Highly Selective *C*-Alkylation of Ambident Anions; Synthesis of 9-Alkyl-9-benzoylfluorene by Phase Transfer Reaction

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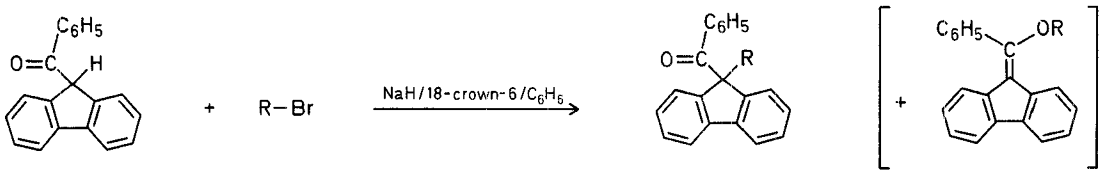
In a previous paper[1], we have shown that alkylation of sodium naphtholate, in the presence of crown ethers, gives high ratios of *O*/*O*+*C*-alkylation, when conducted in various solvents. As an extension of our previous work, we have been interested in seeking examples of the enhancement of reaction by crown ethers in the little studied field of alkylation of ambident anions. It is known[2,3] that the 9-benzoylfluorenide anion is an ambident anion capable of forming covalent bonds either at oxygen or carbon atom on alkylation.

Boisset et al.[3] found that the 9-benzoylfluorenide anion, prepared from the reaction of 9-benzoylfluorene (**1**) with potassium, could be alkylated with primary and secondary alkyl halides and that the basicity of the solvent played a decisive role in determining the reaction course of the ambident anion; in aprotic solvents, the ratio of *C*-alkylation in the alkylation products decreases with a decrease in basicity of the solvents. Furthermore, they suggested that the reaction of primary and secondary alkyl halides with the 9-benzoylfluorenide anion in ethanol gave *C*-alkylation products (**3a-c**) in relatively high yields. Furthermore, Mąkosa et al.[4] found that fluorene is alkylated with alkyl halides in basic aqueous medium in the presence of triethylbenzylammonium chloride as phase transfer catalyst. However, there has been no report of the reaction of *t*-alkyl halide with **1**. The presence of a crown ether may lead to a high degree of selective alkylation (at the C or O atom) and to successful alkylation by *t*-alkyl halides. Therefore, we studied the reaction of **1** with a variety of alkyl halides in the presence of 18-crown-6 as a phase transfer catalyst.

We have found that the 9-benzoylfluorenide anion, generated in a catalytic two phase system, can be alkylated in high selectivity on the carbon atom with alkyl halides. Thus, stirring of **1** with excess alkyl halide and sodium hydride in the presence of 18-crown-6 in benzene leads to the formation of the *C*-alkylated product **3** in moderate to good yield together with a trace of the *O*-alkylation product **4**.



1 **2a-g** **3a-g** **4a-c**

	a	b	c	d	e	f	g
R	CH_3	C_2H_5	*i*-C_3H_7	*t*-C_4H_9	$C_2H_5-C(CH_3)_2-$	*i*-$C_3H_7-C(CH_3)_2-$	*n*-$C_4H_9-C(CH_3)_2-$

However, in the absence of 18-crown-6, the reaction of **1** with alkyl halides gave extremely low yields of the alkylation products **3**. These results are also listed in the Table. The more important finding is that the catalytic two phase reaction is not sensitive to the alkyl halide type. Thus, with *t*-alkyl halides, compounds **3d-g** are obtained. However, in contrast to this alkylation, we could not obtain the alkylated products of **1** using *t*-alkyl halides as alkylating agent by the known methods[2,3]. Therefore, the catalytic alkylation of **1** with alkyl halides in benzene represents a particularly useful method for the selective synthesis of 9-alkyl-9-benzoylfluorene such as **3a-g**. On the other hand, when **1** and primary and secondary alkyl halides were allowed to react in tetrahydrofuran, dimethyl sulfoxide, or diglyme, the corresponding *C*-alkylation products **3** were obtained together with a substantial amount of the *O*-alkylation product, but the yield of the *C*-alkylation product **3** was very poor as compared with the results in the Table.

Alkylation of **1** was also carried out in benzene/aqueous sodium hydroxide solution with 18-crown-6 as a liquid-liquid two phase transfer catalyst. When primary and secondary alkyl halides were employed as alkylating agent, the results were usually quite similar, although a less satisfactory result in the case of **3c** was obtained. However, the reaction of **1** with *t*-alkyl halides under these conditions gave extremely low yields of the corresponding alkylation product **3**. The results with the *t*-alkyl halides must be explained by the competition between dehydrohalogenation and alkylation occurring in the liquid-liquid two phase system.

