[Contribution from the Chemical Laboratory of Northwestern University]

1,6- (OR 2,5-) DISUBSTITUTED NAPHTHALENES[1]

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The present study concerns itself with various new approaches to the problem of attaching substituents at the 1,6 positions of naphthalene, since several compounds of this type were desired for antimalarial investigations. One such approach was the Gattermann reaction with 2-chloronaphthalene, hydrogen cyanide, and aluminum chloride. An aldehyde was obtained, m.p. 100–102°, which changed to 7-chloro-1-naphthoic acid on oxidation. It was, therefore, the previously undescribed 7-chloro-1-naphthaldehyde. The fact that the crude aldehyde melted at 82–85° suggests that 6-chloro-1-naphthaldehyde (m.p. 83–84°) was also present.

Several new compounds were made from Cleve's acid, 5-amino-2-naphthalenesulfonic acid. These included sodium 5-cyano-2-naphthalenesulfonate made by the Sandmeyer reaction, 5-cyano-2-naphthalenesulfonyl chloride, and the corresponding anilide. Interchange of the SO_2Cl group by Cl was attempted by heating with phosphorus pentachloride at 160°, since there is precedent for this type of decomposition (1). In addition to the anticipated conversion of 5-cyano-2-naphthalenesulfonyl chloride into 6-chloro-1-naphthonitrile, there was evidently an extensive concurrent chlorination to a dichloronaphthonitrile.

Cleve's acid was acetylated to sodium 5-acetamido-2-naphthalenesulfonate which, with phosphorus pentachloride, was transformed into 5-acetamido-2-naphthalenesulfonyl chloride. Treatment of this with aniline yielded 5-acetamido-2-naphthalenesulfonanilide. Similar compounds of 1,4-orientation are described by Schroeter (2), and 5-benzamido-2-naphthalenesulfonyl chloride is reported by Schweitzer and Burr (3).

Chloromethylation of 2-chloronaphthalene was accomplished successfully, but the orientation of the chloromethyl group was not established. We confirmed the statement of Rupe and Brentano (4) that the chloromethyl group in benzyl chloride was convertible to an aldehyde group by heating with hexamethylenetetramine. Correspondingly, α-naphthylmethyl chloride and bromide yielded 21% and 44%, respectively, of 1-naphthaldehyde. The same method should apply with the x-chloromethyl-2-chloronaphthalene, but this work still awaits development.

Our experience with nitration of 2-naphthylamine by the method of Friedlaender and Szymanski (5) failed to check their results. They reported 5-nitro-2-naphthylamine, m.p. 143.5°, as the chief product together with a small amount of 8-nitro isomer, m.p. 103.5°. Our product melted at 91–92°. This points to a predominance of the 8-nitro isomer.

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Passing mention may be made to another nitration, carried out in the present investigation. This was the conversion of benzyl acetate by a mixture of nitric and sulfuric acids into a 37% yield of *p*-nitrobenzyl acetate. Also obtained was a substantial quantity of oily product which undoubtedly contained the ortho isomer. Beilstein and Kuhlberg (6) nitrated benzyl acetate with cold nitric acid of the highest concentration and also obtained *p*-nitrobenzyl acetate. They listed no yield.

EXPERIMENTAL

I. *Approaches to chloronaphthaldehyde via Gattermann aldehyde synthesis.* Anhydrous hydrogen cyanide (7.4 ml.) was added dropwise during fifteen minutes into a suspension of 20.6 g. of aluminum chloride in 31 ml. of ice-cooled chlorobenzene. After leaving the mixture fifteen minutes at room temperature to form $AlCl_3 \cdot 2HCN$, 10 g. of 2-chloronaphthalene was added. A slow stream of hydrogen chloride was passed in at 20–25° for fifteen minutes, then at 70° for five hours. The mixture was shaken frequently. The dark thick liquid was poured on ice, acidified, steam distilled to remove chlorobenzene, the residue extracted with ether, the ether extract washed with water and then treated with saturated sodium bisulfite solution. The copious precipitate was separated, washed with ether, and decomposed with sodium carbonate solution. The solid aldehyde which separated melted at 82–85°. Crystallizations from dil. alcohol and from hexane gave 2 g. of light yellow aldehyde, m.p. 100–102° corr. This is evidently the unknown 7-chloro-1-naphthaldehyde, since aqueous permanganate oxidized it to 7-chloro-1-naphthoic acid (7), m.p. and mixed m.p. 240–242°. Probably the lower-melting 6-chloro-1-naphthaldehyde (8) was present in the mother liquors.

