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# ROTATION AND INVERSION BARRIERS IN 2-LITHIO-2-PHENYL-1,3-DITHIANES *

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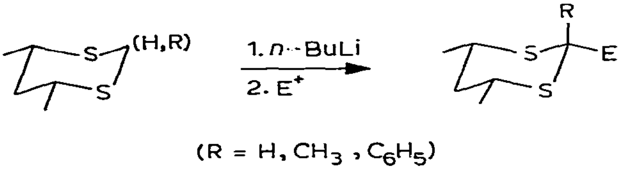
## Summary

The barriers to phenyl rotation in 2-lithio-2-phenyl-*cis*-4,6-dimethyl-, 2-lithio-2-phenyl-4,4,6-trimethyl- and 2-lithio-2-phenyl-*trans*-4,6-dimethyl-1,3-dithiane are compared in tetrahydrofuran (THF) and hexamethylphosphortriamide (HMPA). In the first two cases, the barriers in THF are lower than those in HMPA, presumably because the lithio compound exists as a tight ion pair in THF but as a solvent-separated ion pair (with more delocalization of charge into the phenyl ring) in HMPA. However, in the *trans*-4,6-dimethyl compound the barriers are the same in the two solvents and nearly equal to the barriers for ring reversal. It is concluded that in this compound the rate-determining step for phenyl rotation may actually be ring reversal, at least in solvent HMPA.

## Introduction

Reactions of lithium derivatives of anancomeric (conformationally biased) 1,3-dithianes with electrophilic reagents such as DCl, methyl iodide, formaldehyde, etc. have been shown to proceed with high stereoselectivity to give virtually exclusively equatorial substitution products [1] (Scheme 1).

SCHEME 1



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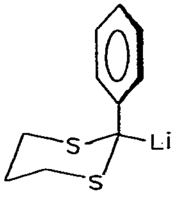
* Dedicated to Professor Herbert C. Brown on the occasion of his 66th birthday.

In a recent publication [2] we have adduced evidence that this high degree of stereoselectivity is intrinsic to the 1,3-dithianyl-2-carbanion (as predicted [3] by quantum-mechanical calculations) rather than being a result of ion pairing between lithium and the carbanion in some particular geometry, as suggested originally [1]. Specifically, it was shown by $^1$H and $^{13}$C NMR spectroscopy that both 2-phenyl-2-lithio- and 2-phenyl-2-potassio-1,3-dithianes exist as two species, one in THF, distinct for Li and K and presumably a tight ion pair, and one in HMPA, identical for Li and K, presumably a solvent-separated ion pair, and that the two species react with very nearly the same high stereoselectivity in reactions with electrophiles.

In efforts to shed additional light on the nature of the species involved we now report results of $^7$Li and $^{31}$P NMR studies as well as additional studies involving $^{13}$C NMR. The results of these experiments lend further support to the conclusion that 2-lithio-2-phenyl-1,3-dithiane (I) exists as two different types of ion pair and shed new light on the mechanisms of inversion and phenyl rotation in these species.



(I)

## Results

Previously [2], the two types of ion pairs corresponding to I had been manifested by differences in chemical shifts of the aromatic protons and ($^{13}$C) carbon nuclei. For example, conversion of 2-phenyl-1,3-dithiane to the lithio derivative I in THF moves the shift of the *para*-carbon in the aromatic ring 15.5 ppm upfield; the corresponding shift for the *para*-hydrogen is 1.09 ppm. Addition of HMPA to the THF solution produces an additional shift of 0.79 ppm for the proton in question and 9.0 ppm for the $^{13}$C nucleus. When the NMR spectrum of the aforementioned proton in I in THF was observed upon addition of small increments of HMPA, the curve shown in Fig. 1 (2 *M* solution of I) was obtained; from this curve and one obtained in more dilute solution it was concluded that 2—3 mol of HMPA added to a solution of one mol of I in THF sufficed to produce the maximum upfield shift of the (presumed) solvent-separated ion.

