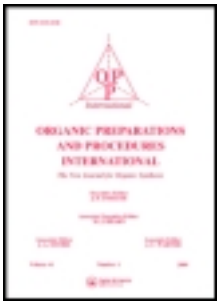


Organic Preparations and Procedures International: The New Journal for Organic Synthesis

Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/uopp20

A SIMPLE ONE-POT PREPARATION OF 4-ALKOXY-AND 4-ALKYLTHIO-CATECHOLS AND o-BENZOQUINONES

Christopher J. Cooksey [a], Edward J. Land [b] & Patrick A. Riley [c]

[a] Department of Chemistry, University College London, 20 Gordon Street, London, WC1H OAJ, UK

[b] CRC Department of Biophysical Chemistry, Paterson Institute for Cancer Research, Christie Hospital NHS Trust, Wilmslow Road, Manchester, M209BX, UK

[c] Department of Molecular Pathology, University College and Middlesex School of Medicine, Windeyer Building, Cleveland Street, London, W1P6DB, UK

Published online: 18 Feb 2009.

To cite this article: Christopher J. Cooksey , Edward J. Land & Patrick A. Riley (1996): A SIMPLE ONE-POT PREPARATION OF 4-ALKOXY-AND 4-ALKYLTHIO-CATECHOLS AND o-BENZOQUINONES, Organic Preparations and Procedures International: The New Journal for Organic Synthesis, 28:4, 463-467

To link to this article: http://dx.doi.org/10.1080/00304949609356553

ORGANIC PREPARATIONS AND PROCEDURES INT., 28 (4), 463-498 (1996)

OPPI BRIEFS

A SIMPLE ONE-POT PREPARATION OF 4-ALKOXY- AND 4-ALKYLTHIO-CATECHOLS AND *o*-BENZOQUINONES

Submitted by (10/11/94)

Christopher J. Cooksey*, Edward J. Land† and Patrick A. Riley††

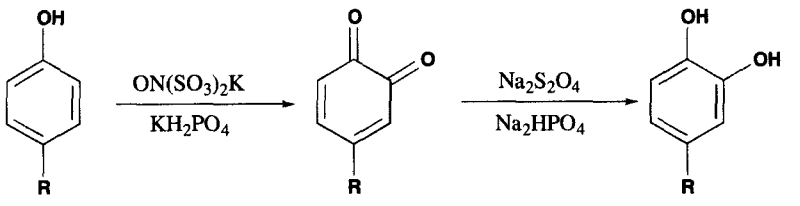
Department of Chemistry, University College London
20 Gordon Street, London WC1H 0AJ, UK

† *CRC Department of Biophysical Chemistry*
Paterson Institute for Cancer Research, Christie Hospital NHS Trust
Wilmslow Road, Manchester M20 9BX, UK

†† *Department of Molecular Pathology*
University College and Middlesex School of Medicine
Windeyer Building, Cleveland Street, London W1P 6DB, UK

In connection with our continuing studies of the reactivity of *o*-benzoquinones with thiols[1] and the tyrosinase-mediated oxidation of 4-substituted phenols,[2] it was desirable to have a convenient synthesis of the corresponding 4-substituted catechols. Although the use of reagents such as O_2/Cu has been reported[3] and two-stage reactions involving acetylation followed by alkaline hydrogen peroxide are known,[4] these and other methods[5] did not appear to be convenient and herein we report a simple one-pot procedure for converting 4-substituted phenols into the corresponding 4-substituted catechols via the *o*-benzoquinones.

The required *o*-benzoquinones are readily obtained in high yield by the oxidation of 4-substituted phenols with Fremy's radical (potassium nitrosodisulfonate).[6] We found that isolation



1 2 3

a) R = MeO b) R = PrO c) R = BuO d) R = MeS e) R = PrS
f) R = BuS g) R = $HOCH_2CH_2S$

and purification of the *o*-benzoquinones is unnecessary and the crude products may be reduced directly with alkaline sodium hydrosulfite to give the required 4-substituted catechols which are

conveniently isolated by flash chromatography. The *o*-benzoquinones were obtained as short-lived solids or solutions by (i) omitting the reduction stage in the above preparation, (ii) by pulse radiolysis of the corresponding catechol[1] or (iii) by oxidation of the corresponding catechol with silver carbonate on Celite.[7] Identical procedures were used for all compounds and no attempt was made to optimize yields. The isolated products had satisfactory spectroscopic properties (Tables 1-4). The catechols