II. *via Cleve's acid,* 5-amino-2-naphthalenesulfonic acid. This acid was obtained from the duPont Company.

(a) *Sodium 5-cyano-2-naphthalenesulfonate.* Cleve's acid (446 g.), dissolved in 1 liter of water containing 80 g. of sodium hydroxide, was diluted with 500 ml. of water and 1 kg. of crushed ice and precipitated by 1 liter of conc'd hydrochloric acid. The suspension was diazotized at 0–5° by the addition of 135 g. of powdered sodium nitrite during three hours. After neutralization to litmus by solid sodium carbonate, it was added during half an hour to a solution of 2.5 moles of cuprous chloride. Temperature was kept at 0–5° by adding ice. After two hours stirring, it was left overnight at room temperature, then 1.5 kg. of sodium chloride was added, and after two hours the precipitated sulfonate was collected and dried in an oven; yield 480 g.

(b) *5-Cyano-2-naphthalenesulfonyl chloride.* Fifty grams of the crude sodium sulfonate was heated by an oil-bath at 130°, for four hours with 70 g. of phosphorus pentachloride, then the mixture was poured on crushed ice, the brown solid was washed by decantation with cold water, ground in a mortar with cold water, filtered off, and dried. The powder was extracted with 200 ml. of benzene, concentrated to 100 ml., diluted with 100 ml. of hexane, and cooled to 0°. The yield of brown crystals, m.p. 149–151°, was 16.6 g. or 33% assuming pure sodium sulfonate. Another crystallization gave yellow crystals, m.p. 151–153° corr. Yields were less if the reaction period was only one hour, and the yield was negligible at room temperature after ten hours.

Anal. Calc'd for $C_{11}H_6ClNO_2S$: N, 5.57. Found: N, 5.86.

(c) *Aniline derivative.* Treatment of the sulfonyl chloride with aniline gave rise to 5-cyano-2-naphthalenesulfonanilide, m.p. 194°.

Anal. Calc'd for $C_{17}H_{12}N_2O_2S$: N, 9.09. Found: N, 9.24.

(d) *Reaction with phosphorus pentachloride at 160°.* Eight grams of 5-cyano-2-naphthalenesulfonyl chloride and 10 g. of phosphorus pentachloride were heated under reflux in an oil-bath at 160–165° for five hours. The mixture was poured on cracked ice, filtered, dried, and crystallized from alcohol. Four grams (66% calc'd as $C_{10}H_6ClCN$) of white crystals was obtained, m.p. 99–101°.

Anal. Calc'd for $C_{11}H_6ClN$: N, 7.47.
Calc'd for $C_{11}H_5Cl_2N$: N, 6.31. Found: N, 6.44, 6.46, 6.20.

Hydrolysis. Refluxing of 8.8 g. of the chlorinated naphthonitrile with 10 g. of sodium hydroxide in 15 g. of water and 50 ml. of alcohol for twenty-four hours liberated ammonia in quantity. The alcohol was distilled off and the residue was filtered and acidified (HCl). The product obtained was crystallized from 50% alcohol; yield 6 g., m.p. 190–200°. With a 5-hour refluxing period, 2.4 g. of nitrile gave rise to 0.2 g. of 6-chloro-1-naphthoic acid, m.p. 217°, and 0.5 g. of alkali-insoluble material.

III. *Other reactions with Cleve's acid.* (a) *Acetylation.* Sodium 5-amino-2-naphthalenesulfonate (117 g.), made from 112 g. of Cleve's acid, was treated with 150 ml. of acetic anhydride. Heat was evolved. After one hour at 100° it was cooled and the sodium 5-acetamido-2-naphthalenesulfonate filtered off and rinsed with alcohol; yield, 128 g. (94%).

(b) *5-Acetamido-2-naphthalenesulfonyl chloride.* Ten grams each of the salt from (a) and phosphorus pentachloride were ground in a mortar. The mixture warmed forming a paste which, in fifteen minutes, was added to crushed ice. The solid was ground with water, filtered off, dried, and extracted with ethyl acetate in a Soxhlet. The yield of light tan crystalline material was 3.3 g. It did not melt up to 250°. Analysis was satisfactory for the sulfonyl chloride.