We now report a similar titration of I in THF with HMPA, but with observation of the $^7$Li spectrum. As seen in Fig. 1, the pattern of chemical shift change of the $^7$Li resonance as a function of the amount of HMPA added is virtually the same as that observed for the *para* hydrogen even though the shift is in the opposite direction; the $^7$Li resonance moves a total of 0.30 ppm downfield. This observation supports the hypothesis that a solvent-separated ion pair is formed upon addition of HMPA: removal of the anion from the vicinity of the Li$^+$ will presumably enhance the effective charge on the lithium nucleus (with solvation

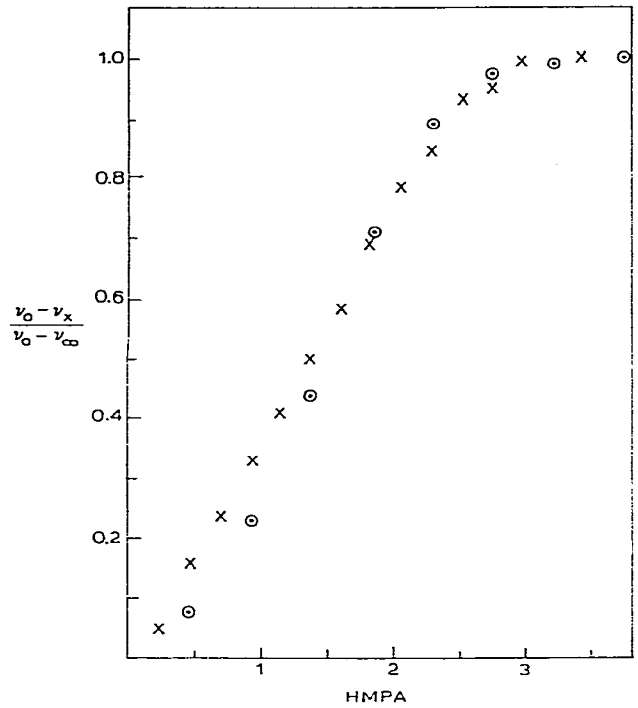


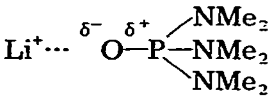
Fig. 1. Proton shifts (crosses) and lithium shifts (circled points) of 2-phenyl-1,3-dithianyllithium in THF upon addition of HMPA. Abscissa: Mol ratio [HMPA]/[RLi]. Ordinate: Incremental shift expressed as a fraction of the maximum shift increment attained at high [HMPA]/RLi] ratio.

The shift in THF ($\nu_0$) is 6.18 ppm for the $^1$H and —1.12 ppm for the $^7$Li nucleus; the corresponding maximum attained shifts ($\nu_\infty$) are 5.39 and —0.82 ppm.

of the lithium ion producing a less than compensating change in the opposite direction) and therefore leads to a downfield shift.

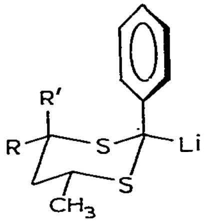
It might be expected that some of the positive charge on lithium is distributed over the HMPA molecules in the solvent sphere of the ion (cf. Scheme 2 [4]) with a resultant increased positive charge on phosphorus. Indeed, examination of the $^{31}$P signal of the HMPA in a 1/1 (mol ratio) solution of I and HMPA in THF/hexane disclosed the expected downfield shift of the phosphorus nucleus (0.93 ppm relative to a solution of HMPA of equal concentration in THF/hexane in the absence of I).

SCHEME 2



$$Li^+\cdots \overset{\delta^-}{O}-\overset{\delta^+}{P}(NMe_2)_3$$

In support of the existence of two discrete ions (presumably a contact ion pair and a solvent-separated ion pair, in rapid equilibrium with each other) we had previously reported [2] low temperature $^{13}$C NMR studies of lithio derivatives II and III in various solvents. Because of the unsymmetrical substitution pattern of the ring, both II and III show discrete signals for the *ortho*-carbons (and III also for the *meta*-carbons) of the aromatic ring. Clearly the phenyl ring is perpendicular to the symmetry plane of the dithiane chair (as observed in similar compounds [5] including 2-phenyl-2-methyl-1,3-dithiane [6]) and rotation around the C(2)—C(ipso) bond becomes slow on the NMR time scale at low temperature.



