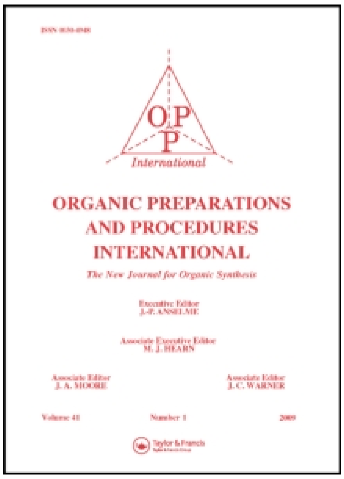

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PREPARATION OF HROMOBENZOIC ACIDS FROM THE CORRESPONDING BROMOTOLUENES VIA THE KROHNKE METHOD

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solution was heated on the water bath for 30 min. The reaction mixture was filtered and concentrated to leave the residue, which was extracted with dichloromethane. The dichloromethane extract was washed with water, dried over Na_2SO_4 and evaporated in vacuo to leave the residue which was chromatographed on silica gel with hexane as an eluent give 149 mg (90%) of III.

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PREPARATION OF BROMOBENZOIC ACIDS FROM THE CORRESPONDING BROMOTOLUENES VIA THE KROEHNKE METHOD

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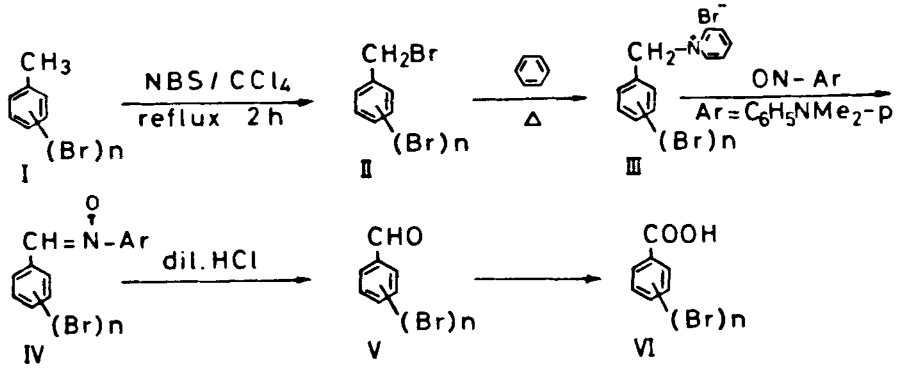
Although oxidation of bromotoluenes (I), which have one or two bromo groups in the ortho positions, was carried out according to the reported methods[1,2] in order to obtain the corresponding bromobenzoic acids, their yields were very poor (a few percent).

We wish to report a convenient preparative route of the title compounds from the corresponding bromotoluenes *via* the Kröhnke method.[3]



a: 2,3-Br_2
b: 2,4-Br_2
c: 2,6-Br_2
d: 2,3,4-Br_3
e: 2,4,5-Br_3

As shown in Scheme I, the preparative route from I to VI is longer than that of direct oxidation of I to VI. However, purification of III and isolation of IV were unnecessary, and the yields in each procedure were good. Handling of each procedure was very easy. Based on the above results this route seems to be a practical method for the preparation of bromobenzoic acids having bromo groups in their ortho positions.

EXPERIMENTAL SECTION

All melting points are uncorrected. Compound Ic is commercially available and the others (Ia-b, Id-e) were prepared according to the reported method.[1]

Reaction of I with NBS. Typical Procedure.- After a mixture of 3 g (12 mmol) of Ia, 2.3 g (13 mmol) of NBS, 0.1 g of benzoyl peroxide in 30 ml of carbon tetrachloride was refluxed for 2 hrs, the formed succinimide was removed by filtration. The filtrate was evaporated *in vacuo* to afford 3 g

(76%) of IIa as colorless needles (hexane), mp. 33.5-34°.

Anal. Calcd. for $C_7H_5Br_3$: C, 25.57; H, 1.53

Found: C, 25.75; H, 1.72

IIb as a colorless oil, lit.[4] mp. 40-41°; yield: 70%.

Anal. Calcd. for $C_7H_5Br_3$: C, 25.57; H, 1.53

Found: C, 25.48; H, 1.63

IIc as colorless needles (hexane), mp. 80-81°, lit.[4] 80°; yield: 76%.

Anal. Calcd. for $C_7H_5Br_3$: C, 25.57; H, 1.53

Found: C, 25.72; H, 1.53

IId as colorless needles (hexane), mp. 66-67°; yield: 74%.

Anal. Calcd. for $C_7H_4Br_4$: C, 20.62; H, 1.00

Found: C, 20.83; H, 1.09

IIe as colorless needles (hexane), mp. 95-96°; yield: 98%.

