The Use of Phase-Transfer Catalysis for the Synthesis of Phenyl and 8-Quinolinyl Ethers

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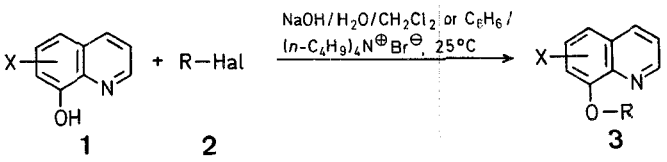
Aromatic ethers such as 2,4-dichlorophenyl 4-nitrophenyl ether, 2,4-dichlorophenyl 3-methoxy-4-nitrophenyl ether, 4-nitrophenyl 2-nitro-4-trifluoromethylphenyl ether and heteroanalogues of diphenyl ether such as 3-(substituted phenoxy)-pyridazines have been found to be useful as pesticides[1-5], fungicides[6], and as selective herbicides for the control of various noxious weeds.

Ethers are generally prepared by the Williamson reaction and the related alkylation of phenols to give aromatic ethers is well known[7]. The phase-transfer catalysis technique has been successfully applied to the Williamson ether synthesis[8,9]. Previously reports had appeared on the application of phase-transfer catalysis to the synthesis of symmetrical ethers[10] and aromatic ethers[11,12,13]. This type of reaction was used for the preparation of methyl, ethyl, butyl, and benzyl ethers from, especially, phenolic alkaloids and hydroxypyridines[14-17].

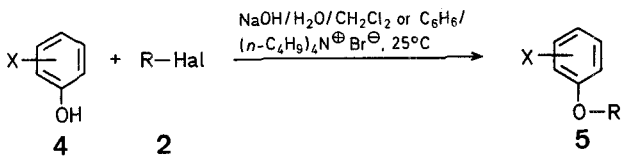
The use of resin-bound phenoxides in a convenient synthesis of nitrophenyl β-D-galacto- and β-D-glucopyranosides has been described[18]. Furthermore, the arylation of phenols by chloropyridines and chloroquinolines under phase-transfer-catalysed conditions has also been published[19]. However, as far as we are aware, no detailed studies on the applications of phase-transfer catalysis to the preparation of 8-quinolinyl ethers from 8-hydroxyquinolines are available.

We now report on the synthesis of 8-quinolinyl ethers **3** from 8-hydroxyquinolines **1** and organic halides **2** under phase-transfer-catalysed conditions (Scheme **A** and Table 1).



Scheme **A**

This reaction has also been extended to the preparation of various phenyl ethers **5** from phenols **4** and organic halides **2** (Scheme **B** and Table 3).

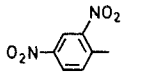
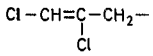
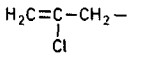
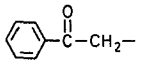
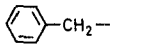
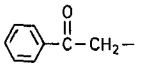
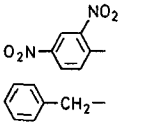
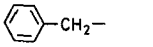
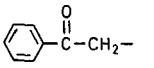
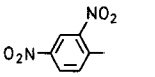
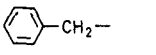
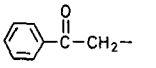
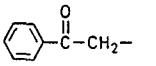
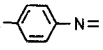


Scheme **B**

The reactions are performed by stirring the reagents **1** or **4** and **2** in a solvent such as dichloromethane or benzene with an aqueous solution of sodium hydroxide (or solid sodium hydroxide) in the presence of tetra-*n*-butylammonium bromide at room temperature or slightly above. The products **3** or **5** are obtained in good yields with the exception of **3h** and **3j** (Tables 1 and 3). In the absence of the catalyst no ether (e.g. **3j**) is formed and the starting materials are obtained unchanged from the organic layer.

0039-7881/82/1032-0858 $ 03.00

Table 1. 8-Quinolinyl Ethers **3a–r** (Scheme A)