(II) R = R' = H
(III) R = R' = $CH_3$
(IV) R = H, R' = $CH_3$

By observing coalescence upon increasing the temperature we had established the barriers for phenyl rotation in the lithiated species summarized in Table 1. In the previous work [2] it was noted that the barrier was higher in HMPA-containing solvents than in pure THF and this was logically explained in terms of the solvent-separated pair postulated to exist in HMPA: greater delocalization of negative charge into the aromatic ring in that ion would lead to more double bond character of the C(2)—C(ipso) bond and thus to a higher barrier. (In support of the hypothesis, it was also observed that C(2) was at lower field, as behooves a $sp^2$ hybridized carbon, in HMPA than in THF.) It was also noted that the barrier was higher in III than in II suggesting contribution of a steric factor (interaction of axial phenyl with *syn*-axial methyl) to the barrier in III. This, in turn, was interpreted to mean that the solvent-separated ion pair could not be entirely planar at the benzylic carbon, C(2), since a flattened ion should experience little *syn*-axial interaction of the phenyl ring with the axial methyl group at C(4).

Compounds II and III are conformationally homogeneous: the equatorial methyl groups at C(4) and C(6) prevent ring reversal. We thought it would be of interest to examine compound IV in which ring reversal (presumably attended by inversion at C(2)) is possible as well as phenyl rotation.

Compound IV indeed displayed the evidence for phenyl rotation being slowed on the NMR time scale at low temperature. (The full experimental data for this compound as well as II and III are given in Table 2.) In addition, the rate of ring

TABLE 1

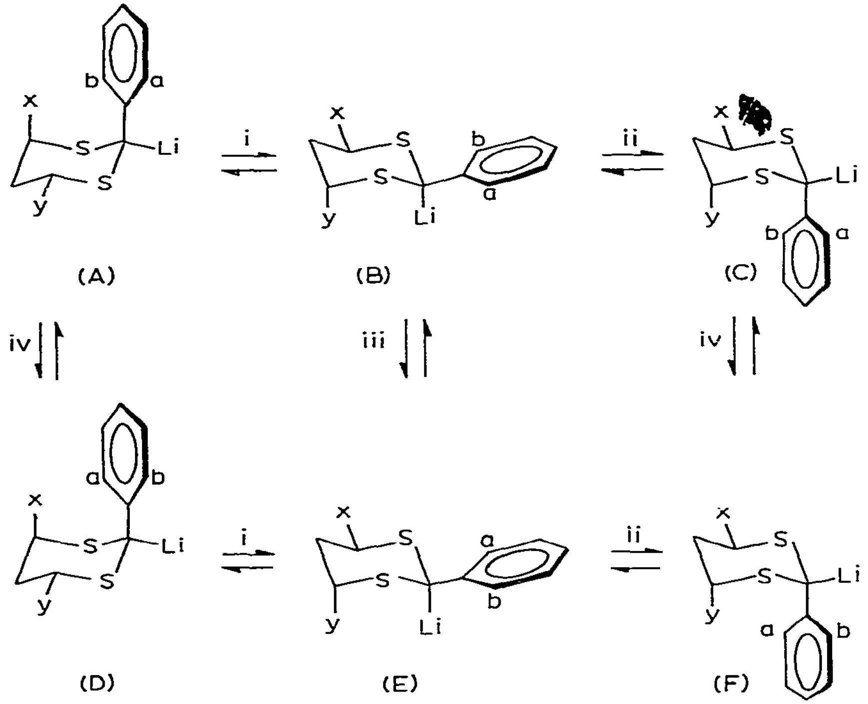
BARRIERS TO PHENYL ROTATION (kcal/mol) [e]

| Compound | Solvent | | | | |
|---|---|---|---|---|---|
| | THF | 1/1 [a] | 2/1 [a] | 3/1 [a] | Ref. |
| II | *b* | *b* | 11.5 | 13.3 | 2 |
| III | 13.0 | 13.6 | 14.4 | 16.4 | 2 |
| IV | 12.6 | *c* | *d* | 12.8 | *c* |

[a] THF/HMPA mixture; the ratio indicates the number of mol of HMPA to the number of mol of RLi.
[b] Because of degeneracy of the *ortho*-carbon signals, the barrier could not be determined. [c] This work.
[d] Not determined. A referee has criticized the determination of activation energies from coalescence measurements at a single temperature. We estimate the error from this source as no greater than ±0.3 kcal/mol; an error of this magnitude would not in the least affect the conclusions reached here.

reversal could be measured by observing the coalescence of the ring methyl groups as a function of temperature. The data for phenyl rotation are summarized in Table 1; the barriers to ring reversal were 13.3 and 12.7 kcal/mol in THF and THF/HMPA, respectively. The picture for the complete process is shown in Scheme 3.

