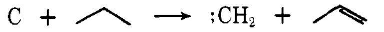
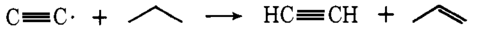
hydrogens by C to produce CH_2 and **8** (eq 6) or abstraction by C_2 to produce acetylene and **8** (eq 7).[21]


(6)


(7)

A Comparison of C–H Insertion by Atomic Carbon with that by Methylene. Studies of the reactions of methylene with hydrocarbons have demonstrated that this species is completely nonselective in its C–H insertions.[22] Molecular orbital calculations of the energetics of the reaction of methylene with methane[23,24] indicate that the insertion proceeds by initial transfer of hydrogen to the methylene in much the same manner as that postulated here for carbon atom insertion. However the results of this investigation indicate that atomic carbon is considerably more selective in its C–H insertions than methylene. A consideration of the thermodynamics of the extreme case of complete hydrogen transfer in each reaction may provide a clue to the reason for the observed selectivity:[25]

$$C(^1D) + CH_4 \rightarrow H\text{—}\dot{C}\text{:}\ (^2\Sigma) + \cdot CH_3 \quad \Delta H = -5\ \text{kcal/mol}$$

$$CH_2(^1A_1) + CH_4 \rightarrow H_3C\cdot + \cdot CH_3 \quad \Delta H = -15\ \text{kcal/mol}$$

Thus heats of reaction indicate that the initial hydrogen transfer is more favorable in methylene insertion than in insertion by atomic carbon.

Conclusion

Experimental evidence indicates that C–H insertion by atomic carbon occurs by preferential attack at the weakest carbon–hydrogen bond. MINDO/3 calculations suggest that this preference is the result of an initial transfer of hydrogen from propane to the attacking carbon. The energetics of this hydrogen transfer dictate a preferential reaction at the secondary C–H bond in propane.

Acknowledgment. We are grateful to Drs. A. P. Wolf and D. R. Christman of Brookhaven National Laboratory for determining the specific activity of the 5-aminotetrazole-^{14}C. Financial support by the National Science Foundation through Grant No. MPS 75-05405 and by the Research Corporation is gratefully acknowledged.

References and Notes

(1) A preliminary account of this research was presented at the First Chemical Congress of the North American Continent, Mexico City, Mexico, Dec 1975, Abstract No. PHSC 178.

(2) For a recent review see C. MacKay in "Carbenes", Vol. II, R. A. Moss and M. Jones Jr., Ed., Wiley-Interscience, New York, N.Y., 1975, pp 1–42.

(3) P. S. Skell, J. J. Havel, and M. J. McGlinchey, *Acc. Chem. Res.*, **6**, 97 (1973).

(4) A. P. Wolf, *Adv. Phys. Org. Chem.*, **2**, 201 (1964).

(5) P. S. Skell and R. R. Engel, *J. Am. Chem. Soc.*, **88**, 4483 (1966).

(6) (a) G. Stocklin and A. P. Wolf, *J. Am. Chem. Soc.*, **85**, 229 (1963); (b) M. J. Welch and A. P. Wolf, *ibid.*, **91**, 6584 (1969); (c) K. K. Taylor, H. J. Aache, and A. P. Wolf, *ibid.*, **97**, 5970 (1975). (b) M. J. Welch and A. P. Wolf, *ibid.*, **91**, 6584 (1969); (c) K. K. Taylor, H. J. Aache, and A. P. Wolf, *ibid.*, **97**, 5970 (1975).

(7) P. B. Shevlin, *J. Am. Chem. Soc.*, **94**, 1375 (1972); (b) S. Kammula and P. B. Shevlin, *ibid.*, **95**, 4441 (1973); (c) *ibid.*, **96**, 7830 (1974); (d) R. H. Parker and P. B. Shevlin, *Tetrahedron Lett.*, 2167 (1975).

(8) V. G. Satzinger, *Justus Leibigs Ann. Chem.*, **638**, 159 (1960).

(9) A preliminary account of this work stated that no 1-butene was produced.[1] This was due to an error in the analytical method which has now been corrected.

(10) (a) F. Martinotti, M. J. Welch, and A. P. Wolf, *Chem. Commun.*, 115 (1968); (b) W. Brown, A. M. Bass, D. D. Davis, and J. D. Simmons, *Proc. R. Soc. London, Ser. A*, **312**, 417 (1969); (c) D. Husain and L. J. Kirsch, *Trans. Faraday Soc.*, **67**, 2025 (1971).

