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The Nonplanar Structure of 2,2′-Dilithio-1,1′-binaphthyl. An Experimental Estimate of the Lithium-Bridging Stabilization Energy for a Dilithiobiaryl

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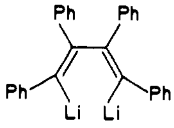
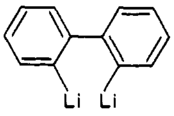
Abstract: Ab initio and semiempirical MO calculations by Schleyer and co-workers have predicted that 2,2′-dilithiobiphenyl is planar with each lithium bridging the 2 and 2′ positions to give a symmetrical structure with C_{2v} symmetry. Recently, this theoretical prediction has been confirmed by the crystal structure of the 2,2′-dilithiobiphenyl·2TMEDA complex. Our experiments establish that 2,2′-dilithio-1,1′-binaphthyl completely retains optical activity in dimethyl ether solution at temperatures from −131 °C to at least −45 °C. Our results place a lower limit on the free energy barrier for racemization of 2,2′-dilithio-1,1′-binaphthyl of >18.4 kcal and, together with Schleyer's results, set limits on the stabilization energy gained by symmetrical bridging of the two lithiums. This stabilization energy can be estimated as at least 2 kcal, but less than 5 to 10 kcal, which is significantly less than the 16.8 kcal predicted by MNDO calculations in the gas phase. The experimental results establish that dilithio derivatives of biaryls with modest barriers to internal rotation (e.g., 1,1′-binaphthyl) can have nonplanar structures and can be obtained in optically active form. This configurational stability is an important factor in the use of dilithiobiaryls as synthetic intermediates, and the existence of substantial rotational barriers provides a unique, new probe into the nature of the bonding in bridged metal–carbon systems.

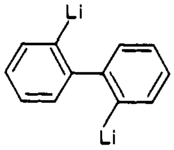
Recent work by Schleyer and co-workers has drawn attention to the structure of 1,4-dilithio butadiene (I) and the related system 2,2′-dilithiobiphenyl (II).[1-3] These structures have been studied by using semiempirical (MNDO) and ab initio molecular orbital calculations.[1,2] In addition, the selectivity in the reaction of *n*-BuLi and TMEDA with biphenyl in hexane has been examined[2] and more recently the crystal structure of II·2TMEDA has been determined.[3] The main theme which evolves from this work is that the dilithio derivatives of the 4π electron butadiene systems favor a structure in which the two Li atoms are symmetrically arranged above and below a planar π system, as indicated below for compound III. The variety of evidence provided by Schleyer and co-workers[1-3] as well as comparison of their results with the intermolecular aggregation (association) found for solutions of alkyl- and aryllithium compounds[4,5] indicates that this symmetrically double bridged structure is the predominant species both in solution and in the solid state.[5]



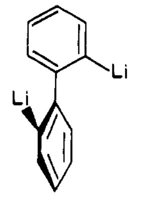
I



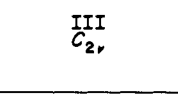
IIa
C_{2v}



IIb
C_{2h}



IIc
C_2



III
C_{2v}

Extension of these results to the structure of 2,2′-dilithio-1,1′-binaphthyl suggests the possibility of a coplanar arrangement of the two naphthalene ring systems, leading to a compound which would exhibit no optical activity.[6] This type of structure, however, would be destabilized to a significant extent by steric interactions (e.g., interference between the 8 and 8′ H atoms), and these steric interactions add an important constraint in regard to the existence of a coplanar structure for the ground state of 2,2′-dilithio-1,1′-binaphthyl. However, the stabilization noted by Schleyer's group for a symmetrically double-bridged structure may be a factor in transition-state stabilization and in lowering the barrier to rotation about the 1,1′ bond of binaphthyl.[7] Consequently, the existence and magnitude of a barrier to internal rotation about the 1,1′ bond of 2,2′-dilithio-1,1′-binaphthyl would be of considerable interest in view of Schleyer's results[1-3] on the dilithiobiphenyl systems.

In the course of preparing optically active 2,2′-disubstituted 1,1′-binaphthyl systems, we have generated 2,2′-dilithio-1,1′-binaphthyl at low temperatures in $(CH_3)_2O$.[8] The reaction of optically pure 2,2′-dihalo-1,1′-binaphthyls with alkyllithium

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(1) A. J. Kos and P. v. R. Schleyer, *J. Am. Chem. Soc.*, **102**, 7928 (1980).

(2) W. Nengebauer, A. J. Kos, and P. v. R. Schleyer, *J. Organomet. Chem.*, **228**, 107 (1982).