SCHEME 3



We note immediately (Table 1) that, unlike in the case of II and III, the barriers to phenyl rotation in IV are independent of solvent (THF or HMPA). Moreover, at least in HMPA, the barriers to rotation and to ring reversal are identical. (In THF the difference between the two barriers is on the edge of being significant.)

## Discussion

Because of the structural similarity of III and IV (save for one sterically and electronically innocuous equatorial methyl group at C(4)) the difference in phenyl rotation behavior of the two species seems, at first sight, surprising. The difference between the two species is that IV can ring invert and III cannot; thus it seems plausible that ring inversion accounts for the difference in behavior. The "anomaly" in IV arises in solvent HMPA (in which the barrier is almost 4 kcal/mol lower than that in III) and we note that in HMPA the barriers to phenyl rotation and to ring reversal are effectively identical (12.7 vs. 12.8 kcal/mol). It would thus appear that in HMPA ring reversal and phenyl rotation are coupled, with the barrier to ring reversal being the rate-determining one for both processes.

Examination of Scheme 3 suggests a plausible explanation. Direct rotation of the phenyl ring in A to give D would involve a barrier of 16.4 kcal/mol (cf. III) which is higher than observed. However, A may ring-reverse to B which can then undergo inversion at the lithiated carbanion to give C. C is structurally identical to A but both the methyl groups (x, y) and the *ortho*-carbons (a, b) have switched environments. In this switch, no phenyl rotation was actually required. It is only necessary to postulate that in the processes i and ii, the highest barrier to be traversed is 12.7 kcal/mol above A. Pure ring reversal ($A \rightleftharpoons F$) or pure rotation ($A \rightleftharpoons D$) must involve either the higher-energy purely rotational step iv ($A \rightleftharpoons D$ by direct interconversion or $A \rightleftharpoons B \rightleftharpoons C \rightleftharpoons F$) or rotation of the equatorial phenyl group ($A \rightleftharpoons B \rightleftharpoons E \rightleftharpoons D$ or $A \rightleftharpoons B \rightleftharpoons E \rightleftharpoons F$, respectively) i.e. step iii. Step iii probably has a high rate constant but the overall interconversion of A and D by this step may still be slow because of the low stationary state concentration of B and E.

Closer examination of step i discloses that it involves a ring reversal whose activation energy may be somewhat lower than the typical inversion barrier in 1,3-dithiane (9.4 kcal/mol, [7]) because of the *syn*-axial $C_6H_5/CH_3$ strain energy in A which disappears partially in the transition state; on the other hand, the process is thermodynamically strongly uphill because an equatorial lithio derivative in the dithiane series is converted to an axial one (estimated [1,3] energy 6—9 kcal/mol). If the transition state energy is somewhat in excess of the energy of B, a value of 12.7 kcal/mol is entirely reasonable. Process ii is an anion inversion. Values in the literature for inversions of alkyllithium compounds are of the order of 15 kcal/mol [8,9]. These values relate to tight ion pairs, however, and the value for a solvent separated ion pair may well be somewhat lower (cf. the difference [10] between dialkylmagnesium, 20 kcal/mol, and alkylmagnesium halide, 11 kcal/mol), so again a value of 12.7 kcal/mol is not unreasonable. We thus come to the conclusion that the simultaneous reversal, rotation path $A \rightleftharpoons B \rightleftharpoons C$ is energetically reasonable.

The situation is probably different in THF. Here the direct rotation path iv ($A \rightleftharpoons D$) is expected to have an activation energy of only 13.0 kcal/mol, by analogy with compound III. The actual barrier to rotation of 12.6 kcal/mol is in agreement; the small difference, if real, may reflect the lesser buttressing and greater deformability of IV compared to III making the *syn*-axial interaction at the rotation barrier slightly less severe in IV. In contrast, the ring reversal barrier of 13.3 kcal/mol is palpably larger which may indicate that in the process $A \rightleftharpoons B \rightleftharpoons C$ the carbanion inversion step ii now becomes rate-determining and we have already surmised that this step is slower in THF than in HMPA. The overall barrier of 13.6 kcal represents the difference between A (or C) and the top of the barrier; that this value is not the same as that in 2-methylbutyllithium (15 kcal/mol [8]) is perhaps not surprising since there are a number of major differences between the two ions.

