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N-BROMOSUCCINIMIDE: DIRECT OXIDATION OF ALDEHYDES TO ACID BROMIDES

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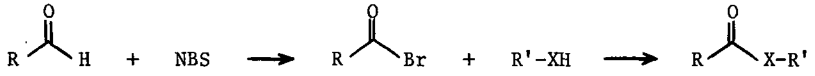
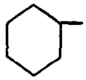
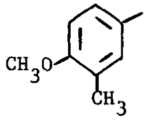
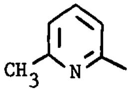
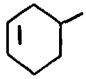
Summary. N-Bromosuccinimide was shown to oxidize aldehydes to the corresponding acid bromides.

N-Bromosuccinimide (NBS) is a versatile synthetic reagent, perhaps most widely used to effect bromination at allylic and benzylic positions.[1] It also oxidizes primary and secondary alcohols to aldehydes and ketones, respectively.[1] Recently, during an attempt to brominate the benzylic methyl group of 4, we observed unexpectedly the exclusive formation of the corresponding acid bromide instead. An extensive search of the literature revealed only a few isolated reports on the reaction of NBS with aromatic aldehydes.[2] In these cases, the presumed aromatic acid bromides were trapped with ammonia to give the corresponding amides in low yields. Realizing this reaction could be a useful alternative for oxidizing aldehydes, we decided to investigate this interesting reaction further. Our initial findings are reported here.

Typically, the aldehyde (10 mmol) was dissolved in solvent (20 ml), and NBS[3] added (see Table I). Under nitrogen, the reaction flask was illuminated with a 150W flood lamp. In cases where spontaneous reflux failed to start, external heating was applied. The reaction was complete in a few minutes.[4] In order to facilitate the isolation of products, the acid bromide

Table I. NBS-Oxidation of Aldehydes



Substrate, R	NBS (equiv.)	Solvent	Reaction Time (min.)	Product, R'-X-	Yield (%)[a]
1 C_6H_5	1.33	CCl_4	10	CH_3O-	84
2 	1.1	"	1.5	CH_3O-	82
3 n-C_3H_7	1.1	"	2.0	ØCH$_2$NH-	66
4 	1.33	"	7.0	CH_3O-	70
5 	1.33	"	12	CH_3O-	55
6 	1.1	"	2.0	CH_3O-	23[b]

[a] Isolated yields. [b] Product mixture isolated by distillation, desired methyl ester estimated by vpc analysis.

was converted in situ to an ester or an amide.

The results in Table I suggest the applicability of this reaction to a variety of aldehydes. The yields are fair to good,[5a,b] although conditions have not been optimized. We have demonstrated that this oxidation reaction is not limited to aromatic aldehydes. It is particularly interesting to note that benzylic positions are not brominated under the conditions described. The fact that heterocyclic and aromatic carboxaldehydes are oxidized is of note since many such aldehydes are easily accessible by either the Vilsmeier-Haack[6a] or Reimer-Tiemann reactions.[6b] Unfortunately, NBS is apparently not selective enough to affect clean oxidation in the presence of olefinic functions (as in 6).

The intermediacy of acid bromides in the reaction sequence presented was established by direct isolation of benzoyl bromide[5a] in 48% yield when benzaldehyde was allowed to react with NBS in benzene.

Although a number of reagents are known to oxidize aldehydes to carboxylic acids, notably chromium[7] and silver compounds,[8] none, except Corey's MnO_2-oxidation of cyanohydrins,[9] offers the advantage of simultaneous oxidation and activation of the resultant carboxyl group. Thus we believe this reaction should prove to be an important addition to the existing synthetic approaches to carboxylic acids and their derivatives.

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3. NBS was recrystallized according to the procedure of H. J. Dauben and L. L. McCoy, J. Amer. Chem. Soc., 81, 4863 (1959).
4. In some cases, up to a few percent of starting material remained unreacted.
5. (a) Spectroscopic data were consistent with the assigned structures. (b) Satisfactory elemental analysis were demonstrated after either recrystallization or preparative vpc of the isolated products.
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7. For a recent example, see E. J. Corey and G. Schmidt, Tet. Lett., 399 (1979).
8. For some examples, see L. F. Fieser and M. Fieser, "Reagents for Org. Syn.," Wiley (New York), 1967, Vol. 1, p. 1012.
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