dihydroabietic, and tetrahydroabietic acids.

This affords conclusive evidence that so-called α-pyroabietic acid is not an isomer of abietic acid, but a product of dehydrogenation and disproportionation.

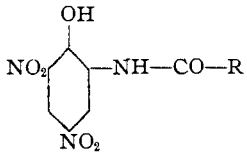
WASHINGTON, D. C. RECEIVED FEBRUARY 23, 1938

[CONTRIBUTION FROM THE CHEMISTRY LABORATORY OF THE UNIVERSITY OF WASHINGTON]

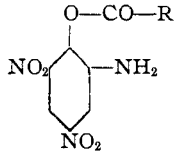
Derivatives of Picramic Acid and Some of their Rearrangements

BY IRWIN A. PEARL AND WILLIAM M. DEHN

Picramic acid yields two types of acetyl derivatives.[1] We have obtained both (I) and (II) in

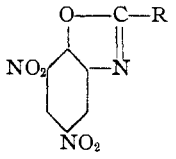


(I)



(II)

acetylation of picramic acid. Our investigation has revealed that a product, reported by Schiff as (II),[2] is in reality a benzoxazole (III), a type previously known to synthesis.[3]



(III)

Our analytical data and the insolubility of the Schiff compound in dilute acids confirm the assigned structure. As might be expected, either acid or caustic hydrolysis yields picramic and acetic acids.

From the acetylation products of picramic acid we have isolated the O-acetyl compound (II), the structure of which was confirmed by its dissolving in dilute acids and by alkaline hydrolysis to picramic and acetic acids.

This derivative melts at 160–161°; the N-acetyl derivative, at 201°; and the benzoxazole, at 193°.

Acetyl-benzoylpicramic acids were investigated and data substantiating the conclusions of Pollard and Nelson[4] and others on the rearrangements of diacyl derivatives of 2-aminophenols were obtained.

By treating N-acetylpicramic acid with benzoyl chloride in benzene solution we obtained an acetyl-benzoylpicramic acid melting at 119.5–120.5° (IV). On warming N-benzoylpicramic acid with acetic anhydride we obtained an acetyl-benzoylpicramic acid melting at 170–171° (V). On hydrolysis with dilute alkali, both of these compounds yielded N-acetylpicramic acid melting at 204–205°.[5] These facts indicate that rearrangement takes place on hydrolysis and that compound (IV) is 4,6-dinitro-2-acetylaminophenylbenzoate, and that compound (V) is 4,6-dinitro-2-benzoylaminophenylacetate.

A number of other new derivatives of picramic acid have been prepared. All are given in Table I and are indicated in the experimental part by asterisks.

In addition to these new derivatives, the following compounds have been prepared in increased yields by improved processes: 3,5-dinitro-2-hydroxyphenylurethan, 1-phenyl-4,6-dinitrobenzoxazole, 4,6-dinitro-2-acetylaminophenol, and 4,6-dinitro-2-benzoylaminophenol.

Experimental

1-Methyl-4,6-dinitrobenzoxazole.*—A mixture of 100 g. of picramic acid,[6] 250 g. of acetic anhydride, and one drop of sulfuric acid was heated in a liter flask on the steam-plate for six hours. The initial precipitate redissolved after a few minutes. On cooling, slightly brownish, transparent needles separated. A yield of 100 g. melting at 192–193° was obtained. Recrystallization from alcohol or xylene gave white needles melting at 193°. When dissolved in nitric or sulfuric acids and then poured into water, or when boiled with dilute alkali, it yielded N-acetylpicramic acid melting at 204–205°.

4,6-Dinitro-2-acetylaminophenol.—The filtrate from above was poured into water and allowed to stand. A yield of 25 g. of 4,6-dinitro-2-acetylaminophenol (N-

(1) Meldola and Wechsler, *Chem. News*, **82**, 254 (1900); Cassella and Company, German Patent 161,341 (1903).

(2) Schiff, *Ann.*, **239**, 366 (1887).