Anal. Calcd. for $C_7H_4Br_4$: C, 20.62; H, 1.00

Found: C, 20.81; H, 1.14

Reaction of II with Pyridine. Typical Procedure.- A solution of 2.96 g (9 mmol) of IIa and 1 ml of pyridine in 20 ml of benzene was refluxed for 1 hr. The precipitated IIIa was collected and washed with a small amount of benzene to give 3.45 g (94%) of IIIa as colorless prisms (water), mp. 257-258° (dec.).

Anal. Calcd. for $C_{12}H_{10}NBr_3$: C, 35.33; H, 2.47; N, 3.43

Found: C, 35.12; H, 2.52; N, 3.78

IIIb as colorless prisms (water), mp. 217-218° (dec.); yield: 91%

Anal. Calcd. for $C_{12}H_{10}NBr_3$: C, 35.33; H, 2.47; N, 3.43

Found: C, 35.32; H, 2.49; N, 3.83

IIIc as colorless prisms (water), mp. 235-238° (dec.); yield: 86%.

Anal. Calcd. for $C_{12}H_{10}NBr_3$: C, 35.33; H, 2.47; N, 3.43

Found: C, 34.89; H, 2.54; N, 3.68

IIId as colorless prisms (water), mp. 275-278° (dec.); yield: 90%.

Anal. Calcd. for $C_{12}H_9NBr_4$: C, 29.60; H, 1.86; N, 2.87

Found: C, 29.65; H, 1.96; N, 3.30

IIIe as colorless prisms (water), mp. 238-240° (dec.); yield: 90%.

Anal. Calcd. for $C_{12}H_9NBr_4$: C, 20.60; H, 1.86; N, 2.87

Found: C, 29.49; H, 2.26; N, 3.10

Preparation of V from III. Typical Procedure.- After a solution of 3 g (7.53 mmol) of IIIa, p-nitrosodimethylaniline (1.2 g, 8 mmol) and 0.5 ml of aq. 10% NaOH in 20 ml of ethanol was stirred for 1 hr*, 20 ml of aq. 10% HCl was added into the reaction mixture and then the mixture was stirred for 30 min. to afford 1.16 g (60% from IIIa) of Va as colorless needles (methanol), mp. 89.5-90.5°.

Anal. Calcd. for $C_7H_4OBr_2$: C, 31.85; H, 1.52

Found: C, 31.75; H, 1.68

IVb as yellow needles (EtOH), mp. 173-175°.

Anal. Calcd. for $C_{15}H_{14}N_2OBr_2$: C, 45.25; H, 3.54; N, 7.03

Found: C, 45.19; H, 3.56; N, 7.29

The other compounds IV were not isolated.

Vb as colorless needles (methanol), mp. 84-85°, lit.[5] mp. 80°; yield: 62% (from IIIb).

Vc as colorless needles (methanol), mp. 92-93°, lit.[6] mp. 90.5°; yield: 77% (from IIIc).

Vd as colorless needles (methanol), mp. 134-135°; yield: 65% (from IIId).

Anal. Calcd. for $C_7H_3OBr_3$: C, 24.52; H, 0.88

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*At that point, sometimes IV precipitated as a crystalline solid. Isolation of IV can be carried out by filtration. For example, IVb was isolated and purified by recrystallization from ethanol.

Found: C, 24.36; H, 0.96

Ve as colorless needles (methanol), mp. 146-147°; yield: 73% (from IIIe).

Anal. Calcd. for $C_7H_3OBr_3$: C, 24.52; H, 0.88

Found: C, 24.50; H, 0.93

Oxidation of V with $KMnO_4$ in Acetone. Typical Procedure.- To a refluxing solution of 0.79 g (3 mmol) of Va in 30 ml of acetone was added a saturated aqueous $KMnO_4$ (1 g) solution. After the disappearance of the color of $KMnO_4$, the warm reaction mixture was filtered to remove precipitated MnO_2 which was washed with acetone. The filtrate and the acetone wash were combined and concentrated in vacuo to leave a residue which was treated with dil. HCl and extracted with CH_2Cl_2. The CH_2Cl_2 solution was washed with water, dried with Na_2SO_4 and evaporated in vacuo to give 2.16 g (72%) of VIa as colorless needles (EtOH-H_2O), mp. 150-151°, lit.[1] mp. 145-150°.

VIb as colorless needles (EtOH-H_2O), mp. 168-169°, lit.[1] mp. 168-169°; yield: 75%.

VIc as colorless needles (EtOH-H_2O), mp. 147-148°, lit.[1] mp. 146-147°; yield: 65%.

VId as colorless needles (EtOH-H_2O), mp. 199-200°, lit.[1] mp. 197-198; yield: 70%.

VIe as colorless needles (EtOH-H_2O), mp. 197-198°, lit.[1] mp. 195-196°; yield: 76%.

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