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Solution Ion Pair Structure of 2-Lithio-1,3-dithianes in THF and THF-HMPA

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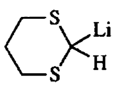
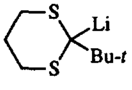
Abstract: An NMR study of 2-lithio-1,3-dithiane and 2-triorganosilyl-, 2-*tert*-butyl- and 2-phenyl-2-lithiodithianes reveals that all are contact ion pair species in THF and all become separated ions with excess HMPA. The dithianes differ greatly in their ease of ion separation, with the parent lithiodithiane the most difficult.

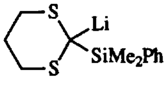
Of the numerous acyl anion equivalents in the literature (metalated thioacetals,[1a, 2a] vinyl ethers,[1b] O-protected cycnohydrins,[1c] and others[1d]), the 2-lithio-1,3-dithianes, developed by Corey and Seebach,[2a] are probably the best known. The chemistry has been extensively reviewed.[2b] Their importance has resulted in theoretical[4] and physical studies in the solid state,[2c, 2d] in solution[3c, 2e, 2f, 5-9] and the gas phase.[10] The properties of dithianes relevant to solution ion pair behavior of the dithianes **1-Li** to **5-Li** in THF and THF-HMPA (hexamethylphosphorictriamide) are summarized below.



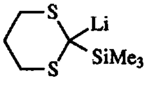
1-Li



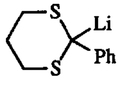
2-Li



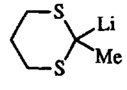
3-Li



4-Li



5-Li

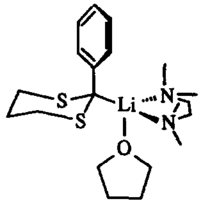


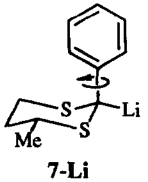
6-Li

Acidity. The kinetic acidity,[5] solution pK_a values in cyclohexylamine,[7a] THF,[7a, 9] and DMSO[8] of various dithianes, as well as the gas phase proton affinity[10] of dithiane anion have been reported. The pKa of dithiane in DMSO is 39, in THF 36.5. Alkyl dithianes are slightly less acidic, with pK_a(THF) = 38.2 for **6-H**. 2-Phenyldithiane is more acidic than dithiane itself in both DMSO and THF.

	1-H	**6-H**	**5-H**
Kinetic (*t*-BuOK/*t*-BuOH) k_{rel}	214	0.39	-
Thermodynamic (THF) pK_a	36.5	38.2	30.5
Thermodynamic (DMSO) pK_a	(39)	-	30.7

Crystal Structures. X-ray crystal structures of two 2-lithiodithianes have been determined: 2-methyl-2-lithiodithiane·TMEDA, a sulfur bridged dimer,[2d] and 2-phenyl-2-lithiodithiane·TMEDA·THF (TMEDA = N,N,N'N'-tetramethylethylenediamine), a contact monomer,[2c] in which the Li has three different ligands: 5^-, TMEDA and THF.





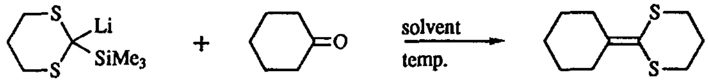
7-Li

Solution Structures. Low-temperature (–100 °C) ^{13}C NMR spectra of 2-(^{6}Li)lithio-2-^{13}C-dithiane, as well as the 2-methyl analog (**6-Li**) in THF,[2e] showed a 1:1:1 triplet (^{2}J ^{6}Li-^{13}C = 10.1 Hz) for C-2, so that both **1-Li** and **6-Li** are either monomeric (one Li per C-2) or sulfur-bridged dimers (as is the case for crystalline **6-Li**·TMEDA[2d]). It was not possible to observe similar ^{13}C-^{6}Li coupling for **5-Li** with ^{13}C labelled C-2 at –130 °C in THF. The ^{13}C chemical shifts of **1-Li**, **5-Li** and **6-Li** have been interpreted in terms of pyramidal carbanions with relatively high charge localization.[10] Cryoscopic measurements indicate that **6-Li** is largely monomeric in THF.[2f]

One of the remarkable features of lithio dithianes is the large equatorial preference for the lithium substituent, sufficient to place even a *tert*-butyl at C-2 >99.7% axial.[6b] This preference is possibly a consequence of the strong stereoelectronic interaction of the C-Li orbital with antiperiplanar C-S bonds and perhaps the avoidance of n_S-n_C repulsions.

Ion pair status in solution has been studied for **5-Li**.[6a] Addition of HMPA to a THF solution of **5-Li** causes the ^{1}H aromatic signals to move upfield until they reach a plateau at 3 equiv of HMPA. This phenomenon was interpreted in terms of the conversion of **5-Li** contact ion pair (CIP) in THF to **5**$^{-}$//Li^{+} separated ion pair (SIP) in THF-HMPA. In a similar study of **7-Li**, addition of 2 molar equiv of HMPA causes the phenyl ortho protons to become non-equivalent due to restricted rotation around the C-Ph bond. Apparently formation of a separated ion which can delocalize more charge into the ring slows the rotation of the phenyl group. The energy barriers increase as HMPA is added, and the amount of separated ion increases.

2-Trimethylsilyl-2-lithiodithiane (**4-Li**) has been used for the formation of ketene thioacetals,[2g, 12] but no solution properties are known. The phenyldimethylsilyl analog **3-Li** has not been reported.



4-Li 62%

The HMPA Titration Technique for Determining Ion Pair Structure. We have reported that Li-P coupling can be observed in low-temperature ^{31}P, ^{7}Li and ^{6}Li NMR spectra of HMPA-complexed organolithium reagents[3] (also discovered independently by Snaith[13a]). Under these conditions, individual solvated species having one to four HMPA molecules attached to lithium can be detected and quantified, and the CIP/SIP transition reliably identified.[14] As a result, solvation properties of lithium reagents long recognized as crucial in understanding reactivity, but for which experimental techniques were lacking or difficult, can be reliably determined. The procedure involves low-temperature (<-100 °C) examination of the progression of individual lithium-HMPA complexes by ^{31}P, ^{7}Li, and/or ^{6}Li NMR spectroscopy (as well as other nuclei where appropriate) as small increments of HMPA are added. In many cases, the stoichiometry of the changes and characteristic chemical shifts and $^{2}J_{Li\text{-}P}$ coupling constants allow determination of aggregation states and the point at which (or whether) deaggregation occurs. Ion pair separation can always be detected if it occurs. The systems studied have included a number of organolithium reagents, including α-lithiosulfides and selenides,[3c, 3e, 3f] lithium ate complexes,[3a-d] lithium halides,[3b, 3d, 13a] lithium amides,[15, 16a] lithium chalcogenides[3c, 3d] and lithium phenoxides.[13b,16b]

