NOTES

Nicotinic Acid. Miscellaneous Esters[1]

By C. O. Badgett and C. F. Woodward

Several esters of nicotinic acid have been reported recently.[2,3] Some new miscellaneous esters have been prepared in this Laboratory, and, since the work has been terminated, we are reporting these compounds and the two additional methods used in their preparation.

The first method used was the direct reaction of the alcohol with nicotinyl chloride hydrochloride. The second method involves the reaction of nicotinic anhydride[4] with the alcohol. The following examples will serve to illustrate the methods.

Method A. Glycol Dinicotinate

Into a round-bottomed, three-necked flask equipped with air-tight stirrer, dropping funnel, and condenser equipped with a calcium chloride drying tube was placed 61.5 g. (0.5 mole) of nicotinic acid. Stirring was started, and 178 g. (1.5 moles) of redistilled thionyl chloride was added dropwise at a fairly rapid rate. After addition was complete, the reaction mixture was refluxed for two hours. The condenser was then set for distillation, and the excess thionyl chloride was distilled off while the reaction mixture was stirred to prevent formation of a hard cake. Approximately 300 cc. of anhydrous benzene was added. The nicotinyl chloride hydrochloride was filtered off, washed twice with 100-cc. portions of anhydrous benzene and sucked almost dry on a Buchner funnel.

The nicotinyl chloride hydrochloride was immediately transferred to a 600-cc. beaker, and 9 g. (0.145 mole) of ethylene glycol was added with stirring. The reaction was exothermic. After evolution of hydrogen chloride had ceased, the mixture was heated to about 100° on a hot-plate with continuous stirring for fifteen minutes. The reaction mixture was then dissolved cautiously in water and made strongly alkaline with concentrated ammonium hydroxide, and the crystalline glycol dinicotinate was filtered off. The product was washed with three 100-cc. portions of dilute ammonium hydroxide and dried. The yield was 36 g. or 91.2% of theoretical. The glycol dinicotinate thus prepared had a m. p. of 127.0–128.0°. Recrystallization from 400 cc. of 40% alcohol following Norit treatment gave 32 g. of product of the same melting point. Three recrystallizations did not raise the melting point.

Method B. Trinicotinin

Into a 200-cc. round-bottomed, three-necked flask equipped with a stirrer and reflux condenser equipped with a drying tube, was placed 20.5 g. (0.09 mole) of nicotinic anhydride, 12 cc. of anhydrous pyridine and 1.84 g. (0.02 mole) of redistilled, anhydrous glycerol. The mixture was heated on the steam-bath for four hours with continuous stirring. The reaction mixture was poured into 100 cc. of water and made strongly alkaline with sodium carbonate solution, and the oil layer was extracted with three 40-cc. portions of chloroform. The chloroform extract was washed with three 25-cc. portions of water and dried over anhydrous sodium sulfate. The chloroform and pyridine were removed by evaporation, leaving an oil which crystallized when scratched with a stirring rod and cooled in an ice-bath. The yield of trinicotinin was the theoretical. The melting point was 87.7–88.8°. The melting point was not raised by repeated recrystallization from acetone-petroleum ether.

Isopropylidene glycerol[5,6] and α-monomyristin[7] were prepared in accordance with the literature methods and used in the preparation of the mixed glycerides. Table I gives the analytical data and physical constants of the new esters.

TABLE I

PROPERTIES OF NICOTINIC ACID ESTERS

Compound[a]	Formula	M. p., °C.	Carbon Calcd.	Carbon Found	Hydrogen Calcd.	Hydrogen Found	Nitrogen Calcd.	Nitrogen Found	Milliequiv. alkali per g. of ester Calcd.	Milliequiv. alkali per g. of ester Found
Nicotinate										
Phenyl	$C_{12}H_9NO_2$	74.2–75.0	72.35	72.69	4.55	4.70	7.03	6.87	5.02	5.01
Cyclohexyl	$C_{12}H_{15}NO_2$	[b]	70.22	70.29	7.37	7.34	6.82	6.79	4.87	4.84
Isopropylidene glycerol[c]	$C_{12}H_{15}NO_4$	41.4–41.9[d]	60.75	60.27	6.37	6.33	5.91	5.85	4.21	4.18
Glycol di-[e]	$C_{14}H_{12}N_2O_4$	126.7–127.1	61.76	62.30	4.44	4.94	10.29	10.29	7.34	7.35
α-Naphthyl	$C_{16}H_{11}NO_2$	70.0–70.6	77.09	77.45	4.41	4.68	5.63	5.62	4.01	4.02
Pentaerythritol tetra-	$C_{29}H_{24}N_4O_8$	162–163	62.58	62.30	4.35	4.49	10.07	9.61	7.20	7.20
Inositol hexa-	$C_{42}H_{30}N_6O_{12}$	254.3–254.9	62.22	62.16	3.73	4.12	10.37	9.97	7.40	7.36
Trinicotinin[f]	$C_{21}H_{17}N_3O_6$	87.6–87.8	61.91	61.42	4.21	4.34	10.31	10.28	7.36	7.39
α-Monomyristin dinicotinin[c]	$C_{29}H_{40}N_2O_6$	58.6–59.2	67.94	68.07	7.87	8.04	5.47	5.42	5.85	5.85

[a] These substances were all made by Method A unless otherwise indicated. [b] B. p. 144.5° at 4.1 mm.; $n^{25}D$ 1.5177; d^{25}_4 1.0941. [c] Used Method B. [d] B. p. 143–144° at 1.2 mm. [e] Yield, Method A, 91.2%; yield, Method B, 93.6%. [f] Used Methods A and B.

(1) Article not copyrighted.

(2) Badgett, Provost, Ogg and Woodward, This Journal, **67**, 1135 (1945).

(3) Huber, Boehme and Laskowksi, *ibid.*, **68**, 187 (1946).

(4) Badgett, *ibid.*, **69**, 2231 (1947).

(5) Irvine, McDonald and Soutar, *J. Chem. Soc.*, **107**, 337 (1915).

(6) Newman and Renoll, This Journal, **67**, 1621 (1945).

(7) Averill, Roche and King, *ibid.*, **51**, 866 (1929).

Eastern Regional Research Laboratory
Philadelphia, Penna. Received July 14, 1947

The Iodination of ω-Cyanoacetophenone

By W. M. Hearon and A. F. Helin

During the course of work with 2-(cyanoacetyl)-coumarone, the material, when treated with iodine

and aqueous sodium hydroxide, gave a yellow precipitate having an odor and melting point like that of iodoform. The material was not iodoform as shown by a mixed melting point.

This reaction has been studied using ω-cyanoacetophenone and found to produce the hitherto unreported triiodoacetonitrile along with benzoic acid. Triiodoacetonitrile is an unstable material, decomposing on standing to give iodine, cyanogen iodide, and an unidentified oil. Heating triiodoacetonitrile with aqueous sodium hydroxide produces carbon tetraiodide, ammonia, sodium carbonate, and an unidentified isocyanide.

