Metal-assisted reactions. Part 27.[1] 3-Benzyloxy-1,2-benzisothiazole 1,1-dioxide: an unusual ether linkage that does not permit heterogeneous catalytic hydrogenolysis

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Aryl or allyl ethers of some heterocyclic systems can be readily hydrogenolysed or cross-coupled catalytically with transition metals to give arenes, alkenes or alkanes. Unexpectedly for transition metals, the corresponding alkyl and, particularly, benzyl ethers are totally inert. An X-ray structure determination on 3-benzyloxy-1,2-benzisothiazole 1,1-dioxide 1 has shown that there is no inherent structural reason for this major difference, apart from the absence of a suitable p-orbital in the benzyl ethers.

Derivatives of 3-oxo-1,2-benzisothiazole 1,1-dioxide (saccharin) **1** are well-known for their biological properties.[2] More

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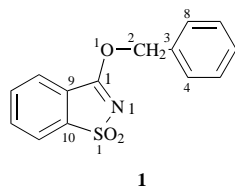
recently, derivatives prepared from such compounds and phenols [pseudosaccharyl ethers, **2** in eqn. (1)] have been used
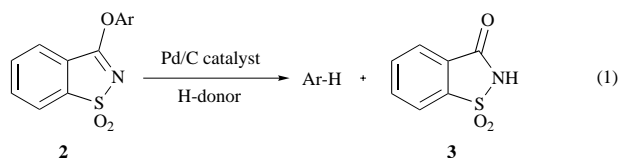
to produce arenes **3** by *ipso* replacement of OH by H through heterogeneous catalytic transfer hydrogenolysis [eqn. (1)][3] and to form substituted arenes [**4**, eqn. (2)] through C–C bond
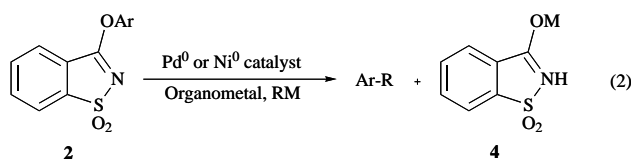
formation on catalytic cross-coupling with organometallic reagents.[4] X-Ray structure determinations on a series of these aryl pseudosaccharyl ethers[5,6] and related aryl tetrazolyl ethers[1] has revealed a remarkable disparity in the two C–O ether bond lengths on converting a parent phenol into its ether **2**. In these compounds, the total C–O–C ether bond distance is close to 2.78 Å but one of the C–O bonds is very long (at about 1.42 to 1.44 Å) and the other is very short (about 1.32–1.33 Å), approaching a bond order of about 1.5. These observations have been discussed extensively in the context of the reactivity of these ethers towards catalytic hydrogenolysis.[1] It was shown that aryl pseudosaccharyl **2** or aryl tetrazolyl ethers and the analogous ethers with allyl in place of aryl[7] are easy to hydrogenolyse by heterogeneous catalysis and that this ease of reaction was at least partly caused by the large C–O bond energy

changes that occur on ether formation (the original phenolic C–O bond is weakened and the new C–O bond to the heterocycle is very strong, giving an overall net bond energy gain of some 170 kJ mol^{-1}).[1] At the same time, it was pointed out that changes in bond energy alone did not appear to be a sufficient criterion for cross-coupling or hydrogenolysis to occur. In particular, alkyl and benzyl pseudosaccharyl or tetrazolyl ethers (*e.g.* the title compound **1**), which are analogous to the aryl pseudosaccharyl or aryl tetrazolyl ethers, do not undergo the same hydrogenolytic reactions. Especially for the benzyl group, this lack of reactivity with a palladium catalyst is in marked contrast to the readiness with which suitable benzylic compounds generally undergo oxidative addition reactions with transition metals.[8] Because one reason for this absence of reactivity could be due to there *not* being one long and one short C–O bond in the benzyl ether **1**, with no favourable accompanying change in overall bond energy, it was decided to determine whether or not the characteristic exceptional long and short C–O ether bond situation found in aryl pseudosaccharyl ethers **2** was repeated in the benzylic analogue **1**.

