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Stereoselective synthesis of highly substituted *trans*-2,3-dihydrofuran and *trans*-1,2-cyclopropane derivatives containing sulfonyl groups

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Abstract

trans-2,3-Dihydrofuran derivatives **3** and *trans*-1,2-cyclopropane derivatives **4** were prepared with high chemoselectivity and moderate overall chemical yield by the reaction of α,β-unsaturated sulfones **1** with arsonium bromides **2** in the presence of potassium carbonate. The structures of products obtained were identified by IR, MS, ^{1}H NMR, elemental analysis, and X-ray diffraction analysis.

1. Introduction

Dihydrofuran derivatives, substituted with a sulfonyl group have attracted considerable interest recently because of their promising utility as building blocks for a series of valuable spirocyclic compounds.[1,2] Cyclopropane derivatives play an equally important role in the field of organic synthesis.[3,4] To date, a number of methods for the synthesis of dihydrofuran and cyclopropane derivatives substituted with sulfonyl groups have been developed.[5–9] In previous papers, we have reported our recent work on stereoselective synthesis of dihydrofurans and cyclopropanes.[10–16] As part of a continuing effort, we report the stereoselective synthesis of *trans*-2,3-dihydrofuran and *trans*-1,2-cyclopropane derivatives containing sulfonyl group via the reaction of α,β-unsaturated sulfones with substituted arsonium ylides.

2. Results and discussion

In the presence of K_2CO_3, α,β-unsaturated sulfones **1a–e** reacted with furoylmethyltriphenylarsonium bromide **2A** or thienoylmethyltriphenylarsonium bromide **2B** at room temperature for 48 h to generate 2-furoyl-3-aryl-4-tosyl-5-phenyl-*trans*-2,3-dihydrofurans **3Aa–3Ae** or 2-thienoyl-3-aryl-4-tosyl-5-phenyl-*trans*-2,3-dihydrofurans **3Ba–3Be** exclusively and with high diastereoselectivity. Alternatively, if sulfones **1d** and **1e** were used as reactants in the presence of K_2CO_3 followed by the addition of arsonium ylide **2B**, 2-thienoyl-3-aryl-4-tosyl-5-phenyl-*trans*-2,3-dihydrofurans **3Bd–3Be** were formed as the major product and *trans*-1-thienoyl-2-aryl-3-tosyl- 3-benzoylcyclopropanes **4Bd–4Be** were generated as a minor reaction product, all with high diastereoselectivity (Scheme 1, Table 1). Products were identified by IR, MS, ^{1}H NMR, and elemental analysis. The conformation of dihydrofuran and cyclopropane products was confirmed via X-ray diffraction analysis (Figs. 1 and 2).[17]

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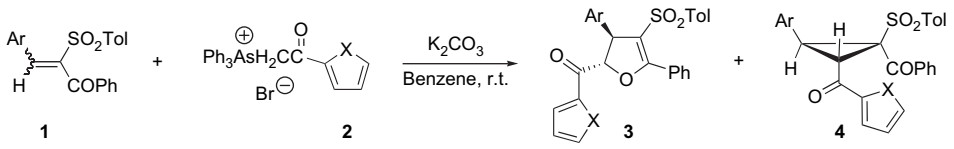


Scheme 1.

1a, **3Aa**, **3Ba**	**1b**, **3Ab**, **3Bb**	**1c**, **3Ac**, **3Bc**	**1d**, **3Ad**, **3Bd**, **4Bd**	**1e**, **3Ae**, **3Be**, **4Be**	**2A**, **3Aa–3Ae**	**2B**, **3Ba–3Be**, **4Bd**, **4Be**
4-$CH_3C_6H_4$	C_6H_5	4-ClC_6H_4	2-ClC_6H_4	4-$NO_2C_6H_4$	X=O	X=S