The structures of the new compounds **3d-g** are in accord with I.R., ^{1}H-N.M.R., Mass, and U.V. spectra, and microanalytical data. Known products were identified by comparison of I.R., N.M.R., and m.p. data with those of authentic samples.

Alkylation of 9-Benzoylfluorene (1); General Procedure:

A mixture of 9-benzoylfluorene (**1**; 2.78 g, 0.01 mol), 18-crown-6 (0.47 g), 50% sodium hydride in oil (0.9 g), and benzene (75 ml) is stirred at the appropriate temperature. After 30 min the alkyl bromide **2** (0.03 mol) is added and the reaction mixture is stirred for several hours. The resultant mixture is washed with water and dried over anhydrous sodium sulfate. The benzene solution is subjected to gas chromatographic analysis (conditions: 1 m × 3 mm; 3% Silicon OV-17 on Chromosorb W; column temp. 220–250°, carrier gas nitrogen). The pure sample of 9-alkyl-9-benzoylfluorene **3** is obtained by the following procedure. The benzene solution is concentrated to 30 ml and then passed through a column of neutral

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Table. Alkylation of 9-Benzoylfluorene (**1**)

Product	Reaction conditions temperature/time	Yield[a] [%]	m.p.	Molecular formula[b] or Lit. m.p.	U.V. (C_2H_5OH) λ_{max} [nm]	^{1}H-N.M.R. ($CDCl_3$/TMS) δ [ppm]	M.S. (70 eV) *m/e* (rel. intensity)
3a	27°/1 h	95 (trace)	101–102°	101.5°[2]	—	—	—
3b	27°/4 h	85 (trace)	129–130°	129.5°[2]	—	—	—
3c	60°/3 h	95 (trace)	69–70°	69–70°[2]	—		313 (1); 208 (3); 105 (100); 43 (1)
3d	80°/5 h	85 (trace)	89–90°	$C_{24}H_{22}O$ (326.4)	302 (3990); 289 (sh, 5880); 258 (18430)	1.06 (s, 9H, t-C_4H_9); 6.85–7.84 (m, $13H_{arom}$)	326 (2); 221 (11); 105 (100); 57 (4)
3e	80°/5 h	82 (trace)	oil	$C_{25}H_{24}O$ (340.4)	302 (3680); 291 (5880); 258 (18430)	0.70 (t, 3H, $J=8$ Hz, CH_3); 1.12 [s, 6H, $C(CH_3)_2$]; 1.35 (q, 2H, $J=8.9$ Hz, CH_2); 6.72–7.82 (m, $13H_{arom}$)	340 (2); 235 (10); 105 (100); 71 (85)
3f	80°/4 h	30 (10)	124–125°	$C_{26}H_{26}O$ (354.5)	303 (3700); 291 (sh, 6700); 253 (19460)	0.67 [d, 6H, $J=7.5$ Hz, $CH(C\underline{H}_3)_2$]; 1.12 [s, 6H, $C(C\underline{H}_3)_2$]; 1.52–1.58 (m, 1H, CH); 6.55–7.85 (m, $13H_{arom}$)	354 (1); 249 (8); 105 (100); 85 (22)
3g	80°/4 h	54 (25)	oil	$C_{27}H_{28}O$ (368.5)	303 (4230); 292 (sh, 5970); 260 (19170)	0.68 (d, 3H, $J=5$ Hz, $CH_2C\underline{H}_3$); 1.12 [s, 6H, $C(CH_3)_2$]; 1.18–1.78 [m, 6H, $(CH_2)_3$]; 6.65–7.90 (m, $13H_{arom}$)	368 (1); 263 (5); 105 (100); 99 (1)

[a] Yields determined by G.L.C.; the values in brackets are obtained in the absence of crown ether; isolated yields are, respectively, **3a**, 91%; **3b**, 80%; **3c**, 88%; **3d**, 81%; **3e**, 70%; **3f**, 22%; **3g**, 40%.

[b] Compounds **3d–f** gave satisfactory microanalyses (C ±0.3, H ±0.3).

alumina eluting with benzene (30 ml each fraction). Fractions 3–7, containing the 9-alkyl-9-benzoylfluorene, are combined and evaporated. Recrystallization of the residue from ethanol gives the pure *9-alkyl-9-benzoylfluorene* **3** (see Table).

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