Experimental

Preparation of Triiodoacetonitrile.—To a solution of 1.0 g. (0.0069 mole) of ω-cyanoacetophenone[1] in 30 ml. of 10% sodium hydroxide diluted to 100 ml. was added 5.3 g. (0.021 mole) of iodine and 10.0 g. of potassium iodide in 75 ml. of water. The yellow precipitate was sucked off, washed with water, and dried at 3° for fourteen hours. The product, 2.3 g. (80% yield) melted at 120–122° dec., and, when mixed with iodoform, melted at 110°. It was soluble in common organic solvents with liberation of iodine.

Anal. Calcd. for C_2I_3N: C, 5.7; H, 0.0; N, 3.3; I, 90.9. Found: C, 5.5; H, 0.06; N, 3.2; I, 90.4. Calcd. for diiodoacetonitrile, C_2HI_2N: C, 8.2; H, 0.34; N, 4.8; I, 86.7.

The product, stable when wet, was unstable dry but could be dried under carbon dioxide or nitrogen. Washing the wet product with aqueous potassium iodide also increased its stability during drying. Triiodoacetonitrile, dried by any of the above methods, decomposed on standing to give iodine, a brown oil, and white needles of cyanogen iodide, which sublimed from the decomposition mixture—m. p. 132–133°; recorded,[2] 146.0°.

Anal. Calcd. for ICN: C, 7.8; H, 0.0; N, 9.2; I, 83.0. Found: C, 8.1; H, 0.2; N, 9.3; I, 80.0.

With quinoline in ether, the cyanogen iodide gave a complex melting at 102–103°; recorded, 104°.[3]

The filtrate from the triiodoacetonitrile preparation gave 1.134 g. crude and 0.461 g. pure (or 55%) benzoic acid which did not depress the melting point of an authentic sample.

Triiodoacetonitrile and Sodium Hydroxide.—One gram of triiodoacetonitrile in 25 ml. of 5% aqueous sodium hydroxide was heated at 60° for one hour with stirring. The reddish-orange solid was sucked off and steam-distilled to remove unchanged triiodoacetonitrile. The red solid remaining was sublimed at 130–140° under 1–2 mm. pressure, giving crystals of carbon tetraiodide.

Anal. Calcd. for CI_4: C, 2.3; H, 0.0; N, 0.0; I, 97.7. Found: C, 2.6; H, 0.05; N, less than 0.1; I, 97.1.

The filtrate above gave a positive test for ammonia, carbonate ion, and an isocyanide by odor and by acid hydrolysis to formic acid.

(1) Prepared by the method of Arndt and Loewe, *Ber.*, **71**, 1630 (1938).

(2) Cook and Robinson, *J. Chem. Soc.*, 1002 (1935).

(3) Mumm and Bruhn, *Ber.*, **68**, 176–183 (1935).

DEPARTMENT OF CHEMISTRY
MASSACHUSETTS INSTITUTE OF TECHNOLOGY
CAMBRIDGE 39, MASSACHUSETTS RECEIVED AUGUST 2, 1947

Purification of Thianaphthene

BY CORWIN HANSCH

In the preparation of thianaphthene by the reduction of 3-thianaphthenol[1,2] with zinc and acetic acid, thianaphthene is obtained which does not have a sharp melting point and apparently contains small amounts of 2,3-dihydrothianaphthene. Refluxing thianaphthene thus prepared with 10% by weight of sulfur for four hours, then isolating the product by steam distillation from a dilute sodium hydroxide solution, gives thianaphthene melting sharply at 32°.

(1) Friedländer, *Ber.*, **41**, 231 (1908).

(2) Hansch and Lindwall, *J. Org. Chem.*, **10** 381 (1945).

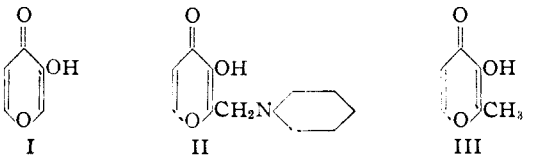
POMONA COLLEGE
CLAREMONT, CALIFORNIA RECEIVED JULY 10, 1947

A Synthesis of Maltol

BY M. A. SPIELMAN AND MORRIS FREIFELDER

Maltol (III) has been isolated from pine needles,[1] larch bark,[2] the destructive distillates of various organic materials[3] and the alkaline hydrolysis products of streptomycin.[4] However, no synthesis has been reported.

We have condensed pyromeconic acid (I) with piperidine and formaldehyde to give the Mannich base (II). There was no evidence of a second



I II III

condensation such as takes place with kojic acid, a similar 3-hydroxy-4-pyrone.[5] Hydrogenation of the base over a palladium catalyst gave maltol (III) in poor yield. Meconic and pyromeconic acids have been made artificially,[6] and the total synthesis of maltol is therefore complete.

Experimental[7]

3-Hydroxy-2-piperidinomethyl-4-pyrone.—To 3.5 g. of pyromeconic acid in 20 ml. of alcohol was added 2.8 ml. of piperidine and 1.4 ml. of 40% aqueous formaldehyde. There was a mild heat of reaction after which the mixture was heated for five minutes on the steam-bath. It was cooled, acidified with ethereal hydrogen chloride, diluted with two volumes of ether and left in the cold for several hours. The precipitate was recrystallized from 1:5 alcohol–acetone. The yield of pure hydrochloride, m. p. 193–195° with foaming, was 2.8 g. and 0.5 g. of less pure product, m. p. 189–190°, was recovered from the mother liquors.

Anal. Calcd. for $C_{11}H_{16}ClNO_3$: N, 5.70. Found: N, 5.73.

The free base was prepared with the aid of silver carbonate. It is very soluble in the usual organic solvents except petroleum ether. After two crystallizations from benzene–petroleum ether, it melted at 125–126°.

Anal. Calcd. for $C_{11}H_{15}NO_3$: N, 6.69. Found: N, 6.61.

(1) Feuerstein, *Ber.*, **34**, 1804 (1901).

(2) Peratoner and Tamburello, *ibid.*, **36**, 3407 (1903).

(3) Brand, *ibid.*, **27**, 806 (1894); Kiliani and Bazlen, *ibid.*, **27**, 3115 (1894); Erdmann and Schaefer, *ibid.*, **43**, 2398 (1910); Reichstein and Beitter, *ibid.*, **63**, 824 (1930); Goos and Reiter, *Ind. Eng. Chem.*, **38**, 132 (1946).

(4) Schenck and Spielman, THIS JOURNAL, **67**, 2276 (1945).

(5) Woods, *ibid.*, **68**, 2744 (1946).

(6) Peratoner, *C. A.*, **6**, 994 (1912); Thoms and Pietrulla, *Ber. pharm. ges.*, **31**, 4 (1921); Wibaut and Kleipool, *Rec. trav. chim.*, **66**, 24 (1947).

(7) Microanalyses by E. F. Shelberg.

Maltol.—To 189 mg. of the above hydrochloride in 10 ml. of water was added 1 ml. of *N* sodium hydroxide and 50 mg. of palladium-on-charcoal catalyst. It was shaken twenty hours at 25° under 20 mm. more than atmospheric pressure of hydrogen. The absorption was 1.05 molar equivalents. The solution was acidified with hydrochloric acid and extracted several times with chloroform. Evaporation of the chloroform left a gummy brown solid from which maltol was isolated by sublimation at 130° followed by crystallization from benzene. The yield was 7 mg., m. p. and mixed m. p. 160–162°.[8]

Anal. Calcd. for $C_6H_6O_3$: C, 57.14; H, 4.80. Found: C, 57.48; H, 4.76.

