Direct NMR Observation of Atropisomerism of a Bisphosphite Dibenzo[d,f][1,3,2]dioxaphosphepin Moiety

Gregory T. Whiteker,* Arnold M. Harrison and Anthony G. Abatjoglou

Union Carbide Corporation, South Charleston Technical Center, P.O. Box 8361, South Charleston, WV 25303-0361, USA

Rapid interconversion of two diastereoisomeric bisphosphite ligands by dibenzo[d,f][1,3,2]dioxaphosphepin epimerization has been observed by variable temperature ^{1}H NMR.

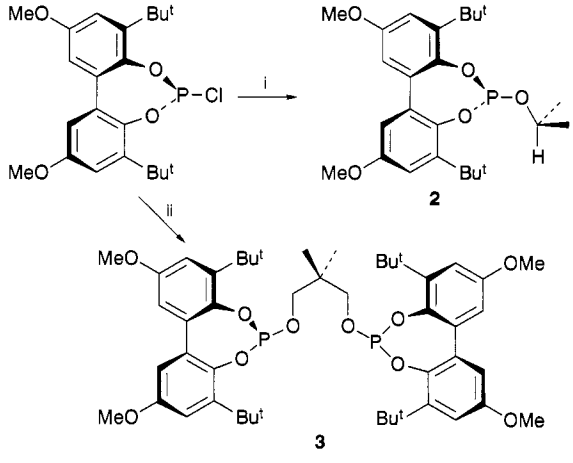
Despite the widespread use of chelating bisphosphine ligands in homogeneous catalysis,[1] applications of bisphosphites have only recently been developed.[2,3] In particular, bisphosphites containing the dibenzo[d,f][1,3,2]dioxaphosphepin moiety offer significant advantages over conventional phosphine ligands. For example, bisphosphite ligands discovered at Union Carbide exhibit exceptionally high regioselectivities in rhodium-catalysed hydroformylation of α-olefines.[3] These rhodium-bisphosphite catalysts, in addition, exhibit widespread tolerance for functional groups which further increases their synthetic utility.[4]

Asymmetric catalysts which contain optically-active bisphosphites of this general class have been reported by Pringle and Takaya.[5] As a consequence of the biaryl stereogenic element, the multiple dibenzo[d,f][1,3,2]dioxaphosphepin units increase the stereochemical possibilities for these bisphosphite ligands. For example, the enantiomerically-pure bisphosphite **1** reported by Takaya has three possible diastereoisomeric forms which differ in the absolute configuration of the biphenyl moieties. Both Takaya and Pringle have attributed the observation of a single ^{31}P NMR resonance for ligands such as **1** to the existence of a single diastereoisomer. Facile interconversion of bisphosphite diastereoisomers by biphenol epimerisation was proposed to be unlikely. This conclusion prompts us to communicate NMR studies which allow for the direct measurement of the barrier to atropisomerism of the dibenzo[d,f][1,3,2]dioxaphosphepin moiety in related bisphosphite ligands.

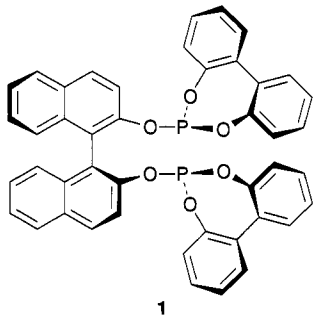
Our initial attempts to study atropisomeric behavior of the dibenzo[d,f][1,3,2]dioxaphosphepin moiety involved the monophosphite **2**.† Phosphites were prepared as depicted in Scheme 1. The *iso*-propyl methyl substituents in **2** are diastereotopic due to the presence of the biphenol stereogenic element. Rotation about the biphenyl bond would interconvert these diastereotopic methyl environments and exchange ligand enantiomers. The room temperature ^{1}H NMR spectrum of **2** exhibited one upfield doublet at δ 1.30 ($^3J_{HH}$ = 6.2 Hz) assigned to the *iso*-propyl methyl substituents. The ^{1}H NMR spectrum of the sample was unchanged when obtained at −90 °C. Similarly, the ^{13}C{^{1}H} spectrum of **2** displayed a single methyl resonance for the *iso*-propyl substituent at 25 °C. Although these observations are consistent with fast exchange (on the NMR time scale) of methyl environments by biaryl rotation, the possibility that the diastereotopic methyl groups give rise to isochronous resonances in both ^{1}H and ^{13}C NMR spectra could not be excluded.[6]