Perhaps the most significant information provided by the HMPA titration technique is the CIP-SIP status of the lithium reagents and the ease or difficulty of ion pair separation.[3d] The signature for a CIP can be seen in several aspects of the lithium and phosphorus NMR spectra. First, the ^{7}Li line width of the contact ion pair at low temperature will usually be broad (>2 or 3 Hz) in THF. Although a broad ^{7}Li line does not uniquely define a CIP, the broad signal is indicative of either the presence of multiple species in slow dynamic exchange or fast quadrupolar relaxation due to an asymmetric environment at ^{7}Li. In either case, the ion is not a single SIP species. Second, since the lithium and phosphorus signals of SIP Lih$_n^+$ (we use "h" as an abbreviation for HMPA) have been shown to be remarkably consistent among SIP systems, the point in the HMPA titration at which the conversion of CIP to SIP occurs can be determined.

The transition of a contact to a separated ion is characterized by a progression of solvated species which differs from systems which are CIP or SIP throughout. For lithium reagents which remain CIP's even with excess HMPA, the appearance of *at most* a doubly HMPA-solvated structure ($RLih_2$) is detected before free HMPA is observed in solution. Contact ions exhibit ^7Li chemical shifts which are often quite distinct from those of separated ions.

For lithium reagents which are already SIP's in THF, an orderly progression of mono, bis, tris and tetrakis HMPA coordinated lithium species can be observed, with a characteristic 20/60/20 ratio of $R^-//Lih_0^+$, $R^-//Lih_1^+$ and $R^-//Lih_2^+$ at one equiv of HMPA, almost pure $R^-//Lih_3^+$ at 3 equiv of HMPA, and significant amounts of free HMPA, $R^-//Lih_3^+$, and $R^-//Lih_4^+$ at 4 equiv of HMPA. In contrast, when a lithium reagent undergoes a CIP to SIP transition, one of the HMPA solvates is absent or present in small amounts, as illustrated for the lithiodithianes discussed below.

For the systems studied, discrete NMR signals for various HMPA solvates and ion pairs can be seen at temperatures as high as -90 °C, although only below about -110 °C can the coupling that allows identification of ions be resolved. It is likely that the energy barriers that allow individual detection of these species arise not from the inherent barriers to the interconversion of CIP's and SIP's, but from the attendant solvation and desolvation of HMPA molecules. Correlation of chemical reactivity of organolithium reagents with the information obtained from spectroscopic experiments must take both the temperature difference as well as the Curtin-Hammett principle into account.

Results

2-Phenyldimethylsilyl-2-lithiodithiane (3-Li). We begin our consideration of the solution structures of lithiodithianes with a study of **3-Li**. This lithium reagent is probably monomeric in THF at −132 °C since the C-2 resonance (^{13}C NMR) showed coupling to only a single ^6Li or ^7Li.[17] The HMPA titration (Fig. 1) is easy to interpret. Addition of small increments of HMPA produced a new species which showed an unusually upfield shift in the ^{31}P NMR with well-

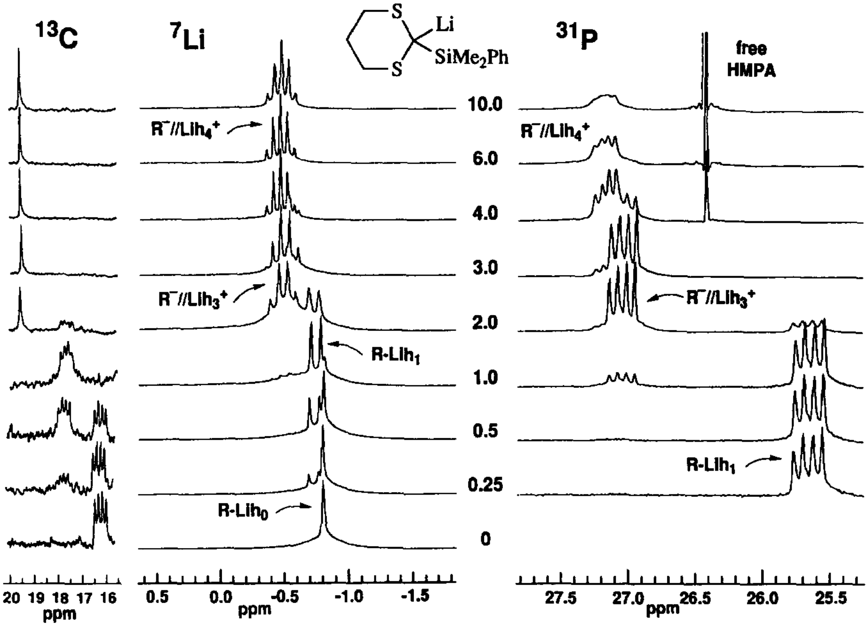


Figure 1. ^{13}C, ^7Li and ^{31}P NMR spectra of **3-Li** with increasing amounts of HMPA in 95:5 THF/hexane at -133 °C. All spectra (Gaussian multiplied) are plotted on the same frequency scale.

resolved ^{31}P-^{7}Li coupling, a doublet in the ^{7}Li NMR spectrum, and detectable ^{7}Li-^{13}C coupling in the ^{13}C NMR spectrum. This is therefore a CIP with one HMPA coordinated to lithium. A dimeric species should behave differently: 0.5 equiv of HMPA should produce (3-Li)$_2$h$_1$; 1 equiv, a second species (3-Li)$_2$h$_2$, as seen for (MeSLi)$_2$.[3d] Further addition of HMPA produces *without any other detectable intermediate species* the characteristic ^{7}Li and ^{31}P signals of SIP 3^-//Lih$_3^+$ and finally 3^-//Lih$_4^+$. The identification of these species as separated ions is supported by the ^{13}C signal of C-2 which shows Li-C coupling for 3-Li and 3-Lih$_1$ but a narrow line for 3^-//Lih$_3^+$ and 3^-//Lih$_4^+$. Apparently, 3-Lih$_2$ is thermodynamically unstable and disproportionates to 3^-//Lih$_3^+$ and 3-Lih$_1$. A similar disproportionation was seen above for 5-Li (for which the THF CIP and bis HMPA SIP were present in larger amounts than the mono HMPA CIP) and is generally seen whenever a CIP to SIP transition occurs (e.g., LiBr,[3d] MeSLi,[3d] R$_3$SiPhSCHLi[3e,3f]).