(3) U. Schubert, W. Nengebauer, and P. v. R. Schleyer, *J. Chem. Soc., Chem. Commun.*, 1184 (1982).

(4) See ref 2, ref 3, and B. J. Wakefield: B. J. Wakefield, "The Chemistry of Organolithium Compounds", Pergamon Press, Oxford, 1974, Chapter 1.

(5) For example, note that the two molecules of TMEDA in the crystal structure of II-2TMEDA can be thought of as playing the role of a coordinating solvent.

(6) Note that 1,1′-binaphthyl and its derivatives exhibit optical activity by virtue of the non-zero dihedral angle between the rings.

(7) The MNDO calculations cited in ref 2 indicate that the planar C_{2h} (IIb) and the planar C_{2v} (IIa) structures for dilithiobiphenyl are higher in energy than the twisted C_2 structure (IIc) by 22.1 and 41.9 kcal, respectively. The MNDO calculations also place the symmetrically bridged structure (III) below the C_2 structure by 16.8 kcal, and the X-ray diffraction analysis by Schubert, Nengebauer, and Schleyer (ref 3) confirms that III is the ground state of dilithiobiphenyl. Taking these results at face value suggests that the lowest minimum energy path for racemization of dilithiobinaphthyl proceeds through a transition state resembling III, rather than IIa or IIb, and implies that the barrier to racemization of 2,2′-dilithio-1,1′-binaphthyl is comparable to or less than the barrier to racemization of 1,1′-binaphthyl.

(8) (a) K. J. Brown, M. S. Berry, K. C. Waterman, D. Lingenfelter, and J. R. Murdoch, *J. Am. Chem. Soc.*, **106**, 4717 (1984); (b) K. J. Brown, M. S. Berry, and J. R. Murdoch, *J. Org. Chem.*, in press.

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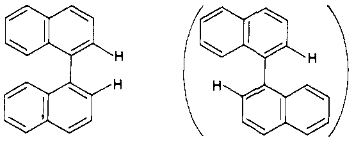
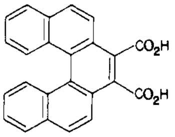
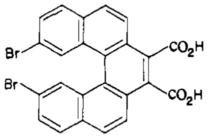
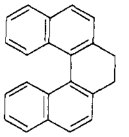
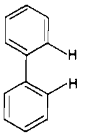
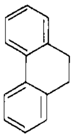
Table I

	structure	$\Delta G_{\mathrm{rac}}^{\ddagger}$,^{b} kcal ($T$, K)	$\Delta H_{\mathrm{rac}}^{\ddagger}$,^{b} kcal	$\Delta S_{\mathrm{rac}}^{\ddagger}$,^{b} eu	ref
A		23.3 (228) 23.8 (298)	21.7	−7.3	9
B		23.0 (298)			10
C		25.2 (228) 24.7 (294)	26.8	+7.0	10
D		29.9 (228)^{a} 29.9 (298)^{a}	30.0	+0.3	10, 11
E		2-3 (298)			13
F		4 (298)			12

[a] 27.9 kcal after correction for the torsional strain associated with the ethane bridge; barrier for ethane = 3 kcal/mol,[12] but only two eclipsed hydrogen atoms are present in D; compare with the difference between the barriers of E and F. [b] Thermodynamic quantities associated with the kinetics of racemization.

reagents to form the corresponding dilithio intermediates, followed by quenching of these intermediates with various electrophiles (PhCHO, Ph_2PCl), has been studied. In particular, it has been demonstrated that no detectable loss of optical activity occurs at any stage of this two-step reaction. The 2,2'-dilithio-1,1'-binaphthyl intermediate gives no evidence of racemization in dimethyl ether at temperatures between −131 and −45 °C over a period of 30 min.[8] On the basis of a limit of detection for the presence of a second enantiomer of 2%,[8] we calculate a maximum rate constant for racemization of 10^{-5} s^{-1} at 225 K. This value leads to a minimum free energy of activation of 18.4 kcal/mol. Since no racemization has actually been detected experimentally, 18.4 kcal/mol is a strictly *lower* limit, and the actual barrier could be substantially higher.

This result allows us to place an upper limit on the stabilization associated with bridging of the two lithiums between the 2 and 2' positions. Specifically, we can state that the stabilization gained by bridging of the two lithiums is not large enough to compensate for the destabilizing steric repulsion associated with bridging the two naphthalene rings into planarity, and thus a substantial barrier to racemization is present for 2,2'-dilithio-1,1'-binaphthyl under our experimental conditions.