Results and discussion

The bond lengths and angles in 3-benzyloxy-1,2-benzisothiazole 1,1-dioxide **1** were determined by X-ray analysis. Relevant atom numbering is shown on structure **1**. Generally, the observed bond lengths and angles in **1** are unremarkable for this type of benzisothiazole 1,1-dioxide, except near the central ether linkage. Table 1 gives a selection of bond lengths and angles. In the crucial sequence of atoms C1–O1–C2–C3 (structure **1**), it is seen that the bond lengths are 1.315(2) Å (C1–O1), 1.454(3) Å (O1–C2) and 1.500(3) Å (C2–C3). The last C–C single bond length is unexceptional for CH$_2$ connected directly to an aryl ring[9] and is not discussed further. However, the O1–C2 single bond is very long for such a linkage; in similar aryl ethers (*e.g.* **2**) it is generally found to be about 1.42 Å, similar to the length in aliphatic ethers.[1] In contrast, the C1–O1 bond is extremely short; in simple diaryl ethers a corresponding C–O bond length is normally about 1.37–1.38 Å and, in the exceptional aryl pseudosaccharyl and aryl tetrazolyl ethers previously surveyed,[1] the short C–O bond is about 1.33–1.34 Å. Thus, in this benzyloxy compound **1**, the *total* C1–O1–C2 ether bond distance of 2.77 Å is very close to the previously reported average of 2.78 Å and is unexceptional.[1] However, one C–O bond length (C1–O1) in the benzyl ether **1** is exceptionally short

compared even with the already short corresponding C–O bonds in aryl pseudosaccharyl ethers; the other C–O bond (O1–C2) is much longer than the corresponding long bonds in aryl pseudosaccharyl ethers.[1] Thus, bond length/bond energy relationships[10] indicate that, in compound **1**, one C–O bond is weak (approximately 327 kJ mol^{-1}) and the other exceptionally strong (approximately 537 kJ mol^{-1}), when compared with average normal values of 355 kJ mol^{-1} found for single C–O bonds. In other words, if catalytic hydrogenolysis depended only on relative bond strength changes in the central ether linkage on forming a pseudosaccharyl ether, then the benzyl pseudosaccharyl ether **1** would be expected to be much easier to hydrogenolyse than are aryl pseudosaccharyl ethers **2**. Instead, the benzyl compound **1** is totally inert to reaction conditions that lead to easy, rapid hydrogenolysis of its aryl counterparts [**2**, eqn. (1)].[3,11]

The C1–O1–C2 bond angle of 117.7(2)° in the benzyl ether **1** is close to the 120° required for sp² hybridization and is in the same small range as that observed for all aryl ethers.[1] The N1–C1–O1–C2 torsional angle is significantly very close to 0°, again as found generally for aryl pseudosaccharyl and aryl tetrazolyl ethers.[1] From the points of view of bond strengths, bond lengths and bond angles there appears to be every reason for the benzyl ether **1** to undergo the easiest of catalytic hydrogenolyses, in stark contrast to its actual inertness.

One reason for a lack of reactivity in these pseudosaccharyl and tetrazolyl systems appears to arise when a suitable nitrogen for binding to the catalyst surface (N*, Scheme 1) is not avail-
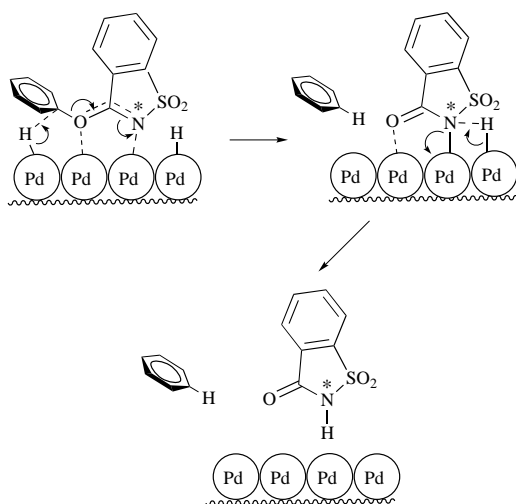
Scheme 1

able.[11] However, this nitrogen is present in the benzyl ether **1** and lack of this nitrogen cannot be the reason for lack of reactivity.

