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A New Selective Synthesis of Aryl 2,2-Diethylbutyl Ethers

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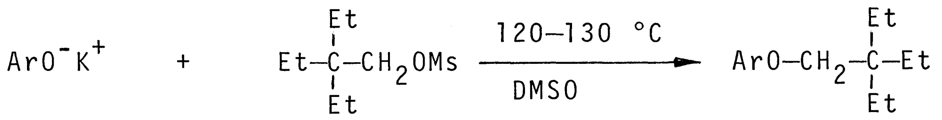
The nucleophilic substitution reactions of hindered 2,2-diethylbutyl methanesulfonate with potassium aryloxides were carried out in dimethyl sulfoxide at higher temperatures. New unrearranged hindered ethers were readily obtained in excellent yields as the desired products.

The S_N2 reactions of neopentyl halide and p-toluenesulfonate with sodium alkoxides are extremely hindered, and believed to be of little use for synthetic purpose.[1-3] In fact, the corresponding unrearranged ethers have been obtained in poor to moderate yields.[4-9]

However, we found that more hindered homologous 2,2-diethylbutyl methanesulfonate reacted with potassium aryloxides to afford new unrearranged ethers in excellent yields under optimum conditions, as shown in Scheme 1.

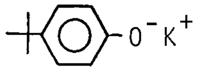
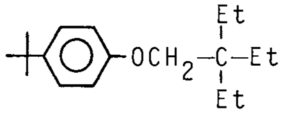
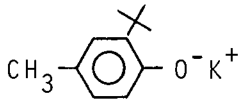
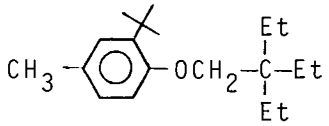
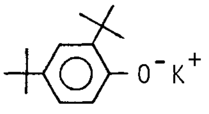
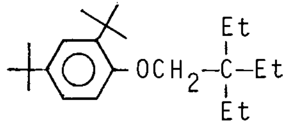
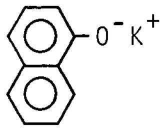
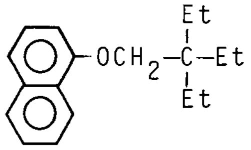
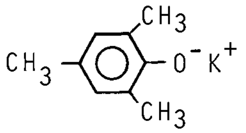
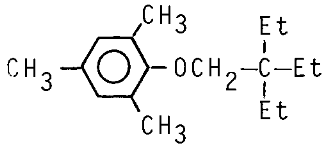
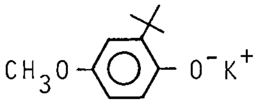
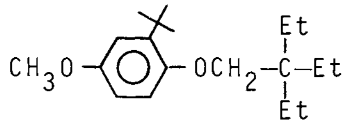


$$ArO^-K^+ \quad + \quad Et\text{—}\overset{Et}{\underset{Et}{C}}\text{—}CH_2OMs \xrightarrow[DMSO]{120\text{—}130\ ^\circ C} ArO\text{—}CH_2\text{—}\overset{Et}{\underset{Et}{C}}\text{—}Et$$

ArO^- = 4-t-Bu—$C_6H_4O^-$, 2-t-Bu-4-Me—$C_6H_3O^-$, 2,4-di-t-Bu—$C_6H_3O^-$,
1-$C_{10}H_7O^-$, 2,4,6-tri-Me—$C_6H_2O^-$, 2-t-Bu-4-MeO—$C_6H_3O^-$

Scheme 1.

Table 1. Reaction of Potassium Aryloxides with 2,2-Diethylbutyl Methanesulfonate[a)]

Run	Nucleophile ArO^-K^+	Temp °C	Time h	Product		Yield[b)]/%
1		120	3		**1**	89 (96)
2		130	3		**2**	88 (100)
3		130	3		**3**	85 (96)
4		130	6		**4**	84 (95)
5		130	6		**5**	82 (100)
6		130	1		**6**	83 (98)

a) Potassium aryloxide 15 mmol, 2,2-diethylbutyl methanesulfonate ($Et_3C{-}CH_2OSO_2CH_3$) 10 mmol, and DMSO (dried and distilled GR grade reagent) 40 cm^3 used under nitrogen. b) Isolated yields of aryl 2,2-diethylbutyl ethers based on $Et_3C{-}CH_2OSO_2CH_3$. Figures in parentheses show the GLPC yields.