(11) (a) R. N. Lambrecht, N. Furukawa, and A. P. Wolf, *J. Phys. Chem.*, **74**, 4605 (1970); (b) T. Rose and C. MacKay, *ibid.*, **77**, 2598 (1973).

(12) J. M. Figuera, J. M. Perez, and A. P. Wolf, *J. Chem. Soc., Faraday Trans. 1*, **71**, 1905 (1975).

(13) T. Migita, C. A. Redvanly, and A. P. Wolf, 155th National Meeting of the American Chemical Society, San Francisco, Calif., March 1968, Abstract No. P226.

(14) M. J. S. Dewar, H. Metiu, P. J. Student, A. Brown, R. C. Bigham, D. H. Lo, C. A. Ramsden, H. Killmar, P. Weiner, and P. K. Bischoff, "MINDO/3; Modified Intermediate Neglect of Differential Overlap", Quantum Chemistry Program Exchange, Indiana University, 1975, Program No. 279.

(15) M. J. S. Dewar, E. Haselbach, and M. Shanshal, *J. Am. Chem. Soc.*, **94**, 9103 (1972).

(16) J. M. Figuera, P. B. Shevlin, and S. D. Worley, *J. Am. Chem. Soc.*, **98**, 3820 (1976).

(17) W. Kirmse, "Carbene Chemistry", 2nd ed., Academic Press, New York, N.Y., 1971.

(18) P. P. Gaspar and G. S. Hammond in ref 2, pp 207–362.

(19) R. S. Mulliken, *J. Chem. Phys.*, **23**, 1833 (1955).

(20) P. B. Shevlin and A. P. Wolf, *J. Am. Chem. Soc.*, **88**, 4735 (1966).

(21) P. S. Skell and R. F. Harris, *J. Am. Chem. Soc.*, **88**, 5933 (1966) have presented evidence for abstraction by C_2.

(22) W. von E. Doering, R. G. Buttery, R. G. Laughlin, and N. Chaudhuri, *J. Am. Chem. Soc.*, **78**, 3224 (1956).

(23) R. C. Dobson, D. M. Hayes, and R. Hoffmann, *J. Am. Chem. Soc.*, **93**, 6188 (1971).

(24) N. Bodor, M. J. S. Dewar, and J. S. Wasson, *J. Am. Chem. Soc.*, **94**, 9095 (1972).

(25) ΔH_f of $CH_2(^1A_1)$ taken as 101 kcal/mol from W. L. Hase, R. T. Phillips, and J. W. Simins, *Chem. Phys. Lett.* **12**, 161 (1971). ΔH_f of $CH(^2\Sigma)$ taken as 142 kcal/mol from A. G. Gayden, "Dissociation Energies and Spectra of Diatomic Molecules", Chapman and Hall, London, 1968.

Cyclopropanes. 39. The Configurational Stability of the 1-Isocyano-2,2-diphenylcyclopropyl Anion[1]

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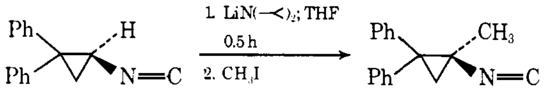
Abstract: In contrast to the 1-cyano-2,2-diphenylcyclopropyl anion, in ether solvents, the 1-isocyano-2,2-diphenylcyclopropyl anion was found to be configurationally stable at −72 °C. The stability was not affected by changing the gegenion from lithium to sodium to potassium. Nor was it affected by change in solvent or by the addition of coordinating agents such as crown ethers, triglyme, and hexamethylphosphoramide (HMPA). The stabilizing effect of the isocyano substituent is discussed.