Variable Temperature Study. A variable temperature experiment of 3-Li (Fig. 2) gives some insight into the exchange processes that occur between the SIP 3^-//Lih$_3^+$ and the CIP 3-Lih$_1$. At −131 °C the ^{13}C-^{7}Li coupling (13.8 Hz) in the ^{13}C NMR spectrum is well resolved, but at −120 °C the two ion pairs begin to exchange anions. The C-2 signals broaden, and eventually the peaks coalesce just below −100 °C. In contrast to these spectra, the ^{7}Li and ^{31}P spectra clearly exhibit ^{7}Li-^{31}P coupling (^2J = 10.9 Hz for the CIP) at −110 °C and still show splitting at −100 °C. Therefore, two different processes are responsible for the ^{13}C and ^{7}Li/^{31}P broadening: one in which the separated carbanion exchanges with the contact carbanion (Eq. 1, this exchanges the SIP carbon signals with the CIP carbon signals), and a second in which HMPA exchanges between separated and contact lithium (Eq. 2, this exchanges the phosphorus CIP and SIP signals, and averages the Li-P coupling). The spectra suggest that the former process occurs at a faster rate than the latter since the carbon signals are the first to coalesce (the frequency separation are comparable, 154 Hz for ^{13}C, 189 Hz for ^{31}P). We estimate from line-shape simulations that exchange of carbanions is 15-20 times as fast as exchange of HMPA (e.g., loss of Li-P coupling of 3-Lih$_1$).

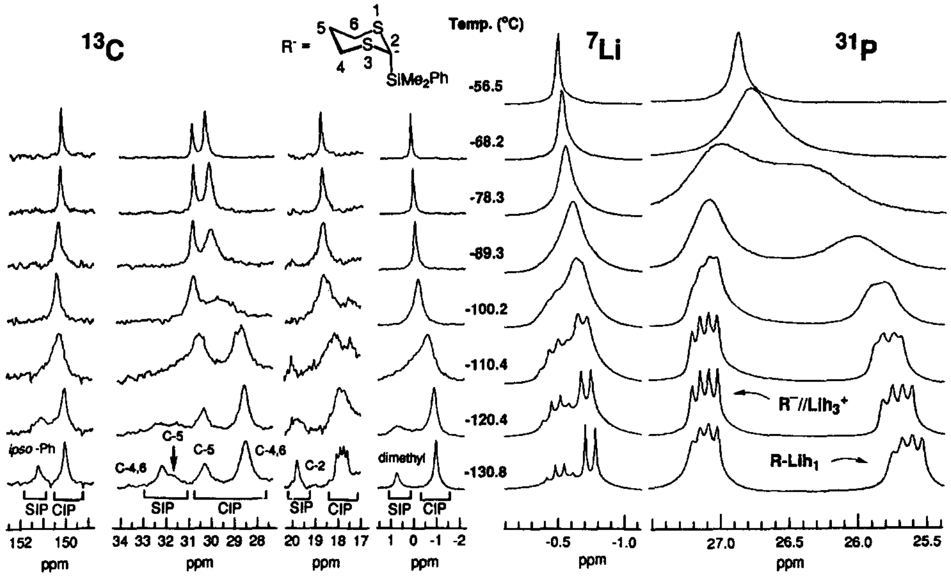


Figure 2. ^{13}C, ^{7}Li and ^{31}P variable temperature NMR spectra of 3-Li (M_0 = 0.16 M) at 1.5 equiv of HMPA in 95:5 THF/hexane. The ^{7}Li and ^{31}P spectra have not been Gaussian multiplied.

$$3^{-}//\mathrm{Lih_3}^{+} \quad + \quad 3^{*}\text{-}\mathrm{Lih_1} \quad \rightleftharpoons \quad 3^{*-}//\mathrm{Lih_3}^{+} \quad + \quad 3\text{-}\mathrm{Lih_1} \qquad \text{(Eq. 1)}$$

$$3^{-}//\mathrm{Lih_3}^{+} \quad + \quad 3\text{-}\mathrm{Lih_1}^{*} \quad \rightleftharpoons \quad 3^{-}//\mathrm{Lih^{*}h_2}^{+} \quad + \quad 3\text{-}\mathrm{Lih_1} \qquad \text{(Eq. 2)}$$

2-Lithiodithiane (1-Li). At the low-temperature limit of THF (≈-128 °C) the signals of **1-Li** were not sufficiently resolved to allow secure identification of all species. Thus the HMPA titration we report in Fig. 3 was carried out in 3:2 THF/Me_2O, rather than in THF as for **3-Li** and **5-Li**, and both ^7Li and ^6Li spectra at natural abundance were measured. At 0 equiv of HMPA, broad ^7Li ($\nu_{1/2}$ > 15 Hz) and sharp ^6Li ($\nu_{1/2}$ = 0.2 Hz) singlets were observed which is consistent with a contact ion. There was no indication of $J_{Li\text{-}H}$ coupling in the ^6Li NMR spectrum. The first HMPA-coordinated species **1-Lih$_1$** (doublet in ^7Li and ^6Li NMR) was also contact, as is indicated most clearly by the ^{31}P NMR signal (27.9 ppm). This signal shows the characteristic sharp triplet due to coupling with the 7.4% ^6Li superimposed on the T_1-broadened, ^7Li coupled signal.[18] The 1:1:1 triplet is not exactly centered on the partially collapsed 1:1:1:1 quartet because of a ^6Li-^7Li isotope shift of the ^{31}P signal.

At 2 equiv of HMPA a second CIP was formed, **1-Lih$_2$**, with triplets in the Li NMR spectra and a similar T_1-broadened signal in the ^{31}P NMR spectrum (27.0 ppm).[18] At this point, small amounts of the separated ion pairs $1^{-}//\mathrm{Lih_3}^{+}$ and $1^{-}//\mathrm{Lih_4}^{+}$ can also be detected, whose concentrations increased slowly as the titration progressed. However, even at 10 equiv of HMPA, **1-Li** is not fully separated: there is still a significant concentration of the CIP **1-Lih$_2$**. The strength of C-Li coordination in **1-Li** is also indicated by the much earlier appearance of free HMPA (at <1 equiv of HMPA), in comparison with **3-Li** and **5-Li** (≈3.5 equiv).

The aggregation state of **1-Li** in THF is not known with certainty. Dimers can sometimes (but not always) have complex HMPA titrations (e.g., MeSLi[3d]). There is no indication in the HMPA titration of any dimeric species.

