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# A NEW APPLICATION OF REDUCTIVE ACETYLATION

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In the reductive acetylation of 2,4,6-tribromoresorcinol, as recently reported (1), 4,6-dibromoresorcinol diacetate was obtained. It therefore seemed desirable also to subject nitro compounds to reductive acetylation, for if the procedure is applicable, acetylated amines would be produced directly.

Our experiments have shown that halogenated *o*-nitrophenols react vigorously with zinc dust in acetic anhydride and acetic acid. The mixture is at first dark, but later lightens. Difficulty was encountered in that the products of apparently identical experiments showed different melting points on recrystallization. This was found to be due to incomplete acetylation, for if the dried crude products were boiled for a time with acetic anhydride, material of constant melting point was obtained. Analyses of these products showed them to be the corresponding triacetates.

2,4-Dibromo-6-nitrophenol (I) and 2,4-dichloro-6-nitrophenol (III) were prepared from phenol as previously described (2). The reductive acetylation of I gave the triacetate of 2,4-dibromo-6-aminophenol (II), that of III gave 2,4-dichloro-6-aminophenol triacetate (IV).

4-Chlorophenol was brominated with one mole of bromine to 2-bromo-4-chlorophenol, which was converted to 2-bromo-4-chloro-6-nitrophenol (V). Reductive acetylation of V yielded 2-bromo-4-chloro-6-aminophenol triacetate (VI). Application of the procedure to 2-chloro-4-bromo-6-nitrophenol (VII) gave similarly 2-chloro-4-bromo-6-aminophenol triacetate (VIII).

*p*-Cresol gives on bromination dibromo-*p*-cresol, which with nitrous acid exchanges a bromine atom for a nitro group to yield 5-bromo-3-nitro-4-hydroxy-1-methylbenzene (3), IX. Reductive acetylation of IX resulted in the triacetate of 5-bromo-3-amino-4-hydroxy-1-methylbenzene (X).

Also, nitro compounds which do not contain a phenolic hydroxyl can be reductively acetylated. The easily accessible 4-bromo-2-nitroanisole (4) (XI) can thus be readily converted to 4-bromo-2-acetamidoanisole (XII).

## EXPERIMENTAL

*Reductive acetylation of 2,4-dibromo-6-nitrophenol (I) to 2,4-dibromo-6-aminophenol triacetate (II).* Ten grams of I is mixed with 70 ml. of acetic anhydride and 15 ml. of gl. acetic acid, 10 g. of zinc dust added cautiously (goggles!), and reflux condenser attached. The reaction is vigorous and the mixture darkens. It is cooled, and zinc dust added from time to time with shaking and breaking of lumps until the liquid is nearly colorless, finally refluxed for a few minutes, and filtered. The zinc dust residue is extracted with acetic acid, the combined filtrates diluted with water, and after a time the white solid is washed with water and dried well in a vacuum. The powdered dry product is refluxed for an hour with 4–5 times its weight of acetic anhydride, poured cold into water, and after a time filtered,

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washed, and crystallized from alcohol; granular rhombohedron-like crystals of m.p. 150°.

*Anal.* Calc'd for $C_{12}H_{11}Br_2NO_4$: C, 36.64; H, 2.80; N, 3.56; Br, 40.71.
Found: C, 37.19; H, 2.92; N, 3.33; Br, 40.68.

*Reductive acetylation of 2,4-dichloro-6-nitrophenol (III) to 2,4-dichloro-6-aminophenol triacetate (IV).* The reductive acetylation of III was carried out in the same manner as the preceding experiment. The product from the acetic anhydride treatment gave from alcohol colorless prisms of m.p. 112°.

*Anal.* Calc'd for $C_{12}H_{11}Cl_2NO_4$: Cl, 23.35; N, 4.61.
Found: Cl, 23.31; N, 4.48.

*2-Bromo-4-chloro-6-nitrophenol (V) to 2-bromo-4-chloro-6-aminophenol triacetate (VI).* The product crystallizes from alcohol in granular crystals of m.p. 144°.

*Anal.* Calc'd for $C_{12}H_{11}BrClNO_4$: C, 41.38; H, 3.16; N, 4.02.
Found: C, 41.43; H, 3.05; N, 3.93.

*4-Bromo-2-chloro-6-nitrophenol (VII) to 2-chloro-4-bromo-6-aminophenol triacetate (VIII).* The compound VIII, obtained by the above procedure, crystallizes from alcohol in granular crystals of m.p. 116°.

*Anal.* Calc'd for $C_{12}H_{11}BrClNO_4$: C, 41.38; H, 3.16; N, 4.02.
Found: C, 40.99; H, 3.29; N, 4.03.

*5-Bromo-3-nitro-4-hydroxy-1-methylbenzene (IX) to 5-bromo-3-amino-4-hydroxy-1-methylbenzene triacetate (X).* IX, prepared by the method of Zincke and Emmerich (3), gives on reduction as described, the compound X, which separates from alcohol in granular crystals of m.p. 110°.

*Anal.* Calc'd for $C_{13}H_{14}BrNO_4$: N, 4.27. Found: N, 4.46.

*4-Bromo-2-nitroanisole (XI) (4) to 4-bromo-2-acetamidoanisole (1-methoxy-2-acetamido-4-bromobenzene) (XII).* The preparation of XII is carried out as in the above examples, except that the crude, damp product from water is dissolved in a little alcohol, and the dark solution allowed largely to evaporate; the mother liquors are removed, and the product purified from water containing a little acetic acid. The dried product is crystallized from benzene-ligroin; leaflets, m.p. 122°.

*Anal.* Calc'd for $C_9H_{10}BrNO_2$: C, 44.26; H, 4.10; N, 5.74; Br, 32.79; $OCH_3$, 12.70.
Found: C, 44.32; H, 4.13; N, 5.75; Br, 33.20; $OCH_3$, 13.01.

## SUMMARY

1. A new application of reductive acetylation is described, in which nitro compounds are converted directly to the acetates of the amino compounds. From 2,4-dibromo-6-nitrophenol, 2,4-dichloro-6-nitrophenol, 2-chloro-4-bromo-6-nitrophenol, 4-chloro-2-bromo-6-nitrophenol, and 5-bromo-3-nitro-4-hydroxy-1-methylbenzene, the triacetates of the corresponding aminophenols were obtained.

2. Nitro compounds containing no phenolic group can also be reductively acetylated; 4-bromo-2-nitroanisole gives thus 4-bromo-2-acetamidoanisole.

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## REFERENCES

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