The chemistry of carbanions has been the subject of extensive investigation.[2-4] The results from these studies have shown that carbanions exist in solution in equilibrium with different types of ion pairs. Spectroscopic studies of alkali metal salts

$$A^-M^+ \rightleftharpoons A^-/S/M^+ \rightleftharpoons A^- + M^+$$

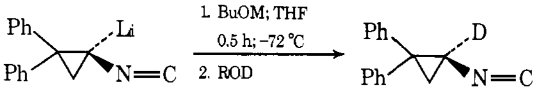
of resonance stabilized carbanions have revealed that such equilibria are affected not only by the structure of the carbanion but also by the gegenion, the solvent polarity, temperature, and the presence of gegenion-coordinating additives.[2b] It has been concluded from these studies that the less associated solvent separated ion pairs ($A^-/S/M^+$) and the free ions are

Table I. Effect of Temperature on the Configurational Stability



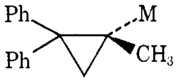
No.	Temp, °C	Yield, %	Optical purity, %
1	-72 ± 2	96	98
2	-52 ± 1	75	93
3	-25 ± 1	92	58
4	-5 ± 1	80	0.3

Table II. Effect of Cation on the Configurational Stability of **5**

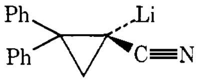


No.	Metal alkoxide	Yield, %	Deuterium, %	Optical purity, %
1		70	98	98
2	*t*-BuONa	78	98	96
3	*t*-BuOK	90	99	99

favored by low concentrations, low temperatures, small cation, and strongly solvating solvents such as, in the extreme, crown ethers. When the carbanionic center is an asymmetric carbon, then the configurational stability of the carbanion can be evaluated.[3,4] To this end, we have focused our attention on the cyclopropyl anion system.



1, M = Li
2, M = Na



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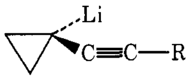

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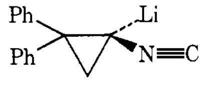
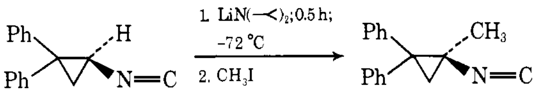


5

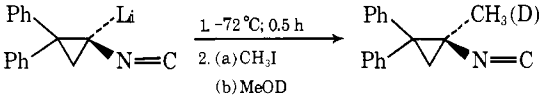
There is ample evidence that the cyclopropane ring possesses considerable strain energy (~26 kcal/mol).[5] Moreover, during the process of inversion the cyclopropyl anions would increase the strain energy even more. Hence, this system provides a built-in energy barrier to pyramidal inversion and makes it a desirable one for the investigation of this process. Thus, it made it possible to demonstrate that the 1-lithium and 1-sodium derivatives of 1-methyl-2,2-diphenylcyclopropane **1** and **2** were capable of maintaining their configurations to a large degree in aprotic solvents.[6,7] A similar result obtains when the 1 substituent in **2** is changed from methyl to other nondelocalizing substituents such as fluoro, chloro, and methoxyl.[8] By contrast, even using aprotic conditions 1-lithio-1-cyano-2,2-diphenylcyclopropane (**3**)[9] or the acetylenic derivative[10] **4** were shown to be incapable of maintaining their configurations. This latter observation is undoubtedly due to the ability of the cyano and acetylenic groups to delocalize the adjacent negative charge and thereby overcome the strain energy barrier induced by the ring. Both of these groups are attached to the cyclopropyl ring by an sp-hybridized carbon. Because of our general interest in the chemistry of the isocyano function[11] and the fact that the nitrogen atom of this group is also sp hybridized we undertook an investigation of the effect of the isocyano function on the configurational stability of 1-lithio-1-isocyano-2,2-diphenylcyclopropane (**5**).[12]

Table III. Effect of Solvent on the Configurational Stability of **5**



No.	Solvent	Yield, %	Optical purity, %
1	Et_2O	84	99
2	THF	96	98
3	THF/DME (2:1)	91	98

Table IV. Effect of Cation Complexing Agents on the Configurational Stability of **5**