The free energy associated with bringing the twisted binaphthyl system into planarity can be estimated by examining the barriers to racemization (Table I) in the related hydrocarbons where interactions involving lithium(s) are obviously absent and where the planar structures (and presumably the steric interactions) are similar to the corresponding analogues of structure III.

Schleyer's results[3] show that the planar structure III is the ground state of 2,2'-dilithiobiphenyl and demonstrate that lithium bridging is sufficiently potent to overcome the free energy barrier to internal rotation in biphenyl (2 to 3 kcal in several different solvents[13]). Our experimental results on the configurational stability of 2,2'-dilithio-1,1'-binaphthyl demonstrate that lithium bridging is *not* strong enough to force planarity in the 1,1'-binaphthyl system. The free energy barrier to internal rotation for binaphthyl is 23.3 kcal (Table I), and the corresponding value for 2,2'-dilithio-1,1'-binaphthyl is >18.4 kcal. Consequently, it could be estimated that the stabilization associated with symmetrical bridging of the two lithiums between the 2,2' positions is somewhere between 2 and 5 kcals. Although the upper limit of 5 kcal might be pushed to as high as 10 kcal by choosing other biaryls (B to D, Table I, footnote *a*) as models for the steric effect, the range of 2–10 kcal is substantially less than the 16.8 kcal obtained from MNDO calculations on 2,2'-dilithiobiphenyl.[2] However, it should be emphasized that our experimental measurements pertain to free energy changes (vs. electronic energy[2]) on dilithiobinaphthyl (vs. dilithiobiphenyl[2,3]) in dimethyl ether (vs. the gas[2] or solid[3] phase) at 228 K (vs. 0 K[2] or 258 K[3]), do not include any effects associated with a powerful chelating agent[3] (TMEDA), and may involve aggregation in solution.

Nonetheless, the experimental results establish that the symmetrical lithium bridging observed in dilithiobiphenyl·2TMEDA[3]

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(9) A. K. Colter and L. M. Clemens, *J. Phys. Chem.*, **68**, 651 (1964).

(10) R. Munday and I. O. Sutherland, *J. Chem. Soc. B*, **80** (1968), and references therein.

(11) D. M. Hall and M. M. Harris, *J. Chem. Soc.*, 490 (1960).

(12) The barrier to inversion in 9,10-dihydrophenanthrene has been estimated at 3–4 kcal/mol. K. Mislow, M. A. W. Glass, H. B. Hopps, E. Simon, and G. H. Wahl, Jr., *J. Am. Chem. Soc.*, **86**, 1710 (1964).

(13) J. P. Lowe, *Prog. Phys. Org. Chem.*, **6**, 1 (1970); R. J. Kurland and W. B. Wise, *J. Am. Chem. Soc.*, **86**, 1877 (1964). The E_a ranges from 0.44 to 1.1 kcal/mol in several solvents. Assuming $\Delta S^* = -7.3$ eu (same as binaphthyl) one calculates $\Delta G^* = 2.0$–2.7 kcal/mol.

is not necessarily a significant factor in the ground-state structures[14] of other dilithiobiaryls in which the parent hydrocarbon has an appreciable barrier to internal rotation. One important, practical consequence is that many dilithiobiaryls will be obtainable in optically active form and can serve as novel intermediates in the synthesis of chiral, bidentate ligands.[8]

The existence of a substantial rotational barrier for 2,2′-dilithio-1,1′-binaphthyl also has significant mechanistic and theoretical applications, since the relative energies of the symmetrical bridged structure (i.e., the transition state for internal rotation) and the unsymmetrical ground-state structure can be studied by simple kinetic techniques as a function of solvent, coordinating ligands, metal, and biaryl. Such measurements would be of interest in elucidating the relative importance of electrostatic[15] and covalent interactions[1-3,16] to the bonding, structure, and reactivity of bridged metal–carbon compounds.

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Registry No. 2,2′-Dilithio-1,1′-binaphthyl, 92218-53-6.