Anal. Calc'd for $C_{12}H_{10}ClNO_3S$: N, 4.94. Found: N, 5.19.

(c) *5-Acetamido-2-naphthalenesulfonanilide.* This derivative was prepared by reaction of the above chloride with aniline. The white crystals from dilute alcohol melted at 215–217° corr.

Anal. Calc'd for $C_{18}H_{16}N_2O_3S$: N, 8.23. Found: N, 8.49.

IV. *via Chloromethylation of 2-chloronaphthalene.* 2-Chloronaphthalene (31.4 g.), 30% formaldehyde (24 ml.), and conc'd hydrochloric acid (41 ml.) were placed in a three-neck flask (300 ml.) equipped with stirrer and funnel. The contents were heated to 60° and held for six hours, during which conc'd sulfuric acid (27 ml.) was added with stirring. Heating and stirring were continued for another twenty-three hours, after which the mixture was cooled and diluted with 85 ml. of cold water. The mixture was extracted with ether, and the extract washed with water, saturated sodium bicarbonate solution, again with water, dried ($MgSO_4$), and filtered through Norit-Celite. Removal of the solvent left 29.0 g. of a thin, light amber oil which crystallized completely when cooled, and partially remelted at room temperature. This oil was distilled at 0.5 mm. to remove 14.1 g. of 2-chloronaphthalene at 65–85° (m.p. 54.5–55.5°). Steam was passed through the 14.9 g. of residue to remove traces of the chloronaphthalene, and the residue was taken up in ether. Removal of the solvent yielded 12.0 g. of amber oil. It was distilled at 1 mm.: 0.6 g. up to 120°; 9.4 g. at 120–123°, n_D^{25} 1.6434; residue 2.0 g. which solidified. The 9.4-g. sample was x-chloromethyl-2-chloronaphthalene.

Anal. Calc'd for $C_{11}H_8Cl_2$: Cl, 33.65. Found: Cl, 33.75.

V. *via Nitration of 2-naphthylamine.* Friedlaender and Szymanski (5) report the nitration of 2-naphthylammonium nitrate, by adding it slowly to conc'd sulfuric acid at −25°, to yield primarily 5-nitro-2-naphthylamine, m.p. 143.5°, and the 8-nitro isomer, m.p. 103.5°, as by-product. In our repetition of this work, we obtained from 124 g. of the nitrate 86 g. of red crystalline material, m.p. 88–89° from alcohol. Crystallization from benzene brought this m.p. to 91–92°.

Nitration of benzyl acetate. Dropwise addition (stirring) of 12.5 g. of benzyl acetate to a cooled (7°) mixture of conc'd sulfuric and conc'd nitric acids (12.5 ml. each) yielded a 2-layer system. A yellow solid separated on pouring into ice-water. After crystallization from alcohol, its m.p. was 67–71°. Another crystallization yielded *p*-nitrobenzyl acetate, m.p. 76–78°, in 6 g. yield (37%). An oily product, probably the ortho isomer, was in the mother liquors.

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SUMMARY

The Gattermann reaction with 2-chloronaphthalene yields 7-chloro-1-naphthaldehyde, but the 6-chloro isomer seems to be formed as well. Chloromethylation of 2-chloronaphthalene is described.

Cleve's acid was used as an intermediate for the synthesis of several derivatives of 5-cyano-2-naphthalenesulfonic acid and of 5-acetamido-2-naphthalenesulfonic acid.

Nitrations of 2-naphthylamine and benzyl acetate were investigated.

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REFERENCES

(1) C. M. SUTER, "Organic Chemistry of Sulfur," Wiley, New York, **1944**, p. 500.
(2) SCHROETER, *Ber.*, **39**, 1566 (1906).
(3) SCHWEITZER AND BURR, U. S. Patent 1,939,025; *Chem. Abstr.*, **28**, 1361 (1934).
(4) RUPE AND BRENTANO, *Helv. Chim. Acta*, **19**, 581 (1936)
(5) FRIEDLAENDER AND SZYMANSKI, *Ber.*, **25**, 2077 (1892).
(6) BEILSTEIN AND KUHLBERG, *Ann.*, **147**, 340 (1868).
(7) GOLDSTEIN AND FISCHER, *Helv. Chim. Acta*, **21**, 1519 (1938).
(8) JACOBS, WINSTEIN, HENDERSON, *et al.*, *J. Org. Chem.*, **11**, 229 (1946).