TABLE 1. ^{1}H NMR Data for Catechols **3**

Cmpd	Solvent	δ/ppm (J/Hz)							
		CH_3	CH_2	CH_2	CH_2	OH	H_3	H_5	H_6
3a	$CDCl_3$	3.73 (s)				4.89	6.50	6.34	6.77
						5.48	(2.9)	(8.7, 2.9)	(8.7)
3b	CD_3COCD_3	0.97	1.70	3.79		7.45	6.46	6.26	6.75
		(7.4)	(7.4)	(6.5)		7.80	(2.9)	(8.5, 2.9)	(8.5)
3c	$CDCl_3$	0.96	1.47	1.73	3.88	5.10	6.50	6.35	6.56
		(6.6)	(6.6)	(6.6)	(6.6)	5.70	(2.8)	(8.6, 2.8)	(8.7)
3d	$CDCl_3$	2.44				5.08	6.88	6.80	6.80
		(s)				5.22	(1.2)	(m)	(m)
3e	$CDCl_3$	0.99	1.62		2.79	5.4	6.95	6.87	6.80
		(7.4)	(7.3)		(7.5)	(2H)	(2.1)	(8.2, 2.1)	(8.2)
3f	$CDCl_3$	0.80	1.31	1.50	2.71	5.20	6.84	6.76	6.70
		(7.5)	(7.6)	(7.7)	(7.3)	5.60	(2.0)	(8.1, 2.0)	(8.1)
3g	CD_3COCD_3		3.63	2.91		2.9 (1H)	6.94	6.78	6.78
			(6.8)	(7.0)		8.02 (2H)	(1.9)	(m)	(m)

TABLE 2. ^{1}H NMR Data for *o*-Benzoquinones **2**

Cmpd	δ/ppm (J/Hz)						
	CH_3	CH_2	CH_2	CH_2	H_3	H_5	H_6
2a[a]	3.85s				5.90	7.04	6.45
					(3.1)	(10.4, 3.0)	(10.5)
2b	1.01	1.82		3.92	5.74	6.84	6.39
	(7.3)	(6.7)		(6.4)	(2.8)	(10.4, 2.8)	(10.4)
2c	0.95	1.44	1.77	3.96	5.74	6.85	6.40
	(7.2)	(7.6)	(8.2)	(6.4)	(3.0)	(10.5, 3.0)	(10.5)
2d	2.51				6.19	6.82	6.42
	(0.5)				(2.4, 0.5)	(10.1, 2.4)	(10.1, 0.5)
2e	1.07	1.79		2.91	6.22	6.71	6.38
	(7.3)	(7.3)		(7.1)	(2.2)	(10.1, 2.2)	(10.1)
2f	0.96	1.4-1.5	1.4-1.5	2.93	6.22	6.77	6.41
	(7.3)	(m)	(m)	(7.1)	(2.2)	(10.2, 2.2)	(10.2)
2g	1.9		3.93	3.13	6.25	6.75	6.38
	(1H brs)[b]		(6.0)	(6.1)	(2.4)	(10.1, 2.4)	(10.5)

a) in CD_3SOCD_3. b) OH

TABLE 3. ^{13}C NMR Data for Catechols **3**

Cmpd	δ/ppm									
	C1	C2	C3	C4	C5	C6	CH_2	CH_2	CH_2	CH_3
3a[a]	137.56	144.64	102.60	153.82	105.28	115.93				55.76
3b[b]	139.47	146.43	103.67	153.87	105.53	116.12	70.20	23.23		10.74
3c[a]	137.22	144.63	103.38	153.84	106.38	115.88	68.54	31.35	19.21	13.80
3d[a]	141.79	143.76	115.75	129.30	121.21	116.20				17.41
3e[a]	142.58	143.56	116.05	127.29	124.27	118.43	37.42	22.43		13.15
3f[a]	143.70	143.66	115.94	127.60	124.13	118.32	35.18	31.30	21.79	13.54
3g[b]	145.96	145.28	116.52	137.56	124.36	119.48	61.40	38.30		

a) $CDCl_3$. b) CD_3COCD_3

TABLE 4. Yields and mps. of Catechols **3** and electronic spectra of Catechols **3** and *o*-Benzoquinones **2**