Product No.	X	R	Hal in **2**	Reaction Conditions[a] time/temperature	Yield [%] of **3**	m.p. [°C] or b.p. [°C]/torr	Molecular formula[b] or Lit. m.p. [°C]	
3 a	H		Cl	4 h/70 °C	92[c]	167–168°	165–166.5°[3]	
3 b	H		Cl	4 h/25 °C	77	105–106°	$C_{12}H_9Cl_2NO$	(254.0)
3 c	H		Cl	4 h/25 °C	52[d]	189–190°/640	$C_{12}H_{10}ClNO$	(219.6)
3 d	H		Br	4 h/25 °C	80	122–123°	$C_{17}H_{13}NO_2$	(263.2)
3 e	H		Cl	4 h/25 °C	90[d]	216–218°/10	$C_{16}H_{13}NO$	(235.2)
3 f	H	$H_2C=CH-CH_2-$	Br	4 h/25 °C	84[d]	150–152°/10	145–150°/8[32]	
3 g	5,7-di–Cl		Br	4 h/25 °C	60	104–105°	$C_{17}H_{11}Cl_2NO_2$	(332.1)
3 h	5,7-di–Cl		Cl	4 h/70 °C	21[c]	170–171°	$C_{15}H_7Cl_2N_3O_5$	(380.1)
3 i	5,7-di–Cl		Cl	4 h/25 °C	90	87.5–88.5°	$C_{16}H_{11}Cl_2NO$	(304.1)
3 j	5,7-di–Cl	$H_2C=C(Cl)-CH_2-$	Cl	4 h/25 °C	35; 0[e]	95–96°	$C_{12}H_8Cl_3NO$	(288.5)
3 k	5,7-di–Cl	$Cl-CH=C(Cl)-CH_2-$	Cl	4 h/25 °C	57	89–91°	$C_{12}H_7Cl_4NO$	(322.9)
3 l	5,7-di–Br		Cl	4 h/25 °C	85	116–117°	$C_{17}H_{11}Br_2NO_2$	(421.0)
3 m	5,7-di–Br		Cl	4 h/70 °C	90	172–173°	$C_{15}H_7Br_2N_3O_5$	(469.0)
3 n	5,7-di–Br		Cl	4 h/25 °C 4 h/25 °C	78 88	108–109°	$C_{16}H_{11}Br_2NO$	(393.1)
3 o	5-HO–SO_2–		Cl	6 h/25 °C	85	134–135°	$C_{17}H_{13}NO_5S$	(343.2)
3 p	5-HO–SO_2–/7-J		Cl	6 h/60 °C	97	123–124°	$C_{17}H_{12}JNO_5S$	(469.1)
3 q	5-HO–SO_2–/7-J	$H_2C=CH-CH_2-$	Br	6 h/60 °C	64	214–215°	$C_{12}H_{10}JNO_4S$	(391.2)
3 r	5-HO–SO_2–  –N=N–	$H_2C=CH-CH_2-$	Br	5 h/75 °C	48[c]		$C_{18}H_{15}N_3O_4S$	(369.4)

[a] 0.1 equivalents of tetra-*n*-butylammonium bromide as catalyst unless otherwise stated.
[b] Satisfactory microanalyses obtained: C ±0.25, H ±0.25, N ±0.22; *exception*: **3r**, C +0.45, N +0.5.
[c] By method B.
[d] Product purified by column chromatography on neutral alumina, eluting with petroleum ether/benzene or benzene/ether.
[e] In the absence of catalyst.

It has been reported[19,20,21] that quaternary ammonium salts are partially dealkylated at higher temperatures or decompose under alkaline conditions. Thus quaternary phosphonium salts have sometimes been employed[19,22,23]. We have circumvented this inconvenience by working at room temperature or only slightly above and have found no evidence for a decomposition of the catalyst. Use of alkyl halides such as 2,3-dichloropropene or 1,2,3-trichloropropene resulted in lower yields of the products **3** or **5**.

8-Quinolinyl (3) and Phenyl (5) Ethers; General Procedures:

Method A: A mixture of dichloromethane (100 ml), water (100 ml), the 8-hydroxyquinoline **1** or phenol **3** (20 mmol), solid sodium hydroxide (1.2 g, 30 mmol), the organic halide **2** (40 mmol) and tetra-*n*-butylammonium bromide (166 mg, 0.5 mmol) is agitated with a vibromixer at room temperature for 4–5 h. The organic layer is separated and the aqueous layer extracted with dichloromethane (2 × 40 ml). The organic layers are combined and evaporated. The residue is mixed with water (50 ml), extracted with ether (3 × 20 ml), the extract is washed with 2 normal sodium hydroxide solution (2 × 20 ml) to remove unreacted **1** or **3**, and then with saturated sodium chloride solution (2 × 20 ml). The extract is dried with sodium sulphate, the solvent is evaporated, and the product purified by distillation or recrystallisation.