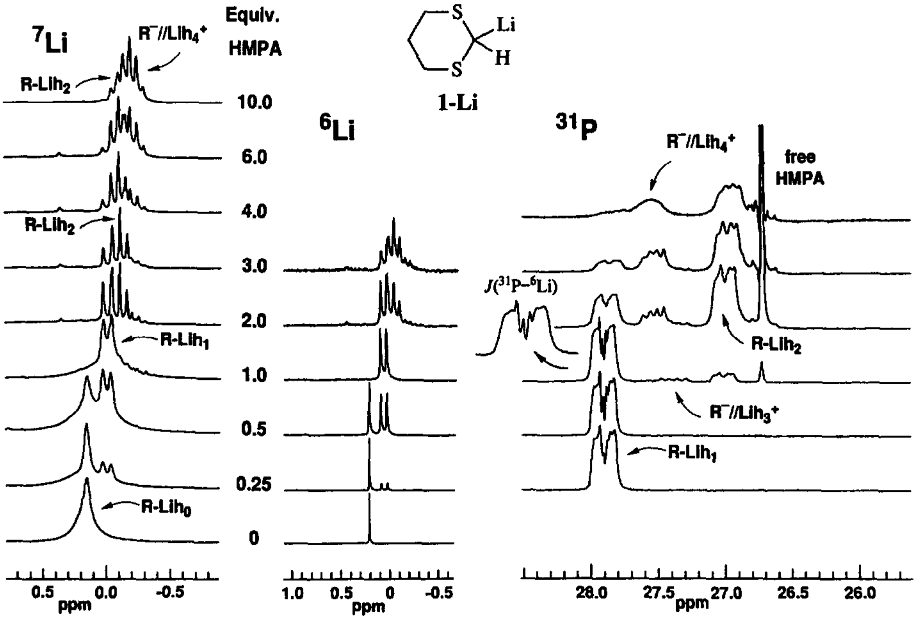


Figure 3. ^7Li, ^6Li and ^{31}P NMR spectra of **1-Li** with increasing amounts of HMPA in 3:2 THF/Me_2O at -135 °C.

2-*tert*-Butyl-2-lithiodithiane (2-Li). We selected **2-Li** as an example of a tertiary alkyldithiane. The interpretation of the HMPA titration, presented in Fig. 4, is unambiguous. The THF species is contact and monomeric, as is shown by the 1:1:1:1 quartet for C-2 in the ^{13}C NMR spectrum ($J_{C\text{-}Li}$ = 18.0 Hz). Both the ^{7}Li and ^{31}P NMR spectra show T_1 broadening effects,[18] as was also found for **1-Li**. The mono HMPA-complexed species (doublet in ^{7}Li NMR at -0.4 ppm) is also contact ($J_{C\text{-}Li}$ = 18.4 Hz). The couplings observed for **2-Li** are smaller than those found for **1-Li** (25.6 Hz) and **6-Li** (9.9 Hz for ^{6}Li, corresponding to 26.1 Hz for ^{7}Li).[2e] No obvious bis HMPA complexed signal (triplet) is observed in the Li NMR spectra; a weak signal in the ^{31}P NMR spectra at 24.5 ppm may be due to **2-Lih$_2$**. Past 1 equiv of HMPA, ion separation occurs, and free HMPA is observed. In contrast to the behavior of **1-Li**, **2-Li** resists coordination of more than trace amounts of a second HMPA to the contact ion.

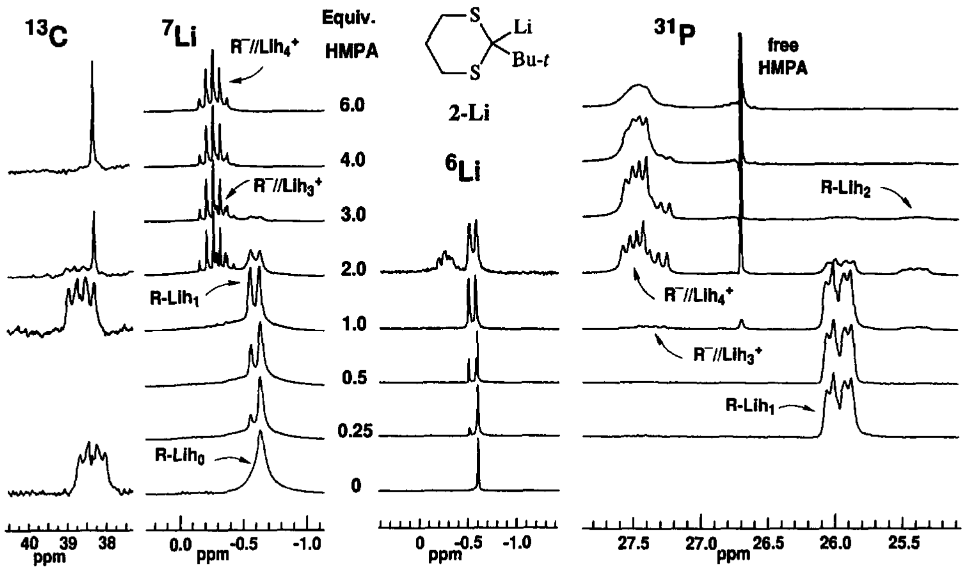


Figure 4. ^{7}Li and ^{31}P NMR spectra of **2-Li** with increasing amounts of HMPA in 3:2 THF/Me_2O at -135 °C.

2-Phenyl-2-lithiodithiane (5-Li). The interaction of **5-Li** with HMPA has been reported previously.[6a] The HMPA titration, as observed by low-temperature ^{7}Li and ^{31}P NMR in THF solution, is presented in Fig. 5. The ^{7}Li NMR spectrum at 0 equiv of HMPA showed a relatively broad singlet ($\nu_{1/2}$ = 7.4 Hz) which is consistent with a contact ion in THF. Upon addition of 0.25 equiv of HMPA, the ^{7}Li NMR spectrum does not show much detail, but the ^{31}P NMR spectrum shows two new species. We have assigned the upfield ^{31}P species is to **7-Lih$_1$** (contact lithium with one HMPA molecule) and the downfield ^{31}P signal (27.1 ppm) to $5^-//Lih_2^+$ (separated lithium with two HMPA molecules). The corresponding lithium signals are superimposed. Between the two ^{31}P NMR signals is a single peak which has the same ^{31}P chemical shift as $5^-//Lih_3^+$ seen later in the titration. The observation of at least three species at 0.25 and 0.5 equiv in the ^{31}P NMR spectrum (a significant departure from systems that are truly solvent-separated in THF) confirms that **5-Li** is contact in THF. By 2 equiv of HMPA the ion pair is completely separated, and the rest of the titration follows systems that are separated in THF.[3d]

