THE STABILITY OF CYCLOPROPYLLITHIUM IN DIETHYL ETHER AND IN TETRAHYDROFURAN*

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It is known that secondary alkyllithium reagents generally cleave ethers quite rapidly at room temperature[1]. The cleavage rate is much greater for secondary than for primary organolithium reagents[2]. Thus the half-lives of ethyl-, *n*-propyl-, and *n*-butyllithium in refluxing diethyl ether solution were found to be 31, 11 and 17 h respectively. Ether solutions of isopropyl-, cyclohexyl-, and *sec*-butyllithium decreased to one-half the initial concentration within thirty minutes without external heating. Indeed, in the latter case, the addition of diethyl ether to a hydrocarbon solution of the lithium reagent resulted in a reaction sufficiently exothermic to cause the solution to reflux. Generally the stability of a lithium reagent is lower in tetrahydrofuran than in diethyl ether. Thus a solution of *n*-butyllithium in tetrahydrofuran which was 0.79*M* at —25° decreased in concentration to 0.23*M* when maintained at room temperature for one hour[3].

The rate of reaction of organolithium reagents with ethers appears to be dependent on the nucleophilic character of the carbanionic center. The order of reactivity of lithium reagents towards ethers (tertiary > secondary > primary) may be explained in terms of increased nucleophilic character of the carbon atom bearing the lithium due to the inductive effect of the alkyl groups. The high stability of vinyllithium in ether solution[4] is consistent with the expectation that a vinyl carbanion would be less nucleophilic than an alkyl carbanion due to the higher electronegativity of carbon in the sp^2 state[5].

It therefore was of theoretical as well as of practical interest to determine the stability of cyclopropyllithium in diethyl ether and in tetrahydrofuran. Although cyclopropyllithium is a secondary lithium reagent, the cyclopropyl group may be able to accommodate a partial negative charge better than a simple alkyl group because of its "unsaturated" character, and for this reason one might expect that cyclopropyllithium is more stable toward ethers than is isopropyllithium. The "unsaturated" nature of the cyclopropyl group (*i.e.*, hybridization of the cyclopropyl carbon atoms approaches sp^2) is indicated by a wide range of experimental and theoretical studies[§].

We have investigated the stability of cyclopropyllithium at room temperature

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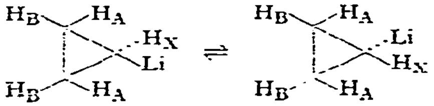
[§] For reviews see ref. 6.

in diethyl ether and in tetrahydrofuran. The cyclopropyllithium solutions were prepared by dissolving solid cyclopropyllithium (obtained by the transmetalation procedure from tetracyclopropyltin[7]) in the solvent of interest. The stability studies were carried out by determining the concentration of active organolithium reagent as a function of elapsed time by the modified Gilman double titration procedure in which 1,2-dibromoethane is used in place of benzyl chloride[8]. It was found that the half-life of cyclopropyllithium in diethyl ether solution at room temperature is approximately 138 h. This is to be compared with values at room temperature of 153 h for *n*-butyllithium, 30 h for *n*-propyllithium, 54 h for ethyllithium and less than 30 min for cyclohexyl- and isopropyllithium. It is clear that in its stability toward ether, cyclopropyllithium resembles a primary organolithium reagent and is much more stable than expected for a secondary lithium reagent.

In tetrahydrofuran a similar situation obtains. A solution of *n*-butyllithium in this solvent, originally $0.79 M$, was completely decomposed after 2 h at 20° (See ref. 3). In this solvent cyclopropyllithium is more stable than *n*-butyllithium, and the data obtained suggest that cyclopropyllithium may be stabilized by the products of its reaction with the solvent. Thus a solution of cyclopropyllithium in tetrahydrofuran, prepared from the solid reagent and found to be $0.175 M$ 4 min after the solution had been prepared, contained 0.064 moles per liter of cyclopropyllithium after 5 h at room temperature. However, after 43.5 h, its concentration had decreased only to $0.055 M$. This result was confirmed by a nuclear magnetic resonance study, the peaks due to the cyclopropyl protons in cyclopropyllithium having a relative area of 1.5 five hours after the solution had been prepared and a relative area of 1.0 after four days at room temperature.