Many hydrogenations were conducted, and the above is typical. The highest yield of maltol (17%) was obtained when the Mannich base hydrochloride was hydrogenated in absolute alcohol over palladium-on-charcoal at 100° and 100 atmospheres pressure. Adams platinum oxide catalyst and Raney nickel led to no maltol whatever. Chemical reduction with sodium methoxide[9] also failed.

The benzoate of synthetic maltol was prepared with benzoyl chloride in pyridine. It melted at 112–113° and the mixed m. p. was 113–114°.

(8) We are indebted to The Cliffs Dow Chemical Corporation of Marquette, Michigan, for a sample of pure maltol from wood distillates.

(9) Cornforth, Cornforth and Robinson, *J. Chem. Soc.*, 682 (1942); Woodward and Doering, THIS JOURNAL, **67**, 863 (1945).

ABBOTT LABORATORIES
NORTH CHICAGO, ILLINOIS RECEIVED JULY 11, 1947

On the Correlation of the Spectroscopic and Thermal Energy Differences between the Fluorescence and Phosphorescence Levels of Dye Molecules

BY M. KASHA AND R. E. POWELL

A general interpretation of the fluorescence and phosphorescence properties of polyatomic molecules on the basis of potential curve crossing suggests a limitation in the validity of the mechanism of luminescence of dyes proposed by Jablonski.[1] Whereas the scheme proposed by Jablonski uses a line energy level diagram, the new interpretation involves a radiationless intersystem "crossing" of potential curves for the first two electronic states above the ground state,[2] as shown in the figure. The potential curves as drawn represent time-average cross-sections, of the potential energy hypersurfaces for the electronic states, along the critical coördinate involved in the excitation of the triplet state[3] of the molecule. An analysis of the rates of the various processes occurring in the S′ state led to the conclusion that for a maximum probability of interaction[4] between the S′ and T states, the "crossing" must occur at the lowest point of the upper curve.

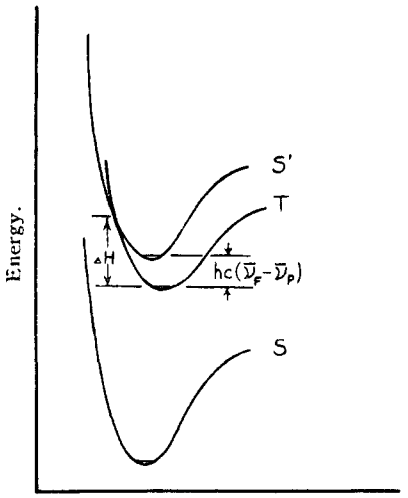


Fig. 1.—Schematic potential energy curves for the three lowest electronic states of a dye molecule.

According to the line energy level scheme of Jablonski, the spectroscopic energy difference between the zero-point energy levels of the fluorescent (unstable) and phosphorescent (metastable) states of a dye should be equal to the heat of activation required for lifting molecules from the phosphorescent to the fluorescent state. This theorem apparently was confirmed by the experiments of Lewis, Lipkin and Magel,[5] in which the fluorescence–phosphorescence energy difference for acid fluorescein dye in boric acid glass was found spectroscopically to be 9 kcal., while the heat of activation as determined by the temperature coefficient of the alpha process[6] of phosphorescence was found to be 8 ± 1 kcal.

However, according to the mechanism of excitation of the phosphorescent state based on potential curve crossing, the two experimental energy quantities may differ considerably in magnitude, if the point of crossing is not at the lowest point of the upper curve. This is shown in the figure, which compares schematically the two energy values for a case of high crossing. According to this picture, the heat of activation should equal or exceed the spectroscopic difference between the zero-point levels of the fluorescent and phosphorescent states.

For the best demonstration of this lack of correlation between the two energy values, (a) the dye should have as small an interval as possible between the zero-point levels of the S′ and T states, and (b) the emission spectra should have

(1) A. Jablonski, *Z. Physik*, **94**, 38 (1935).

(2) M. Kasha, *Chem. Rev.*, in process of publication.

(3) The triplet state theory of phosphorescence as developed by Lewis and Kasha (THIS JOURNAL, **66**, 2100 (1944); **67**, 994 (1945)) is assumed in this treatment, although metastability of an electronic level may be due to various causes. However, the spectroscopic and magnetic studies of the phosphorescent state conducted in this laboratory have given strong evidence that the relatively long-lived, temperature-independent luminescence (β-phosphorescence) occurring 2000 to 12,000 cm.$^{-1}$ lower than the normal absorption band is, in general, due to a triplet–singlet transition.

(4) In the absence of heavy or paramagnetic atoms, and strong fields.

(5) Lewis, Lipkin and Magel, THIS JOURNAL, **63**, 3005 (1941).

(6) α-Phosphorescence involves a T–S′ thermal activation, followed by S′–S emission. Thus, although relatively long-lived, its spectrum is identical with the normal fluorescence spectrum. β-Phosphorescence corresponds to spontaneous T–S emission.

sharply defined structure, to permit an accurate determination of the interval between the zero-point levels[7] of the electronic states. Furthermore, a low relative quantum yield of phosphorescence (α plus β), compared with fluorescence, indicating a high point of crossing, should correspond to a large discrepancy of the two energy values as shown in the figure. The luminescence properties of such molecules as porphyrin, phthalocyanine and chlorophyll makes them especially suited for use in experiments to test these ideas.

In the case of acid fluorescein dye, aside from uncertainties in determining the spectroscopic energy value due to diffuseness of the emission bands, the high relative quantum yield of phosphorescence probably favored the correlation between the spectroscopic and thermal values.

A recent paper on the luminescence of inorganic crystalline impurity "phosphors" by Williams and Eyring[8] proposes an energy-coördinate diagram somewhat similar to the one discussed here. However, it will be noted that the physical systems and some aspects of the phenomena differ considerably in the two cases. Thus, in the present case the system consists of dilute solutions of the complex molecule in a homogeneous rigid *glassy* medium. Furthermore, the process of luminescence consists of transition between electronic levels of the complex molecule itself, with no electron transfer to the medium. In the phenomena treated by Williams and Eyring, energy levels of the crystal lattice are involved, with electron transfer from the absorbing center.

Although Williams and Eyring studied thermal properties of the inorganic phosphors, no spectroscopic data such as required for the correlation described above were included, although it is possible that an analogous relationship of spectroscopic and thermal energies may exist for inorganic luminescent materials.

(7) The frequency of maximum intensity of a diffuse emission band (such as is obtained for an ionic dye) does not, of course, give the fundamental energy of the excited state, but merely the frequency of most probable emission, according to the Franck-Condon principle.

(8) F. E. Williams and H. Eyring, *J. Chem. Phys.*, **15**, 289 (1947).

