Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry
Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/lsyc20

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Published online: 16 Feb 2007.

To cite this article: Zhen-Zhong Liu , Heng-Chang Chen , Sheng-Li Cao & Run-Tao Li (1994): A Novel Method for Synthesis of Aryl Glycidyl Ethers, Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry, 24:6, 833-838

To link to this article: http://dx.doi.org/10.1080/00397919408011305

SYNTHETIC COMMUNICATIONS, 24(6), 833-838 (1994)

A NOVEL METHOD FOR SYNTHESIS OF ARYL GLYCIDYL ETHERS

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ABSTRACT: A solid-liquid phase-transfer catalytic method for the synthesis of aryl glycidyl ethers has been described, and the factors affecting the reaction yield have been examined.

Aryl glycidyl ethers ($ArOCH_2\underset{\diagdown\,O\,\diagup}{CH}—CH_2$) are key intermediates for the synthesis of aminopropanol cardiovascular drugs ($ArOCH_2CHOHCH_2NR^1R^2$), and there are several synthetic methods reported in the literatures. One is Williamson synthesis of ether, i. e. treating sodium phenolate with epichlorohydrin,[1] another is phenol reacting with epichlorohydrin in acetone in the presence of potassium carbonate.[2] Furthermore, the reaction of phenol with epichlorohydrin can be carried out in aqueous sodium hydroxide,[3] and also a method using liquid-liquid phase-transfer catalysis is reported.[4] Although these methods were used frequently, they all have the drawbacks such as long reaction time, low yield and cumbersome processes.

We here report a solid-liquid phase-transfer catalytic method for the synthesis of aryl glycidyl ethers. With this method, the aryl glycidyl ether can be obtained through

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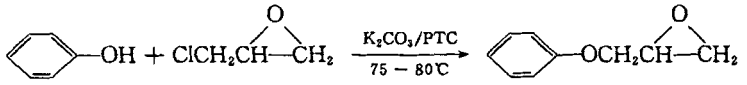
TABLE 1



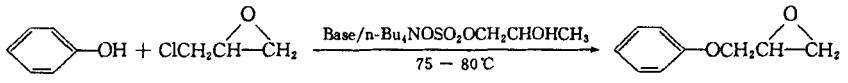
No.	Phase-transfer catalyst	Reaction time[a] (h)	Yield[b] (%)
1	no PTC	1.5	66
2	$PhCH_2NEt_3Cl$	1.5	69
3	$n\text{-}Bu_4NBr$	1.5	75
4	$n\text{-}Bu_4NOSO_2OCH_2CHOHCH_3$ [5]	1.5	91

a. With $n\text{—}Bu_4NOSO_2OCH_2CHOHCH_3$ and K_2CO_3 as catalyst and base, respectively, the reaction monitored by TLC was over within 1.5h. Under the same reaction conditions, the effect of different catalyst on the reaction rate can be compared by the yield.

b. Isolated yields; the same in table 2 and 3.

The results listed in table 1 show that the yield after 1.5h of reaction time with

TABLE 2



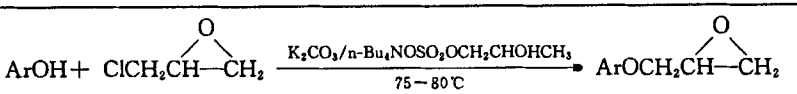
No.	Base	Reaction time (h)	Yield (%)
1	KOH	1.5	78
2	$KOH\text{-}K_2CO_3$	1.5	88
3	K_2CO_3	1.5	91

reacting the corresponding phenol with excess epichlorohydrin in the presence of tetraalkylammonium salt and potassium carbonate.

The effect of different catalyst on the reaction rate, and consequently on the reaction yield has been examined with the aid of the model reaction of phenol with epichlorohydrin (see table 1).

PTC is higher than that of the reaction without PTC and, furthermore, $n\text{-}Bu_4NOSO_2OCH_2CHOHCH_3$ is the best of three catalysts in table 1.

TABLE 3



No.	Ar	Reaction time (h)	Yield (%) observed	Yield (%) reported
1	C_6H_5	1.5	91	60[2]
2	o—$CH_3C_6H_4$	1.5	91	66[7]
3	m-$CH_3C_6H_4$	1	91	82[8]
4	o-$CH_3OC_6H_4$	1	90	67[9]
5	o-ClC_6H_4	1	89	60[10]
6	p-ClC_6H_4	1	90	71[4]
7	2.4-$Cl_2C_6H_3$	1.5	85	10[3]
8	o-$NO_2C_6H_4$	2.5	93	[a]
9	m-$NO_2C_6H_4$	2	93	[b]
10	p-$NO_2C_6H_4$	3	93	50[11]

a. b. Not found in the literature.