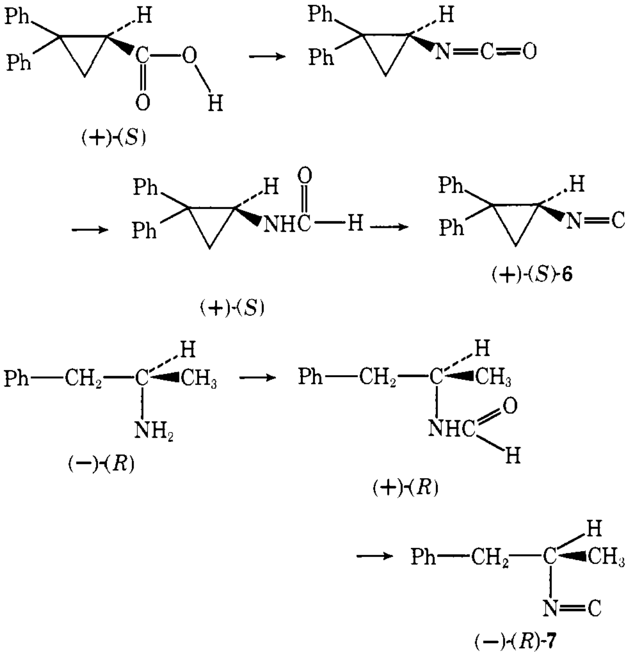
No.	Solvent	Agent (equiv)	Workup	Yield, %	Optical purity, %
1	Pentane[a]	TMEDA (1)	b	70[b]	93
2	THF	TMEDA (1)	a	70	99
3	THF	Triglyme (2)	b	84	99
4	THF	HMPA (4)	b	80 (90)	>99

[a] Heterogeneous reaction. [b] The ratio of **6** to **8** is 7:3.

Results

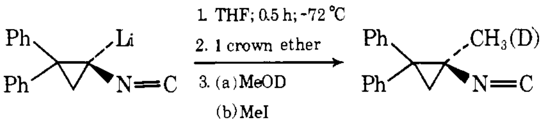
It was decided that a viable approach to this problem would be to study the α-metalation of a chiral cyclopropyl isocyanide such as 1-isocyano-2,2-diphenylcyclopropane (**6**) and to compare the results with a chiral acyclic isocyanide, 1-phenyl-2-isocyanopropane (**7**).

The chiral isocyanides **6** and **7** were prepared as shown[11b] from known starting materials (+)-(*S*)-2,2-diphenylcyclopropanecarboxylic acid[9] and (−)-(*R*)-1-phenyl-2-aminopropane (amphetamine), whose absolute configurations have been previously established.[13] Since the reactions leading to the syntheses of **6** and **7** are known to be stereochemically clean, the absolute configurations of **6** and **7** are thereby established.



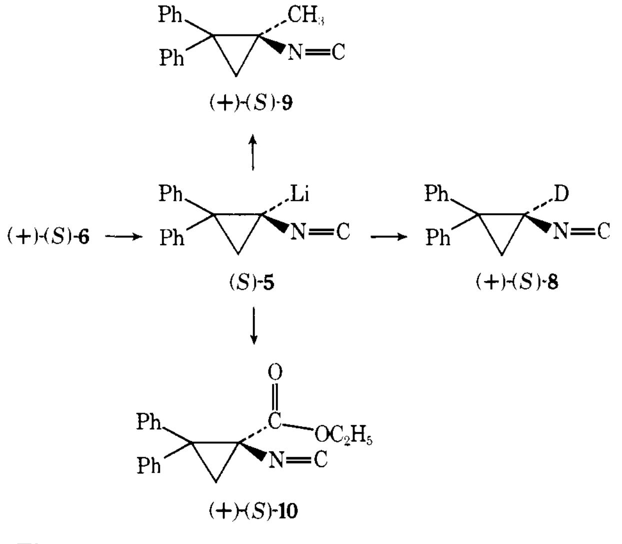
Chiral 1-Isocyano-2,2-diphenylcyclopropyllithium (5). Generation of chiral 1-isocyano-2,2-diphenylcyclopropyl-

Table V. Effect of 1 Equiv of Crown Ether on the Configurational Stability of 5



No.	Crown ether	Work-up	Yield, %	D %	CH_3	Optical purity, %
1	12-Crown-4	b	95		100	100
2	15-Crown-5	a	75	87		100
3	18-Crown-6	a	50	70		93
4	Dicyclohexyl-18-crown-6	b	79		100	100