DEPARTMENT OF CHEMISTRY
UNIVERSITY OF CALIFORNIA
BERKELEY, CALIFORNIA RECEIVED MAY 7, 1947

One-Step Synthesis of 1,2,3,4-Tetrahydrocarbazole and 1,2-Benzo-3,4-dihydrocarbazole

BY CROSBY U. ROGERS AND B. B. CORSON

1,2,3,4-Tetrahydrocarbazole has previously been synthesized in two steps—isolation of cyclohexanone phenylhydrazone followed by ring closure.[1] We have found that certain hydrocarbazoles, such as 1,2,3,4-tetrahydrocarbazole and 1,2-benzo-3,4-dihydrocarbazole, can be prepared by a one-step process which by-passes the isolation of the intermediate phenylhydrazones. There is considerable merit in this abbreviation of the synthesis because these phenylhydrazones are not stable. For example, cyclohexanone phenylhydrazone, although a clean, crystalline compound when first prepared, decomposes in a few days to a sticky, brown mass. An organic acid such as formic, acetic, or propionic can be used as combination solvent and catalyst, or the reaction medium can be water or aqueous alcohol with hydrochloric, phosphoric or sulfuric acid as catalyst.

(1) Drechsel, *J. prakt. Chem.*, **38**, 69 (1888); Baeyer and Tutein, *Ber.*, **22**, 2178 (1889); Baeyer, *Ann.*, **278**, 88 (1893); Borsche, *ibid.*, **359**, 49 (1908); Perkins and Plant, *J. Chem. Soc.*, **119**, 1825 (1921); Ghigi, *Gazz. chim. ital.*, **60**, 194 (1930).

Experimental

Organic Acid Method.—Phenylhydrazine (108 g., 1 mole) was added during one hour to a stirred, refluxing solution of 98 g. (1 mole) of cyclohexanone in 360 g. of glacial acetic acid. After refluxing and stirring an additional hour, the mixture was cooled to 5° and filtered. The crude solid was washed with water, 75% methyl alcohol, and air dried (yield, 150 g., 88%). Crystallization from methyl alcohol gave a first crop of 120 g. and a second crop of 24 g. The reaction goes equally well if acetic acid is replaced by formic or propionic acid. The solubilities of 1,2,3,4-tetrahydrocarbazole in 10 cc. of various solvents are: methyl alcohol, 0.5, 1.2, 1.8 g. at 10, 35, 55°, respectively; acetic acid, 0.5, 1.1, 2.0, 3.0 g. at 20, 39, 58, 68°, respectively; cyclohexane, 0.1, 0.5, 0.9, 1.5 g. at 1, 54, 69, 77°, respectively.

Aqueous Mineral Acid Method.—To a stirred, refluxing mixture of 500 cc. of water and 172 cc. (2 moles) of concentrated hydrochloric acid (d. 1.18) was added 108 g. of phenylhydrazine during five minutes. α-Tetralone[2] (145 g., 1 mole) was added during one hour, and the mixture was stirred and refluxed for an additional four hours. Worked up as above, the first crop was 123 g. and the second crop was 74 g.; 90% total yield. The solubility of 1,2-benzo-3,4-dihydrocarbazole in 10 cc. of methyl alcohol is 0.2, 0.5 and 0.8 g. at 0, 30 and 50°, respectively.

Aqueous Alcohol–Mineral Acid Method.—A mixture of 108 g. of phenylhydrazine, 920 cc. of 75% ethyl alcohol and 1.5 moles of hydrochloric acid was stirred and refluxed while 98 g. of cyclohexanone was added during one hour. The yield of air-dried 1,2,3,4-tetrahydrocarbazole was about 95%.

Where phosphoric acid was substituted for hydrochloric acid, the usual yield of tetrahydrocarbazole was obtained, but the product was contaminated by ammonium phosphate, although it was readily purified by crystallization from methyl alcohol. Where formic acid was employed in the aqueous alcohol–mineral acid method, the product was β-formylphenylhydrazine.[3] The latter was converted to tetrahydrocarbazole by boiling with an acetic acid or formic acid solution of cyclohexanone. β-Acetylphenylhydrazine remained unchanged upon similar treatment.

Inapplicability of Acetic Acid and Mineral Acid Methods for Synthesis of 6-Nitro-1,2,3,4-Tetrahydrocarbazole.—Refluxing a glacial acetic acid solution containing equivalent amounts of *p*-nitrophenylhydrazine and cyclohexanone produced an 80% yield of β-acetyl-*p*-nitrophenylhydrazine melting at 211–212°. The previously reported melting point of this compound was 205–206°.[4]

Anal. Calcd. for $C_8H_9N_3O_3$: C, 49.2; H, 4.7; N, 21.5. Found: C, 48.9; H, 4.8; N, 21.5.

(2) Where the α-tetralone was not pure, owing to contamination with 5–10% of α-tetralol, the appropriate excess was added to compensate for the lack of purity. The ketone-alcohol mixture was analyzed according to Bryant and Smith, THIS JOURNAL, **57**, 57 (1935).

(3) Hirst and Cohen, *J. Chem. Soc.*, **67**, 829 (1895).

(4) Freund and Haase, *Ber.*, **26**, 1316 (1893); Hyde, *ibid.*, **32**, 1811 (1899).

TABLE I

YIELDS AND CONSTANTS OF HYDROCARBAZOLES

Carbazoles	% Yield, crude	M. p., °C. (cor.)	Analyses, % Calculated C	H	N	Mol. wt.	Found C	H	N	Mol. wt.
1,2,3,4-Tetrahydro-[a]	88[d]–95[e]	117–118	84.2	7.7	8.2	171	84.2	8.0	8.5	170
2-Methyl-1,2,3,4-tetrahydro-[b]	65[d]	98–100[g]	84.3	8.2	7.6	185	84.2	8.6	7.2	190
3-Methyl-1,2,3,4-tetrahydro-[b]	70[d]	108–111[h]	84.3	8.2	7.6	185	84.3	8.0	7.5	184
2,4-Dimethyl-1,2,3,4-tetrahydro-[a]	60[d]	103–106[i]	84.4	8.6	7.0	199	84.2	8.6	7.0	202
1,2-Benzo-3,4-dihydro-[a]	80[d]	163–164[j]	87.6	6.0	6.4	219	87.7	5.8	6.8	217
6-Nitro-1,2,3,4-tetrahydro-[c]	60[f]	169–172[k]	66.7	5.6	13.0	216	66.7	5.2	12.8	221

[a] From methyl alcohol. [b] From methyl alcohol or cyclohexane. [c] Red-brown crystals from 95% ethyl alcohol. [d] Acetic acid method. [e] Alcohol–hydrochloric acid method. [f] Aqueous mineral acid method; contaminated by *p*-nitrophenylhydrazone. [g] Borsche, *Ann.*, **359**, 62 (1908), reported 94° as m. p.; Plancher and Carrasco, *Atti. accad. Lincei*, [5] **13**, I, 632 (1904), reported 98–99°. [h] Plant and Rosser, *J. Chem. Soc.*, 2454 (1928). [i] Braun and Haensel (*Ber.*, **59**, 1999 (1926)) reported m. p. to be 96–99°; their product was red, ours was faintly yellow. [j] Ghigi, *Gazz. chim. ital.*, **60**, 194 (1930). [k] Borsche, *Ann.*, **359**, 49 (1908).