This study, which demonstrates a high degree of stability for cyclopropyllithium in ethers, which is quite uncharacteristic of secondary organolithium reagents, suggests that the partial negative charge on the carbon atom to which the lithium atom is attached is indeed absorbed to some extent by the cyclopropyl group as a whole, probably due to the "unsaturated" nature of the cyclopropyl group. The intermediate character of the cyclopropyl group is demonstrated by the fact that cyclopropyllithium is definitely less stable than vinyllithium in ether solvents.

The configurational stability of the lithium reagents derived from 1-bromo-2-methylcyclopropane[9] and 1-bromo-1-methyl-2,2-diphenyl-cyclopropane[10] has been demonstrated by chemical means. The NMR spectrum of cyclopropyllithium in tetrahydrofuran solution is that of an ABX system, and this suggests that this reagent also is configurationally stable. The NMR data ($\delta_{AB} = 34.4$ c.p.s.) implies that the cyclopropyllithium is stable to inversion (equation 1) for at least $^{1}/_{80}$ sec.,



(1)

but it is certain that the lifetime of a particular configuration is many orders of magnitude greater in terms of previous chemical evidence obtained with substituted cyclopropyllithiums[9,10].

Previous preparations of cyclopropyllithium used the reaction of metallic lithium with cyclopropyl chloride[11], since this was the most accessible cyclopropyl halide. Cyclopropyl bromide is now very readily prepared in yields of ca. 70 % via a procedure[12] developed by Meek[*], which involves the reaction of cyclopropanecarboxylic acid, bromine and mercuric oxide in *sym*-tetrachloroethane at temperatures below 40°, and cyclopropyl bromide reacts readily with lithium wire in diethyl ether at about 0° to give cyclopropyllithium in high yield. For synthetic purposes this is now the method of choice, and the preparations of cyclopropyltrimethylsilane (78 %) and tetracyclopropyltin (88 %) using this procedure are described in the experimental section. The good stability of cyclopropyllithium in diethyl ether is evidenced by the fact that the yield of cyclopropyltrimethylsilane was 75 % when the formation of the lithium reagent was allowed to proceed under auto-reflux conditions.

In addition to these studies in ether solvents, the preparation of cyclopropyllithium by the reaction of cyclopropyl bromide with lithium in pentane was examined briefly. Best results were obtained when lithium wire containing ca. 1 % sodium was used. This procedure permitted the preparation of cyclopropyllithium in yields of approximately 50 %.

EXPERIMENTAL[**]

Stability of cyclopropyllithium in diethyl ether at room temperature

Solid cyclopropyllithium was prepared from 0.018 mole of tetracyclopropyltin and 0.036 mole of *n*-butyllithium in pentane[7]. To the solid reagent was added 300 ml of ether; a clear solution resulted. This solution was transferred to a storage tube with buret attached and maintained under an argon atmosphere. Aliquots were withdrawn periodically and titrated with acid for total base content (0.1N HCl, back titration with 0.1N NaOH) and for cyclopropyllithium content by a double titration. In the latter determination the aliquots were added directly to a flask whose bottom was just covered with 1,2-dibromoethane (ca. 10 ml); after a few minutes these mixtures were titrated with 0.1N HCl. The experimental data are summarized in Table 1. The first column gives the time interval between withdrawal of the first aliquot and

TABLE 1

STABILITY OF CYCLOPROPYLLITHIUM IN DIETHYL ETHER

Time (h)	*Aliquot (ml)*	*Cyclopropyllithium Normality*
0	20.0	0.1067
1	20.0	0.1043
4	20.0	0.1022
6	20.0	0.1009
16.5	20.0	0.0976
32.5	10.0	0.0902
97.5	10.0	0.0664
308	10.0	0.0642

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[*] We are greatly indebted to Prof. J. S. MEEK of the University of Colorado for informing us about details of this excellent method prior to publication.