Secondly, the effect of base on the reaction yield has been examined (see table 2).

From table 2, it can be seen that the yield of the reaction using K_2CO_3 or the mixture of KOH and K_2CO_3 is higher than that of the reaction only using KOH. Presumably, the by-product water, formed in the reaction using KOH as base, is not favorable to the reaction, whereas K_2CO_3 can not only acts as base but also absorb the by-product water, thereby promoting the reaction.[6]

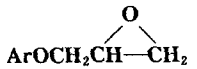
At last, a variety of aryl glycidyl ethers have been synthesized from phenols with various substituent, and the results are given in table 3.

The experimental results demonstrate that in this method the yield is high, the reaction time is short and the operation is simple. The structure of all propared products were confirmed with IR and ^{1}H-NMR, and the analytical data are given in table 4.

EXPERIMENTAL

Melting points were determined on the microscope melting point apparatus and are uncorrected. IR spectra were obtained with a FTS-40 infrared spectrophotometer either

TABLE 4



No.	Ar	m. p. (℃)or b. p. (℃/mmHg) (lit.)	^{1}H-NMR(δ,ppM)	IR(cm^{-1})
1	C_6H_5	87—90/3 (116/5)[2]	6.97(m,5H,ph); 4.0(m,2H,OCH_2) 3.34(m,1H,ring CHO); 2.77(m,2H,ring CH_2O)	3062 3003 2927 2875 1600 1496 1456 1244 1040 916 815 756 693
2	p-$CH_3C_6H_4$	97—99/3 (90—94/0.2)[2]	7.04(m,4H,Ar); 4.10(m, 2H, OCH_2); 3.36(m,1H,ring CHO); 2.81(m,2H, ring CHO); 2.25(s,3H,CH_3)	3060 3002 2927 2875 1602 1496 1457 1123 1037 1245 917 841 754
3	m-$CH_3C_6H_4$	92—94/3 (107—115/0.1)[7]	6.96(m,4H,Ar); 4.07(m,2H,OCH_2); 3.35(m,1H,ring CHO); 2.81(m,2H,ring CH_2O); 2.32(s,3H,CH_3)	3052 3002 2924 2873 1603 1491 1454 1263 1158 1041 911 861 776 691
4	o-$CH_3OC_6H_4$	114—116/2 (152—158/5)[9]	6.93(m,4H,Ar); 4.17(m,2H,OCH_2); 3.97(s,3H, OCH_3); 3.39(m,1H,ring CHO); 2.79(m,2H,ring CH_2O)	3065 3005 2932 2837 1593 1507 1456 1256 1226 1125 1028 916 837 747
5	o-ClC_6H_4	116—118/2 (118/1)[12]	7.21(m,4H,Ar); 4.14(m,2H,OCH_2) 3.38(m,1H,ring CHO); 2.84(m,2H,ring CH_2O)	3067 3001 2930 2875 1590 1487 1447 1248 1062 1025 916 837 751
6	p-ClC_6H_4	109—111/2 (132/3)[4]	7.0(m,4H,Ar); 4.06(m,2H,OCH_2) 3.34(m,1H,ring CHO); 2.78(m,2H,ring CH_2O)	3062 3007 2929 2876 1593 1493 1456 1243 1094 1034 916 826 768
7	2.4—$Cl_2C_6H_3$	124—126/3 (107—109/1)[3]	7.14(m,3H,Ar); 4.16(m,2H,OCH_2) 3.37(m,1H,ring CHO); 2.85(m,2H,ring CH_2O)	3073 3004 2928 2879 1589 1485 1455 1254 1063 1023 916 865 805
8	o-$NO_2C_6H_4$	49—51 (51—51.5)[13]	7.41(m,4H,Ar); 4.23(m,2H,OCH_2) 3.35(m,1H,ring CHO); 2.85(m,2H,ring CH_2O)	3085 3041 2940 2892 1610 1583 1487 1437 1529 1358 1285 913 820 739
9	m-$NO_2C_6H_4$	60—62 (62.4)[13]	7.52(m,4H,Ar); 4.15(m,2H,OCH_2) 3.37(m,1H,ring CHO); 2.81(m,2H,ring CH_2O)	3097 3008 2932 1622 1582 1527 1486 1350 1260 912 858 739
10	p-$NO_2C_6H_4$	68—70 (67—68)[13]	7.6(m,4H,Ar); 4.19(m,2H,CH_2O) 3.39(m,1H,ring CHO); 2.83(m,2H,ring CH_2O)	3097 3016 2944 1609 1597 1508 1498 1459 1338 1264 909 846 754