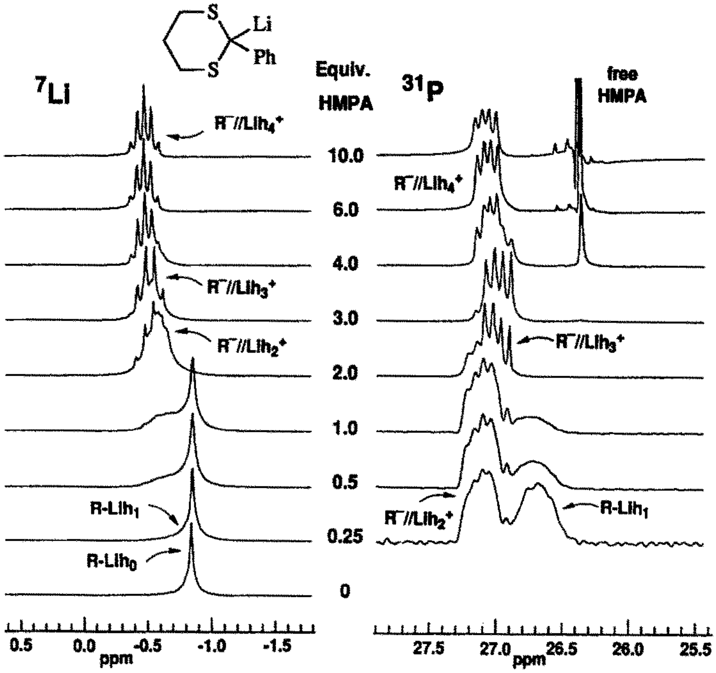


Figure 5. ^{7}Li and ^{31}P NMR spectra of **5-Li** (M_0 = 0.16 M) with increasing amounts of HMPA in 95:5 THF/hexane at -115 to -119 °C.

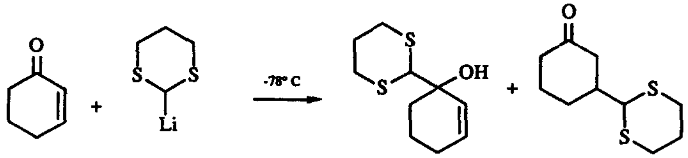
Discussion

Ion Separation. All of the dithianes studied undergo substantial or complete ion separation when excess HMPA is present. In each case the point in the titration at which ion separation occurs is indicated by an intermediate coordination state that is either absent or is present only in minor amounts: h_1 for **5-Li**, h_2 for **3-Li**, h_2 and h_3 for **2-Li**, h_3 for **1-Li**. The relative ease of ion separation is clearly defined by "skipped-over" coordination numbers and more or less follows expectations based on the basicity of the carbanions.

A significant exception to the correlation between basicity and ease of ion separation is the carbanion **2**$^-$ which separates slightly more easily than does **1**$^-$, even though it is more basic.[20] The origins of this effect are likely to be complex: the tertiary carbanion may have better charge delocalization, some relief of strain may accompany lithium decoordination and the attendant possible planarization,[3e] and there is likely to be some steric inhibition of solvation of lithium in the contact ion. Steric hindrance to solvation is the best explanation for the unusual sequence of ion pairs in **2-Li**, which shows only a mono HMPA CIP before ion separation occurs to form predominantly a tetrakis HMPA SIP. Lithio dithiane itself (**1-Li**) also forms a tetrakis HMPA SIP on ion separation, but the precursor is a bis HMPA contact ion. Although the silyl-substituted dithianes **3-Li** and **4-Li** also show only a mono HMPA contact ion, they undergo ion pair separation to form both tris and tetrakis HMPA species, and free HMPA does not appear until later in the titration.

We can confirm Abatjoglou, Eliel and Kuyper's observation[6a] that **5-Li** undergoes easy ion separation in THF-HMPA and that the carbanion is a poor ligand for Li$^+$. This is reasonable considering that C-2 is somewhat hindered and that **5**$^-$ has effective charge delocalization (as indicated by a 15 ppm upfield shift of the *para* carbon[11]). These results also provide a reasonable explanation for why Seebach et al.[2e] could not observe ^{6}Li-^{13}C coupling even at −130 °C.

Effect of HMPA on 1,2- vs 1,4-Addition to Enones. Brown and Yamaichi[21] studied the addition of **1-Li** to cyclopentenone, cyclohexenone and cycloheptenone. In each case, there was nearly complete reversal of regiochemistry from 1,2-addition in THF to 1,4-addition when 2 equiv of HMPA was present. The 1,4-adduct was kinetically formed since the lithium alkoxide from the 1,2-addition did not rearrange to the 1,4-adduct at room temperature for 24 h. The silyl-substituted dithiane **4-Li** behaves similarly: it undergoes 1,2-addition to α,β-unsaturated aldehydes and ketones in THF, but with the addition of 1 to 2 equiv of HMPA conjugate addition to cyclic α,β-unsaturated ketones is promoted. These observations have since been generalized with many types of α-thio and α-seleno substituted lithium reagents.[22, 23] Similar effects have been observed with the HMPA mimic, DMPU.[2h] There are occasional exceptions where HMPA favors 1,2- over 1,4-addition.[23b]



THF	>99/<1
THF, 1 equiv HMPA	12/88
THF, 2 equiv HMPA	5/95

The proposal has been made[24] that contact ions favor 1,2-addition and separated ions 1,4-addition. One rationale for this proposal is that coordination between the lithium of a CIP and the carbonyl group of an endocyclic enone can lead to the 1,2-product but not the 1,4-product without charge separation. On the other hand, the charge is already separated in the SIP, so the thermodynamically favored 1,4 addition product could be favored. Cohen, Abraham and Myers[24a] have provided some experimental evidence in favor of this proposal by the observation that lower temperatures, which favor the conversion of CIP's to SIP's, also increase the fraction of 1,4-addition. The role of HMPA in these reactions would then be to provide higher concentrations of SIP's. There are, however, other effects of HMPA that may be important. For example, the Lewis acid character of Li^+ may essentially disappear in $R^-//Li(HMPA)_4$ SIP's.[25]

The HMPA titration technique allows the quantitative assessment of CIP to SIP ratios, and thus a possible test of the role of SIP's in controlling 1,2- vs 1,4-addition. The Curtin-Hammett principle states that direct information about the role of CIP's and SIP's (reactive intermediates which are in equilibrium with each other) in these reactions can only be obtained if the rate of their interconversion is slower than the rate of their reaction with substrate.