[**] All reactions were performed under an atmosphere of argon or of prepurified nitrogen.

withdrawal of successive aliquots. The time interval between addition of ether to the solid cyclopropyllithium and withdrawal of the first aliquot was 0.67 h. The second column designates the volume of the aliquot withdrawn. The normalities recorded in the third column were calculated from the titration data by subtracting the volume of the acid solution required for the titration of the aliquot which had been treated with 1,2-dibromoethane from the volume of acid required to titrate the total base content in an aliquot of equal volume. The plot of log c_0/c *vs.* time (c_0 = concentration at time 0; c = concentration at time t) was essentially linear up to time 97.5 h. From these data the half-life of cyclopropyllithium in diethyl ether was calculated to be 138 h. At longer times (see value for 308 h) it may be that the reagent becomes stabilized in solution, possibly by complex formation with the products formed in its reaction with the solvent (lithium ethoxide in this case).

Stability of cyclopropyllithium in tetrahydrofuran

The experimental procedure was identical to that described above. The time interval between the addition of tetrahydrofuran to the solid cyclopropyllithium and the withdrawal of the first aliquot was 4 min. Table 2 lists the normalities determined by double titrations. On the basis of the total volume of solution and the initial normality, the yield of solid cyclopropyllithium was calculated to be 77 %.

TABLE 2

STABILITY OF CYCLOPROPYLLITHIUM IN TETRAHYDROFURAN

Time (h)	*Aliquot (ml)*	*Cyclopropyllithium Normality*
0	20.0	0.1753
0.67	20.0	0.1364
1.17	10.0	0.1161
1.67	10.0	0.1045
2.17	10.0	0.0990
2.66	10.0	0.0887
3.17	10.0	0.0852
3.80	8.0	0.0754
4.71	8.0	0.0644
13.4	10.0	0.0562
19.7	5.0	0.0551
43.4	5.0	0.0545

The NMR spectrum of cyclopropyllithium

Solid cyclopropyllithium was dissolved in a minimal amount of tetrahydrofuran. The reagent solution was transferred to an NMR tube with a hypodermic syringe. Both tube and syringe had been dried carefully and flushed with nitrogen. The spectrum was recorded within 20 min. of the first addition of the solvent. The NMR spectrum was recorded using a Varian Associates HR-60 NMR spectrometer and also on a Varian Associates A-60 NMR spectrometer. The spectrum observed is shown in Fig. 1. The peaks above 1 ppm are due to tetrahydrofuran. The peak at 0.22 ppm is due to the presence of cyclopropane (confirmed by partial hydrolysis of a sample with resulting increase in this peak's intensity). This peak increased sevenfold in intensity over the course of four days, suggesting that cyclopropyllithium reacts with tetrahydrofuran *via* an initial metalation reaction.

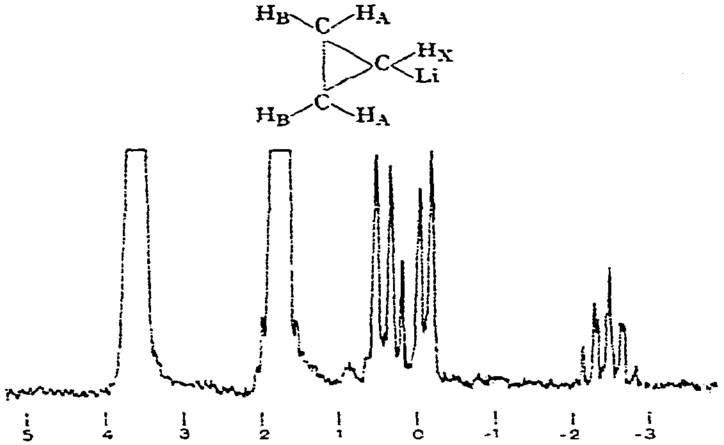

Fig. 1. Cyclopropyllithium in tetrahydrofuran. Assignments: H_B doublet centered at +0.46 ppm; H_A doublet centered at —0.05 ppm; H_X 9 peaks centered at — 2.5 ppm. Calibrated by audiosideband method. Cyclopropane used as internal standard at +0.22 ppm with respect to tetramethylsilane in tetrahydrofuran.

