,N'*-alkylenebis-2-substituted glycines are listed in Table III and some details of their preparation are given in the experimental section.

EXPERIMENTAL

Schiff bases. These were synthesized in the usual manner by reaction of the appropriate aldehyde with the proper anhydrous diamine in alcohol in a 2:1 molar ratio. Purification was accomplished by recrystallization from alcohol. In the case of the 2-pyridine aldehyde- and 6-methyl-2-pyridinealdehyde-derived Schiff bases, reaction was conducted under a blanket of nitrogen using a few drops of glacial acetic acid to expedite reaction. Ligroin (66–75°)

(1) Present address: Chas. Pfizer and Co., Inc., Brooklyn, New York.

(2) H. H. Freedman, A. E. Frost, S. J. Westerback, and A. E. Martell, *Nature*, **179**, 1020 (1957); *J. Am. Chem. Soc.*, **80**, 530 (1958).

(3) Concurrent with our initial publication, a communication appeared by H. Kroll, M. Knell, J. Powers, and J. Simonian, *J. Am. Chem. Soc.*, **79**, 2024 (1957), which reported the synthesis of this compound by a method substantially identical to ours.

(4) N. Schlesinger, *Ber.*, **45**, 1486 (1912).

(5) H. Zahn and H. Wilhelm, *Ann.*, **579**, 1 (1953).

(6) J. Plöchl, *Ber.*, **13**, 2118 (1880).

TABLE I

BIS-SCHIFF BASES R—CH=N—Y—N=CHR

	R	Y	M.P.	Yield, %	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found	Nitrogen, % Calcd.	Nitrogen, % Found
1	Phenyl	Ethylene	52[a]	75.8						
2	*o*-Hydroxyphenyl	Ethylene	126–127[b]	Quant.						
3	*o*-Hydroxyphenyl	1,2-Propylene	Oil[c]	75.0						
4	*o*-Hydroxyphenyl	Trimethylene	54–55[d]	91.3						
5	*o*-Hydroxyphenyl	*o*-Phenylene	164–169[e]	36.4						
6	*m*-Hydroxyphenyl	Ethylene	198–200[f]	68.7						
7	*p*-Hydroxyphenyl	Ethylene	222–226	68.3	57.8	56.8	4.9	6.2	8.4	11.0
8	*o*-Methoxyphenyl	Ethylene	117–119[g]	68.5						
9	*p*-Methoxyphenyl	Ethylene	112–114[h]	79.5						
10	*o*-Chlorophenyl	Ethylene	88–89	76.4	63.0	62.7	4.6	4.6	9.2	9.2
11	*o*-Toluyl	Ethylene	55–56	41.7						
12	*p*-Toluyl	Ethylene	158–160	72.0	81.8	81.5	7.6	7.8	10.6	10.7
13	1-Naphthyl	Ethylene	136.5–138	83.2	85.7	85.7	6.0	6.0	8.3	8.4
14	2-Thienyl	Ethylene	91.5–93[i]	34.0						
15	2-Furyl	Ethylene	53–54[j]	60.0						
16	2-Pyridyl	Ethylene	67–68[k]	67.2						
17	2-Lutidyl	Ethylene	69–72	—	72.2	72.4	6.8	6.8	21.0	20.7
18	*o*-Hydroxyphenyl	Imino*bis*-ethylene	Oil							
19	2,5-Dihydroxyphenyl	Ethylene	248 (dec.)	Quant.	64.0	64.0	5.4	5.4	9.3	9.3
20	2,4-Dihydroxyphenyl	Ethylene	192 (dec.)	—	64.0	63.6	5.4	5.4	9.3	9.2
21	2-Hydroxy-5-chlorophenyl	Ethylene	183–185	66.4	57.0	57.0	4.2	4.2	8.3	8.3
22	2-Hydroxy-5-nitrophenyl	Ethylene	260	Quant.	53.6	53.9	3.9	4.2	15.7	15.9
23	1-(2-Hydroxynaphthyl)	Ethylene	311 (dec.)[d]	—						
24	1-(4-Hydroxynaphthyl)	Ethylene	250 (dec.)	—	78.2	77.8	5.5	5.5	7.6	7.8
25	2-(3-Hydroxynaphthyl)	Ethylene	285	64.0						
26	1-(2-Methoxynaphthyl)	Ethylene	292–294	90.0	78.8	78.6	6.1	5.9	7.1	7.4
27	*o*-Hydroxyphenyl (H=CH_3)	Ethylene	202–203	Quant.	73.0	72.8	6.8	6.7	9.5	9.6