Cmpd	Yield (%)	mp. [bp./0.01mm] (°C)	UV λ_{max}(log ε)	Cmpd	UV λ_{max}(log ε)
3a	34	45-47[a]	230(3.21), 292(3.27)	**2a**	420(3.24)
3b	72	99-101	223(3.65), 288(3.48)	**2b**	420(3.25)
3c	58	98-100		**2c**	420(3.10)
3d	42	56.8[b]		**2d**	330(3.77), 460(3.42)
3e	55	[118-124]		**2e**	330(3.87), 470(3.51)
3f	87	oil		**2f**	330(3.81), 470(3.49)
3g	47	oil	254(3.81), 291(3.54)	**2g**	330(4.09), 460(3.31)

a) Ref. 8, 49-51°. b) Ref 5c, 50-52°

which were obtained as oils (**3e-3g**) were converted to the corresponding *bis*-4-nitrobenzyl ethers by reaction with 4-nitrobenzyl bromide and K_2CO_3 in acetone, for elemental analysis purposes (Table 5). An important limitation was revealed from an attempt to react 4-methylselenyl- or 4-bromophenol under these conditions which led to recovery of unreacted starting materials.

EXPERIMENTAL SECTION

Melting points were determined with an Electrothermal Digital Melting Point Apparatus. NMR spectra were recorded on Varian XL-200 or VXR-400 spectrometers, referencing to residual proton or ^{13}C signals of the solvent. Mass spectra were obtained from a VG7070 spectrometer and GC-MS data from a Hewlett Packard 5890 Series II GC with 5971 mass selective detector. TLC was performed on silica gel on aluminum foil backed plates and flash chromatography used silica gel 60 (230-400 mesh) with ethyl acetate - cyclohexane solvent mixtures. The starting phenols (**1a-1g**) were either commercial samples (**1a**, **1c** and **1d**) or were prepared by selective alkylation of hydroquinone.[2]

TABLE 5. MS data and elemental analysis data for *bis*-4-Nitrobenzylethers of Catechols **3**

Cmpd	EI-MS m/z (%)	HRMS (Calcd)	Elemental Analyses (Calcd)		
			C	H	N
3a	140(100) 125(91) 110(22) 107(32)	140.0480(140.0486)			
3b	168(50) 126(100)		64.30 (64.27)	7.04 (7.19)	
3c	182(20) 126(100)	182.0956(182.0943)	65.69 (65.92)	7.81 (7.81)	
3d	156(100) 141(64)				
3e	184(95) 155(30) 142(100) 110(40)		60.78 (60.65)[a,d]	4.88 (4.70)	6.16 (6.09)
3f	198(68) 155(61) 142(100) 141(77)		61.53 (61.24)[b,d]	5.16 (5.14)	5.98 (5.80)
3g	187(33) 186(72) 156(21) 155(69)	186.0358(186.0351)	57.89 (57.69)[c,d]	4.42 (4.22)	6.14 (6.02)

a) Yellow solid from ethanol, mp. 136-138°. b) Yellow crystals from ethanol, mp. 116°. c) Orange crystals from ethanol, mp. 141-142°. d) As *bis*-(4-nitrobenzyl) ethers.

Typical Procedures. Synthesis of 4-Methylthiocatechol (3d).- A solution of KH_2PO_4 (10g) in water (200 mL) was mechanically stirred in a 2L round bottom flask and ice (200g) added. The flask was cooled in ice-ethanol mixture and $ON(SO_3)_2K$ (6g) added followed by 4-methylthiophenol (1.0g) in ethyl ether (20 mL). The mixture was stirred for 1h during which time it became dark red. The resulting mixture was rotoevaporated at 20° to remove the ethyl ether and extracted with chloroform (3 x 50 mL). Without delay, the chloroform extract was shaken with a solution of $Na_2S_2O_4$ (6g) and Na_2HPO_4 (2.2g) in water (30 mL). The chloroform was separated, dried ($MgSO_4$) and evaporated to give a residue which was flash chromatographed on silica gel 60 (50g) eluting with ethyl acetate-cyclohexane. Evaporation of the appropriate fractions gave **3d** as a cream solid (42%), mp. 56.8° (lit[5c] 50-52°), ^{1}H NMR ($CDCl_3$): δ 2.44 (3H, s), 5.08 (1H, brs) 5.22 (1H, brs), 6.80 (2H, m), 6.88 (1H, d, J 1.2 Hz). ^{13}C NMR: δ 17.41 (q, CH_3), 115.75 (d, C3), 116.20 (d, C6), 121.21 (d, C5), 141.79 (s, C1), 143.76 (s, C2) . MS (EI) m/z (%) 156 (100), 141 (64).

