Regiospecific Introduction of Amino-alkene Functionality into 1,2,3-Triols, 1,3-Dihalogenopropan-2-ols, and 2,3-Dihalogenopropanols promoted by Fluoride Anion

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Regiospecific transformations of 1,2,3-triol, 1,3-dihalogenopropan-2-ol, and 2,3-dihalogenopropanol derivatives into oxazolidin-2-ones and/or oxazol-2(3*H*)-ones promoted by fluoride anion are described.

We report a group of new chemo- and regio-specific transformations which use the naked fluoride anion[1] as a chemoselective base to initiate the conversion of 1,2,3-triol derivatives into oxazolidinones and oxazolones[2] that are useful synthons and precursors for a variety of amino ketones, aldehydes, and alcohols.

The carbamate (**1a**)[3] was treated with tetra-n-butylammonium fluoride (TBAF) and methanesulphonyl fluoride (MsF)[4] in tetrahydrofuran (THF) at 50 °C to give the oxazolidinone (**3a**) exclusively.† This compound was readily converted into the aminomethyl ketone (**5a**) on treatment with sodium methoxide (1.1. equiv.) in methanol at room temperature. Results for other reactions of compounds (**1**) with TBAF–MsF are summarized in Table 1.

We next found that the dihalogeno compounds (**2**) underwent a similar type of reaction with TBAF to give methyleneoxazolidinone (**4**) and/or methyloxazolone (**7**) in good yields.

When R = alkyl in (**2**), the reaction gave the exocyclic methylene product (**4**) exclusively or predominantly, whereas aryl carbamates (R = Ar) gave the exocyclic methylene compound (**4**) or the ring-unsaturated isomer (**7**) selectively, depending on temperature. At room temperature (**4**) was formed exclusively, whereas (**7**) was the sole product at 50 °C. Subsequent methanolysis afforded aminomethyl ketones in good yields.

An interesting selectivity was also observed in the case of the 2,3-dihalogenopropyl phenylcarbamate (**8**). Treatment of (**8**; X = Cl) with TBAF at room temperature gave (**10**) exclusively, whereas at 50 °C the exocyclic methyleneoxazolidinone (**9**) was obtained. In contrast to the chloride (**8**; X = Cl), the bromo analogue (**8**; X = Br) gave the exocyclic isomer (**9**) selectively regardless of temperature. This selectivity provides a simple alternative preparation of (**9**) and (**10**) to that previously reported.[5] Compound (**10**) was also readily converted into the amino-aldehyde (**11**) in 62% yield upon treatment with sodium methoxide in methanol. Reactions of 1,3- or 2,3-dihalogeno derivatives are listed in Tables 2 and 3.

$PhNCO_2CH(CH_2Br)CH_2CH_2Br$ and $PhSO_2CH_2CO_2CH(CH_2Cl)_2$ also participate in this type of reaction to give the cyclized products (**12**) (82%) and (**13**) (65%), respectively.

The phase transfer catalyst–KF system[6] offers further interesting selectivity; the reaction ceased at the cyclization stage, and no unsaturated product was formed under these

† A typical procedure is as follows: to a solution of TBAF·$3H_2O$, (1.75 mmol; Aldrich, used without further purification) and molecular sieves 4A (1.0 g) in THF (2 ml) was added a mixture of (**1a**) (0.30 mmol) and MsF (1.14 mmol) in THF (2 ml) at room temperature, and the mixture was stirred at that temperature for 2 h and then at 50 °C for 5.5 h. The mixture was filtered, dried ($MgSO_4$), and evaporated to give a crude oil (92 mg). Purification on preparative t.l.c. (eluant: AcOEt–n-hexane, 1 : 2) gave (**3a**) (49 mg, 67%) as a mixture of *E*- and *Z*-isomers. These isomers isomerized to 5-hexyl-3-phenyl-2(3*H*)-oxazolone on treatment with activated silica gel in n-hexane at room temperature.

Table 1. Reactions of compounds (**1**).[c]

	R	(**2**), % yield[a] (*E* : *Z*)[b]	(**3**), % yield[a]
a;	Ph	67 (75 : 25)	76
b;	c-C_6H_{11}	64 (63 : 37)	80
c;	Me	50 (68 : 32)	85

[a] Isolated yield. All compounds gave satisfactory spectral data. [b] Determined by n.m.r. measurement of the alkene protons. [c] An 82 : 18 mixture of *anti* and *syn* isomers of (**1**). See ref. 3.