A major difference between the benzyl ether **1** and aryl pseudosaccharyl ethers **2** lies in the presence of a p-orbital on the aryl carbon, which is joined to the ether oxygen in **2**; this p-orbital is ideally placed for accepting an incoming hydrogen atom during hydrogenolysis (Scheme 1). In reaction (1), arenes **3** can be formed from ethers **2** by transfer of a hydrogen to the *ipso* position, with C–H bond formation as one of the ether C–O bonds begins to break (Scheme 1). However, for the benzyl analogue **1**, such transfer to a p-orbital is not possible because the carbon of the benzylic CH₂ joined to the ether oxygen of **1** is sp³ hybridized and has no suitable hydrogen-acceptor p-orbital.

Conclusion

The present X-ray evidence shows conclusively that, of three criteria for ready catalytic hydrogenolysis of pseudosaccharyl

Table 1 Selected geometric parameters (bond lengths/Å, angles/°) for ether **1**[a]

S1–C10	1.771(3)	C1–O1–C2	117.7(2)	O1–C2–C3–C4	−165.8(2)
S1–N1	1.656(2)	O1–C1–N1	124.8(2)	O1–C2–C3–C8	13.9(4)
O1–C1	1.315(2)	O1–C1–C9	116.3(2)	N1–C1–O1–C2	2.8(4)
O1–C2	1.454(3)	O1–C2–C3	107.7(2)	C1–O1–C2–C3	171.6(2)
N1–C1	1.288(3)	C2–C3–C4	117.9(2)	C2–O1–C1–C9	−177.5(2)
C1–C9	1.475(3)				
C2–C3	1.500(3)				
C9–C10	1.384(3)				

[a] Atom numbering is given on structure **1**. Complete data are available from CCDC.[13] For torsion angles, the sign is positive if, when looking from atom 2 to atom 3, a clockwise motion of atom 1 would superimpose it on atom 4.

or tetrazolyl ethers, the benzyl compound **1** easily meets two of them (favourable changes in bond energies on formation of the ether and the presence of a suitable nitrogen for binding to the catalyst surface). A third criterion, the need for a suitably placed receptor p-orbital, is not met and it appears that such a receptor p-orbital is of crucial importance for heterogeneous catalytic hydrogenolysis to occur, even though, in many transition metal catalysed reactions with benzyl compounds, this restriction does not appear to be important. This suggests that heterogeneous hydrogenolysis of pseudosaccharyl ethers requires more than simple oxidative addition of a C–O bond to the catalyst metal for reaction to occur. A mechanism that requires concurrent transfer of hydrogen to carbon as the C–O bond breaks appears to be applicable and would be in keeping with earlier kinetic data.[3,11]

Experimental

General procedures
Melting points were recorded on a Reichert microscopic apparatus and are uncorrected. Mass spectra were obtained on a VG 7070E mass spectrometer by electron ionization (EI), at 70 eV. IR spectra were recorded on a Perkin-Elmer 1720X FT-IR spectrometer as a KBr disk. ¹H NMR spectra were obtained on a Bruker WM 250 MHz FT spectrometer, using tetramethylsilane as internal standard. *J* Values are given in Hz. X-Ray analysis was carried out on a Rigaku AFC-6S four circle diffractometer. Toluene was dried and distilled before use. Other chemicals were used as purchased.