The HMPA titration of **4-Li**, which is virtually identical to **3-Li** (Fig. 1), shows that **4-Li** is contact in THF but is mostly separated at 2.0 equiv of HMPA. This is consistent with (but does not require) a direct role of CIP/SIP in controlling 1,2- vs 1,4-addition. It should be noted, however, that the spectroscopic and reactivity studies were performed at different temperatures (-120 vs -78° C), so the correlation should be viewed as strictly qualitative. Additional product studies with intermediate amounts of HMPA would be required to establish a direct correlation.

2-Lithiodithiane (**1-Li**) provides a different picture. Here also the product ratio changes dramatically when two equiv of HMPA are added. However, the spectroscopic studies (Fig. 3) clearly show that dithiane is only slightly ion-separated at this point. At the higher temperature (-78 °C) of the chemical experiment there would be even less SIP present.[26] Thus we conclude that *either* the Curtin-Hammett limitation applies (i.e., the ion pairs interconvert faster than they react) or the 1,2- to 1,4-addition ratios are determined by other effects of HMPA than the formation of SIP's.

Experimental Section

General. THF and ether were freshly distilled from sodium benzophenone ketyl before use. Dimethyl ether was condensed into a graduated test tube, dried with BuLi, and distilled into the NMR tube. Hexamethylphosphoric triamide (HMPA) was obtained from Aldrich, distilled from CaH_2 at reduced pressure and stored under N_2 over molecular sieves. Glassware was dried overnight in a 110 °C oven. Common lithium reagents were titrated with propanol (or isopropanol) in THF using 1,10-phenanthroline as indicator.

Precautions. HMPA has long been recognized to have low to moderate acute toxicity in mammals.[27a] The American Conference of Governmental Industrial Hygienists have classified HMPA under "Industrial Substances Suspect of Carcinogenic Potential for Man".[27b] Adequate precautions must be taken to avoid all forms of exposure to HMPA.

Starting materials. 1,3-Dithiane and BuLi were obtained from Aldrich. The 2-substituted 1,3-dithianes were prepared by literature procedures.[2a, 2g]

NMR Spectroscopy. ^1H nuclear magnetic resonance (NMR) spectra were obtained on Bruker WP-200 or WP-270 spectrometers. All multinuclear low-temperature NMR experiments were run on a wide-bore AM 360 spectrometer at 139.962 MHz (^7Li), 52.998 MHz (^6Li), 145.784 MHz (^{31}P), or 90.56 MHz (^{13}C) with the spectrometer unlocked. Digital resolution was 0.5 Hz for ^7Li, 0.4 Hz for ^6Li, and 0.6 Hz for ^{31}P and ^{13}C. For a 0.15 M solution, 40 transients for the ^7Li spectrum and 80-120 scans for the ^{31}P spectrum afforded an excellent signal to noise ratio, while for a natural abundance ^6Li and ^{13}C spectrum 300 and 600 scans, respectively, were required for an adequate signal to noise ratio. (Note: Although the spectrometer was unlocked during acquisition, the field was generally very stable and only rarely did an experiment have to be abandoned due to a field shift.)

General Procedure for HMPA Titration of Lithium Reagents. Samples of the lithium reagent (0.66 mmol) in THF or other solvent (3.5 mL) were prepared in 10-mm thin-walled NMR tubes, which were N_2 flushed, oven-dried, and fitted with a septum (9 mm i.d.). The outside top portion of the tube was lightly greased to make a better seal for the septa, which were held securely by parafilm. Silicon grease was placed on the septa tops to seal punctures, and the tubes were stored at −78 °C until the experiment was performed. After adjustment of the shim values for the $CDCl_3$ lock sample, the AM 360 spectrometer was unlocked, the probe was cooled (−120 to −135 °C), and the temperature was measured before and after the experiment using a calibrated RTD (resistance temperature device) accurate to 0.03 °C. The reading was taken 10-15 min after the RTD element had been lowered into the probe. (The reading fluctuated within ~0.1 °C at this point.) The sample was inserted and the spectrometer tuned. Since deuterated solvents were not used, the field was tuned on the ^{13}C FID of C-3 of THF, and NMR spectra of ^7Li, ^{31}P, and other nuclei were measured. The sample was ejected, placed in a -78 °C bath, and for example, 0.25 equiv of HMPA (28.0 µL, 0.161 mmol, 28.8 mg) was added. In order to get the HMPA to dissolve, the tube had to be repeatedly warmed slightly and shaken. The sample was placed in the probe, and after about 10 min the ^7Li and ^{31}P NMR spectra were taken. For techniques used to reference ^7Li and ^{31}P NMR spectra see ref. 1d.

^7Li, ^{31}P and ^{13}C NMR Spectroscopy of an HMPA Titration of 2-(Phenyldimethylsilyl)-1,3-dithian-2-yllithium in 3/2 THF/Ether. To a 10-mm NMR tube containing 2-(phenyldimethylsilyl)-1,3-dithiane (150 µL, 0.165 g, 0.65 mmol) in 2.1 mL of THF and 1.6 mL ether cooled to −78 °C was added PhLi (0.31 mL, 0.715 mmol, 2.28 M in THF).

^{13}C, ^{7}Li and ^{31}P NMR spectra were obtained with a probe temperature between −133.1 and −130.2 °C. NMR analysis of the quenched lithium reagent gave a 72% yield of 2-methyl-2-(phenyldimethylsilyl)-1,3-dithiane and a 6.5% recovery of starting material.

The procedure for the generation of 2-(trimethylsilyl)-1,3-dithian-2-yllithium is the same as above but with the metalation requiring 50 min at −15 to −20 °C (dry ice/ethylene glycol). The solution turned a pale yellow upon addition of BuLi.

Variable Temperature ^{13}C, ^{7}Li and ^{31}P NMR Spectroscopy of 0.16 M 2-(Phenyldimethylsilyl)-1,3-dithian-2-yllithium at 1.5 Equiv of HMPA in 3:2 THF/Ether. To a sample, prepared as detailed above, was added 1.5 equiv of HMPA. A variable temperature experiment was carried out with the temperature being measured before the ^{7}Li spectra were acquired and after the ^{31}P spectra were acquired. The temperature ranges (°C) for the sample were −130.8 to −130.2, −120.4 to −120.7, −110.4 to −111.4, −100.2 to −104.0, −89.3 to −86.5, −78.3 to −78.3, −68.2 to −67.8 and −56.5 (for ^{7}Li and ^{31}P spectra only). NMR analysis of the quenched lithium reagent gave a 89% yield of 2-methyl-2-(phenyldimethylsilyl)-1,3-dithiane and a 1% recovery of the starting material.