The alcohol–mineral acid method produced the *p*-nitrophenylhydrazone of cyclohexanone (m. p. 144–145°), which was converted to 6-nitro-1,2,3,4-tetrahydrocarbazole by boiling with 10% sulfuric acid according to the directions of Borsche.[5]

Purification of Hydrocarbazoles.—It has been reported that tetrahydrocarbazole quickly turns yellow-brown in the air and that it has a fecal odor.[6] We fractionally crystallized tetrahydrocarbazole from methyl alcohol and obtained a colorless, odorless product which was unchanged on standing three months in air and light. 1,2-Benzo-3,4-dihydrocarbazole was also easily purified, but the methyl-substituted tetrahydrocarbazoles became yellowish upon removal from the solvent, although the analytical values were satisfactory.

Freezing and Melting Points of 1,2,3,4-Tetrahydrocarbazole.—Four successive cooling curve determinations were made on a sample of highly purified tetrahydrocarbazole. The slope of the first plateau was zero within the accuracy of the determination, but the slopes of the subsequent plateaus became successively greater. The extrapolated freezing points were 118.4, 117.2, 115.4 and 111.7°, respectively. Purified tetrahydrocarbazole showed a capillary melting point (cor.) of 117–118° with the usual rate of heating; but with slow heating (1° per min.), the melting point was 113–114°, and the sample started to soften at 109°.

(5) Borsche, *Ann.*, **359**, 52 (1908).

(6) Zanetti, *Ber.*, **26**, 2006 (1893).

MULTIPLE FELLOWSHIP ON TAR SYNTHETICS
KOPPERS CO., INC.
MELLON INSTITUTE
PITTSBURGH, PENNA.

RECEIVED JULY 3, 1947

The Preparation of 4-Thiazolidones by the Reaction of Thioglycolic Acid with Schiff Bases

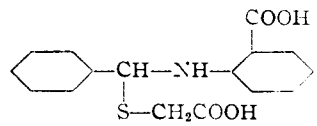
BY ALEXANDER R. SURREY

The appearance of a paper by Erlenmyer and Oberlin[1] on the reaction of Schiff bases with thioglycolic acid prompts the writer to report on similar work in this field carried out in this Laboratory.

We have found that in many instances 4-thiazolidones (Table I) can be prepared conveniently by the reaction of thioglycolic acid with Schiff bases in refluxing benzene. By removing the water continuously as it forms, it was possible to follow the condensation and determine the reaction time. In some cases the Schiff base was prepared in the same solvent. When the calculated amount of water had separated, the thioglycolic acid was added and refluxing was continued. The initial step, the addition of the thiol group to the anil, was usually accompanied with the evolution of heat. Where the Schiff base was only slightly soluble in benzene, vigorous mechanical stirring was employed.

Several other procedures were tried in the preparation of 2,3-diphenyl-4-thiazolidone. At room temperature, in the absence of solvent a 35% yield of the product was obtained; in alcohol or glacial acetic acid, the yield was 12%. The reaction of ethyl thioglycolate with benzylideneaniline in refluxing Skellysolve E for sixteen hours gave an 8% yield of the thiazolidone.

When thioglycolic acid was added to a stirred suspension of benzylidene-2-carboxyaniline in benzene an exothermic reaction occurred and a clear solution resulted. In a short time, a solid which proved to be the addition compound, separated from the benzene solution. When the



reaction was run in refluxing benzene for twenty-four hours, approximately 75% of the calculated amount of water was collected. Although thiazolidone formation is indicated, the product has not yet been isolated from the reaction mixture.

Experimental Part[2]

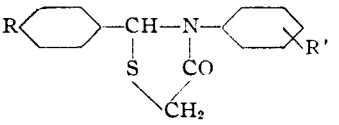
General Procedure for the Preparation of the 4-Thiazolidones.—The following general directions for the preparation of the thiazolidones (Table I) includes the procedure for the preparation of the Schiff base in the same solvent. A mixture of 0.2 mole of benzaldehyde and 0.2 mole of aniline in 100 cc. of dry benzene was refluxed with a water separator connected to the apparatus. After about 3.5 cc. of water had been collected, 20 g. of thioglycolic acid was added and refluxing continued until an additional 3.5 cc. of water had separated. The amount of water collected

(1) Erlenmyer and Oberlin, *Helv. Chim. Acta*, **30**, 1329 (1947).

(2) All melting points are uncorrected unless otherwise indicated.

TABLE I

2,3-SUBSTITUTED-4-THIAZOLIDONES



R	R'	Reflux time, hr.	Yield,[a] %	Recryst. solvent	M. p., °C. (corr.)	Analyses, %[b] Nitrogen Calcd.	Nitrogen Found	Sulfur Calcd.	Sulfur Found
H	H	4	60	Benzene–ether	131.6–132.2[c]	5.49	5.37	13.55	12.63
H	3-Cl	[d]	38	Methanol	128.6–129.6	4.84	4.76	11.05	11.05
H	4-Cl	12	50	Benzene	110.8–112.2	4.84	4.59	11.05	10.80
H	2-OH	8	66	Ethanol	222–224	5.17	5.07	11.80	12.03
H	4-OH	6	61	Ethanol	191.8–193	5.17	5.10	11.80	11.94
H	3-COOH	12	63	Isopropanol	186.5–188	4.68	4.61	10.7	11.0
H	4-COOH	17	25	Isopropanol	244–245.1	4.68	4.65	10.7	10.70
H	4-$COOC_2H_5$	15	28	Benzene–ether	126.8–128.8	4.28	4.20	9.79	9.88
OCH_3	4-OCH_3	12	52	Methanol	118.9–119.8	4.44	4.47	10.16	9.96

[a] No attempt was made to obtain maximum yields, since our interest was chiefly in the scope of the reaction. [b] Analyses were performed by the analytical staff of these Laboratories. [c] Erlenmeyer and Oberlin report a m. p. 130–131°. [d] Reaction carried out at room temperature for five days.

usually approached the theoretical. After most of the benzene had been removed, the residue was dissolved in ether and seeded. In some instances, the thiazolidone separated directly from the benzene solution and was filtered off and purified by recrystallization.

Reaction of Thioglycolic Acid with Benzylidene-2-carboxyaniline.—Five grams of thioglycolic acid was added to a well-stirred suspension of 11.3 g. of benzylidene-2-carboxyaniline in 75 cc. of benzene. An exothermic reaction occurred and a clear solution resulted. The product which precipitated in a matter of a few minutes proved to be the addition compound. After several recrystallizations from a mixture of ether-Skellysolve A, it melted at 101–102°.

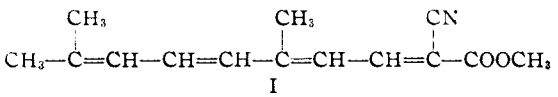
Anal. Calcd. for $C_{16}H_{15}NO_4S$: S, 10.1. Found: S, 9.96.