Table 1
Preparation of compounds **3** and **4**

Entry	Ar	X	Product	Yield (%)	Mp (°C)
1	4-$CH_3C_6H_4$	O	**3Aa**	51.1	167.3–167.5
2	C_6H_5	O	**3Ab**	62.5	166.4–166.6
3	4-ClC_6H_4	O	**3Ac**	55.6	168.5–168.9
4	2-ClC_6H_4	O	**3Ad**	56.7	147.8–148.7
5	4-$NO_2C_6H_4$	O	**3Ae**	43.2	194.8–195.7
6	4-$CH_3C_6H_4$	S	**3Ba**	57.2	160.0–160.9
7	C_6H_5	S	**3Bb**	40.6	173.2–174.2
8	4-ClC_6H_4	S	**3Bc**	60.7	175.4–175.7
9	2-ClC_6H_4	S	**3Bd**	52.3	230.1–230.9
10	4-$NO_2C_6H_4$	S	**3Be**	12.5	202.5–203.2
11	2-ClC_6H_4	S	**4Bd**	12.4	213.0–213.9
12	4-$NO_2C_6H_4$	S	**4Be**	40.9	182.4–183.8

The proposed reaction mechanism shown in Scheme 2 accounts for the highly diastereoselective formation of both dihydrofuran and cyclopropane products. Initial attack of the α,β-unsaturated sulfone **1** via the carbanion derived from arsonium bromide and base produces two intermediates, stabilized carbanion **I** and sulfonyl stabilized enolate **II** containing chiral carbon atoms C_2 and C_3. An intramolecular substitution reaction occurred at intermediate **I** to form the *trans*-cyclopropane **4**, whereas the intramolecular attack of the oxygen enolate to the pendent arsonium-containing carbon resulted in the occurrence of a substitution reaction of **II**. Two possible scenarios occur when the enolate oxygen attacks C_2 from the backside of leaving group (Ph_3As^+) such as **III** and **IV** as shown in Scheme 2. Conformation **III** is relatively more stabilized compared to conformation **IV** in which the repulsion of two large groups (Ar and CO–Fu) exists. Reaction through conformation **III** is preferred, producing the *trans*-dihydrofuran **3**. Generally, enolate intermediate **II** is much more stable than carbanion **I**, so dihydrofuran **3** is produced to the near exclusion of cyclopropane **4**.

In summary, this work provides a simple procedure for the synthesis of sulfonyl-substituted *trans*-2,3-dihydrofuran and *trans*-1,2-cyclopropane derivatives. Moreover, high diastereoselectivity with moderate chemical yield was achieved for these reactions.

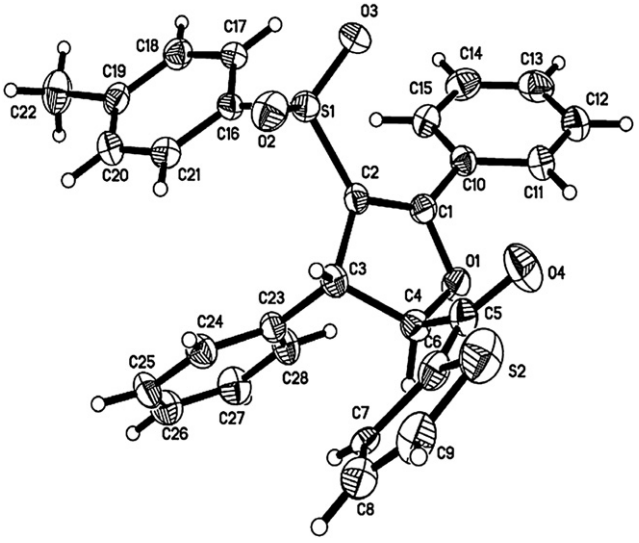


Figure 1. X-ray structure of **3Bb**.

