# Alumina Catalysed Inversion of Bridged Biphenyls

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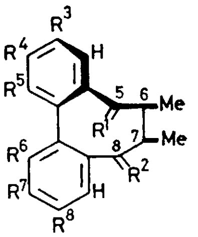
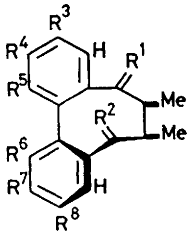
*Summary* Hindered bridged biphenyls which, in the bridging ring, contain a carbonyl group adjacent to one of the aromatic rings, are shown to undergo effectively rotational isomerization when adsorbed on alumina.

THE free energy of inversion about the biaryl bond of some biphenyls can be influenced to a certain extent by the medium in which the inversion occurs.[1] It has also been shown that the racemization of 1,1′-binaphthyl is enhanced by carbon black[2] and that the synthetic usefulness of photoracemization of bridged biphenyls is limited to hydrocarbons.[3] We report herein that adsorption on alumina is highly effective in decreasing the rotational barrier of some bridged biphenyls which are otherwise too hindered to be interconverted.

In the course of recent work on the synthesis of schizandrin-type lignans[4] we obtained pairs of diastereomers (**1**)—(**3**) in which the nonequivalence within each pair arises from restricted biaryl rotation in addition to the presence of chiral centres of given (6,7-*cis*-dimethyl) configuration in the bridging ring. In an attempt to measure the rotational barrier and to establish the relative stability of rotamers from their ratio at equilibrium it was found that the biaryl inversion occurs only at elevated temperatures (in diglyme or neat) with significant decomposition before equilibrium is attained. By contrast, adsorption of (**1a**, **b**)—(**3a**, **b**) on an alumina support[†] resulted in rotational isomerization under mild conditions in forward or reverse processes, affording quantitative equilibrium mixtures from each pure rotamer. Thus, the ketone (**1a**), m.p. 177 °C, which on heating (diglyme, 184 °C, 2 h) partly isomerized (31%) to the more stable (**1b**), m.p. 126 °C, afforded by adsorption on alumina the same ratio of isomers at 38 °C after 30 min. A similar effect was observed in (**4a**, **b**) in which the inversion barrier is increased by *ortho*-methyl substitution (Table). A rough estimate of $\Delta G^{\ddagger}$ values[‡] showed that the rotational barrier decreased by 12·5—15·5 kcal/mol in compounds (**1a**, **b**)—(**4a**, **b**) owing to adsorption on alumina. Silica (Merck, G) was found to be less effective.[§]



(a)



(b)

We found that the ketone group in the bridging ring is necessary for the alumina catalysis: in the less hindered system (**5a**, **b**), the rotation was unaffected by alumina, whereas the C-5 *cis*-methyl ethers derived from (**1a**) and (**1b**) were unaltered when heated (180 °C, 30 min) on alumina. Use of deuteriated alumina[5] for interconversions of (**1**)—(**3**) did not result in hydrogen exchange and therefore Brønsted acidity is not likely to be involved in the mechanism of inversion. Furthermore, these systems were very reluctant to undergo acid or base enolization.[4b,¶]

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[†] The compounds in $CH_2Cl_2$ solution were mixed with a 100-fold excess of alumina (neutral, Merck, activity I), the solvent was eliminated (flow of $N_2$), the solid mixture was kept under $N_2$ under the conditions shown, and the substrate was then separated by filtration ($CH_2Cl_2$).

[‡] The rate constants in diglyme and on alumina were determined from two kinetic data points by n.m.r. monitoring during equilibration. The accurate $\Delta G^{\ddagger}$ values will be included elsewhere.

[§] Observed decrease of $\Delta G^{\ddagger}$ on silica was 4—8 kcal/mol for the investigated compounds. Heating on carbon black[2] (BDH, Merck Darco-60, and Kodak Nuchar-C-190) or diatomaceous earth did not catalyse the inversion.

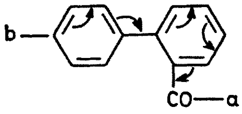
[¶] Unsaturation in the bridging ring of a biaryl system should increase the inversion barrier. See *e.g.*, M. Hall in 'Progress in Stereochemistry,' vol. 4, Butterworths, London, 1969, p. 1.

**Table.** Influence of the alumina surface on the inversion conditions.[a]

| | | Temp./°C | Time/min | Ratio (**a**) : (**b**) | Ratio (**a**) : (**b**) at equilibrium |
|---|---|---|---|---|---|
| (**1**) | $R^1 = O$; $R^2 = H_2$; $R^3$—$R^8$ = OMe[b] | 184[c] | 120 | 69 : 31 | 16 : 84 |
| | | 38[d] | 50 | 49 : 51 | |
| (**2**) | $R^1 = O$; $R^2 = H_2$; $R^3$, $R^4$ = $-OCH_2O-$; $R^5$—$R^8$ = OMe[b] | 187[c] | 120 | 85 : 15 | 24 : 76 |
| | | 40[d] | 55 | 41 : 59 | |
| (**3**) | $R^1$, $R^2 = O$; $R^3$, $R^4$ = $-OCH_2O-$; $R^5$—$R^8$ = OMe[b] | 163[c] | 210 | 82 : 18 | 50 : 50 |
| | | 23[d] | 20 | 74 : 26 | |
| (**4**) | $R^1 = O$; $R^2 = H_2$; $R^3$, $R^5$, $R^6$, $R^8$ = Me; $R^4$, $R^7$ = H[b] | 208[c] | 120 | 65 : 35 | 29 : 71 |
| | | 24[d] | 55 | 45 : 55 | |
| (**5**) | $R^1$ = $-OCH_2CH_2O-$; $R^2 = H_2$; $R^3$—$R^8$ = H[b] | 90[c] | 60 | 45 : 55 | 0 : 100 |
| | | 90[d] | 30 | 57 : 43 | |

[a] Data refer to the inversion of the minor (**a**) rotamer. [b] For the synthesis of (**1**)—(**3**) see ref. 4; the preparation of (**4**) and (**5**) will be reported elsewhere. The conformational structures of (**1**)—(**4**) are based on synthetic and spectral evidence: in rotamers (**a**) the C-5 ketone is not co-planar with the adjacent aromatic ring, whereas in (**b**) it attains coplanarity; in (**5a**, **b**) the conformations were not determined. [c] In diglyme, sealed tubes under argon. [d] On alumina.

The unprecedented extent by which $\Delta G^{\ddagger}$ decreases in a thermal biphenyl inversion can be rationalized by the intermediacy of a species (A) in which the biaryl ketone unit is bound to the Lewis (acid–base) pair site of the alumina surface.[6] Such a mechanism would imply the co-ordination of ketones with the acid sites of alumina[7] and the possibility of delocalization and disruption of a ring $\pi$-system[8] in the transition state.



(A)

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