as thin films or as KBr disks. ^{1}H-NMR spectra were recorded on a Ac-80 spectrometer using TMS as internal standard, $CDCl_3$ as solvent.

Typical procedure

1-Phenoxy-2,3-epoxypropane:

A mixture of phenol(2.0g, 21.3mmol), epichlorohydrin (13.4mL, 172mmol), potassium carbonate (5.9g, 42.6mmol), and n-$Bu_4NOSO_2OCH_2CHOHCH_3$ (0.2g,0.5mmol) was stirred at 75-80℃ for 1.5h. The reaction was monitored by thin-layer chromatography (silica gel GF_{254}, $CHCl_3$). After cooling to room temperature, the inorganic salts were filtered off and washed with epichlorohydrin. The combined organic solution was evaporated and the residue was distilled under reduced pressure to give 2.9g (91%)of 1-phenoxy-2,3-epoxypropane as a colorless oil.

1—(2—Nitrophenoxy)—2,3—epoxypropane:

A mixture of 2—nitrophenol (2.0g, 14.4mmol), epichlorohydrin (10ml, 129mmol), potassium carbonate (4.0g, 28.9mmol), and n—$Bu_4NOSO_2OCH_2CHOHCH_3$(0.14g, 0.4mmol) was stirred at 75—80℃ for 2.5h. After cooling to room temperature, the inorganic salts were filtered off and washed with epichlorohydrin. The combined organic solution was evaporated and the residue was recrystallized from diethyl ether—petroleum ether (1 : 1) to give 2.6g (93%) of 1—(2—nitrophenoxy)—2,3—epoxypropane as white crystal.

REFERENCES

1. Obase,H.; Tatsuno, H.; Goto, K.; Shigenobu, K.; Kasuya, Y.; Yamada, Y.; Fujii, K. and Yada, S. Chem. Pharm. Bull. 1978, 26(5), 1443
2. Erhard, P. W.; Woo, C. M.; Gorczynski, R. J. and Anderson, W. G. J. Med. Chem. 1982, 25(12),1402
3. Newman, M.S.; Fones, W.; Renoll, M. J. Am. Chem. Soc. 1947, 69, 718
4. DiMenna, W.S. and Piantadosi, C. J. Med. Chem. 1978, 21(10), 1073
5. Zhang, L.; Xu, B.Z.; Chen, S.X. and Tang, H.T. Huaxue Shiji 1990, 12 (1),40; Chem. Abstr. 1990,113, 114596f
6. Schmolka, S.J.; Zimmer, H. Synthesis 1984, 29
7. Schulz, H. Pharmazie 1968, 23(5), 240
8. Hoekstra, M.S. Eur. Pat. Appl. EP 165 682, 1985
9. Ji, Y. W.; Chen, H.C.; Liu, Z.Z.; Guo, Y.C.; Hang. Z.X.; Fan,Y.G.; Wu, S.J.; Nie, C.M. Yiyao Gongye 1985, 16(4), 168;Chem. Abstr. 1985, 103, 141546q
10. Efendiev, Z. B.; Magaev, A. Ukr. Khim. Zh. (Russ. Ed.) 1974, 40(4), 411; Chem. Abstr. 1974, 81, 25241q

11. Weissermel. K. ; Fischer, E. ; Haefner, K. H. ; Cherdon, H. Angew. Makromol. Chem. 1968, (4/5), 168; Chem. Abstr. 1969, 70, 29422v
12. Petrow, V. ; Stephenson, O. J. Pharm. Pharmacol. 1953, 5, 359
13. Chizhevskaya, I. I. ; Idel'chik, Z. B. ; Yakimovich, L. A. and Shadurski, K. S. Vestsi Akad. Navuk Belarus. S. S. R. , Ser. Fiz.-Tekh. Navuk 1957, 2,115; Chem. Abstr. 1958, 52, 9009i

(Received in the USA 21 July 1993)