Method B: A mixture of the 8-hydroxyquinoline **1** or phenol **3** (0.05 mol) and 50% w/w sodium hydroxide solution (0.1 mol) is magnetically stirred at room temperature for 50 min. Benzene (50 ml), the organic halide **2** (0.05 mol), and tetra-*n*-butylammonium bromide (498 mg, 1.5 mmol) are then added. The mixture is heated at the temperature and for the time given in the Tables. Water (80 ml) is added and the mixture is extracted with ether (3 × 30 ml). The extract is washed

Table 2. Spectral Data for 8-Quinolinyl Ethers **3a–r**

Product	I.R. (KBr) ν [cm^{-1}]					^{1}H-N.M.R. ($CDCl_3$/TMS) δ [ppm]
	ν_{CH}	$\nu_{C=O}$	$\nu_{C=C}$	ν_{NO_2}	ν_{C-O-C}	
3a	3100, 3050	—	1600	1520, 1335	1260	6.70 (d, 1 H); 7.35 (s, 1 H); 7.58 (q, 1 H); 7.2–8.5 (m, 6 H)
3b	3020	—	1600	—	1250	5.25 (s, 2 H); 6.47 (s, 1 H); 7.1–7.6 (m, 3 H); 7.4–9.1 (m, 3 H)
3c	3040	—	1620	—	1250	5.37 (s, 2 H); 6.37 (s, 2 H); 7.2–8.6 (m, 6 H)
3d	—	1690	1590	—	1220	5.68 (s, 2 H); 7.0–8.5 (m, 11 H)
3e	3040	—	1580	—	1260	5.50 (s, 2 H); 7.3–8.5 (m, 11 H)
3f	2960	—	1610	—	1250	5.60 (q, 4 H); 7.0–8.4 (m, 6 H); 7.4 (m, 1 H)
3g	—	1700	1580	—	1210	5.88 (s, 2 H); 7.53 (s, 5 H); 7.66 (s, 1 H); 8.0–8.3 (m, 3 H)
3h	3015	—	1600	1515, 1340	1260	6.72 (d, 1 H); 7.35 (s, 1 H); 7.59 (q, 1 H); 7.80 (s, 1 H); 8.1–9.1 (m, 3 H)
3i	3040	—	1580	—	1220	5.50 (s, 2 H); 7.3–7.7 (m, 5 H); 8.43 (s, 1 H); 8.1–9.0 (m, 3 H)
3j	3060, 2920	—	1590	—	1240	5.37 (s, 2 H); 6.37 (s, 2 H); 8.47 (s, 1 H); 7.5–9.0 (m, 3 H)
3k	3080	—	1580	—	1240	5.37 (s, 3 H); 6.37 (s, 1 H); 8.47 (s, 1 H); 7.4–9.0 (m, 3 H)
3l	3060	1680	1600	—	1200	5.90 (s, 2 H); 7.63 (s, 5 H); 8.50 (s, 1 H); 8.1–8.9 (m, 3 H)
3m	—	—	1610	1540, 1340	1260	6.65 (d, 2 H); 7.35 (s, 1 H); 7.56 (q, 1 H); 7.93 (s, 1 H); 8.2–9.0 (m, 3 H)
3n	3020	—	1590	—	1220	5.56 (s, 2 H); 7.4–7.7 (br s, 5 H); 8.50 (s, 1 H); 8.1–9.0 (m, 3 H)
3o	3040	1680	1600	—	1220	4.70 (d, 2 H); 5.30 (d, 2 H); 6.0 (m, 1 H); 7.5–8.8 (m, 4 H); 9.37 (s, 1 H)[a]
3p	2960	—	1680	—	1220	4.50 (s, 2 H); 7.4 (m, 5 H); 7.5–8.8 (m, 4 H); 9.30 (s, 1 H)[a]
3q	—	—	1625	—	1230	4.58 (s, 2 H); 7.5 (m, 5 H); 7.8–8.5 (m, 5 H); 9.30 (s, 1 H)[a]
3r	—	—	1600	—	1260	—

[a] DMSO-d_6 solution.

Table 3. Phenyl Ethers **5a–s** (Scheme **B**)