Interconversion of atropisomers was directly observed in the related bisphosphite **3** by variable temperature NMR. Bisphosphite **3** was chosen since the diastereoisomeric forms could be easily identified by NMR spectroscopy. Due to the symmetry of **3** the *neo*-pentyl bridge provides an ideal spectroscopic probe for diastereoisomer interchange by a mechanism involving biphenol epimerization. For **3**, only two diastereoisomeric forms are possible (Fig. 1). The *SS* (*RR*) diastereoisomer contains a C_2 axis of symmetry and exists as a D,L pair of enantiomers. The *RS* diastereoisomer is a *meso* compound which contains a mirror plane. The *SS* and *RS* diastereoisomers, therefore, differ in the number of inequivalent *neo*-pentyl methyl substituents. The *SS* diastereoisomer contains equivalent methyl groups as a result of C_2 symmetry. The *RS* diastereoisomer contains two inequivalent methyl substituents.

The ^{1}H NMR spectrum‡ of **3** at 25 °C contains resonances readily assigned to the tetra-substituted dibenzo[d,f][1,3,2]-dioxaphosphepin and the *neo*-pentyl bridge. A single *neo*-pentyl methyl resonance was observed at δ 0.81. In addition, the diastereoisotopic *neo*-pentyl CH_2 substituents gave rise to only one doublet at δ 3.61 ($^3J_{PH}$ = 6.2 Hz). Upon cooling to −90 °C, the ^{1}H NMR spectrum of **3** exhibited two sets of aromatic, methoxy and *tert*-butyl resonances in an approximately 1 : 1 ratio. Moreover, three broadened methyl resonances were



Scheme 1 *Reagents and conditions*: i, propan-2-ol + BuLi, toluene, reflux; ii, 2,2-dimethyl-propane-1,3-diol (0.5 equiv.), NEt_3, toluene, reflux



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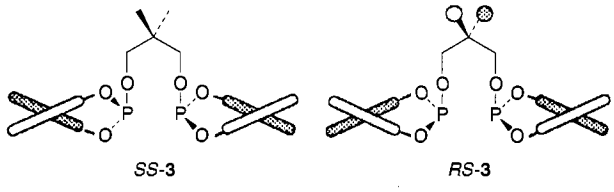

Fig. 1 Schematic representation of *SS*- and *RS*-diastereoisomers of bisphosphite **3**

observed near δ 0.7 in an approximate 1 : 1 : 2 ratio (Fig. 2). The resonances due to the *neo*-pentyl CH_2 substituents broadened at −90 °C and were not well-resolved from resonances due to -OMe and THF-[$^2H_8$]. Upon warming the solution, coalescence of the aromatic resonances was observed at −74 °C, and the room temperature spectrum was reproduced. The three upfield methyl resonances began to broaden above −90 °C and coalesced to a broad singlet at −70 °C. Notably, variable temperature $^{31}P\{^1H\}$ NMR spectra of **3** exhibited only one resonance between −100 and 25 °C and was insensitive to atropisomerism.