(3) Ladenburg, *Ber.*, **9**, 1525 (1876); Hubner and Haarhaus, *Ann.*, **210**, 394 (1881). These authors prepared the phenyldinitrobenzoxazole.

(4) Pollard and Nelson, THIS JOURNAL, **53**, 996 (1931). This article gives a complete bibliography.

(5) Although the melting point for N-acetylpicramic acid is given in the literature as 201°, we have found that repeated crystallizations from xylene, benzene, toluene, or alcohol give shiny yellow needles melting at 204–205°.

(6) Ammonium picramate was prepared by the method of Dehn [U. S. Patent 1,472,791 (1923)]. The ammonium salt was dissolved in water and neutralized with dilute acetic acid. The free picramic acid separated as dark red needles melting at 169°.

TABLE I

Name of compound	Recrystallizing solvent	Crystalline form and color	M. p., °C.	Formula	%N Calcd.	%N Found
1-Methyl-4,6-dinitrobenzoxazole	Xylene	Small white needles	193	$C_8H_5O_5N_3$	18.8	18.7
4,6-Dinitro-2-aminophenylacetate	Benzene	Yellow prisms	160–161	$C_8H_7O_6N_3$	17.4	17.2
4,6-Dinitro-2-chloroacetylaminophenol	Alcohol	Long yellow needles	150	$C_8H_6O_6N_3Cl$	15.2	15.3
4,6-Dinitro-2-dichloroacetylaminophenol	Alcohol	Fine yellow plates	118–119	$C_8H_5O_6N_3Cl_2$	13.5	13.5
4,6-Dinitro-2-benzenesulfonaminophenol	Alcohol	Dark yellow needles	202–203	$C_{12}H_9O_7SN_3$	12.4	12.1
3,5-Dinitro-2-hydroxydiphenylthiourea	Alcohol	Bright yellow needles	247–248	$C_{13}H_{10}O_5SN_4$	16.7	16.7
4,6-Dinitro-2-benzenesulfonaminophenylacetate	Alcohol	Bright yellow leaflets	178–179	$C_{14}H_{11}O_8SN_3$	11.0	10.8
4,6-Dinitro-2-benzoylaminophenylacetate	Benzene	Small white needles	170–171	$C_{15}H_{11}O_7N_3$	12.2	12.4
4,6-Dinitro-2-acetylaminophenylbenzoate	Water	White prisms	119.5–120.5	$C_{15}H_{11}O_7N_3$	12.2	12.2

acetylpicramic acid) separated. Recrystallization from xylene gave bright yellow needles melting at 204–205°. The mixed melting point with N-acetylpicramic acid, prepared by the method of Cassella and Co.,[1] was 204–205°. When ammonium picramate was warmed for six hours with an excess of acetic anhydride and the mixture was poured into water, a quantitative yield of N-acetylpicramic acid was obtained. A mixture of 100 g. of picramic acid, 50 g. of acetyl chloride, and 300 cc. of benzene was heated on the steam-bath for two hours. The mixture was cooled and filtered. A yield of 110 g. of crude N-acetylpicramic acid was obtained. Evaporation of the benzene and recrystallization of the residue from alcohol gave 10 g.; thus the yield was quantitative. The N-acetylpicramic acid was heated on the steam-bath with an excess of acetic anhydride. Cooling gave 1-methyl-4,6-dinitrobenzoxazole melting at 193°.

4,6-Dinitro-2-aminophenylacetate.*—A mixture of 100 g. of picramic acid, 200 cc. of acetic anhydride, and one drop of sulfuric acid was warmed on the steam-bath for two hours and then allowed to stand overnight. The yellow precipitate of N-acetylpicramic acid was filtered off and the filtrate was poured into water and stirred to decompose the excess anhydride. The precipitate that separated was filtered, dried, and extracted with xylene. The yield was 25 g. Recrystallization from benzene yielded yellow prisms of 4,6-dinitro-2-aminophenylacetate (O-acetylpicramic acid) melting at 160–161°. When boiled with 5% sodium hydroxide solution and acidified with dilute hydrochloric acid, it yielded picramic and acetic acids. When boiled with 0.2 *N* sodium hydroxide and neutralized in the same manner, it rearranged to its isomer, N-acetylpicramic acid. When boiled with an excess of acetic anhydride, it yielded 1-methyl-4,6-dinitrobenzoxazole melting at 193°.