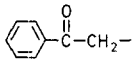
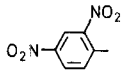
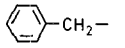
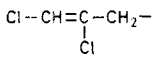
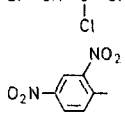
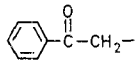
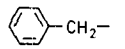
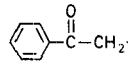
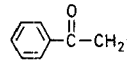
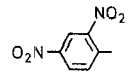
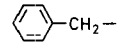
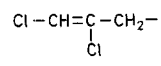
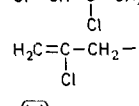
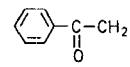
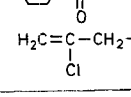
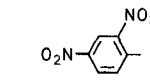
Product No.	X	R	Hal in **2**	Reaction conditions[a] time/ temperature	Yield [%] of **5**	m.p. [°C] or b.p. [°C]/torr	Molecular formula[b] or Lit. m.p. [°C]	I.R. (KBr) ν [cm^{-1}]
5 a	2-H_3C		Br	4 h/25 °C	76	60–61°	63°[24]	3050, 1680, 1590, 1210
5 b	2-H_3C		Cl	4 h/25 °C	82	88–89°	88–89°[13]	3080, 1600, 1525, 1345, 1260
5 c	2-H_3C		Cl	4 h/25 °C	97[c]	150–152°/10	284°/760[25]	3020, 2940, 1600, 1240
5 d	2-O_2N		Cl	4 h/55 °C	10	86–87°	$C_9H_7Cl_2NO_3$ (248.0)	3060, 2910, 1500, 1510, 1340, 1240
5 e	2-*i*-C_3H_7/5-H_3C		Cl	4 h/25 °C	97	63–64°	64.5–66.5°[18]	3100, 2960, 1600, 1520, 1330, 1260
5 f	2-*i*-C_3H_7/5-H_3C		Br	4 h/25 °C	93	55–56°	52[26]	2960, 1700, 1620, 1230
5 g	2-*i*-C_3H_7/5-H_3C		Cl	7 h/40 °C	92[c]	190–192°/10	221–223°/35[28]	3040, 2960, 1600, 1250
5 h	2-*i*-C_3H_7/5-H_3C	$H_2C=CH-CH_2-$	Br	4 h/25 °C	87[c]	116–118°/10	132–133°/23[29]	2940, 1610, 1570, 1250
5 i	2,3-l–CH=CH–$)_2$–		Br	4 h/25 °C	72	71–72°	68°[26]	3060, 1710, 1590, 1220
5 j	2,4-di–Cl		Br	4 h/30 °C	71	73–74°	73.5–74.5[27]	2900, 1705, 1600, 1240
5 k	2,4-di–Cl		Cl	5 h/30 °C	91	115–116°	118–118.5°[13]	3040, 1620, 1540, 1350, 1260
5 l	2,4-di–Cl		Cl	5 h/30 °C	45[c]	60–61°	60°[25]	3020, 2920, 1600, 1260
5 m	2,4-di–Cl		Cl	5 h/30 °C	44[c]	206–207°/640	$C_9H_6Cl_4O$ (271.9)	3080, 1590, 1250
5 n	2,4-di–Cl		Cl	5 h/30 °C	21[c]; 0[d]	222–223°/640	$C_9H_7Cl_3O$ (237.4)	2980, 2920, 1680, 1580, 1250
5 o	2-H_3CO		Br	5 h/25 °C	51	106–107°	106°[24]	2920, 1690, 1600, 1250
5 p	2-H_3CO		Cl	8 h/25 °C	22[c]	127–129°/10	78°/0.6[31]	2920, 1590, 1250

Table 3. (Continued)

Product No.	X	R	Hal in **2**	Reaction conditions[a] time/ temperature	Yield [%] of **5**	m.p. [°C] or b.p. [°C]/torr	Molecular formula[b] or Lit. m.p. [°C]	I.R. (KBr) ν [cm^{-1}]
5 q	2-H_3CO	$Cl-CH=C(Cl)-CH_2-$	Cl	8 h/25 °C	16[c]	217–219°/640	$C_{10}H_{10}Cl_2O_2$ (233.0)	2920, 1600, 1250
5 r	2-H_3CO		Cl	5 h/25 °C	94	94–95°	92.5–94°[13]	3060, 1600, 1540, 1350, 1265
5 s	2-H_3CO	$H_2C=CH-CH_2-$	Br	5 h/60 °C	82[c,e]	107–109°/10	111–113°/13[30]	2940, 1630, 1260

[a] 1 equivalent of tetra-*n*-butylammonium bromide as catalyst unless otherwise stated.
[b] Satisfactory microanalyses obtained: C ±0.20, H ±0.18, N ±0.25; exceptions: **5p, 5s,** C ±0.35, H ±0.30.
[c] Product purified by column chromatography on neutral alumina, eluting with benzene/ether.
[d] In the absence of catalyst.
[e] Method B.

with water (3 × 40 ml), dried with sodium sulphate, and the solvent evaporated. Most of the products are purified by recrystallisation from ethanol.

Deng Duo, Xu Pengki, Zhang Qinghai, and Liang Zupei participated in part of the work.

