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A NEW GENERAL METHOD FOR THE INTRODUCTION OF THE ALDEHYDE FUNCTION IN AROMATIC COMPOUNDS

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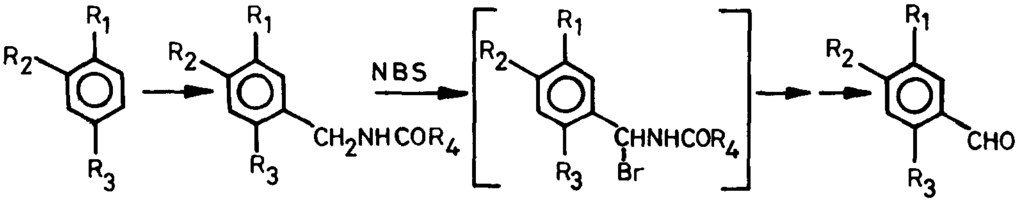
Abstract: Side chain bromination of aromatic amidomethylated compounds yields aldehydes.

A variety of methods are available for the introduction of aldehyde function into aromatic rings. They fall into two categories, viz. (i) direct formylation[1] or (ii) introduction of an appropriate substituent[2] - generally by electrophilic substitution - which is later converted to an aldehyde group. None of these existing methods are applicable to deactivated aromatic rings carrying substituents like nitro, alkoxycarbonyl, etc.

Unlike chloromethylation[3] and Friedel-Crafts acylation reactions[4], amidomethylation reactions can be used to substitute even highly deactivated rings[5]. We have found that amidomethyl derivatives can be conveniently converted to the aldehydes by side chain bromination with N-bromosuccinimide (NBS), and subsequent dehydrobromination and hydrolysis in a single-pot sequence.

We find that the amidomethyl group is preferentially brominated even in the presence of methyl groups. Consequently, the amidomethylation-bromination sequence becomes applicable to a variety of aromatic substrates (see Table).



(a) $R_1 = R_2 = R_3 = H$, $R_4 = CH_3$
(b) $R_1 = R_2 = R_3 = H$, $R_4 = CH_2Cl$
(c) $R_1 = R_3 = H$, $R_2 = CH_3$, $R_4 = Ph$
(d) $R_1 = R_3 = H$, $R_2 = CH_3$, $R_4 = CH_2Cl$
(e) $R_1 = H$, $R_2 = R_3 = CH_3$, $R_4 = CH_3$
(f) $R_1 = H$, $R_2 = R_3 = CH_3$, $R_4 = CH_2Cl$
(g) $R_1 = NO_2$, $R_2 = R_3 = H$, $R_4 = CH_2Cl$
(h) $R_1 = COOMe$, $R_2 = R_3 = H$, $R_4 = CH_2Cl$
(i) $R_1 = COOH$, $R_2 = R_3 = H$, $R_4 = CH_2Cl$
(j) $R_1 = R_3 = Br$, $R_2 = H$, $R_4 = CH_2Cl$

Table

Amidomethylated Product	Aldehyde	Yield (%)	Amidomethylated Product	Aldehyde	Yield (%)
a	Benzaldehyde	70	f	2,4-Dimethylbenzaldehyde	50
b	Benzaldehyde	82	g	m-Nitrobenzaldehyde	70*
c	p-Tolualdehyde	60	h	Isophthalaldehydic acid	25
				Isophthalaldehydic acid methyl ester	35
d	p-Tolualdehyde	65	i	Isophthalaldehydic acid	90*
e	2,4-Dimethylbenzaldehyde	55	j	2,5-Dibromobenzaldehyde	75*

* Method B

The following procedures are typical.

Method A: A mixture of the amidomethylated compound (30 mmol), NBS (30 mmol), CCl_4 (200 ml) and dibenzoylperoxide (200 mg) was refluxed on the water bath for 3-5 h. Solvent was removed in vacuo and the residue was steam distilled after hydrolysing with 2M HCl. Steam distillate was extracted into ether and the crude aldehyde was purified by distillation or recrystallization.

Method B: An intimate mixture of the amidomethylated compound (1 mmol), NBS (2 mmol) and dibenzoylperoxide (10 mg) was heated on the water bath for 1 h. The reaction mixture was then refluxed with ethanolic HCl (10 min) and the aldehyde was isolated as the 2,4-DNP derivative.

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