Preparation of [*formyl*-^{2}H]- and [*formyl*-^{3}H]-Aldehydes

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ALDEHYDES, labelled with deuterium or tritium in the formyl group, are of value in mass-spectrometric and biosynthetic studies. The preparation of [*formyl*-^{2}H]aldehydes by decarboxylation of the corresponding deuterated glyoxylic acids (RCO·CO_2D) has recently been reported.[1] We now describe a simple method, of general application to aromatic aldehydes, which employs the readily accessible morpholino-nitriles (I).[2,3]

Aryl aldehydes were heated at 60° in morpholine containing morpholine perchlorate (1·1 mole) to form the corresponding iminium salts. Aqueous sodium cyanide (1·1 mole) was added and the mixture heated at 80° to give the derivatives (I) in high yield. The morpholino-nitriles were treated with sodium hydride (2 moles) in dry dimethylformamide, under nitrogen, at room temperature or, for the α-naphthyl derivative, at 40°, to form the corresponding benzylic anions.[4] Addition of deuterium oxide (*ca.* 5 moles) followed by thionyl chloride or excess of carbon dioxide gave the α-deuterated morpholino-nitriles (method *a*). Tritiation was effected in the same way. Alternatively, direct exchange of the α-hydrogen was carried out in dimethylformamide containing D_2O or [^{3}H]H_2O at 100° in a sealed tube for *ca.* 5 hr. This technique (method *b*) was preferred for labelling with tritium at high activity. Generally, hydrolysis of the labelled morpholino-nitriles with 2N-aqueous-ethanolic or aqueous hydrochloric acid under reflux gave the formyl-labelled aldehydes in high yield without loss of label. With the *m*-nitro-, *p*-cyano-, and *p*-nitro-phenyl derivatives, however, considerable loss of label occurred during hydrolysis. The following procedure (method *c*) was then adopted. Direct exchange of the morpholino-nitrile (as above) was carried out in sulpholan at 100°. Hydrolysis was effected at 100° after addition of thionyl chloride or sulphuryl chloride to generate [^{2}H]- or [^{3}H]-HCl. The results are tabulated.

Oxidation of veratraldehyde, *m*-nitrobenzaldehyde, and *p*-cyanobenzaldehyde, labelled with tritium by method *b*, to the corresponding acids

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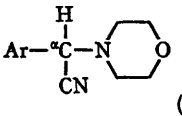
TABLE



(I)

Deuteration of aromatic aldehydes (Ar·CHO)

Ar	M.p. of (I)	Method	% D* in (I)	% D* in ArCHO
Phenyl	ref. 2	*a*	92	89
		b	*ca.* 100	—
3,4-Dimethoxyphenyl	ref. 3	*a*	99	99
4-Benzyloxy-3-methoxyphenyl	110—112°	*a*	*ca.* 100	*ca.* 100†
p-Nitrophenyl	147—149°	*c*	—	*ca.* 100
m-Nitrophenyl	88—89°	*c*	—	*ca.* 100
p-Cyanophenyl	128—129°	*a*	95	68
		c	—	96
p-Dimethylaminophenyl	139°	*a*	94	72
α-Naphthyl	103—104°	*a*	97	97

* % D in the α-position determined by n.m.r. spectroscopy.
† [*formyl*-^{2}H]Vanillin was also obtained as a by-product.

removed at least 99·5% of the tritium. Examination of the various deuterated aldehydes by n.m.r. spectroscopy also showed that labelling was confined to the aldehydic proton. When oxygen was passed through a solution of the anion derived from (I; Ar = 3,4-dimethoxyphenyl) by the action of sodium hydride, *N*-veratroylmorpholine was the major product.

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