Received: March 4, 1982

[1] H. Martin, *Pesticide Manual,* British Crop Protection Council, 1972.
[2] P. R. Driscoll, *U. S. Patent* 3495969 (1970), Mobil Oil Co.; *C. A.* **72,** 90310 (1970).
[3] K. Fujikawa, K. Kondo, I. Yokomichi, F. Kimura, T. Haga, R. Sishiyama, *Agr. Biol. Chem.* **34,** 68 (1970).
[4] T. Tetsuo, K. Makoto, T. Yasumoto, *Weed Sci.* **23,** 57 (1975).
[5] T. Saburo, K. Tetuomi, *Japan Patent* 11900 (1968), Sankyo Co.; *C. A.* **70,** 28933 (1969).
[6] P. R. Driscoll, *U. S. Patent* 3574841 (1971), Mobil Oil Co.; *C. A.* **74,** 141551 (1971).
[7] C. A. Buehler, D. E. Pearson, *Survey of Organic Syntheses,* Vol. 2, John Wiley & Sons, New York, London, Sydney, Toronto, 1977.
[8] W. P. Weber, G. W. Gokel, *Phase Transfer Catalysis in Organic Synthesis,* Springer Verlag, Berlin, Heidelberg, New York, 1977.
[9] E. V. Dehmlow, S. S. Dehmlow, *Phase Transfer Catalysis,* Verlag Chemie, Weinheim, 1980.
[10] R. A. Dubois, H. H. Freedman, *U. S. Patent* 4061682 (1977), Dow Chemical Co.; *C. A.* **88,** 50280 (1978).
[11] A. Mckillop, J. C. Fiaud, R. P. Hug, *Tetrahedron* **30,** 1379 (1974).
[12] P. M. Quan, S. R. Kron, *Ger. Offen. (DOS)* 2634419 (1977), Imperial Chemical Industries Ltd.; *C. A.* **86,** 189480 (1977).
[13] J. D. Reinheimer, J. P. Douglass, H. Leister, M. B. Voelkel, *J. Org. Chem.* **22,** 1743 (1957).
[14] B. R. Baker, F. J. McEvoy, *J. Org. Chem.* **20,** 136 (1955).
[15] A. Cohen, J. W. Haworth, E. H. Hughes, *J. Chem. Soc.* **1952,** 4374.
[16] J. Ugelstad, T. Ellingsen, A. Berge, *Acta Chem. Scand.* **20,** 1593 (1966).
[17] R. L. Merker, M. J. Scott, *J. Org. Chem.* **26,** 5180 (1961).
[18] T. Iversen, R. Johansson, *Synthesis* **1979,** 823.
[19] H. Alsaidi, R. Gallo, J. Metzger, *Synthesis* **1980,** 921.
[20] E. V. Dehmlow, M. Slopianka, H. Heider, *Tetrahedron Lett.* **1977,** 2361.
[21] H. J.-M. Dou, R. Gallo, P. Hassanaly, J. Metzger, *J. Org. Chem.* **42,** 4275 (1977).
[22] G. W. Gokel, W. P. Weber, *J. Chem. Ed.* **55,** 350 (1978).
[23] C. Starks, *Chem. Tech.* **1980,** 110.
[24] Y. Saburi, Y. Yoshimoto, K. Minami, *Nippon Kagaku Zasshi,* **12,** 1326 (1962); *C. A.* **69,** 35630 (1968).
[25] Q. Hla Baw, *J. Indian. Chem. Soc.* **3,** 101 (1926); *C. A.* **20,** 3695 (1926).
[26] R. Royer, E. Bisagni, *Helv. Chim. Acta* **42,** 2364 (1959); *C. A.* **54,** 16455 (1960).
[27] W. L. F. Armarego, *Austr. J. Chem.* **13,** 1, 95 (1960).
[28] B. Prager, P. Jacobson, *Beilsteins Handbuch der Organischen Chemie,* Vierte Auflage, **6,** 536, Deutschen Chemischen Gesellschaft, 1923.
[29] F. Richter, *Beilsteins Handbuch der Organischen Chemie.* Vierte Auflage, II, **6,** 494, Deutschen Chemischen Gesellschaft, 1944.
[30] R. S. Livshits et al., *Zh. Obshch. Khim.* **21,** 1354 (1951); *C. A.* **46,** 5050 (1952).
[31] W. K. Anderson, E. J. LaVoie, J. C. Bottaro, C. Jeffrey, *J. Chem. Soc. Perkin Trans. 1* **1976,** 1.
[32] T. Nógrádi, L. Vargha, G. Iványovics, I. Koczka, *Acta. Chim. Acad. Sci. Hung.* **6,** 287 (1955); *C. A.* **51,** 5078 (1957).

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