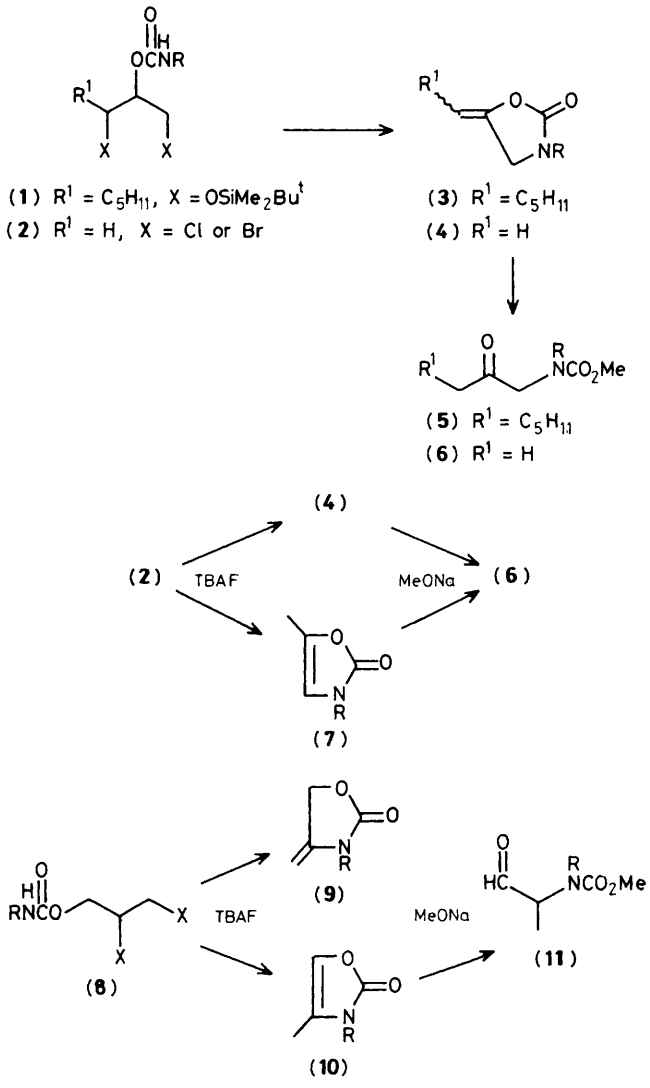


Table 2. Reactions of compounds (2).[a]

	R	X	% Yield[b] (4)	(7)	(6)
a;	Ph	Cl[c]	76	0	80
		Cl	0	72	88
		Br	0	79	—
		F	0	9	—
b;	4-ClC$_6$H$_4$	Cl	0	65	—
		Br	0	71	—
c;	1-Naphthyl	Cl	0	75	—
d;	c-C$_6$H$_{11}$	Cl[c]	90	0	77
		Cl	78	12	—
e;	Me	Cl	72	0	80

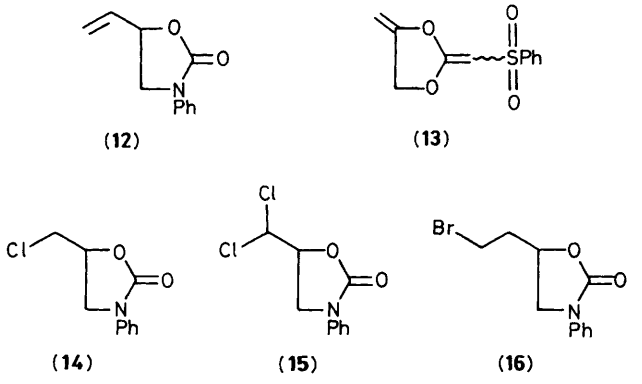
[a] Reactions were carried out with (2) : TBAF = 1.0 : 2.5—3.0 in THF at 50 °C unless otherwise noted. The methanolysis was performed with 1.1 equiv. of MeONa in MeOH at 50 °C unless otherwise noted. [b] Isolated yield. All compounds gave satisfactory spectral data. [c] At room temperature.

conditions: *e.g.* (**2**; R = Ph, X = Cl), PhNCO$_2$CH(CH$_2$Cl)-CHCl$_2$, and PhNCO$_2$CH(CH$_2$Br)CH$_2$CH$_2$Br gave (**14**) (83%), (**15**) (91%), and (**16**) (74%), respectively with 10 mol% of benzyltriethylammonium chloride and 4 equiv. of KF in toluene–water at 50—90 °C.

Table 3. Reactions of compounds (8).

R	X	Temp./°C	% Yield[b] (9)	(10)
Ph	Cl	R.t.	0	51
	Cl	50	69	0
	Br	R.t.	80	0
	Br	50	68	0
c-C$_6$H$_{11}$	Cl	R.t.	0	17

[a] Reactions were carried out with (8) : TBAF = 1.0 : 2.5—3.0 in THF at room temp. or 50 °C. [b] Isolated yield. All compounds gave satisfactory spectral data.



Thus, TBAF is an excellent chemoselective base for the introduction of amino-alkene functionality into 1,2,3-triol, 1,3-dihalogenopropan-2-ol, and 2,3-dihalogenopropanol derivatives, offering a versatile synthesis of oxazolidinones and oxazolones. Use of KF in a phase transfer catalyst system furnishes a selective approach to halogeno-oxazolidinones.

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