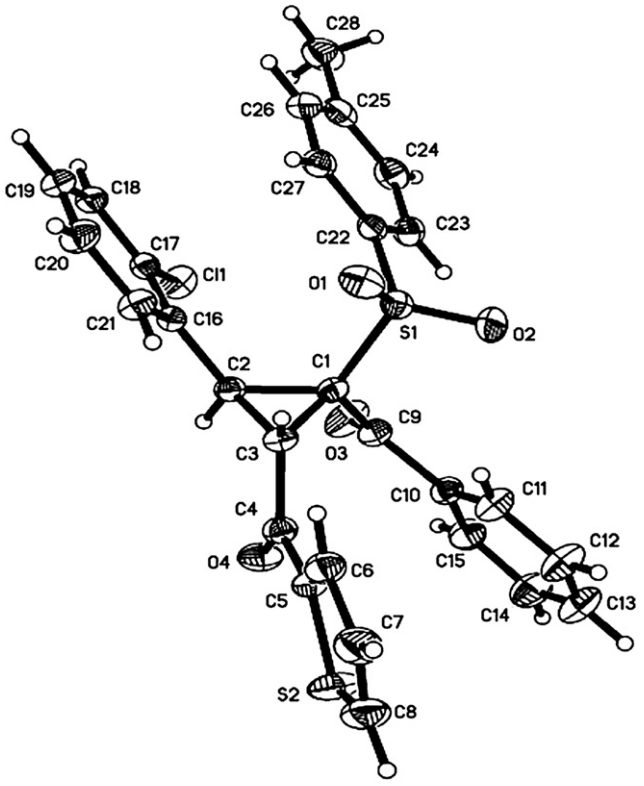
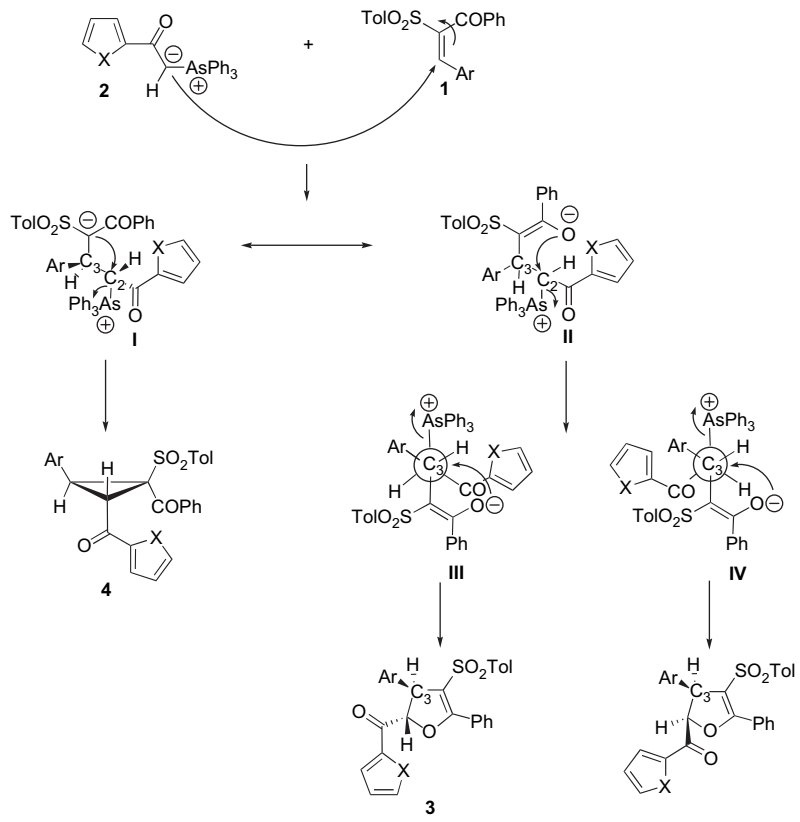


Figure 2. X-ray structure of **4Bd**.



Scheme 2.

3. Experimental

3.1. General

All reagents and solvents were obtained from commercial sources and used without purification. Melting points were determined using a WRS-1 melting point apparatus and are uncorrected. IR spectra were determined on a Bruker spectrometer and expressed in cm^{-1} (KBr disc). ^1H NMR spectra were recorded on a Bruker AVANCE-300 MHz NMR using $CDCl_3$ as solvent. *J* values are given in hertz. Elemental analysis was performed on the Elementar Vario EL-III instrument. Mass spectra were run on an HP5989A mass spectrometer. X-ray analysis was performed on a Bruker Smart Apex CCD Spectrometer.

α,β-Unsaturated sulfone derivatives **1**[10] and arsonium bromide **2**[18] were prepared as described in the literature and references cited therein.

3.2. General procedure for the synthesis of compounds *3Aa–3Ee*

To a solution of 1,3-diphenyl-2-tosyl-prop-2-en-1-one (**1**, 1.0 mmol) in benzene (12 ml) were added arsonium bromide (**2**, 1.1 mmol) and K_2CO_3 (3.0 mmol). The mixture was stirred at ambient temperature for 48 h. The solid residue was filtered and the solvent was evaporated under reduced pressure. The residue was purified by column chromatography on silica gel using ethyl acetate/petroleum ether (v/v=1:5–1:4) as eluent to give *trans*-2,3-dihydrofuran **3** or *trans*-1,2-cyclopropane **4**, respectively. Further purification can be carried out by recrystallization from ethyl acetate/petroleum ether.