X-Ray structure analysis
Data collection and cell refinement used MSC/AFC Diffractometer Control Software (Molecular Structure Corporation, 1988). Data reduction was effected with TEXSAN Process. The programmes used for structure refinement were TEXSAN LS and material for publication was produced by TEXSAN FINISH.[12] Particular selected geometric details appear in Table 1. Crystal data and details of structure determination factors for compound **1** are given in Table 2. Atomic coordinates, bond lengths and angles, and thermal parameters have been deposited with the Cambridge Crystallographic Data Centre (CCDC).[13]

Preparation of 3-benzyloxy-1,2-benzisothiazole 1,1-dioxide 1
A mixture of 3-chloro-1,2-benzisothiazole 1,1-dioxide (pseudosaccharyl chloride, 1.29 g, 6.4 mmol), benzyl alcohol (0.6 ml, 5.8 mmol) and triethylamine (2 ml) in toluene (40 ml) was stirred under reflux for 45 min. Dichloromethane (200 ml) was added to the cooled reaction products and the whole was washed with dilute HCl (1 M, 3 × 200 ml), aqueous sodium hydrogen carbonate (3 × 200 ml) and brine (3 × 200 ml), before being dried (Na₂SO₄). After filtration from the drying agent, the filtrate was set aside to evaporate slowly at room temperature to form pale yellow crystals, which were filtered off by gentle suction, washed with cold toluene and then allowed to dry in the open

Table 2 Crystal data and details of data collection and refinement for compound 1[a]

Formula	$C_{14}H_{11}NO_3S$	$a/°$	90	μ/cm^{-1}	2.51
M_r	273.31	$\beta/°$	112.97(2)	Form	Prism
System	Monoclinic	$\gamma/°$	90	Size/mm³	$0.250 \times 0.200 \times 0.200$
Space group	$P2_1/n$	$V/Å^3$	1240.5(8)	Colour	Colourless
$a/Å$	13.437(4)	Z	4		
$b/Å$	6.848(4)	$D_c/Mg\ m^{-3}$	1.463		
$c/Å$	14.642(4)	$\theta/°$	18.17–22.51		
		Parameters[b]	18		

Data collection[c]			*Data refinement*[d]	
Measured reflections	2488		R	0.036
Independent reflections	2383		wR	0.044
Observed reflections $I > 3\sigma(I)$	1491		S	1.74
$\theta_{max}/°$	25.0		Reflections	1491
h	$0 \to 16$		Parameters	172
k	$0 \to 8$		$(\Delta/\sigma)_{max}$	0.001
l	$-17 \to 17$		$\Delta/\rho_{max}/e\ Å^{-3}$	0.26
Intensity decay (%)	-0.5		$\Delta/\rho_{min}/e\ Å^{-3}$	-0.33

[a] For all determinations, Mo-Kα radiation at $\lambda = 0.7107$ Å was used. The crystal density was not determined directly. The temperature of measurement was 153 K. [b] Parameters = the number of reflections used to determine the cell parameters. [c] Rigaku AFC-6S diffractometer; ω–2θ scans; no absorption correction; 3 standard reflections monitored every 150 reflections. [b] Refinement on F; H-atom positions were found from ΔF synthesis and included with $U_{iso}(H) = 1.2\,U$eq(C); $\omega = 4F_o^2/\sigma^2(F_o^2)$; no correction for extinction; atomic scattering factors from *International Tables for X-Ray Crystallography* (1974, vol. VI).

to give the desired product **1** (1.25 g, 72%), mp 128–129 °C (Found: C, 61.5; H, 4.1; N, 5.1. $C_{14}H_{11}NO_3S$ requires C, 61.5; H, 4.1; N, 5.1%); δ_H(CDCl$_3$) 5.59 (s, 2H), 7.46 (m, 5H), 7.78 (d of t, 2H, J 7.5), 7.70 (d, 1H, J 7.5), 7.89 (d, 1H, J 7.5); v_{max}/cm^{-1} 1617, 1456, 1416, 1323, 1175, 1157; m/z 273 (M$^+$).

Acknowledgements

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