The results are summarized in Table 1. For example, potassium 4-t-butylphenoxide (15 mmol) was heated with 2,2-diethylbutyl methanesulfonate (10 mmol) in DMSO (40 cm^3) at 120 °C for 3 h under nitrogen atmosphere. The reaction mixture was extracted with hexane (40 cm^3 ×2). The extract was washed with ethylene glycol (40 cm^3 ×10) and with water (40 cm^3), dried and fractionated under reduced pressure to give 2.336 g

(89%) of 4-t-butylphenyl 2,2-diethylbutyl ether **1** (Run 1). More hindered aryloxides also reacted with 2,2-diethylbutyl methanesulfonate at 130 °C to give the new corresponding ethers; 2-t-butyl-4-methylphenyl 2,2-diethylbutyl ether **2**, 2,4-di-t-butylphenyl 2,2-diethylbutyl ether **3**, 2,2-diethylbutyl 1-naphthyl ether **4**, 2,2-diethylbutyl 2,4,6-trimethylphenyl ether **5**, and 2-t-butyl-4-methoxyphenyl 2,2-diethylbutyl ether **6** (Runs 2–6). These desired products were characterized by IR, ^{1}H-NMR, and high-resolution mass spectra (HRMS). GLPC analysis proved that by-products were scarcely given in all runs.

The reaction rate was appreciably depressed by the steric hindrance of aryloxide (Runs 1, 3, and 5), while the functional groups in aryloxide (CH_3 and CH_3O) also affected the reaction time (Runs 2 and 6).

On the other hand, potassium 2,4,6-trimethylphenoxide (15 mmol) was allowed to react with neopentyl methanesulfonate (10 mmol) at 130 °C for 2 h in DMSO (40 cm^3) to give neopentyl 2,4,6-trimethylphenyl ether in 90% (99% GLPC) yield.

The kinetics showed typical second-order reactions, first-order both for mesylate and for aryloxide. The rate constants, k_2 for the reactions of 2,4,6-trimethylphenoxide with neopentyl and 2,2-diethylbutyl mesylates were $(7.74\pm0.06)\times10^{-3}$ and $(2.15\pm0.02)\times10^{-3}$ dm^3 mol^{-1} s^{-1}, respectively, at 130±0.1 °C in DMSO. The reactions were not retarded by the addition of radical scavengers, m-dinitrobenzene and galvinoxyl (10^{-3}–10^{-2} mol dm^{-3}).

Mosher et al elucidated that the S_N reaction of S-(–)-neopentyl-1-d tosylate with sodium ethoxide in HMPA gave R-(+)-ethyl neopentyl-1-d ether at 130 °C in 34% yield (97±3% ee).[8)]

These results suggest that our nucleophilic substitution reactions in DMSO proceed by S_N2 pathway.

References

1) P. Sykes, "A Guidebook to Mechanism in Organic Chemistry," 6th ed, Longman Scientific & Technical, Harlow, Essex (1986), pp 86 and 111.
2) R. T. Morrison and R. N. Boyd, "Organic Chemistry," 6th ed, Prentice

Hall, Englewood Cliffs, New Jersey (1992), p. 188.

3) J. March, "Advanced Organic Chemistry," 4th ed, John Wiley & Sons, New York (1992), p. 339.

4) G. M. Fraser and H. M. R. Hoffmann, J. Chem. Soc., (B), 1967, 425.

5) F. C. Whitmore, E. L. Wittle, and A. H. Popkin, J. Am. Chem. Soc., 61, 1589 (1939).