STERLING-WINTHROP RESEARCH INSTITUTE
RENSSELAER, NEW YORK RECEIVED SEPTEMBER 23, 1947

Polyenes. VI. Methyl Dehydrocitrylidenecyanoacetate[1]

BY WILLIAM G. YOUNG AND SEYMOUR L. LINDEN

For a research program which was later abandoned we wished to prepare dehydrocitrylidenecyanoacetate (I) from dehydrocitral and cyanoacetic acid followed by esterification. Dehydrocitral has been prepared previously[2] by the self condensation of β-methylcrotonaldehyde. The isolation of the dehydrocitral and its separation from isomers and other condensation products, however, is accomplished only by tedious redistillations and recrystallizations. Fortunately, for the purpose of this investigation it was found unnecessary to carry out such purifications since treatment of the main fraction from the condensation reaction with a basic aqueous solution of cyanoacetic acid yielded directly pure crystalline dehydrocitrylidenecyanoacetic acid. The methyl ester was then prepared by treatment of the silver salt of the acid with methyl iodide.



I

The absorption spectra of dehydrocitrylidenecyanoacetic acid (λ_{max} 390 mμ, ε 41200) and its methyl ester (λ_{max} 405 mμ, ε 43300) correspond well in both wave length and extinction with that expected of a new group of alkylidenecyanoacetic acid and esters with four conjugated carbon–carbon double bonds.[3]

The usual procedure for the preparation of β-methylcrotonaldehyde[4] *via* α-bromoisovaleraldehyde diethyl acetal (followed by dehydrobromination and hydrolysis of the acetal) was found by us to be both time consuming and expensive. The over-all yield from isovaleraldehyde is seldom better than 10%. We have found, on the other hand, that β-methylcrotonaldehyde can be prepared readily from γ,γ-dimethylallyl bromide by the method of Sommelet.[5] The γ,γ-dimethylallyl bromide is conveniently prepared in large quantities by the addition of hydrogen bromide to isoprene.[6] The reaction of the bromide with hexamethylenetetramine is almost quantitative and the decomposition of the salt thus obtained is readily carried out by steam distillation. The yield from the allylic bromide is 35%.

We wish to thank Mr. Joseph Rule for the preparation of the γ,γ-dimethylallyl bromide. The micro-analyses reported were carried out at the California Institute of Technology through the courtesy of Professor Haagen-Smit.

Experimental

Dehydrocitral and Dehydrocitrylidenecyanoacetic Acid.—The process employed for the preparation of dehydro-

(1) This work was made possible by a research grant from Sharp and Dohme, Inc.

(2) Fischer and Hultzsch, *Ber.*, **68**, 1726 (1935); Fischer, Holtzsch and Plaig, *ibid.*, **70**, 370 (1937).

(3) Andrews, Cristol, Lindenbaum and Young, THIS JOURNAL, **67**, 715 (1945).

(4) McElvain, Clarke and Jones, *ibid.*, **64**, 1966 (1942); Fischer, Ertel and Lowenberg, *Ber.*, **64**, 30 (1931).

(5) Sommelet, *Compt. rend.*, **157**, 852 (1933); Delaby, *Bull. soc. chim.*, [5] **3**, 2375 (1936).

(6) Staudinger, Kries and Schilt, *Helv. Chim. Acta*, **5**, 743 (1922).

citral is a modification of the procedure of Fischer and co-workers.[2] A mixture of 11.7 g. (0.14 mole) of freshly distilled β-methylcrotonaldehyde, 1.5 ml. of glacial acetic acid and 0.15 ml. of piperidine was heated under nitrogen in a small Claisen flask on a steam-bath for twenty-three minutes. The reaction mixture turned very dark red almost at once and gradually thickened. After removing the flask from the steam-bath and cooling, a nitrogen filled capillary was inserted and the material was distilled at reduced pressure. In addition to some low boiling substance (unreacted β-methylcrotonaldehyde) which collected in a Dry Ice trap, three fractions were obtained: (1) b. p. 30–100° (2 mm.), wt. 0.7 g.; (2) b. p. 100–112° (2 mm.) (dark red), wt. 1.6 g.; (3) b. p. above 112° (2 mm.), bath temp. above 200°, wt. 0.5 g. The principal fraction (2) displayed a high sharp absorption spectra maximum at 338 mμ in 95% ethanol. Fraction (2) was treated directly with a slightly basic solution of 2 g. of cyanoacetic acid in 12 ml. of water and shaken vigorously for one-half hour during which time all of the oil dissolved. The basic aqueous solution was extracted three times with ether and acidified. A dark red oil appeared which crystallized at once to dark red shiny crystals. These were washed with water and dried; yield 1.82 g. A 300-mg. portion of these crystals was recrystallized three times from water–acetic acid yielding 149 mg. of pure dehydrocitrylidenecyanoacetic acid with the following physical properties: m. p. 195–198° (dec.), λ_{max} 390 mμ (ε 41200) in 95% ethanol. *Anal.* Calcd. for $C_{13}H_{15}O_2N$: C, 71.86; H, 6.96; N, 6.45. Found: C, 71.63; H, 6.99; N, 6.25. Quantitative catalytic hydrogenation showed 5.58 moles of hydrogen absorbed per mole. The compound contains four carbon–carbon double bonds and a nitrile group. In view of the unexpected hydrogenation result, quantitative hydrogenations were carried out on samples of very pure α-cyanocrotonic acid[7] which contains one carbon–carbon double bond and a nitrile group. This substance absorbed 2.73 and 2.57 moles of hydrogen per mole in duplicate experiments. This indicates that the nitrile group absorbs *ca.* 1.6 moles of hydrogen. Thus, the absorption of 5.58 moles of hydrogen by the dehydrocitrylidenecyanoacetic acid indicates the presence of four carbon–carbon double bonds.

Because of the large loss accompanying the formation of β-methylcrotonaldehyde from its diethyl acetal (usually 50–60% yield) and because of the large amount of side reaction loss attending the self-condensation of the aldehyde it was thought possible to perform the condensation using the acetal under conditions in which the aldehyde might be formed *in situ*. Attempts at such a reaction using, for example, wet acetic acid and piperidine failed. No dehydrocitral was obtained and usually 70–90% of the starting material could be recovered although it had been partially converted to the aldehyde.

Methyl Dehydrocitrylidenecyanoacetate.—The dry silver salt prepared from 1.52 g. of the dehydrocitrylidenecyanoacetic acid was refluxed and stirred with methyl iodide and ether for twenty-four hours. Evaporation of the ether after filtration and drying left 1.59 g. (98% yield) of methyl dehydrocitrylidenecyanoacetate. Recrystallization from methanol yielded a pure sample of the ester with the following physical properties: m. p. 115–118°, λ_{max} 405 mμ (ε 43300) in 95% ethanol. Molecular weight (in camphor)[8] was 235 ± 3, calcd. 231.

An attempt was made to condense β-cyclocitral with methyl dehydrocitrylidenecyanoacetate in a Knoevenagel type reaction. It was thought that some methyl axerophthylidenecyanoacetate might be formed in the reaction. Absorption spectrum measurements on the reaction mixture unfortunately failed to indicate unambiguously the presence or absence of the desired product. Molecular weight determinations,[8] however, indicated that perhaps the reaction had proceeded to a certain extent. A biological test performed with the purified reaction mixture failed to show any vitamin A activity.

(7) Young, Andrews, Lindenbaum and Cristol, THIS JOURNAL, **66**, 810 (1944).

(8) Smith and Young, *J. Biol. Chem.*, **75**, 289 (1927).

