

An efficient and convenient method for preparation of 2,2-disubstituted and 2-monosubstituted 1,3-benzodioxoles from ketones and aldehydes with catechol catalysed by ZrO_2/SO_4^{2-}

Tong-Shou Jin*, Su-Ling Zhang, Xiao-Feng Wang, Jun-Jie Guo and Tong-Shuang Li

Department of Chemistry, Hebei University, Baoding 071002, Hebei Province, P. R. China

The title compounds have been synthesised by reaction of catechol with ketones and aldehydes catalysed by ZrO_2/SO_4^{2-} solid superacid in high yields. Ketones gave better yields than aldehydes.

Keywords: catechol, benzodioxoles, ketone, aldehydes

1,3-Benzodioxole derivatives are widely employed for the protection of catechols compounds in multistep organic syntheses.^{1–5} They were also applied as pesticides or pesticide intermediates,^{6–8} herbicides,⁹ antioxidants,^{10,11} antimicrobial¹² and medicinal.^{13,14} The acetal ring is stable to a variety of commonly used reagents such as HNO_3 ,¹⁵ $Pb(OAc)_4$,¹⁶ and $BuLi$,¹⁷ and is cleaved by $NaI-AcCl$,¹⁸ boron tribromide,¹⁹ and $NaN(SiMe_3)_2$ or $Li(i-Pr)$.²⁰ In general, 1,3-benzodioxoles are prepared by protic or Lewis acid catalysed condensation of carbonyl compounds with catechol. Several types of Lewis acid catalysts have been used previously for this purpose, including boron tribromide,¹⁹ phosphorus pentoxide,²¹ phosphorus trichloride,²² trimethylsilyl chloride²³ and protic acids such as *p*-toluenesulfonic acid.¹⁵ These methods are not very satisfactory due to the long reaction time (8–120 h, ref. 15), low yields, tedious workup and the problem of corrosion and pollution. Some of the catalysts are not easily obtained, expensive and non-recoverable. More recently, montmorillonite clay²⁴ was also used for this reaction to obtain better results.

Solid superacids have been recently used as efficient catalysts for a variety of organic reactions.^{25–29} We have recently developed an easy procedure for the synthesis of diacetals catalysed by ZrO_2/SO_4^{2-} .²⁸ This suggested the use of ZrO_2/SO_4^{2-} to catalyse the synthesis of 2,2-disubstituted and 2-substituted 1,3-benzodioxoles from ketones and aldehydes with catechol. Herein we wish to report an efficient and convenient procedure for the synthesis of substituted 1,3-benzodioxoles by condensation of catechol with ketones and aldehydes catalysed by ZrO_2/SO_4^{2-} solid superacid in refluxing benzene or toluene.

When catechol **1** in the presence of ZrO_2/SO_4^{2-} solid superacid was heated with several ketones or aldehydes **2** in refluxing benzene or toluene, the corresponding 2,2-disubstituted and 2-monosubstituted 1,3-benzodioxoles **3** were

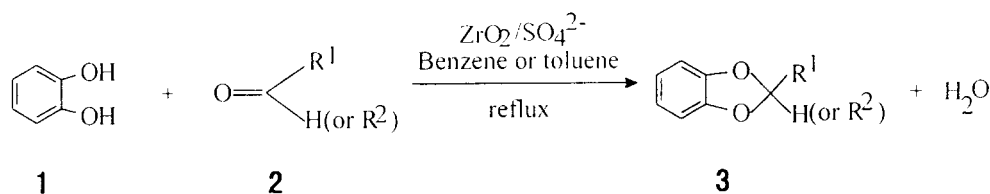
obtained in good to high yield except for anthrone (**1n** no reaction), the result is summarised in Tables 1 and 2.