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[14] The fact that dilithiobinaphthyl can be obtained in optically active form rules out the symmetrically bridged planar structure III as the ground state. The actual ground-state structure is unknown at present and could be similar to the "classical" structure IIc, where each lithium atom replaces one of the hydrogens at the 2,2′ positions, and the aryl rings are rotated out of planarity to some degree (e.g., ~90°). An alternative is a distorted bridge structure where each lithium spans the 2,2′ positions in unsymmetrical fashion, which may also allow twisting of the naphthalene rings with respect to each other. Other structures can also be imagined. The calculations by Nengebauer, Kos, and Schleyer[2] estimate the bridging stabilization energy (16.8 kcal) from the energy difference between the twisted, classical structure IIc (C_2 symmetry) and III (C_{2v} symmetry). Even though the MNDO calculations place the C_2 structure of dilithiobiphenyl at an energy minimum, it is possible that the ground state of dilithiobinaphthyl may not correspond exactly to the classical, twisted structure (C_2 symmetry) and may be shifted toward an unsymmetrically bridged structure, where the naphthalene rings are twisted out of coplanarity. This possibility may alter the present estimates of the stabilization to be gained by symmetrical bridging of the two lithiums to give structure III, since the MNDO estimates and the experimental estimates may refer to different ground-state structures. However, since the steric interactions associated with rotation around the 1,1′ bond are substantially higher for dilithiobinaphthyl than for dilithiobiphenyl, and since the lithium/carbon and lithium/lithium interactions are similar (or possibly reduced in magnitude for dilithiobinaphthyl), it is likely that the energy-minimized C_2 structure for dilithiobinaphthyl exhibits a comparable (or higher) degree of asymmetry in lithium–carbon bond distances and a comparable (or higher) degree of twisting between the aryl rings compared to the analogous structure of dilithiobiphenyl.

[15] J. Klein, D. Kost, W. G. Schriver, and A. Streitweiser, Jr., *Proc. Natl. Acad. Sci. U.S.A.*, **79**, 3922 (1982).

[16] (a) W. E. Rhine, J. H. Davis, and G. Stucky, *J. Organomet. Chem.*, **134**, 139 (1977). (b) H. Dietrich, *Acta Crystallogr.*, **16**, 681 (1963). (c) E. Weiss and G. Hencken, *J. Organomet. Chem.*, *2*, 197 (1964).

A General Approach to the Quantitation of Synthetic Efficiency in Solid-Phase Peptide Synthesis as a Function of Chain Length[⊥]

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Abstract: A model peptide, Leu-Ala-Gly-Val, was synthesized by solid-phase methods at increasing distances from a 1% cross-linked polystyrene resin support. The efficiency of the synthesis was evaluated by quantitatively measuring the amounts of the deletion peptides Leu-Ala-Val and Leu-Gly-Val that were produced during the synthesis of the tetrapeptide. By inserting an oxymethylphenylacetyl group between this test peptide and the peptide chains used to provide spacers from the support, it was possible to selectively evaluate the quality of the tetrapeptide without interference by the spacer. Low and constant levels of deletion peptides were found. No significant effect of distance from the support or of peptide loading on the synthetic efficiency could be detected up to a chain length of 60 residues and a peptide-to-resin weight ratio of 4:1.

The essential feature of solid-phase peptide synthesis[1] is the covalent attachment of the growing peptide chain to an insoluble solid support during the course of the chain assembly. This has obvious advantages which include rapid purification of the product peptide at each step by simple filtration and washing and low handling losses. However, since the early days of the solid-phase method it has frequently been assumed that a price is paid for this speed and simplicity in the form of a negative influence of the insoluble resin support on reaction kinetics, leading to incomplete reaction at each step, with the consequent accumulation of resin-bound peptide byproducts and generation of a complex product mixture after cleavage from the resin.[2-4] In particular, there has been a general feeling that there must be resin-imposed steric limitations to stepwise solid-phase peptide synthesis.[2] Some workers feel that reactions will be less efficient close to the polymer backbone,[3] while others feel that there will be significant declines in yields as the peptide is elongated, due to temporary steric occlusion of peptide chains within the polymer network.[4]

To resolve such conflicting views, we have determined experimentally the efficiency of solid-phase synthesis as a function of peptide chain length. Previous attempts to address this question have either been indirect or poorly defined and controlled. We report here a general experimental approach that allows direct

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[⊥] This paper is dedicated to the memory of our friend and colleague, Dr. Balz Gisin.

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(2) Bayer, E.; Eckstein, H.; Hägele, K.; König, W. A.; Brüning, W.; Hagenmaier, H.; Parr, W. *J. Am. Chem. Soc.* **1970**, *92*, 1735–1738.

(3) Wünsch, E. *Angew. Chem., Int. Ed. Engl.* **1971**, *10*, 786.

(4) Fankhauser, P.; Brenner, M. In "The Chemistry of Polypeptides"; Katsoyannis, P. G., Ed.; Plenum Press: New York, 1973; pp 389–411.

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