3.2.1. 2-Furoyl-3-(4-methylphenyl)-4-tosyl-5-phenyl-trans-2,3-dihydrofuran (*3Aa*)

^1H NMR ($CDCl_3$, 300 Hz) δ: 2.31 (s, 3H), 2.35 (s, 3H), 4.62 (d, *J*=3.85, 1H), 5.51 (d, *J*=3.85, 1H), 6.59 (dd, *J*=3.57, 1.64, 1H), 6.95–7.51 (m, 7H), 7.62 (dd, *J*=1.64, 0.55, 1H), 7.82–7.86 (m, 2H); IR (KBr) *ν*: 1680, 1595, 1512, 1490, 1317, 1152 cm^{-1}; MS *m/z* (%) (EI): 329 (14), 105 (100), 95 (79), 91 (87). Anal. Calcd for $C_{29}H_{24}O_5S$: C, 71.88; H, 4.99. Found: C, 72.15; H, 4.65.

3.2.2. 2-Furoyl-3-phenyl-4-tosyl-5-phenyl-trans-2,3-dihydrofuran (*3Ab*)

^1H NMR ($CDCl_3$, 300 Hz) δ: 2.32 (s, 3H), 4.68 (d, *J*=3.85, 1H), 5.52 (d, *J*=3.85, 1H), 6.61 (dd, *J*=3.57, 1.64, 1H), 6.99–7.47 (m, 7H), 7.65 (dd, *J*=1.64, 0.55, 1H), 7.82–7.87 (m, 2H); IR (KBr) *ν*: 1685, 1623, 1595, 1492, 1317, 1152 cm^{-1}; MS *m/z* (%) (EI): 315 (100), 220 (23), 191 (22), 105 (50). Anal. Calcd for $C_{28}H_{22}O_5S$: C, 71.47; H, 4.99. Found: C, 71.65; H, 4.75.

*3.2.3. 2-Furoyl-3-(4-chlorophenyl)-4-tosyl-5-phenyl-trans-2,3-dihydrofuran (**3Ac**)*

^{1}H NMR ($CDCl_3$, 300 Hz) δ: 2.31 (s, 3H), 4.62 (d, J=3.96, 1H), 5.49 (d, J=3.96, 1H), 6.62 (dd, J=3.57, 1.65, 1H), 6.90–7.56 (m, 7H), 7.58 (dd, J=1.65, 0.55, 1H), 7.85–7.87 (m, 2H); IR (KBr) ν: 1677, 1627, 1596, 1325, 1153 cm^{-1}; MS *m/z* (%) (EI): 409 (5), 349 (74), 254 (27), 95 (100). Anal. Calcd for $C_{28}H_{21}O_5SCl$: C, 66.60; H, 4.19. Found: C, 66.87; H, 3.92.

*3.2.4. 2-Furoyl-3-(2-chlorophenyl)-4-tosyl-5-phenyl-trans-2,3-dihydrofuran (**3Ad**)*

^{1}H NMR ($CDCl_3$, 300 Hz) δ: 2.39 (s, 3H), 3.82 (d, J=4.25, 1H), 4.71 (d, J=4.25, 1H), 6.62 (dd, J=3.57, 1.65, 1H), 7.08–7.51 (m, 7H), 7.60 (dd, J=1.65, 0.55, 1H), 7.85–7.88 (m, 2H); IR (KBr) ν: 1683, 1647, 1595, 1490, 1317, 1153 cm^{-1}; MS *m/z* (%) (EI): 349 (76), 254 (42), 225 (40), 105 (100). Anal. Calcd for $C_{28}H_{21}O_5SCl$: C, 66.60; H, 4.19. Found: C, 66.35; H, 4.44.