[a] Mason, *Ber.*, 20, 267 (1887) reports m.p. 53–4°. [b] Ref. a, reports m.p. 125–126°. [c] Strache, *Ber.*, 21, 2358 (1888) reports a yellow oil. [d] Pfeiffer, *et al.*, *J. Prakt. Chem.*, 149, 217 (1937) report a yellow oil. [e] Ref. d, m.p. 163°. [f] Bogoslovskii, *J. Gen. Chem.* (*U.S.S.R.*), 14, 995 (1944), m.p. 189–191.5°. [g] Ref. a, m.p. 113°. [h] Ref. a, m.p. 110–111°. [i] Eichhorn and Bailar, *J. Am. Chem. Soc.*, 75, 2905 (1953). [j] Ramceau, *Rec. trav. chim.*, 57, 194 (1938). [k] Busch and Bailar, *J. Am. Chem. Soc.*, 78, 1137 (1956).

TABLE II

N,N'-ALKYLENEBIS[(2-SUBSTITUTED)GLYCINONITRILES]

Compd.[d]	M.P.	Yield, %	Carbon Calcd.	Carbon Found	Hydrogen Calcd.	Hydrogen Found	Nitrogen Calcd.	Nitrogen Found
1	118–123 dec.[a]	75.8	74.5	74.2	6.3	6.2	19.3	19.3
2	125–126 dec.[b]	99.0	67.1	67.1	5.7	5.6	17.4	17.2
3	Oil	—						
4	Oil	—		(Crude oil hydrolyzed without purification)				
5	Oil	—						
6	Oil	—						
7	130 dec.	83.4	67.1	67.6	5.6	6.6	17.4	16.6
8	Oil	—						
9	95–97 dec.	81.4	68.6	68.5	6.3	6.5	16.0	15.5
10	80–99 indef.	—						
11	Amorphous	—	75.4	75.2	7.0	7.0	17.6	17.5
12	127–132 dec.	Quant.	75.4	75.3	7.0	7.1	17.6	17.3
13	152 dec.	Quant.	80.0	79.8	5.7	5.6	14.4	14.1
14	87–90 dec.	—						
14[c]			—	—	—	—	14.9	14.9
15	87–91 dec.	—	62.2	58.7	5.2	5.0	20.7	20.5
15[c]			48.0	47.4	4.7	4.6	16.3	15.9
16	96–102 dec.	—	65.7	65.6	5.5	5.8	28.7	27.9
17	Oil	—	72.2	72.4	6.8	6.8	21.0	20.7
18	Oil	—	65.9	65.0	6.4	7.3	19.2	18.6

[a] Ref. 4 gives m.p. 122–123°. [b] Ref. 3 gives m.p. 113–115°. [c] Dihydrochloride. [d] The numbers refer to the parent compounds as given in Table I.

TABLE III

N,N-ALKYLENEBIS[(2-SUBSTITUTED)GLYCINES]

Compd.[d]	M.P.	Yield, %	Hydrolysis Method	Analyses					
				Carbon		Hydrogen		Nitrogen	
				Calcd.	Found	Calcd.	Found	Calcd.	Found
1	>280[a]	Quant.	II	65.8	65.1	6.2	6.2	8.5	8.6
2	234–235 (dec.)[b]	75	I	60.0	59.8	5.6	5.8	7.8	7.9
4	234–238 (dec.)	53	I	60.9	60.6	6.5	6.2	7.5	7.6
7	240–245 (dec.)	29	II	60.0	58.2	5.6	5.9	7.8	7.5
9	246 (dec.)	25	I	61.8	59.7	6.23	6.0	7.2	7.0
10	202–207 (dec.)	10	II	54.4	52.9	4.6	4.6	7.1	6.4
18[c]	—	17[c]	I	47.0	46.8	5.3	5.8	8.2	9.4

[a] Ref. 4 reports m.p. >250°. [b] Ref. 3 gives no m.p. [c] As the trihydrochloride, Cl, Calcd. 20.7, Found 20.7. [d] See footnote d, Table II.

was used as recrystallizing solvent. Pertinent data are reported in Table I.