^{7}Li and ^{31}P NMR Spectroscopy of an HMPA Titration of 1,3-Dithian-2-yllithium in 3:2 THF/Me$_2$0 at -135 °C. To a 10-mm NMR tube containing 1,3-dithiane (84.2 mg, 0.70 mmol) in 2.1 mL THF cooled to -78 °C was added *n*-BuLi (0.35 mL, 0.70 mmol, 2.0 M in pentane). The colorless solution was shaken and stored in a -20 °C freezer for 2 h. Dimethyl ether (1.4 mL) was condensed into the tube and NMR spectra were acquired with a probe temperature of -135 °C. The sample was quenched with 0.3 mL (4.8 mmol) of iodomethane to give a 40% NMR yield (pentachloroethane standard) of 2-methyl-1,3-dithiane and 18% recovery of 1,3-dithiane. No sign of decomposition was apparent, and the low yield was likely due to product volatility.

^{13}C, ^{7}Li, ^{6}Li and ^{31}P NMR Spectroscopy of an HMPA Titration of 0.18 M 2-*tert*-Butyl-1,3-dithian-2-yllithium in 3:2 THF/Me$_2$0 at -135 °C. To a 10-mm NMR tube containing 2-*tert*-butyl-1,3-dithiane (123 mg, 0.70 mmol) in 2.1 mL THF cooled to -78 °C was added BuLi (0.35 mL, 0.70 mmol, 2.0 M in pentane). The colorless solution was shaken and stored in a -20 °C freezer for 6 h. Dimethyl ether (1.4 mL) was condensed into the tube and NMR spectra were acquired with a probe temperature of -135 °C. ^{13}C NMR of THF CIP (THF/Me$_2$O, 90.556 MHz, -135 °) δ 27.2 (2C), 29.5 (1C), 33.2 (3C), 38.4 (1:1:1:1 quartet, $J_{C\text{-}Li}$ = 18.1 Hz), 44.9 (1C); ^{13}C of SIP (with 4.0 equiv of HMPA) δ 29.1, 32.2, 34.4, 38.3 (carbanion carbon), 45.1. The sample was quenched with 0.3 mL (4.8 mmol) of iodomethane to give a 71% NMR yield (pentachloroethane standard) of 2-*tert*-butyl-2-methyl-1,3-dithiane and 21% recovery of 1,3-dithiane.

^{7}Li and ^{31}P NMR Spectroscopy of an HMPA Titration of 2-Phenyl-1,3-dithian-2-yllithium in THF at -115 to -119 °C. To a 10-mm NMR tube containing 2-phenyl-1,3-dithiane (0.126 g, 0.64 mmol) was added 1.0 equiv of BuLi and the pale yellow solution was stored at −40 °C for 1.5 h. ^{7}Li and ^{31}P NMR spectra were obtained with a probe temperature between −115.1 °C and −118.8 °C. NMR analysis of the quenched lithium reagent gave a 91% yield of 2-methyl-2-phenyl-1,3-dithiane.

References and Notes

1. (a) Fröling, A.; Arens, J. F. *Rec. Trav. Chim.* **1962**, *81*, 1009. Truce, W. E.; Roberts, F. E. *J. Org. Chem.* **1963**, *28*, 961.
   (b) Schöllkopf , U.; Hänssle, P. *Liebig's Ann. Chem.* **1972**, *763*, 208. Baldwin, J. E.; Höfle, G. A.; Lever, Jr.; O. W. *J. Am. Chem. Soc.* **1974**, *96*, 7125. Hartmann, J,; Stähle, M.; Sclosser, M. *Synthesis* **1974**, 888.
   (c) Stork, G.; Maldonado, L. *J. Am. Chem. Soc.* **1971**, *93*, 5286. Deuchert, K.; Hertenstein, U. Hünig, S. *Synthesis* **1973**, 777.
   (d) Hase, T. A.; Koskimies, J. K. *Aldrichimica Acta* **1981**, *14*, 73.
2. (a) Seebach, D.; Corey, E. J. *J. Org. Chem.* **1975**, *40*, 231. Corey, E. J.; Seebach, D. *Angew. Chem., Int. Ed. Engl.* **1965**, *4*, 1075. Gröbel, B. T.; Seebach, D. *Synthesis* **1977**, 357.
   (b) Page, P. C. B.; van Niel, M. B.; Prodger, J. C. *Tetrahedron* **1989**, *45*, 7643.
   (c) Amstutz, R.; Dunitz, J. D.; Seebach, D. *Angew. Chem., Int. Ed. Engl.* **1981**, *20*, 465.
   (d) Amstutz, R.; Seebach, D.; Seiler, P.; Schweizer, B.; Dunitz, J. D. *Angew. Chem., Int. Ed. Engl.* **1980**, *19*, 53.
   (e) Seebach, D.; Gabriel, J.; Hässig, R. *Helv. Chim. Acta* **1984**, *67*, 1083.
   (f) Bauer, W.; Seebach, D. *Helv. Chim. Acta* **1984**, *67*, 1972.
   (g) Seebach, D.; Kolb, M.; Gröbel, B. T. *Chem. Ber.* **1973**, *106*, 2277.
   (h) Seebach, D.; Siegel, H.; Gabriel, J.; Hässig, R. *Helv. Chim. Acta* **1980**, *63*, 2046.
   (ih) Mukhopadhyay, T.; Seebach, D. *Helv. Chim. Acta* **1982**, *65*, 385.
3. (a) Reich, H. J.; Green, D. P.; Phillips, N. H. *J. Am. Chem. Soc.* **1989**, *111*, 3444.
   (b) Reich, H. J.; Green, D. P. *J. Am. Chem. Soc.* **1989**, *111*, 8729.
   (c) Reich, H. J.; Borst, J. P. *J. Am. Chem. Soc.* **1991**, *113*, 1835.
   (d) Reich, H. J.; Borst, J. P.; Dykstra, R. R.; Green, D. P. *J. Am. Chem. Soc.* **1993**, *115*, 8728.
   (e) Reich, H. J.; Dykstra, R. R. *J. Am. Chem. Soc.* **1993**, *115*, 7041.
   (f) Reich, H. J.; Dykstra, R. R. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 1469.
   (g) Reich, H. J.; Borst, J. P.; Dykstra, R. R. *Organometallics* **1993**, *12*, 0000 (in press).
4. Borden, W. T.; Davidson, E. R.; Andersen, N. H.; Denniston, A. D.; Epiotis, N. D. *J. Am. Chem. Soc.* **1978**, *100*, 1604.
5. Oae, S.; Tagaki, W.; Ohno, A. *Tetrahedron* **1964**, *20*, 427.
6. (a) Abatjoglou, A. G.; Eliel, E. L.; Kuyper, L. F. *J. Am. Chem. Soc.* **1977**, *99*, 8262.
   (b) Eliel, E. L.; Hartmann, A. A.; Abatjoglou, A. G. *J. Am. Chem. Soc.* **1974**, *96*, 1807.
7. (a) Streitwieser, A., Jr.; Ewing, S. P. *J. Am. Chem. Soc.* **1975**, *97*, 190.
   (b) Xie, L.; Bors, D. A.; Streitwieser, A. *J. Org. Chem.* **1992**, *57*, 4986.
8. Bordwell, F. G.; Bares, J. E.; Bartmess, J. E.; Drucker, G. E.; Gerhold J.; McCollum, G. J.; Van Der Puy, M.; Vanier, N. R.; Matthews, W. S. *J. Org. Chem.* **1977**, *42*, 326. Bordwell, F. G.; Drucker, G. E.; Andersen, N. H.; Denniston, A. D. *J. Am. Chem. Soc.* **1986**, *108*, 7310.
9. Fraser, R. R.; Bresse, M.; Mansour, T. S. *J. Chem. Soc., Chem. Commun.* **1983**, 620.
10. Bartmess, J. E.; Hays, R. L.; Khatri, H. N.; Misra, R. N.; Wilson, S. R. *J. Am. Chem. Soc.* **1981**, *103*, 4746.
11. Browne, S. E.; Asher, S. E.; Cornwall, E. H.; Frisoli, J. K.; Harris, L. J.; Salot, E. A.; Sauter, E. A.; Trecoske, M. A.; Veale, P. S., Jr. *J. Am. Chem. Soc.* **1984**, *106*, 1432.
12. Jones, P. F.; Lappert, M. F. *J. Chem. Soc., Chem. Commun.* **1972**, 526. Carey, F. A.; Court, A. S. *J. Org. Chem.* 1972, *37*, 1926. Kolb, M. *Synthesis* **1990**, 171.