*3.2.5. 2-Furoyl-3-(4-nitrophenyl)-4-tosyl-5-phenyl-trans-2,3-dihydrofuran (**3Ae**)*

^{1}H NMR ($CDCl_3$, 300 Hz) δ: 2.35 (s, 3H), 4.72 (d, J=4.12, 1H), 5.65 (d, J=4.12, 1H), 6.61 (dd, J=3.57, 1.65, 1H), 6.90–7.56 (m, 7H), 7.58 (dd, J=1.65, 0.55, 1H), 7.92–7.95 (m, 2H); IR (KBr) ν: 1680, 1643, 1593, 1519, 1318, 1153 cm^{-1}; MS *m/z* (%) (EI): 339 (10), 236 (26), 105 (41), 95 (100). Anal. Calcd for $C_{28}H_{21}NO_7S$: C, 65.23; H, 4.11; N, 2.72. Found: C, 65.52; H, 4.30; N, 2.92.

*3.2.6. 2-Thienoyl-3-(4-methylphenyl)-4-tosyl-5-phenyl-trans-2,3-dihydrofuran (**3Ba**)*

^{1}H NMR ($CDCl_3$, 300 Hz) δ: 2.32 (s, 3H), 2.38 (s, 3H), 4.62 (d, J=4.12, 1H), 5.56 (d, J=4.12, 1H), 6.99 (dd, J=4.94, 3.84, 1H), 7.12–7.39 (m, 6H), 7.42 (dd, J=3.84, 1.10, 1H), 7.60–7.65 (m, 1H), 7.76 (dd, J=4.94, 1.10, 1H), 7.83–7.86 (m, 1H); IR (KBr) ν: 1660, 1599, 1511, 1491, 1318, 1147 cm^{-1}; MS *m/z* (%) (EI): 344 (54), 234 (28), 111 (100), 105 (78), 91 (52), 77 (44). Anal. Calcd for $C_{29}H_{24}O_4S_2$: C, 69.57; H, 4.83. Found: C, 69.58; H, 4.88.

*3.2.7. 2-Thienoyl-3-phenyl-4-tosyl-5-phenyl-trans-2,3-dihydrofuran (**3Bb**)*

^{1}H NMR ($CDCl_3$, 300 Hz) δ: 2.28 (s, 3H), 4.72 (d, J=4.12, 1H), 5.58 (d, J=4.12, 1H), 6.99 (dd, J=4.94, 3.84, 1H), 7.02–7.39 (m, 7H), 7.42 (dd, J=3.84, 1.10, 1H), 7.59–7.61 (m, 1H), 7.76 (dd, J=4.94, 1.10, 1H), 7.83–7.86 (m, 1H); IR (KBr) ν: 1662, 1579, 1480, 1436, 1309, 1158 cm^{-1}; MS *m/z* (%) (EI): 375 (2), 331 (59), 330 (49), 111 (100), 105 (94), 91 (55), 77 (51). Anal. Calcd for $C_{28}H_{22}O_4S_2$: C, 69.12; H, 4.65. Found: C, 69.11; H, 4.56.

*3.2.8. 2-Thienoyl-3-(4-chlorolphenyl)-4-tosyl-5-phenyl-trans-2,3-dihydrofuran (**3Bc**)*

^{1}H NMR ($CDCl_3$, 300 Hz) δ: 2.31 (s, 3H), 4.60 (d, J=4.12, 1H), 5.72 (d, J=4.12, 1H), 7.01 (dd, J=4.94, 3.84, 1H), 7.10–7.37 (m, 6H), 7.42 (dd, J=3.84, 1.10, 1H), 7.44–7.46 (m, 1H), 7.79 (dd, J=4.94, 1.10, 1H), 7.83–7.86 (m, 1H); IR (KBr) ν: 1677, 1628, 1597, 1413, 1311, 1151 cm^{-1}; MS *m/z* (%) (EI): 256 (3), 254 (7), 225 (11), 111 (12), 105 (100), 91 (62), 77 (87). Anal. Calcd for $C_{28}H_{21}O_4S_2Cl$: C, 64.54; H, 4.06. Found: C, 64.60; H, 4.21.

