

CATALYTIC ALKYLATION OF ALDEHYDES

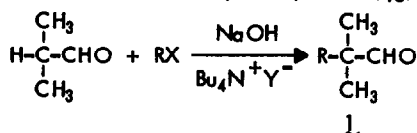
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As Solodar¹ pointed out, the successful completion of synthetic organic reactions involving an inorganic reactant hinges upon proper, intimate contact between the inorganic species, which is often water-soluble, and the organic species, which is often water-insoluble. Tetraalkylammonium ions have been used as catalysts in reactions which involve sodium or potassium hydroxide as a reactant, e.g., the alkylation of aryl-acetonitriles or ketones.^{2,3}

We found that aldehydes containing only one α -hydrogen atom, such as isobutyraldehyde or 2-ethylhexanal, can be transformed into alkylated products when treated with certain organic halides in the presence of 50% aqueous NaOH and catalytic amounts of tetrabutylammonium ions. Thus, isobutyraldehyde was treated with reactive organic halides to give C-alkylated products, \downarrow , according to the following scheme:



The specific reactants used and the products and yields obtained are listed in Table I.

TABLE I

ALKYLATION OF ISOBUTYRALDEHYDE					
R	X	Y	Temp, °C	Product	Yield, %
CH ₃ -	I	I	42	(CH ₃) ₃ CCHO	15
CH ₂ =CHCH ₂ -	Cl	I	20	CH ₂ =CHCH ₂ C(CH ₃) ₂ CHO	30
CH ₂ =CHCH ₂ -	Cl	I	60	CH ₂ =CHCH ₂ C(CH ₃) ₂ CHO	56
CH ₂ =CHCH ₂ -	Br	Cl	20	CH ₂ =CHCH ₂ C(CH ₃) ₂ CHO	35
CH ₃ CH=CHCH ₂ -	Cl	I	65	CH ₃ CH=CHCH ₂ C(CH ₃) ₂ CHO	54
C ₆ H ₅ CH ₂ -	Cl	I	20	C ₆ H ₅ CH ₂ C(CH ₃) ₂ CHO	34
C ₆ H ₅ CH ₂ -	Cl	I	70	C ₆ H ₅ CH ₂ C(CH ₃) ₂ CHO	75
(CH ₃) ₂ CH-	Br	I	20	Condensation products of isobutyraldehyde	

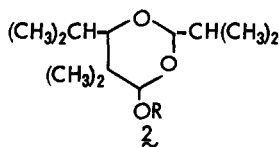
In a typical alkylation, a mixture of 140 g (3.5 mole) NaOH, 140 g water, 200 ml benzene, and 14.7 g (0.04 mole) tetrabutylammonium iodide was warmed to 70°C. While this mixture was being stirred, a

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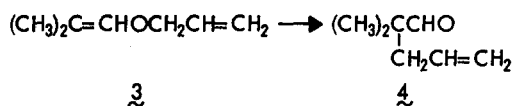
solution of 288 g (4.0 mole) isobutyraldehyde and 380 g (3.0 mole) benzyl chloride was added dropwise over a 5-hr period. Stirring was continued at 70°C for an additional 2 hr, and subsequent distillation of the organic portion afforded 364 g (75%) 2,2-dimethyl-3-phenylpropionaldehyde (bp 95°C at 7.2 torr).

The tendency of isobutyraldehyde toward base-catalyzed self-condensation is a considerable problem in these reactions. To avoid this self-condensation, we added a mixture of isobutyraldehyde and the halide dropwise to a stirred mixture of an inert solvent (such as benzene), the base, and the quaternary ammonium salt catalyst (preferably the iodide). It was advantageous to carry out the reactions at elevated temperatures (50 to 80°C) to avoid excessive formation of an O-alkylated trimer of isobutyraldehyde, **2**.

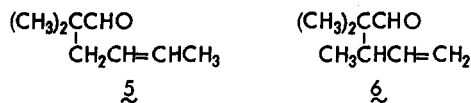


In general, reactive allylic halides and benzylic halides can be used with reasonable success in the alkylation of isobutyraldehyde: with less reactive halides the alkylation reaction cannot compete successfully with base-catalyzed self-condensation.

The alkylation of isobutyraldehyde gives C-alkylation products only. These C-alkylation products do not arise from O-alkylation products by a Claisen rearrangement, e.g., the rearrangement of **3** to **4**,



since the reaction with 1-chloro-2-butene gave only **5** and none of **6**, the product expected from a Claisen rearrangement.



Further, in the reaction of isobutyraldehyde with benzyl chloride, any enol-ether formed could not have undergone rearrangement, and no such enol-ether was detected.

2-Ethylhexanal gave higher yields of alkylated products than isobutyraldehyde owing to the greater stability of the former toward sodium hydroxide. Some O-alkylation (formation of enol-ethers) was observed in 2-ethylhexanal reactions, presumably because the attack at the α -carbon atom is more sterically hindered in 2-ethylhexanal than in isobutyraldehyde (see Table II).

TABLE II
ALKYLATION OF 2-ETHYLHEXANAL

<u>Halide</u>	<u>Catalyst</u>	<u>Temp, °C</u>	<u>Product</u>	<u>Yield, %</u>
$(\text{CH}_3)_2\text{CHBr}$	Bu_4NI	20	$\text{Bu}(\text{Et})\text{C}=\text{CHOCH}(\text{CH}_3)_2$	21
$\text{C}_6\text{H}_5\text{CH}_2\text{Cl}$	Bu_4NI	65	$\text{Bu}(\text{Et})\overset{\text{C}}{\underset{\text{CH}_2\text{C}_6\text{H}_5}{\text{C}}}\text{CHO}$	55
			$\text{Bu}(\text{Et})\text{C}=\text{CHOCH}_2\text{C}_6\text{H}_5$	35
$\text{CH}_2=\text{CHCH}_2\text{Cl}$	Bu_4NCl	40	$\text{Bu}(\text{Et})\overset{\text{C}}{\underset{\text{CH}_2\text{CH}=\text{CH}_2}{\text{C}}}\text{CHO}$	85
$\text{CH}_3\text{CH}=\text{CHCH}_2\text{Cl}$	Bu_4NI	65	$\text{Bu}(\text{Et})\overset{\text{C}}{\underset{\text{CH}_2\text{CH}=\text{CHCH}_3}{\text{C}}}\text{CHO}$	65
			$\text{Bu}(\text{Et})\text{C}=\text{CHOCH}_2\text{CH}=\text{CHCH}_3$	25
$(\text{CH}_3)_2\text{C}=\text{CHCH}_2\text{Cl}$	Bu_4NI	50	$\text{Bu}(\text{Et})\overset{\text{C}}{\underset{\text{CH}_2\text{CH}=\text{C}(\text{CH}_3)_2}{\text{C}}}\text{CHO}$	60
			$\text{Bu}(\text{Et})\text{C}=\text{CHOCH}_2\text{CH}=\text{C}(\text{CH}_3)_2$	30

This new method of alkylation provides a convenient route for the synthesis of certain substituted aldehydes which are otherwise not conveniently accessible.

REFERENCES

1. J. Solodar, *Tetrahedron Lett.*, 287 (1971) and references therein.
2. M. Makosza, *Tetrahedron Lett.*, 677 (1969).
3. A. Yonczyk, B. Serafin, and M. Makosza, *Tetrahedron Lett.*, 1351 (1971).