The observation of these three methyl resonances at low temperature is strong evidence for the presence of both *SS* and *RS* diastereoisomers of **3** at low temperature. The interconversion of these diastereomers can be accomplished only by biphenyl epimerization. These results demonstrate that facile atropisomerism of the dibenzo[d,f][1,3,2]dioxaphosphepin moiety in bisphosphite **3** occurs with $\Delta G^{\ddagger}$ −74 °C = 10 kcal mol^{-1} (based on the coalescence behavior of a pair of aromatic resonances, 1 cal = 4.184 J). Interconversion of diastereotopic forms of optically active bisphosphites of this type should be considered likely under catalytic conditions.

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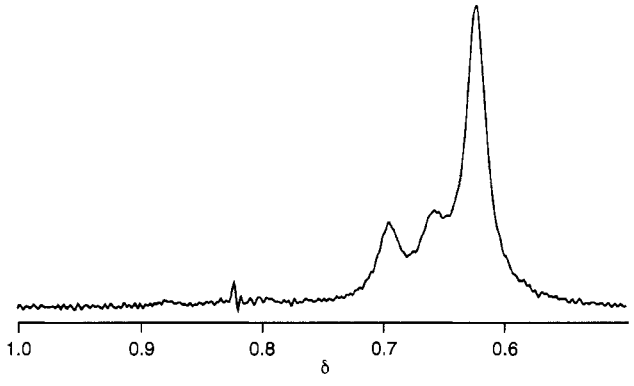

Fig. 2 Resolution enhanced *neo*-pentyl methyl region of ^1H NMR spectrum (−90 °C) of **3**

Footnotes

† *Spectroscopic data* for compound 2. ^1H NMR (300.519 MHz, acetone-[$^2H_6$]) δ 1.30 (d, *J* 6.2 Hz, 6 H, $CHMe_2$), 1.45 (s, 18 H, Bu^t), 3.81 (s, 6 H, OMe), 4.59 (d of septets, J_{PP} 8.1, J_{HH} 6.3 Hz, 1 H, $CHMe_2$), 6.77 (d, *J* = 3.0 Hz, 2 H, aromatic) and 6.96 (d, *J* 3.0 Hz, 2 H, aromatic). $^{13}C\{^1H\}$ NMR (75.477 MHz, acetone-[$^2H_6$]) δ 24.8 (d, J_{PC} 4.1 Hz, $POCHMe_2$), 31.3 (s, CMe_3), 35.7 (s, CMe_3), 55.6 (s, OMe), 70.2 (d, J_{PC} 14.7 Hz, $POCHMe_2$), 113.5 (s, 6, 6′-), 114.7 (s, 4, 4′-), 134.5 (s, 1, 1′-), 142.7 (s, 3, 3′-), 142.7 (d, J_{PC} 6.2 Hz, 2, 2′-) and 156.4 (s, 5, 5′-). $^{31}P\{^1H\}$ NMR (121.666 MHz, acetone-[$^2H_6$]) δ 146.42.

‡ *Spectroscopic data* for compound 3. ^1H NMR (300.519 MHz, 25 °C, THF-[$^2H_8$]) δ 0.81 (s, 6 H, *neo*-pentyl Me), 1.43 (s, 36 H, Bu^t), 3.61 (d, J_{PH} 6.2 Hz, 4 H, $POCH_2$), 3.78 (s, 12 H, OMe), 6.73 (d, *J* 3.0 Hz, 4 H, aromatic) and 6.95 (d, *J* 3.0 Hz, 4 H, aromatic). $^{13}C\{^1H\}$ NMR (75.477 MHz, 25 °C, THF-[$^2H_8$]) δ 21.8 (s, *neo*-pentyl Me), 31.3 (d, J_{PC} 3.0 Hz, CMe_3), 35.9 (s, CMe_3), 55.6 (s, OMe), 69.8 (s, CH_2O), 113.7 (s, 6,6′-), 114.9 (s, 4,4′-), 134.6 (d, J_{PC} 3.7 Hz, 1,1′-), 142.6 (s, 3,3′-), 142.9 (d, J_{PC} 5.9 Hz, 2,2′-) and 156.8 (s, 5,5′).

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