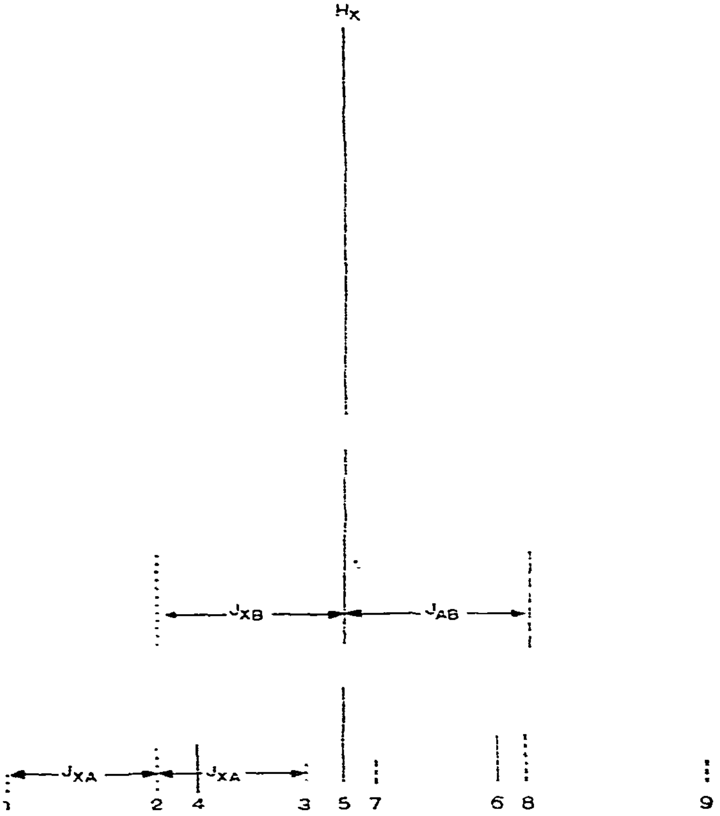

Fig. 2. Nine-line spectrum due to H_X in cyclopropyllithium

The NMR spectrum of cyclopropyllithium[*] [doublet at 0.46 ppm (J_{XB} = 11.8 c.p.s.); doublet at —0.05 ppm (J_{XA} = 9.5 c.p.s.); multiplet of nine peaks at —2.5 ppm] is in complete agreement with the following interpretation. The spin of proton H_X splits the equivalent protons H_B into a doublet with J_{XB} of 11.8 c.p.s. and the equivalent protons H_A into a doublet with a coupling constant of 9.5 c.p.s. We would expect the peak due to H_X to be split into a triplet of intensity ratio 1:2:1 by the H_B protons with a coupling constant of 11.8 c.p.s. and each member of the triplet to be split into another analogous triplet with a coupling constant of 9.5 c.p.s. On this basis it is possible to construct the actual observed nine-line spectrum for the proton bonded to the carbon atom bearing the lithium (H_X), as shown in Fig. 2. From the size of the coupling constants, it is seen that the nine-line spectrum would appear as a quintet with the inner peaks split 2:3:2. For the composite spectrum of H_X we should therefore see a quintet in the ratio 1:4:6:4:1. Furthermore, the coupling constants J_{2-5} and J_{5-8} should equal 11.8 c.p.s. In addition, the following constants should be 9.5 c.p.s.: J_{1-2}, J_{2-3}, J_{4-5}, J_{5-6}, J_{6-7}, J_{7-8} and J_{8-9}. Since all the above considerations are true of the observed spectrum, there can be little doudt that it is the hydrogen atom bonded to the carbon atom bearing the lithium that is responsible for splitting H_A and H_B protons into doublets. In addition to the above-mentioned splittings, the doublets due to H_A and H_B are further split with a small coupling constant of *ca.* 1 c.p.s. It is uncertain whether this represents *gem* or *cis-trans* coupling. No attempt was made to further characterize H_A and H_B as being *cis* or *trans* to H_B. In substituted cyclopropanes J_{cis} usually is larger than J_{trans}[**]. On this basis one would assign H_B as the *cis* protons.