β-Methylcrotonaldehyde.—Freshly distilled γ,γ-dimethylallyl bromide[6] ($n^{20}D$ 1.4900), 34.5 g. (0.23 mole), was added to a solution of hexamethylenetetramine in dry chloroform. The white precipitate which resulted was washed with ether and dried under vacuum. This salt was then dissolved in water and added dropwise to rapidly boiling water under a slow stream of nitrogen. The distillate was kept slightly acid by adding dilute sulfuric acid periodically. The distillate was extracted several times with ether and the combined ether extracts were dried over sodium sulfate. Removal of the ether and distillation of the residue through a small Vigreux column yielded 6.5 g. (0.078 mole, 35% yield) of β-methylcrotonaldehyde, b. p. 68–72° (95 mm.).

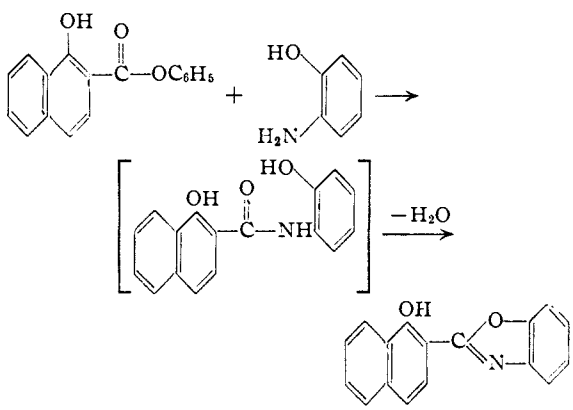
DEPARTMENT OF CHEMISTRY
UNIVERSITY OF CALIFORNIA AT LOS ANGELES
LOS ANGELES, CALIFORNIA RECEIVED MARCH 1, 1947

The Salol Reaction

BY JAMES A. VANALLAN

The "salol procedure"[1] is very convenient for preparing amides of salicylic acid, particularly from sensitive amines such as the aminophenols. By the use of the phenyl ester of 1-hydroxynaphthalene-2-carboxylic acid, homologs in the naphthalene series can be obtained. In the accompanying table there are listed the amines used with salol and with phenyl 1-hydroxynaphthalene-2-carboxylate (Table I), with the properties of the resulting compounds.

When the reaction is applied to *o*-aminophenols or *o*-diamines, a secondary loss of water gives rise to a cyclic compound instead of the open-chain amide.



In addition to the methods listed,[1] salicyl and hydroxynaphthoylamides have been prepared by the action of a dehydrating agent on mixtures of the acid and amine in an inert solvent[2,3,4,5]; from an aryl bromide and salicylamide[6,7]; from the anhydride of 2-hydroxy-3-naphthoic acid and an amine[8]; from 2-hydroxy-3-naphthoic acid and

(1) Allen and VanAllan, "Organic Syntheses," **26**, 94 (1946)
(2) Semer and Shepard, *J. Chem. Soc.*, **95**, 441 (1909).
(3) German Patent 293,897 (1913) [*Frdl.*, **12**, 912 (1914–1916)].
(4) German Patent 291,139 [*Frdl.*, **12**, 182 (1914–1916)].
(5) German Patent 284,997 [*Frdl.*, **12**, 183 (1914–1916)].
(6) Loevenich and Loeser, *Ber.*, **60**, 322 (1927).
(7) Goldberg, *ibid.*, **39**, 1691 (1906).
(8) German Patent 295,183 [*Frdl.*, **12**, 914 (1914–1916)].

TABLE I

AMIDES AND HETEROCYCLIC COMPOUNDS FROM PHENYL SALICYLATE AND FROM PHENYL-1-HYDROXYNAPHTHALENE-2-CARBOXYLATE

Amine used	M. p., °C.	Yield, %	Formula	% Nitrogen Calcd.	% Nitrogen Found
		With Phenyl Salicylate			
Piperidine	142–143	69	$C_{12}H_{15}NO_2$	6.8	6.9
Cyclohexylamine	85–86	79	$C_{13}H_{17}NO_2$	6.4	6.4
Benzylamine	135–136	77	$C_{14}H_{13}NO_2$	6.2	6.2
n-Butylamine[11]	[a]	81			
Laurylamine	71–72	75	$C_{19}H_{31}NO_2$	4.6	4.6
Diethylamine	[b]	68	$C_{11}H_{15}NO_2$	7.3	7.2
Ethylenediamine	183–184	69	$C_{16}H_{16}N_2O_4$	9.4	9.5
Chloroaniline	155	83	$C_{13}H_{11}ClNO$	15.3[c]	15.0[c]
Aminobiphenyl	110	85	$C_{19}H_{15}NO_2$	[d]	[d]
o-Aminophenol	125	22.4	$C_{13}H_9NO_2$	6.63[e]	6.63[e]
p-Aminophenol[12]	176	57			
m-Aminophenol	184	58	$C_{13}H_{11}NO_2$	6.11	6.10
5-Aminoindazole	230	37	$C_{14}H_{11}N_3O_2$	16.62	16.57
6-Aminoindazole	234–235	31	$C_{14}H_{11}N_3O_2$	16.62	16.56
m-Phenylenediamine[12]	199–200	49			
5-Aminobenzotriazole	245	42	$C_{13}H_{10}N_4O_3$	22.03	21.74
1,2,3,4-Tetrahydroquinoline	138–139	34	$C_{16}H_{15}NO_2$	5.5	5.6
		With Phenyl-1-hydroxynaphthalene-2-carboxylate			
Diethylamine	[f]	63	$C_{15}H_{17}NO_2$	5.77	5.6
o-Phenylenediamine	>265	78	$C_{17}H_{12}N_2O$	[g]	[g]
o-Aminophenol	188	89	$C_{17}H_{11}NO_2$	[h]	[h]

[a] B. p. 153–156° (3 mm.). [b] B. p. 146–148° (4 mm.). [c] Chlorine. [d] Calcd.: C, 78.80; H, 5.18. Found: C, 78.8; H, 5.1. [e] Calcd.: C, 73.8; H, 4.3. Found: C, 74.24; H, 4.53. [f] B. p. 130–133° (1 mm.). [g] Calcd.: C, 78.40; H, 4.6. Found: C, 78.6; H, 4.4. [h] Calcd.: C, 78.0; H, 4.22. Found: C, 77.9; H, 4.3.

acetanilide[9] or aniline[10], from methyl salicylate and an aliphatic amine.[11,12]

(9) German Patent 289,027 [*Frdl.*, **12**, 184 (1914–1916)].
(10) Schöpff, *Ber.*, **25**, 2740 (1892).
(11) Hurd, Fancher and Bonner, THIS JOURNAL, **68**, 2745 (1946).
(12) Fargher, Galloway and Probert, *J. Textile Inst.*, **21**, 245T (1930) [*C. A.*, **24**, 6026 (1930)].

COMMUNICATION NO. 1154
KODAK RESEARCH LABORATORIES
ROCHESTER 4, NEW YORK RECEIVED JULY 10, 1947

A New Process for the Preparation of Thioglycolylamides

BY JAMES A. VANALLAN

It is known that thioglycolylamides may be obtained by alkaline hydrolysis of carbamyl thioglycolylanilides[1] but the yields are low (15%) and several steps are required to obtain the product. Also acetothioglycolylamides, which are obtained from the acid chloride and an amine, may be saponified to the required thioglycolylamides but the intermediate acid chloride[2] is difficult to obtain, and again the process consists of several steps.