The above discussion is based on the assumption that the 2-lithio-1,3-dithianes are monomeric in both HMPA and THF. The evidence on this point is not conclusive, but the invariability of the proton and carbon NMR spectra of I in THF to addition of tetramethylethylenediamine [2] suggests that the species is monomeric.

The exploitation of dithianyllithium species in the determination of carbanion inversion barriers may have significance going beyond that of the present investigation.

TABLE 2

$^{13}C$ NMR AND COALESCENCE DATA FROM II, III and IV IN THF AND THF/HMPA

| | | II (THF)[a] | II (HMPA)[b] | III (THF)[c] | III (HMPA)[d] | IV (THF)[e] | IV (HMPA)[f] |
|---|---|---|---|---|---|---|---|
| *Chemical shift (ppm)*[g] | C(2) | 43.4 | 48.6 | 40.7 | 45.9 | 39.0 | 42.9 |
| | C(4) | 32.8 | 37.0 | 42.9 | 42.3 | 39.4 | 39.0 |
| | C(5) | 39.2 | 40.2 | 53.4 | 54.7 | 45.4 | 46.4 |
| | C(6) | 28.2 | 32.6 | 29.5 | 32.6 | 25.9 | 29.7 |
| | C(7) | 22.3 | 22.0 | 22.2 | 22.0 | 22.5 | 22.1 |
| | C(8) | — | — | 31.6 | 31.0 | — | — |
| | C(9) | — | — | 28.3 | 27.3 | 21.9 | 20.3 |
| | *ipso* | 157.2 | 154.2 | 157.6 | 155.3 | 159.0 | 156.4 |
| | *ortho* | 122.2 | 116.5 | 121.1 | 116.5 | 121.0 | 116.0 |
| | *meta* | 127.3 | 126.8 | 127.0 | 126.7 | 126.9 | 126.7 |
| | *para* | 113.2 | 103.2 | 112.2 | 103.3 | 112.0 | 102.7 |
| *C(2)—phenyl rotation* | | | | | | | |
| max $\Delta\nu$ (*ortho*)(Hz) | | 0 | 7.6 | 58.5 | 21.9 | 63.0 | 20.6 |
| Coalescence temp. (°C) | | ? | −21 | −5 | 44 | −13 | −20 |
| $\Delta G$ (kcal/mol) | | ? | 13.3 | 13.0 | 16.4 | 12.6 | 12.8 |
| *Ring inversion* | | | | | | | |
| max $\Delta\nu$ (C(7)—C(9)) (Hz) | | — | — | — | — | 17.0 | 46.9 |
| Coalescence temp. (°C) | | — | — | — | — | −13 | −13 |
| $\Delta G$ (kcal/mol) | | — | — | — | — | 13.3 | 12.7 |

[a] 1.4 *M* solution of II in THF. [b] 0.8 *M* solution of II in THF containing 3 molar equivalents of HMPA.
[c] 1.0 *M* solution of III in THF. [d] 0.7 *M* solution of III in THF containing 3 molar equivalents of HMPA.
[e] 1.0 *M* solution of IV in THF. [f] 0.7 *M* solution of IV in THF containing 3 molar equivalents of HMPA.
[g] Downfield from tetramethylsilane.

## Experimental

Compound IV was previously prepared [11] by Dr. V.S. Rao. The preparation [1] and spectral examination [2] of the lithio derivatives has been described earlier. $^7$Li and $^{31}$P spectra were recorded on a Varian XL-100 pulsed Fourier transform nuclear magnetic resonance spectrometer. The $^7$Li spectra were recorded at 38.87 MHz and are reported upfield from external LiCl, 1 *M* in $D_2O$ (lock). The $^{31}$P spectra were recorded at 40.50 MHz and are reported downfield from external $H_3PO_4$, 0.5 *M* in $D_2O$ (lock). The titration and low-temperature experiments have been previously described [2]; the results of the barrier measurements are recorded in Table 2.

## Acknowledgement

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