Synthesis of 4-Methylthio-*o*-benzoquinone (2d).- This compound was obtained in 86% yield by evaporation of the chloroform extract (above) before reaction with $Na_2S_2O_4$ as a crimson solid, mp 92°. UV: λ_{max} (log ε) 330 (3.77), 460 (3.42) (H_2O); ^{1}H NMR ($CDCl_3$): δ 2.51 (3H, d, J 0.5), 6.19 (1H, d of qui, J 2.4, 0.5), 6.42 (1H, dq, J 10.1, 0.5 Hz), 6.82 (1H, dd, J 10.1, 2.4 Hz).

Acknowledgements.- We thank Dr. A. T. Dronsfield at The University of Derby for GC-MS measurements and the Cancer Research Campaign and the Association for International Cancer Research for support.

REFERENCES

1. a) C. J. Cooksey, E. J. Land, P. A. Riley, T. Sarna, and T. G. Truscott, *Free Radical Res. Commun.* **4**, 131, (1987); b) E. J. Land, C. J. Cooksey and P. A. Riley, *Biochem. Pharmacol.*, **39**, 1133 (1990); c) C. J. Cooksey, K. Jimbow, E. J. Land and P. A. Riley, *Melanoma Res.*, **2**, 283 (1992); d) C. J. Cooksey, E. J. Land, C. A. Ramsden and P. A. Riley, *Anti-Cancer Drug Design*, **10**, 119 (1995).

2. S. Naish-Byfield, C. J. Cooksey, A. M. Latter, C. I. Johnson and P. A. Riley, *Melanoma Res.*, **1**, 273 (1991).

3. P. Capdevielle and M. Maumy, *Tetrahedron Lett.*, **23**, 1577 (1982).

4. H. Bretschneider, K. Hohenlohe-Oehringen, A. Kaiser and U. Wolcke, *Helv. Chim. Acta.*, **56**, 2857 (1973).

5. a) **3a** from the aldehyde, G. W. Kabalka, N. K. Reddy and C. Narayana, *Tetrahedron Lett.* **33**, 865 (1992); b) **3** (R = octyloxy and R = decyloxy, in 4 steps from 3,4-dihydroxybenzaldehyde), Y. Naito, M. Sugiura, Y. Yamaura, C. Fukaya, K. Yokoyama, Y.Nakagawa, T. Ikeda, M. Senda and T. Fujita, *Chem. Pharm. Bull. Jpn*, **39**, 1736 (1991); c) **3d** by pyrolysis of a dimethylsulfonium salt, A. Winkler, *Ger. Offen.* DE 2644591 (1978); *Chem. Abstr.*, **89**, 23960 (1978).

6. H. J. Teuber, *Chem. Rev.*,**71**, 229 (1971).

7. V. Balogh, M. Fetizon and M. Golfier, *J. Org. Chem.*, **36**, 1339 (1971).

8. D. H. Rosenblatt and R. W. Rosenthal, *J. Am. Chem. Soc.*, **75**, 4607 (1953).

****

REDUCTION OF AROMATIC SULFONYL CHLORIDES TO DISULFIDES

Submitted by (11/15/95)

M. H. Zhang*, M. Zheng, T. Cheng and S. X. Wang

Teaching and Research Section of Organic Chemistry of Agriculture College Yangzhou University, Yangzhou 225002, Jiangsu, P. R. CHINA

Lalancette and Arnac first reported the preparation of sodium selenated borohydride ($NaBH_2Se_3$) by the reaction of sodium borohydride and selenium powder in diglyme in 1969.[1] This reagent, similar to the sodium sulfurated borohydride ($NaBH_2S_3$), could be useful as a new stereoselective reducing agent.[2] However, no further reports concerning the reducing capacity of $NaBH_2Se_3$ have appeared. We now report that sodium triselenoborohydride ($NaBH_2Se_3$)[1] reduces aromatic