Preparation of cyclopropyllithium in diethyl ether solution

To a three-necked flask (equipped with a thermometer, nitrogen inlet tube, mechanical stirrer and addition funnel) was added 17.9 g (2.6 g atoms) of lithium wire pieces and 650 ml of diethyl ether. The flask was immersed in an ice bath, and a solution of 145 g (1.2 moles) of cyclopropyl bromide in 350 ml of ether was added dropwise over the course of 90 min. The lithium became bright after the first portion of the bromide had been added. The reaction mixture was stirred for an additional 90 min. after which time only a very small amount of lithium remained. To this solution was added 65 g (0.25 mole) of tin tetrachloride dropwise and with gentle stirring. After the addition was complete, the mixture was allowed to warm to room temperature. Stirring was continued for 18 h. The mixture was cooled, then hydrolyzed with 300 ml of ice water. The ether layer was washed with a water-methanol solution of potassium fluoride; no precipitate resulted. The dried ether layer was distilled to give 62.2 g (88 %) of tetracyclopropyltin, b.p. 69 70°/0.25, n_D^{25} 1.5200 (lit.[14] n_D^{25} 1.5202). The infrared spectrum of this material was identical to that of tetracyclopropyltin prepared by the Grignard procedure. Very little (< 0.5 g) remained as distillation residue[***].

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[*] Chemical shifts are given in ppm downfield from tetramethylsilane.

[**] For leading references see 13.

[***] The Grignard route to tetracyclopropyltin[14] usually gave yields of only 60 %, and considerable amounts of hexacyclopropylditin were formed as well. The latter was not isolated in earlier studies; it has now been characterized: n_D^{25} 1.5627. (Found: C, 44.77; H, 6.19. ($C_{15}H_{30}Sn_2$ Calcd.: C, 44.68; H, 6.25 %.) Hexacyclopropylditin decolorizes iodine solutions; tetracyclopropyltin does not, at room temperature.

A similar procedure was used in the preparation of cyclopropyltrimethylsilane. Cyclopropyllithium was prepared from 0.23 g atom of lithium and 0.1 mole of cyclopropyl bromide in 70 ml of ether. To this solution, at 0°, was added 0.118 mole of trimethylchlorosilane. Fifteen min after the addition was complete, the solution was allowed to warm to room temperature, kept at 25° for 15 min, then cooled and hydrolyzed with 30 ml of water. The ether layer was dried and analyzed for cyclopropyltrimethylsilane (identified by retention time and infrared spectrum[14]), using benzene as an internal standard, by gas chromatography (Dow Corning 710 Silicone Fluid, 30% on 60-80 mesh Chromosorb P, jacket at 70°, preheater at 126°, 12.2 p.s.i. He). This procedure established that the desired silane had been formed in 78% yield.

In another experiment no attempt was made to control the temperature below the reflux temperature of the ether solvent during the preparation of the cyclopropyllithium reagent. The yield of cyclopropyltrimethylsilane in this case was 75%.

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SUMMARY

The half-life of cyclopropyllithium in diethyl ether is *ca.* 138 h at room temperature, which roughly equals the stability of *n*-butyllithium in this solvent and which is far greater than the stability of other secondary organolithium reagents in ether. In tetrahydrofuran cyclopropyllithium is more stable than is *n*-butyllithium. The NMR spectrum of cyclopropyllithium in tetrahydrofuran solution is reported. The preparation of cyclopropyllithium in high yield by the reaction of cyclopropyl bromide with lithium in diethyl ether is described.

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