*3.2.9. 2-Thienoyl-3-(2-chlorolphenyl)-4-tosyl-5-phenyl-trans-2,3-dihydrofuran (**3Bd**)*

^{1}H NMR ($CDCl_3$, 300 Hz) δ: 2.39 (s, 3H), 3.86 (d, J=4.12, 1H), 5.58 (d, J=4.12, 1H), 7.09 (m, 4H), 7.25 (dd, J=4.94, 3.84, 1H), 7.27–7.70 (m, 7H), 7.76 (dd, J=3.84, 1.10, 1H), 8.06–8.09 (m, 2H), 8.10 (dd, J=4.94, 1.10, 1H); IR (KBr) ν: 1673, 1645, 1595, 1512, 1417, 1324, 1152 cm^{-1}; MS *m/z* (%) (EI): 254 (17), 225 (6), 111 (100), 105 (94), 91 (55), 77 (51). Anal. Calcd for $C_{28}H_{21}O_4S_2Cl$: C, 64.54; H, 4.06. Found: C, 65.50; H, 4.32.

*3.2.10. 2-Thienoyl-3-(4-nitrolphenyl)-4-tosyl-5-phenyl-trans-2,3-dihydrofuran (**3Be**)*

^{1}H NMR ($CDCl_3$, 300 Hz) δ: 2.31 (s, 3H), 4.92 (d, J=4.40, 1H), 5.48 (d, J=4.40, 1H), 7.01–7.04 (m, 2H), 7.18 (dd, J=4.94, 3.84, 1H), 7.25–7.55 (m, 7H), 7.71 (dd, J=3.84, 1.10, 1H), 7.79 (dd, J=4.94, 1.10, 1H), 8.02–8.05 (m, 4H); IR (KBr) ν: 1674, 1627, 1597, 1490, 1319, 1152 cm^{-1}; MS *m/z* (%) (EI): 360 (7), 111 (100), 105 (45), 77 (33). Anal. Calcd for $C_{28}H_{21}NO_6S_2$: C, 63.26; H, 3.98; N 2.63. Found: C, 63.13; H, 4.28; N, 2.92.

*3.2.11. 1-Thienoyl-2-(2-chlorophenyl)-3-tosyl-3-benzoyl-trans-1,2-cyclopropane (**4Bd**)*

^{1}H NMR ($CDCl_3$, 300 Hz) δ: 2.31 (s, 3H), 5.58 (d, J=4.12, 1H), 4.72 (d, J=10.6, 1H), 6.10 (d, J=10.6, 1H), 6.92–7.09 (m, 7H), 7.29–7.90 (m, 9H); IR (KBr) ν: 1673, 1646, 1595, 1513, 1416, 1320, 1153; MS *m/z* (%) (EI): 254 (17), 111 (93), 105 (100), 91 (48), 77 (63). Anal. Calcd for $C_{28}H_{21}O_4S_2Cl$: C, 64.54; H, 4.06. Found: C, 64.52; H, 4.55.

*3.2.12. 1-Thienoyl-2-(4-nitrophenyl)-3-tosyl-3-benzoyl-trans-1,2-cyclopropane (**4Be**)*

^{1}H NMR ($CDCl_3$, 300 Hz) δ: 2.40 (s, 3H), 3.82 (d, J=7.69, 1H), 4.60 (d, J=7.69, 1H), 7.05 (dd, J=4.94, 3.84, 1H), 7.16–7.29 (m, 5H), 7.38 (dd, J=3.84, 1.10, 1H), 7.55–7.59 (m, 1H), 7.80 (dd, J=4.94, 1.10, 1H), 8.01–8.20 (m, 2H); IR (KBr) ν: 1676, 1629, 1598, 1490, 1316, 1157 cm^{-1}; MS *m/z* (%) (EI): 360 (28), 111 (100), 105 (54), 77 (45). Anal. Calcd for $C_{28}H_{21}NO_6S_2$: C, 63.26; H, 3.98; N, 2.63. Found: C, 63.23; H, 4.22; N, 2.41.

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17. CCDC-651155 (**3Bb**) and CCDC-651154 (**4Bd**) contain all crystallographic details of this publication and are available free of charge at www.ccdc.cam.ac.uk or can be ordered from the following address: Cambridge Crystallographic Data Centre, 12 Union Road, GB-Cambridge CB21EZ; fax: +44 1223 336 033; or deposit@ccdc.cam.ac.uk. Unit cell parameters (**3Bb**): *a*: 16.145(3) Å; *b*: 9.4331(16) Å; *c*: 31.436(5) Å; *β*: 91.109(2); space group: *C*2/*c*. Unit cell parameters (**4Bd**): *a*: 12.1587(10) Å: *b*: 14.8794(12) Å; *c*: 26.595(2) Å; space group: *Pbca*.
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