We have developed an efficient and convenient procedure for the preparation of 1,3-benzodioxoles catalysed by ZrO_2/SO_4^{2-} . The reactions were completed within 3.0–15 h to give satisfactory yields in most cases. The crude products could be easily obtained by filtration of the catalyst followed by evaporation of the solvent. The present procedure gives reproducibly high yields but needs much shorter reaction time than with *p*-toluenesulfonic acid catalyst.¹⁵ For example, with *p*-toluenesulfonic acid catalyst and heating for 36, 24 and 120 h, **3a**, **3d** and **3h** were obtained in 83, 79 and 76% yield respectively. However, our procedure with ZrO_2/SO_4^{2-} catalyst and heating for 7, 6.5 and 15 h gave **3a**, **3d** and **3h** in 86, 88 and 76% yield respectively.

We found that the reaction rate is markedly influenced by the size of ring. Five and six-membered ring ketones gave high yields of products. For example, cyclopentanone **1e** gave **3e** for 3 h in 82% yield, and cyclohexanone **1f** provided **3f** for 3 h in 88% yield. However, cycloheptanone **1g** gave **3g** for 10 h in 76% yield. The explanation for this result may be due to the ring strain.

We have also found that aldehydes gave an intractable mixture of complex by-products in this reaction and acetals were obtained only in moderate yields (22–80%). This might be due to the aldehyde group being too reactive and accompanying side reactions such as oxidation, polymerisation, and tar formation, etc.

In conclusion, we have provided an efficient and convenient method for the synthesis of a variety of 2,2-disubstituted and 2-monosubstituted 1,3-benzodioxoles catalysed by ZrO_2/SO_4^{2-} . Ketones give high yields while aldehydes give moderate yields. The present method has operational simplicity, high yields, short reaction time and a non-corrosive and environment friendly catalyst.



Scheme 1

* To receive any correspondence. E-mail: orgsyn@mail.hbu.edu.cn

† This is a Short Paper, there is therefore no corresponding material in *J. Chem. Research (M)*.

Table 1 Synthesis of 2,2-disubstituted 1,3-benzodioxoles catalysed by ZrO_2/SO_4^{2-}

Entry	Ketones	Solvent/ reaction time (h)	Ratio ^a	Products	Isolated yield/%	Mp/°C	or	b.p./torr
						found		reported
1a	Acetone	None/7	1:5	3a	86	80–82/30		50–51/2.5 ¹⁵
1b	Butanone	None/8	1:5	3b	85	95–97/30		64–65/2.5 ¹⁵
1c	Hexan-2-one	Benzene/9.5	1:3	3c	82	125–127/30		84–86/1.5 ¹⁵
1d	Methyl- -isobutylketone	Toluene/6.5	1:3	3d	88	126–128/30		96–97/5 ¹⁵
1e	Cyclopentanone	Benzene/3	1:3	3e	82	130–132/2		114–115/4.5 ¹⁵
1f	Cyclohexanone	Benzene/3	1:3	3f	88	46–48		45–48 ¹⁵
1g	Cycloheptanone	Toluene/10	1:3	3g	76	56–58		55–57 ¹⁵
1h	Acetophenone	Benzene/15	1:3	3h	76	168–170/10		122–124/1.0 ¹⁵
1i	2-Chloro- acetophenone	Toluene/10	1:2	3i	84	49–50		49–50 ²⁴
1j	<i>p</i> -Methoxy- acetophenone	Benzene/11	2:1	3j	52	66–68		67–68 ²⁴
1k	<i>p</i> -Nitro- acetophenone	Toluene/11	2:1	3k	98	100–102		–
1l	Benzophenone	Toluene/10	2:1	3l	21	87–89		85–87 ¹⁵
1m	Dibenzyl ketone	Toluene/10	2:1	3m	52	100–101		–
1n	Anthrone	Toluene/12	2:1	3n	0	–		–

^aCatechol:ketone (mol:mol).**Table 2** Synthesis of 2-monosubstituted 1,3-benzodioxoles catalysed by ZrO_2/SO_4^{2-}

Entry	Ketones	Solvent/ reaction time (h)	Ratio ^a	Products	Isolated yield/%	Mp/°C	or	b.p./torr
						found		reported
1o	<i>n</i> -Butylaldehyde	Benzene/10	1:3	3o	68	110–112/30		75–80/3.5 ¹⁵
1p	Benzaldehyde	Toluene/7.5	1:3	3p	22	55–56		54–56 ¹⁵
1q	Cinnamaldehyde	Toluene/6	1:3	3q	80	60–61		60–61 ²⁴
1r	<i>p</i> -Methyl- benzaldehyde	Toluene/10	1:2	3r	52	57–58		57–58 ²⁴
1s	<i>p</i> -Methoxy- benzaldehyde	Toluene/5	1:2	3s	48	58–59		59–60 ¹⁵
1t	<i>m</i> -Nitro- benzaldehyde	Toluene/9	2:1	3t	34	85–87		88–89 ²⁴

^aCatechol:aldehyde (mol:mol).