It has now been found that thioglycolylamides may be made in excellent yield and in a high state of purity without protecting the thiol group. The process consists of mixing an amine and thioglycolic acid in molecular proportions with benzene as a solvent and utilizing a Clarke–Rahrs ester column[3] to remove the water as it is formed. The reactants are at all times in an atmosphere of benzene during the course of the reaction, which minimized the formation of disulfide. The crude product, therefore, usually possesses a higher degree of purity than that obtained by other processes. The process is illustrated by the preparation of thioglycolylanilide.

Thioglycolylanilide.—Thioglycolic acid (46 g.) and aniline (45 g.) are mixed in 250 ml. of benzene. This solution is refluxed, using an ester column, until approximately 9 ml. of water has separated (about nine hours). The benzene solution is then treated with an equal volume of petroleum ether and chilled. The product (70 g., 85%) separates as a mass of white crystals; m. p. 103–105°. A recrystallization from dilute alcohol raises the melting point to 110°.

(1) Beckurts and Frerichs, *J. prakt. Chem.*, [2] **66**, 174 (1902).
(2) Benary, *Ber.*, **46**, 2105 (1913).
(3) Eastman Kodak Company, "Syn. Org. Chem.," **9**, No. 3, May (1936).

COMMUNICATION NO. 1156
KODAK RESEARCH LABORATORIES
ROCHESTER 4, NEW YORK RECEIVED JULY 26, 1947

Resonance and Hydrogen Bond Effects on the Basic Strengths of Certain Arylalkyl Azomethines

BY CHARLES D. WAGNER AND EDWARD D. PETERS

When aliphatic primary amines are treated with most of the common aromatic aldehydes, azo-

methines are readily and quantitatively formed which ordinarily are considerably less basic than the aliphatic amines. This fact has been utilized as the basis of a method by which secondary plus tertiary aliphatic amines may be determined in the presence of primary amines and ammonia.[1]

Reference has been made[1] to the fact that the titration of a mixture of an aliphatic secondary amine and the azomethine of a primary amine leads to the sharpest satisfactory differentiation between the two compounds when the azomethine is derived from salicylaldehyde. (Of benzaldehyde, *p*-hydroxybenzaldehyde, anisaldehyde, *o*-methoxybenzaldehyde, cinnamaldehyde, piperonal and *m*-nitrobenzaldehyde, the last-named formed an azomethine which was less basic than that derived from salicylaldehyde, but the compound formed was easily hydrolyzed in the presence of water and dilute acid and was therefore not used in the analytical method.)

Interesting differences were observed in the titration curves obtained by treating a mixture of di-*n*-amylamine and *n*-amylamine with different aromatic aldehydes and titrating in the usual way[1] using methanol as a solvent. Since benzaldehyde reacts to a significant extent with unsubstituted straight-chain secondary amines, the reaction time for benzaldehyde with the mixture was shortened to five minutes in comparison to twenty minutes used with the other aldehydes.

In each experiment 10 ml. of an isopropyl alcohol solution containing 1.80 millimoles of di-*n*-amylamine and 2.08 millimoles of *n*-amylamine was added to 80 ml. of methanol containing 40 millimoles of aldehyde (carboxylic acid-free). After the mixture stood at room temperature for twenty minutes, it was titrated potentiometrically, using 0.5 *N* hydrochloric acid in isopropyl alcohol.

Curves obtained using benzaldehyde, salicylaldehyde, *p*-hydroxybenzaldehyde, anisaldehyde and *o*-methoxybenzaldehyde are presented in Fig. 1. From these it is noted that in the absence of phenolic aldehydes, the portions of the curves representing titration of secondary amine are almost identical. The phenolic aldehydes in the basic solutions cause decreased basicities corresponding to the relative acid strengths of the two aldehydes.

The portions of the curves representing titrations of azomethines demonstrate that azomethines from the methoxyaldehydes and *p*-hydroxybenzaldehyde are stronger bases (about 1 pK unit) than that from benzaldehyde, and about 1.5 pK units stronger than the azomethine from salicylaldehyde. These observations, which were confirmed qualitatively and almost quantitatively using the primary and secondary isobutylamines and isopropylamines, may be ascribed to resonance and hydrogen bond effects in the azomethines:

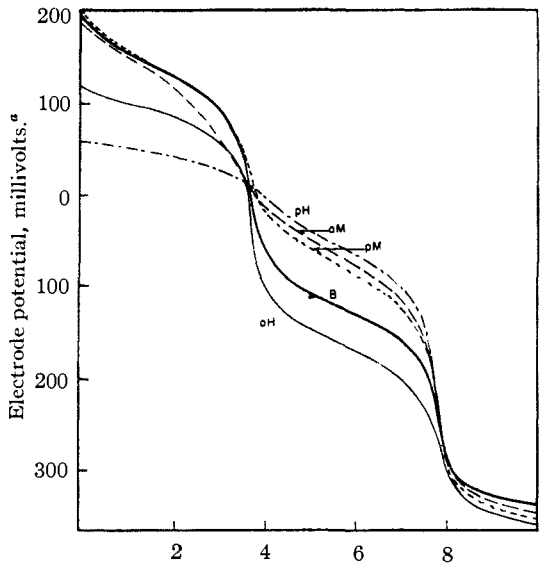
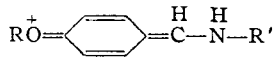


Fig. 1.—Acidimetric titrations of di-*n*-amylamine-*n*-amylamine mixtures in methanol after treatment with certain aromatic aldehydes: 1.8 milliequivalents of di-*n*-amylamine, 2.08 milliequivalents of *n*-amylamine treated with 40 millimoles of aldehyde in 80 ml. of methanol: ——, B, benzaldehyde; ——, *o*H, salicylaldehyde; —·—·—, *p*H, *p*-hydroxybenzaldehyde; — — —, *o*M, *o*-methoxybenzaldehyde; - - - - -, *p*M, anisaldehyde.

[a] Zero on electrode potential scale is approximately equivalent to a *p*H of 7 with the electrodes in aqueous solution.

1. Base strength of an azomethine from an ortho- or para-hydroxybenzaldehyde or *o*- or *p*-methoxybenzaldehyde tends to be increased over that of the benzaldehyde derivative because of the greater resonance energy of the conjugate acid of the azomethine, due primarily to the following resonance structure



where R equals either methyl or hydrogen and where the substituents may be either ortho or para.

2. The resonance effect in the case of the salicylaldehyde compound is more than compensated by hydrogen bonding between the ortho oxygen and the nitrogen atoms, which tends to decrease the basic character of the nitrogen atom of the azomethine so that the result is a compound somewhat less basic than the benzaldehyde derivative.

SHELL DEVELOPMENT COMPANY
EMERYVILLE, CALIFORNIA RECEIVED MARCH 10, 1947

(1) C. D. Wagner, R. H. Brown, and E. D. Peters, **69**, 2609 (1947).