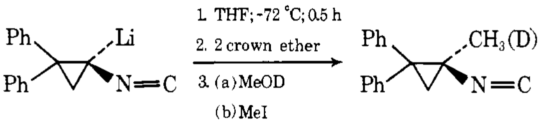
lithium (**5**) was accomplished by treating (+)-(*S*)-**6** dissolved in tetrahydrofuran with lithium diisopropylamide at −72 °C. In separate experiments, the reaction mixture, kept at −72 °C for 30 min, was hydrolyzed with methanol-*O*-*d* to yield (+)-(*S*)-1-deuterio-1-isocyano-2,2-diphenylcyclopropane (**8**), with methyl iodide to yield (+)-(*S*)-1-methyl-1-isocyano-2,2-diphenylcyclopropane (**9**), and with ethyl chloroformate to produce ethyl (+)-(*S*)-1-isocyano-2,2-diphenylcyclopropanecarboxylate (**10**). Both the alkylation[11b] and hydrolysis proceeded with complete retention of optical activity and configuration. By analogy it is expected that a similar result obtains in the reaction with ethyl chloroformate. These observations clearly illustrate that **5** is capable of maintaining its configuration at −72 °C using tetrahydrofuran as a solvent. With these encouraging results in hand we next undertook an investigation of various reaction parameters that might affect the stability of **5**: temperature, cation, solvent, and cation complexing reagents.



The temperature at which the reaction is run has a profound effect on the configurational stability of **5**, as shown in Table I. As the temperature of the reaction is raised there is a gradual loss of optical purity and at −5 °C the lithium reagent **5** has essentially racemized. It should be pointed out that the configurational stability of **5** at temperatures between −52 and −72 °C contrasts dramatically with the results obtained with its isomer 1-cyano-2,2-diphenylcyclopropyllithium, which racemizes rapidly at these temperatures.[9]

Grovenstein[14] and also Lochman and Lim[55] have demonstrated that cation exchange occurs between alkyllithium reagents and sodium or potassium alkoxides. Based on these results tetrahydrofuran solutions of **5** at −72 °C were treated with sodium and potassium *tert*-butoxide. The results shown in Table II indicate that changing the cation from lithium to sodium or potassium has no effect on the configurational stability. It has also been observed that changing the concentration of **5** in solution has no effect on the optical purity of the product. A fivefold increase or a threefold decrease in the concentration resulted in no appreciable change.

Table VI. Effect of 2 Equiv of Crown Ether on the Configurational Stability of 5



No.	Crown ether	Work-up	Yield, %	D %	CH_3	Optical purity, %
1	12-Crown-4	b	80		65[a]	
2	15-Crown-5	b[b]	77	5[b]	0	98
3	15-Crown-5	a	86	11		100
4	18-Crown-6	a	50	80		93
5	Dicyclohexyl-18-crown-6	b	77		0	92

[a] Based on NMR analysis of the reaction product mixture. [b] The starting material in this case was **8**, with 88% D.

The solvent study was limited by the insolubility of **5** in hydrocarbon solvents. However, within the limited range of ethereal solvents it was observed that changing from diethyl ether to a better solvating medium such as tetrahydrofuran or a mixture of tetrahydrofuran and 1,2-dimethoxyethane did not change the stereochemical results (Table III). Again this observation contrasts markedly from that reported by Kobrich,[10] who showed that although **4** existed in a pyramidal configuration in benzene solution the addition of a small amount of tetrahydrofuran caused a rapid inversion of configuration.

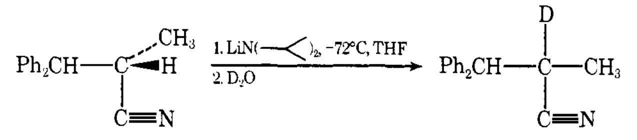
Recently Panek[16] reported that the rate of geometric isomerization of 1-lithio-1-phenyl-1-butene in hexane solution was enhanced by the addition of cation complexing reagents and the following order was observed; *N*,*N*,*N*,*N*-tetramethylethylenediamine (TMEDA) > 1,2-dimethoxyethane > tetrahydrofuran > diethyl ether. An investigation of the effect of complexing reagents on **5** was undertaken and the results are given in Tables IV–VI.

As can be seen from Table IV the addition of 1 equiv of TMEDA to a pentane or tetrahydrofuran solution of **5** has no effect on the configurational stability of **5**. Moreover, the addition of 2 equiv of triglyme or 4 equiv of HMPA to a solution of **5** did not alter the configurational stability of **5**.

The results on the addition of 1 equiv of various crown ethers to a tetrahydrofuran solution of **5** are shown in Table V. It is evident from the observed optical purity of the product that **5** maintains its configuration completely. A similar result was obtained when 2 equiv of crown ether was added (Table VI). However, in the case of the addition of 1 equiv of crown ether alkylation or deuterolysis of **5** was observed but in the presence of 2 equiv of crown ether the alkylation and deuterolysis product was markedly reduced. The extent of this reduction was dependent on the structure of the crown ether added.