6) V. W. Gash, J. Org. Chem., 37, 2197 (1972).

7) R. Davis and J. Hudec, J. Chem. Soc., Perkin Trans. 2, 1975, 1395.

8) B. Stephenson, G. Solladie, and H. S. Mosher, J. Am. Chem. Soc., 94, 4184 (1972).

9) H. Masada, K. Tajima, K. Taniguchi, and T. Yamamoto, Chem. Lett., 1991, 753.

10) Spectral data are as follows. **1** : bp 145 °C/173 Pa; IR (neat) 1247 and 1182 cm^{-1} (C–O–C); ^{1}H NMR ($CDCl_3$) δ=0.79 (9H, t, J=7.6 Hz, CH_3), 1.29 (9H, s, t-Bu), 1.38 (6H, q, J=7.6 Hz, CH_2), 3.60 (2H, s, CH_2), 6.83 (2H, d, J=8.8 Hz, aromatic), and 7.29 (2H, d, J=9.0 Hz, aromatic); HRMS Found: m/z 262.2287. Calcd for $C_{18}H_{30}O$: M, 262.2294. **2** : bp 135 °C/133 Pa; IR (neat) 1225, 1095, and 1027 cm^{-1} (C–O–C); ^{1}H NMR ($CDCl_3$) δ= 0.80 (9H, t, J=7.2 Hz, CH_3), 1.38 (9H, s, t-Bu), 1.43 (6H, q, J=6.4 Hz, CH_2), 2.28 (3H, s, CH_3-Ar), 3.62 (2H, s, CH_2O), and 6.8–7.1 (3H, m, aromatic); HRMS Found m/z 276.2451. Calcd for $C_{19}H_{32}O$: M, 276.2451. **3** : bp 146 °C/80 Pa; IR (neat) 1248, 1093, and 1028 cm^{-1} (C–O–C); H^1 NMR ($CDCl_3$) δ=0.80 (9H, t, J=7.1 Hz, CH_3), 1.31 (9H, s, t-Bu), 1.40 (9H, s, t-Bu), 1.44 (6H, q, J=6.7 Hz, CH_2), 3.64 (2H, s, CH_2O), and 6.8–7.4 (3H, m, aromatic); HRMS Found : m/z 318.2926. Calcd for $C_{22}H_{38}O$: 318.2921. **4** : bp 160 °C/133 Pa; IR (neat) 1270, 1240, and 1101 cm^{-1} (C–O–C); ^{1}H NMR ($CDCl_3$) δ=0.86 (9H, t, J=7.8 Hz, CH_3), 1.52 (6H, q, J=7.6 Hz, CH_2), 3.82 (2H, s, CH_2O), and 6.7–8.3 (7H, m, aromatic); HRMS Found: m/z 256.1821. Calcd for $C_{18}H_{24}O$: M, 256.1825. **5** : bp 125 °C/267 Pa; IR (neat) 1215 and 1147 (C–O–C) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ= 0.87 (9H, t, J=7.8 Hz, CH_3), 1.45 (6H, q, J=7.5 Hz, CH_2), 2.22 (6H, s, Ar-CH_3), 2.45 (3H, s, Ar-CH_3), 3.46 (2H, s, CH_2O), and 6.80 (2H, s, aromatic); HRMS Found: m/z 248.2121. Calcd for $C_{17}H_{28}O$: M, 248.2138.
6 : bp 150 °C/267 Pa; IR (neat) 1213 and 1056 cm^{-1} (C–O–C); ^{1}H NMR ($CDCl_3$) δ=0.80 (9H, t, J=7.1 Hz, CH_3), 1.38 (9H, s, CH_3), 1.43 (6H, q, J=7.6 Hz, CH_2), 3.68 (2H, s, CH_2O), 3.77 (3H, s, CH_3O), and 6.00–6.95 (3H, m, aromatic); HRMS Found m/z 292.2379. Calcd for $C_{19}H_{32}O_2$: M, 292.2400.

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