Experimental

The catalyst ZrO_2/SO_4^{2-} solid superacid was prepared as follows. $Zr(OH)_4$ was obtained by hydrolysing $ZrOCl_2 \cdot 8H_2O$ with aqueous ammonium hydroxide, washing the precipitate, and drying it at 110–120°C for 4 h, and then powdering the precipitate to below a 100 mesh. The hydroxides were treated with 1N H_2SO_4 for 4 h, filtering, drying, calcined in electric furnace at 650°C for 4 h, and finally stored in a desiccator until use. The products were characterised by ¹H NMR spectra and comparison of their melting or boiling points with literature values.

General procedure for the preparation of 1,3-benzodioxoles: The catalyst ZrO_2/SO_4^{2-} (200mg) was added to a solution of catechol 1 (2.00mmol) and ketone or aldehyde 2 in benzene or toluene (15ml) as indicated in Tables 1 and 2. The mixture was stirred under reflux for the length of time as shown in Tables 1 and 2 and the water was separated from the reaction system by azeotropic distillation with a water separator. The progress of the reaction was monitored by TLC. After completion of the reaction, the benzene or toluene was removed by distillation, Et_2O (10ml) was added, the catalyst was filtered off and washed with Et_2O . The solvent was evaporated under reduced pressure and the crude product was purified by column chromatography on silica gel (light petroleum-diethyl ether as eluent) to give the corresponding product 3.

For **3i**: δ_H (300MHz), 4.00 (2H, s, 2- CH_2Cl), 6.81–6.89 (4H, m, 5,6,7,8- H_4), 7.40–7.64 (5H, m, ph- H_2); **3j**: δ_H (300MHz), 1.97 (3H, s, 2- CH_3), 3.80(3H,s, 4'- OCH_3), 6.79 (4H, s, 5,6,7,8- H_4), 6.89 (2H, d, 3',5'- H_2), 7.52 (2H, d, 2',6'- H_2); **3k**: δ_H (200MHz), 1.987 (3H, s, 2- CH_3), 5.81–5.82 (4H, m, ph- H_4), 7.75–8.24 (4H, m, 5,6,7,8- H_4); **3l**: δ_H (200MHz), 6.79–6.92 (4H, m, 5,6,7,8- H_4), 7.61–7.34 (10H, m, ph- H_{10}); **3m**: δ_H (300MHz), 3.19 (4H, s, 2-1',2-1''di- CH_2), 6.66 (4H, s, 5,6,7,8- H_4), 7.18–7.29 (10H, m, ph- H_{10}); **3q**: δ_H (300MHz), 6.83 (4H, s, 5,6,7,8- H_4), 6.60 (1H, d, 2- H), 6.37 (1H, d, 1'- H), 6.92 (1H, d, 2'- H), 7.31–7.47 (5H, m, ph- H_2); **3t**: δ_H (300MHz), 6.90 (4H, s, 5,6,7,8- H_4), 7.04 (1H, s, 2- H), 8.46 (1H, t, 2'- H), 8.31 (1H, d, 4'- H), 7.64 (1H, t, 5'- H), 7.93 (1H, d, 6'- H).

The project was supported by National Natural Science Foundation of China (29872011 and 29572039), Educational Ministry of China and Educational Department of Hebei Province (990104).