Reaction with liquid hydrogen cyanide: Preparation of N,N'-alkylenebis(2-substituted)glycinonitriles. The general procedure consisted in adding to the Schiff base at 5–10° with efficient stirring, a 4 to 5 molar excess of liquid hydrogen cyanide or an amount sufficient to give a good slurry.[7] When reaction took place, solution of the Schiff base occurred within a few min., followed in some instances, by precipitation of the adduct. In such cases separation was affected by filtration followed by air drying or by adding a ten-fold volume of water and stirring thoroughly, followed by filtration and further washing with water. When precipitation did not occur, the excess liquid hydrogen cyanide was removed by aspiration or by evaporation at room temperature since the application of heat usually caused decomposition of the adducts. The adducts were generally analytically pure requiring no further purification. Pertinent data are listed in Table II. For convenience, reaction was conducted in a flask fitted with a sintered glass disc and stop-cock arrangement to minimize handling of the liquid hydrogen cyanide.

Hydrolysis of adducts. Preparation of N,N'-alkylenebis(2-substituted)glycines. Method I. The first general procedure involved adding 4–5 ml. of cold concentrated hydrochloric acid per gram of nitrile and, once the initial exothermic reaction had subsided, heating the mixture on a steam bath for a few min. The acids often separated as their hydrochlorides from which the free acids were obtained by neutralization. When separation did not occur, the free acids were isolated by neutralization with 30% sodium hydroxide to *p*H 4–5 followed by filtration and thorough washing with water, in which most were insoluble. Recrystallizations were effected from methanol.

Method II. The second general procedure was that of Schlesinger.[4] This consisted in adding 10 ml. of a concentrated hydrochloric acid-concentrated sulfuric acid mixture (1–5 by volume) per gram of nitrile at a temperature below 35°. After three days at room temperature, an equal volume of water was added, the mixture heated to reflux for one hour, and the acid isolated as above. Data on the various acids are summarized in Table III.

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(7) Inasmuch as the reaction may be vigorously exothermic after passing through an induction period, it is strongly recommended that all the usual precautions for working with liquid hydrogen cyanide be observed and that the reaction be limited to a 0.1 mol. scale.

[CONTRIBUTION FROM THE POLYMER RESEARCH LABORATORY, THE DOW CHEMICAL CO.]

Organic Chemistry of α-Methylstyrene. I. Reactions Leading to *N*-(α,α-Dimethyl-substituted-benzyl)acrylamides

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The reactions of α-methylstyrene, *p*-chloro-α-methylstyrene, *p*-bromo-α-methylstyrene, and *m*-trifluoromethyl-α,α-dimethylbenzyl alcohol with acrylonitrile have been investigated and three of the corresponding *N*-substituted acrylamides prepared. α-Methylstyrene or *p*-substituted-α-methylstyrenes (*p*-substituent *ortho-para* directing) under the above reaction conditions preferentially dimerize rather than react with acrylonitrile. The carbonium ion from *m*-trifluoromethyl-α,α-dimethylbenzyl alcohol or the dehydration product appears to be less reactive with another *m*-trifluoromethyl-α-methylstyrene than with the nitrogen of acrylonitrile; the product obtained in good yield is *N*-(*m*-trifluoromethyl-α-α-dimethylbenzyl)-acrylamide.

The reaction of 2-phenyl-2-propanol with acid leads to the formation of 2-phenylpropene (α-methylstyrene) as the major product. If 2-phenylpropene is let stand in an acid medium under various conditions of solvent, acid strength, and temperature, three dimeric products result: 2,4-diphenyl-4-methylpentene-1 (II), 2,4-diphenyl-4-methylpentene-2 (III), and 1,1,3-trimethyl-3-phenylindane (IV). These products may be considered to arise from the reaction of a cumyl carbonium ion with 2-