13. (a) Barr, D.; Doyle, M. J.; Mulvey, R. E.; Raithby, P. R.; Reed, D.; Snaith, R.; Wright, D. S. *J. Chem. Soc., Chem. Commun.* **1989**, 318.
    (b) Raithby, P. R.; Reed, D.; Snaith, R.; Wright, D. S. *Angew. Chem., Int. Ed. Engl.* **1991**, *30*, 1011.
14. Lithium-phosphorus coupling has also been detected in an α-lithiophosphoryl compound: Denmark, S. E.; Miller, P. C.; Wilson, S. R. *J. Am. Chem. Soc.* **1991**, *113*, 1468.
15. Romesburg, F. E.; Collum, D. B. *J. Am. Chem. Soc.* **1992**, *114*, 2112.
16. (a) Jackman, L. M.; Scarmoutzos, L. M.; Porter, W. *J. Am. Chem. Soc.* **1987**, *109*, 6524.
    (b) Jackman, L. M.; Chen, X. *J. Am. Chem. Soc.* **1992**, *114*, 403.
17. The ^{7}Li-^{13}C coupling is 14.6 Hz.[3c] In principle **3-Li** could also be dimerized through the sulfur as in the crystal structure of 2-methyl-2-lithiodithiane·TMEDA.[2d] However, considering that 2-methyl-2-lithiodithiane (**6-Li**) is mostly monomeric in THF solution, **3-Li**, which bears a better carbanion stabilizing group and is more sterically encumbered, is likely also monomeric.
18. The ^{31}P and ^{7}Li NMR signals of THF and HMPA complexed SIP's are only slightly broadened by ^{7}Li quadrupolar (T_1) relaxation.[3d] Quadrupolar relaxation causes the 1:1:1:1 quartet of many CIP's to collapse first to a broad doublet and then to a singlet. Under these conditions, the sharp signal of natural abundance ^{6}Li can be seen in the valley of the broad doublet.[3d, 2h, 19] This behavior is distinct from that observed by broadening due to dynamic exchange (T_2 relaxation). This distortion has been demonstrated and simulated for ^{19}F in BF_3 and ClO_3F: Bacon, J.; Gillespie, R. J.; Quail, J. W. *Can. J. Chem.* **1963**, *41*, 3063.
19. Bauer, W.; Winchester, W. R.; Schleyer, P. v. R. *Organometallics* **1987**, *6*, 2371.
20. The pK_a of **2-H** is not known, but 2-ethyldithiane is slightly less acidic than 2-methyldithiane, therefore, we expect the *tert*-butyl analog to have an even higher pK_a.[7]
21. Brown, C. A.; Yamaichi, A. *J. Chem. Soc., Chem. Commun.* **1979**, 100 and references therein.
22. Ager, D. J.; East, M. B. *J. Org. Chem.* **1986**, *51*, 3983.
23. (a) Krief, A. *Tetrahedron* **1980**, *36*, 2531.
    (b) Dumont, W.; Lucchetti, J.; Krief, A. *J. Chem. Soc., Chem. Commun.* **1983**, 66.
24. (a) Cohen, T.; Abraham, W. D.; Myers, M. *J. Am. Chem. Soc.* **1987**, *109*, 7923.
    (b) Dolak, T. M.; Bryson, T. A. *Tetrahedron Lett.* **1977**, 1961.
25. Lefour, J.-M.; Loupy, A. *Tetrahedron* **1978**, *34*, 2597.
26. Lower temperatures favor SIP structures. Hogen-Esch, T. E.; Smid, J. *J. Am. Chem. Soc.* **1966**, *88*, 307.
27. (a) Kimbrough, R.; Gaines, T. B. *Nature* **1966**, *211*, 146. Shott, L. D.; Borkovec, A. B.; Knapp, W. A., Jr. *Toxicol. Appl. Pharmacol.* **1971**, *18*, 499.
    (b) Mihal, C. P., Jr. *Am. Ind. Hyg. Assoc. J.* **1987**, *48*, 997. American Conference of Governmental Industrial Hygienists: *TLVs-Threshold Limit Values and Biological Exposure Indices for 1986-1987*; ACGIH: Cincinnati, OH, Appendix A2, p 40.

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