Received 8 January 2001; accepted 24 February 2001
Paper 01/703

Reference

- T.W. Green and P.G.M. Wuts, *Protective Groups in Organic Synthesis*, 2nd Ed. John Wiley, New York, 1991, PP 170.
- G. Majetich and S. Liu, *Synth. Commun.* 1993, **23**, 2331.
- E.J. Corey and S.D. Hurt, *Tetrahedron Lett.*, 1977, 3923.
- K. Ogura and G. Tsuchihashi, *Tetrahedron Lett.*, 1971, 3151.
- U. Eder, G. Sauer, G. Haffer, J. Ruppert, R. Wiechert, A. Fuerst and W. Meier, *Helv. Chim. Acta*, 1976, **59**, 999.
- M. Anderson, A.G. Brinnand and R.E. Woodall, *Eur. Pat.*, 469686, 1990; *Chem. Abstr.*, 1992, **116**, 235642 p.
- M. Anderson, A.G. Brinnand and R.E. Woodall, *Eur. Pat.*, 512379, 1991; *Chem. Abstr.*, 1993, **119**, 95537 t.
- C. Devakumar and V.S. Saxina, *Shashpa*, 1994, **1**, 47.
- F. Arndt and H. Franke, *Ger. Pat.*, 2624822, 1976; *Chem. Abstr.*, 1978, **88**,105307 a.
- T. Isobe and H. Seino, *Yukagaku*, 1994, **43**, 1017; 1990, **39**, 931.
- T.H. Minh, E.R. Cole and G. Grank, *Australian Pat.*, 577866, 1980; *Chem. Abstr.*, 1984, **101**, 191878 d.
- T. Isobe and H. Seino, *Bokin Bobai*, 1988, **16**, 453; 1985, **13**, 485.
- H. Akimoto, K. Ootsu and F. Ito, *Jap. Pat.*, 0509170, 1990; *Chem. Abstr.*, 1993, **119**, 8798 n.
- Y. Kumagai, J.M. Fukuto and A.K. Cho, *Curr. Med. Chem.*, 1994, **1**, 254.

- 15 E.R. Cole, G. Crank and H.T.H. Minh, *Aust. J. Chem.*, 1980, **33**, 675.
- 16 E.R. Cole, G. Crank and H.T.H. Minh, *Aust. J. Chem.*, 1980, **33**, 527.
- 17 S. Bengtsson and T. Hogberg, *J. Org. Chem.*, 1989, **54**, 4549.
- 18 L. Corda, A.M. Fadda, A. Maccioni, A.M. Maccioni and G. Podda, *J. Heterocyclic Chem.*, 1988, **25**, 311.
- 19 E. Napolitano, R. Fiaschi and E. Mastrorilli, *Synthesis*, 1986, 22.
- 20 J.R. Hwu, F.F. Wong, J.J. Huang and S.C. Tsay, *J. Org. Chem.*, 1997, **62**, 4097.
- 21 H. Iwagami, M. Yatagal, M. Nakazawa, H. Orlta, Y. Honda, T. Ohnuki and T. Yukawa, *Bull. Chem. Soc. Jpn.*, 1991, **64**, 175.
- 22 R.R. Bikbulatov, T.V. Timofeeva, L.N. Zorina, O. G. Safiev and V.V. Zorin, *Zh. Obshch Khim.*, 1996, **66**, 1854.
- 23 Y. Nishida, M. Abe, H. Ohri and H. Meguro, *Tetrahedron: Asymmetry*, 1993, **4**, 1431.
- 24 T.S. Li, L.J. Li, B. Lu and F. Yang, *J. Chem. Soc. Perkin Trans.*, 1998, 3561.
- 25 T.S. Jin, Y.R. Ma, X. Sun, D. Liang and T.S. Li, *J. Chem. Research (s)*, 2000, 96.
- 26 T.S. Jin, X. Sun and T.S. Li, *J. Chem. Research (s)*, 2000, 128.
- 27 T.S. Jin, Y.R. Ma, Y. Li, X. Sun and T.S. Li, *Synth. Commun.*, 2001, **31** (13).
- 28 T.S. Jin, Y.R. Ma, Y.G. Wang and T.S. Li, *Indian J. Chem.*, 2000, **39B**, 858.
- 29 X. Sun, X.F. Wang, T.S. Jin and T.S. Li, *Chinese J. Hebei University*, 2001, **21**, 49.