4,6-Dinitro-2-benzoylaminophenol.—A mixture of 100 g. of picramic acid, 75 g. of benzoyl chloride, and 250 cc. of benzene was heated on the steam-bath for two hours. The red color disappeared and very fine greenish-yellow needles separated. The mixture was cooled and filtered. The 4,6-dinitro-2-benzoylaminophenol (N-benzoylpicramic acid), after washing well with benzene and drying, weighed 125 g. and melted at 220–221°. Recrystallization from xylene yielded bright yellow prisms melting at 226–227°. A mixture with N-benzoylpicramic acid, prepared by the method of Kym,[7] melted at 226–227°. This compound was also prepared by heating under reflux for two days on the steam-bath a mixture of 8.5 g. of picramic acid, 11 g. of benzoic anhydride, and 50 cc. of benzene. The yield was 10 g. Recrystallization from xylene gave bright yellow prisms melting at 226–227°.

1-Phenyl-4,6-dinitrobenzoxazole.[8]—A mixture of 100 g. of N-benzoylpicramic acid, 150 cc. of acetic anhydride, and a drop of sulfuric acid was heated under a reflux on the steam-bath for five hours. The greenish crystals were replaced by silvery leaflets. The crude phenyldinitrobenzoxazole weighed 50–55 g. and melted at 219–220°. Recrystallization from xylene gave white plates melting at 220–221°.

4,6-Dinitro-2-benzoylaminophenylacetate.*—The filtrate from above was poured into an excess of cold water and stirred to decompose the excess acetic anhydride. The solution was partially neutralized with ammonium hydroxide. After filtering and drying, the yellow precipitate weighed 45–50 g. Recrystallization from benzene gave small white needles of dinitrobenzoylaminophenylacetate melting at 170–171°. Hydrolysis with dilute alkali gave N-acetylpicramic acid melting at 204–205°.

4,6-Dinitro-2-acetylaminophenylbenzoate.*—A mixture of 50 g. of N-acetylpicramic acid, 40 g. of benzoyl chloride, 100 cc. of benzene, and one drop of sulfuric acid was heated under reflux on the steam-bath for six hours. The benzene was then evaporated and the residue was cooled, powdered and well washed with 5% sodium carbonate solution to remove the benzoic acid. The precipitate (35 g.) was filtered and washed successively with sodium carbonate solution and dilute hydrochloric acid. Recrystallizations from water gave shiny white needles melting at 119.5–120.5°. On hydrolysis with dilute alkali, this compound yielded N-acetylpicramic acid melting at 204–205°. A mixture with the N-acetylpicramic acid formed by the hydrolysis of the isomeric diacyl melted at the same temperature.

3,5-Dinitro-2-hydroxyphenylurethan.[8]—Picramic acid was heated under reflux with an excess of ethyl chlorocarbonate for five hours. The mixture was then poured into an excess of water. A dark yellow precipitate of the urethan separated (90–95%). Recrystallization from alcohol gave bright yellow silky needles melting at 152–153°.

Other New Picramic Acid Derivatives.—The 4,6-dinitro-2-chloroacetylaminophenol,* 4,6-dinitro-2-dichloroacetylaminophenol,* 4,6-dinitro-2-benzenesulfonaminophenol,* and 3,5-dinitro-2-hydroxydiphenylthiourea* were prepared from picramic acid by treatment in the standard manner, respectively, with chloroacetyl chloride, dichloroacetyl

(7) Kym, *Ber.*, **32**, 1429 (1899).