α-Metalation of Acyclic Isocyanides. The metalation of (−)-(*S*)-1,1-diphenyl-2-cyanopropane[3a] (**11**) was carried out under aprotic conditions at −70 °C using lithium diisopropylamide as the base. The reaction mixture was quenched with deuterium oxide after 0.5 h to yield the deuterated product which had >95% D incorporated and was found to be completely racemized.

Under the conditions used for the reaction of **11** the reaction of (−)-(*R*)-**7** yielded a product which was 68% racemized but had no deuterium incorporated. Using a stronger base, lithium 2,2,6,6-tetramethylpiperidide,[17] in tetrahydrofuran resulted in total racemization but again no deuterium was found in the



(−)-(S)-11 (±)

product. Only when methylcyclohexane was used as the solvent and TMEDA-lithium 2,2,6,6-tetramethylpiperidide as the base system[18] was the product completely deuterated but again completely racemized. However, in contrast to the previous reactions this latter reaction was heterogeneous. Apparently under homogeneous conditions the conjugate base of **7** is strong enough to react with the medium.

Discussion

This investigation was undertaken to gain some insight into the question of how the isocyano group acts as a substituent to increase the activity of an α-hydrogen atom and also into the effect it would have on the geometry of an α carbanion. It was concluded from previous studies[3,6-9] that substituents which activate the α hydrogen by a resonance effect would favor a planar configuration for the resultant carbanion whereas substituents which operate by an inductive effect would favor a pyramidal configuration. Kobrich[10] has pointed out that the geometry of the carbanion depends not only on the substituents but also on the nature of the ion pair in solution. It will be demonstrated that in the case of **5**, with the isocyano group as an α substituent, the anion is capable of maintaining its configuration whether it exists as a contact ion pair, solvent separated ion pair, or a free ion pair and that the isocyano group operates chiefly through an inductive effect.

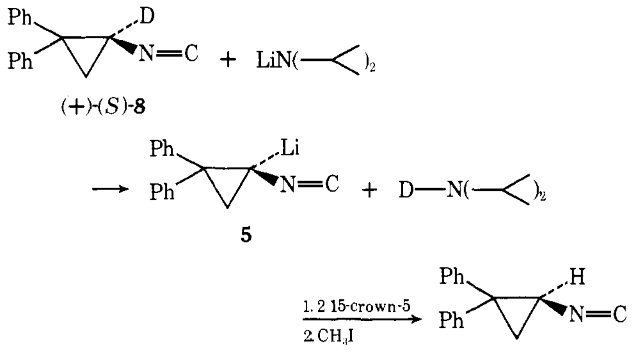
$$R^-M^+ \rightleftharpoons R^-/S/M^+ \rightleftharpoons R^- + M^+$$

There is ample evidence[2,19] that alkali metal salts of carbon acids, in aprotic solvents, exist as an equilibrium mixture of contact, solvent separated, and free ion pairs. The important factors that have been shown to affect the equilibrium in favor of solvent separated ion pairs may be summarized as follows: solvent separated ion pairs decrease in the order of the size of cation Li > Na > K > Cs;[14,20] lower temperatures;[20,21] cation complexing ability of solvent, 1,2-dimethoxyethane > tetrahydrofuran > diethyl ether;[20,22] addition of cation complexing reagents such as polyglycol dimethyl ethers,[23] HMPA,[23] and crown ethers.[24-28]

The experiments, the results of which are reported in Tables I-VI, were performed under conditions which should have resulted in the formation of solvent separated ion pairs. However, it can be seen that at −72 °C, the configuration of **5** was maintained regardless of the change of cation, solvent, or the addition of complexing reagents. In other words, **5** is capable of maintaining its configuration as a solvent separated ion pair.

Carbanion 5 as a "Free Ion Pair". Table V shows that the addition of 1 equiv of 15-crown-5 to a tetrahydrofuran solution of **5** followed by quenching with methanol-*O-d* resulted in the isolation of optically pure 1-deuterio-2,2-diphenylcyclopropyl isocyanide (**8**) in 75% yield and with 87% deuterium incorporated. However, under identical conditions except that 2 equiv of 15-crown-5 was added, the product contained only 11% deuterium. In order to establish that **5** was formed in the reaction the following experiment was carried out. The deuterated (88%) isocyanide **8** was reacted with lithium diisopropylamide, 2 equiv of 15-crown-5 was added, and after 0.5 h methyl iodide was added to the reaction mixture. The results showed that no methylated product was formed and that the product consisted only of 5% **8** and 95% **6** showing that **5** was indeed formed under the reaction conditions.

The question that arises is the source of the proton in the above reactions. Under the reaction conditions used there are three possible sources: (a) the diisopropylamine produced in the α-metalation step; (b) the crown ether; and (c) the tetrahydrofuran solvent. The above reaction where **8** was used as starting material and the product was found to contain only 5% deuterium clearly shows that the diisopropylamine cannot be the chief proton source. In order to evaluate whether the solvent was involved the reaction of **6** was carried out using tetrahydrofuran-d_8 as the solvent, adding 2 equiv of 15-crown-5 and then methyl iodide. No alkylated product was formed and the product consisted of 71% **6** and 29% **8**. It is concluded from these results, by elimination, that the main source of proton is the crown ether. Moreover, it should be pointed out that the reaction of **5** with the solvent or crown ether is complete before the addition of methyl iodide. These results show that with the addition of 1 equiv of crown ether **5** is stable but that the addition of the second equivalent causes **5** to react.

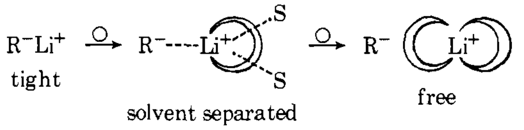


(+)-(S)-8

5

6

Is the second equivalent of crown ether necessary or will other cation complexing reagents also suffice? To clarify this point the following experiments were performed and the results shown in Table VII. As can be seen from the first entry, when 5 equiv of 1,2-dimethoxyethane-d_{10} was added to **5** followed by the addition of 1 equiv of 15-crown-5, or entry 3, the addition of a crown ether followed by 5 equiv of 1,2-dimethoxyethane-d_{10}, or as in the second entry, the addition of 15-crown-5 followed by 1 equiv of TMEDA, the results were identical with those when 2 equiv of crown ether was added.



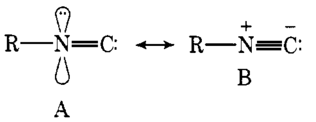
Earlier it was indicated that the addition of 1 equiv of crown ether to a tetrahydrofuran solution of **5** resulted in the formation of a solvent separated ion pair. The cation is surrounded by the crown and the anion is located at one face of the crown and solvent molecules at the other face.[29] It is proposed that the addition of a second equivalent of crown initiates a competition for the cation between the solvent molecules and the added crown ether in which the crown ether displaces the solvent molecules. This results in a strongly complexed sandwiched[28] cation which then leaves a "free" or "naked"[25a] carbanion in solution. A similar situation obtains, regardless of the order of addition, when 1 equiv of crown ether and 5 equiv of 1,2-dimethoxyethane are added to **5**. The addition of 1 equiv of TMEDA to the solvent separated ion pair produced by the addition of crown ether to **5** gives a similar result. The resulting "free" carbanion produced under these conditions, being a tertiary carbanion as well, will be extremely reactive and will abstract an available proton from its immediate surroundings largely from the crown ether, resulting in the formation of **6**. Notice the high retention of optical activity and configuration that is observed indicating that the "free carbanion" is capable of maintaining its stereochemical integrity.

The data in Table VI provide a means of comparing the ability of various crown ethers to complex the lithium cation in tetrahydrofuran solution. It can be seen that in the presence of 2 equiv of 12-crown-4, the α-isocyanocyclopropyl anion **5** yielded upon workup with methyl iodide a mixture of both **6** and **9** in yields of 35 and 65%, respectively. The addition of 2 equiv of 15-crown-5 resulted only in the regeneration of the starting material **6**. However, in the case of the addition of 2 equiv of 18-crown-6 the isolated product was mainly due (80%) to the reaction of **5** with the quenching reagent (CH_3OD). A comparison of these three crown ethers for their capacity to complex the lithium cation in order to produce the "free ion pair" shows the following order: 15-crown-5 > 12-crown-4 > 18-crown-6. Dicyclohexyl-18-crown-6 behaves more like 15-crown-5 than the unsubstituted 18-crown-6. The presence of the cyclohexane rings may be causing an interesting conformational effect in which the oxygen atoms are positioned favorably for complexing the lithium cation. The exact nature of this effect requires further investigation.