(8) Rudolf, *J. prakt. Chem.*, [2] **48**, 439 (1893).

chloride, benzenesulfonyl chloride, and phenyl isothiocyanate. The 4,6-dinitro-2-benzenesulfonaminophenylacetate* was prepared from the corresponding amine and benzenesulfonyl chloride in alkaline solution.

Summary

A number of new derivatives of picramic acid were prepared. Also several known derivatives were prepared by greatly improved processes. A study of the rearrangements of certain derivatives of picramic acid substantiated previous work on acyl-2-aminophenols. The error in the previously reported O-acetylpicramic acid is clarified.

SEATTLE, WASH. RECEIVED FEBRUARY 23, 1938

[CONTRIBUTION FROM THE THOMPSON LABORATORY OF THE PHILLIPS EXETER ACADEMY]

The Racemization of an Optically Active Acid and its Methyl Ester

BY C. L. BICKEL

It is well known that optically active acids whose asymmetric carbon atom holds both a hydrogen and the carboxyl group, $R-\underset{\displaystyle CO_2H}{\overset{|}{C}}H-R'$, are racemized by bases with more difficulty than are their esters.[1-5] In all but one of the cases studied, the racemization of the ester was accompanied by hydrolysis. And in this one case,[3,4] although the rate of racemization of the ester was measured, the racemization of the acid was not studied quantitatively. In consequence it is impossible to compare, except in a qualitative way, the rates of racemization of an ester and the corresponding acid in any known instance.

The preparation and use of the active forms of β-benzoyl-α-phenylpropionic acid, I, in connection with another problem indicated that they are unusually stable in the presence of bases, no racemization being detected under ordinary conditions. On the other hand, the methyl esters, II, of the optically active forms of the acid are racemized with ease even in very dilute solutions of a base at room temperature.

$$C_6H_5-\underset{\displaystyle COOH}{\overset{|}{C}}H-CH_2-CO-C_6H_5$$

I

$$C_6H_5-\underset{\displaystyle COOCH_3}{\overset{|}{C}}H-CH_2-CO-C_6H_5$$

II

Concentrations of sodium hydroxide which produce measurable rates of racemization in methyl alcoholic solution do not cause any saponification of the ester. Under these conditions the only product is the inactive ester. Higher concentrations of sodium hydroxide, which racemize the active ester much too fast to make measurements possible, cause saponification of the ester. Concentrated aqueous sodium hydroxide, with enough added acetone to give solubility, saponifies the active esters with but partial racemization. This behavior agrees with that shown by the compounds studied by McKenzie[1,2] and by Wren.[3,4]

Basic solutions which racemize the active ester in a few minutes have no measurable effect on the active acid over a period of at least a month. A higher temperature and a more concentrated solution of the base are required to racemize the active acid at a rate which can be measured conveniently. In fact, hydrobromic acid or hydriodic acid seem to be as effective as sodium hydroxide in racemizing the active acid.

The fact that acids and bases seem to be equally effective in racemizing the active acid does not imply that the high temperature is solely responsible for the racemization. The active acid undergoes no racemization when held slightly above its melting point (181°) for some hours in a Pyrex melting point tube.

The rate of racemization of the active ester increases with an increase in the concentration of base. The rate of racemization of the active acid increases with an increase in the concentration of base and also increases with temperature. The effect of a change in temperature on the racemization of the active ester was not investigated.

No attempt has been made to draw any exact relationship between the concentration of base and the rate of racemization, since one case does not warrant a general conclusion. The facts are presented in the light of utility and it is hoped

(1) McKenzie and Thompson, *J. Chem. Soc.*, **87**, 1019 (1905).
(2) McKenzie and Wren, *ibid.*, **115**, 602 (1919).
(3) Wren and Williams, *ibid.*, **109**, 576 (1916).
(4) Wren, *ibid.*, **113**, 213 (1918).
(5) Gadamer, *J. prakt. Chem.*, **195**, 389 (1913).