In summary, we have shown that the 1-isocyano-2,2-diphenylcyclopropyllithium (**5**) is capable of retaining its configuration as a contact, solvent separated, and free ion pair.

Isocyanide as a Substituent. The above observations have a bearing on how one should view the isocyano group as a substituent. If a substituent attached to a carbanion center is capable of delocalizing a negative charge, then the tendency to delocalize the electron pair is enhanced as the contact ion pair is converted to a solvent separated ion pair and the probability of such resonance delocalization should be at a maximum for the free ion pair. The observations made by Kobrich[10] and Panek[16] discussed earlier are in accord with this conclusion. It is clear from the results obtained with **5** that the isocyano group does not serve such a purpose and that the α-isocyano carbanion favors a pyramidal configuration.

An explanation for this behavior may be found in the structure of the isocyanide moiety itself. In resonance terminology the canonical structure A makes a much larger contribution to the overall structure than does B with its unfavorable distribution of charge. In structure A the nitrogen and the isocyano carbon atoms have their nonbonding electron pairs in a p orbital and an sp orbital, respectively. In addition the carbon is left with a vacant p orbital. Recently various ab initio calculations[30] have been reported to show, from the gross atom charges on nitrogen (−0.36) and carbon (+0.14), that the gross dipole moment of the isocyano group is directed from the terminal carbon toward the nitrogen[31]



$$\overset{\longleftarrow\!\!+}{(\mathrm{N{-}C})}$$

and not the reverse

$$\overset{+\!\!\longrightarrow}{(\mathrm{N{-}C})}$$

as has previously been believed. These data would be consistent with a nonbonding pair of electrons residing on the nitrogen atom such as in structure A.

The inversion mechanism for an α-substituted carbanion involving a planar intermediate is shown as follows:

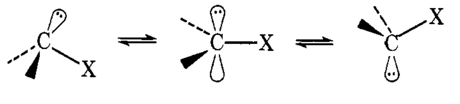
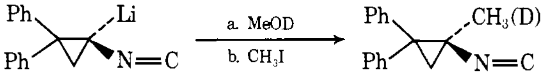


Table VII. Effect of the Addition of 1 Equiv of Crown Ether and Another Coordinating Reagent on the Configurational Stability of **5**



No.	Crown ether	Coord agent	Work-up	Yield, %	D %	CH_3	Optical purity, %
1	15-Crown-5 (1)	DME-d_{10} (5)	b	86	0	0	88
2	15-Crown-5 (1)	TMEDA (1)	a	86	<2		97
3	Dicyclohexyl-18-crown-6 (1)	DME-d_{10} (5)	b	88	0	0	88

The rate of inversion of a carbanion depends on how readily the planar intermediate or transition state is formed. The substituent X will have a marked influence on this rate with good delocalizing substituents (cyanide, carbonyl, etc.) increasing the rate owing to stabilization of the planar intermediate and poor ones (fluorine, chlorine) decreasing it by destabilizing the planar form. The destabilization by fluorine and chlorine of the planar intermediate is due to the repulsive interaction between the nonbonding pair of electrons in a p orbital of the heteroatom and the adjacent electron pair in a p orbital on carbon.[32] A striking example is the nitrogen analogue of the cyclopropyl anion, the aziridine system. *N*-Chloro, *N*-methoxyl, and *N*-amino aziridines exist as stable pyramidal structures at room temperature.[33] A comparable destabilization of the planar intermediate which would be involved in the inversion of **5** is possibly due to the repulsive interaction of the electron-rich p orbital of the nitrogen atom of the isocyano group and the electron pair of the carbanion.

The isocyanide moiety, based on our observations, does not act as a delocalizing substituent. It behaves as an electron-withdrawing group operating largely through an inductive effect. This conclusion is supported by the positive σ^+ value found for the isocyanide group.[34] It should also be noted that in contrast to the cyclopropyl system **6**, the acyclic system **7** racemized. The enhanced acidity of **6** over that of **7** is due to the greater s character associated with the cyclopropyl carbon. The larger configurational stability of **5** as compared to the anion of **7** is due to the strain in the ring system.

Experimental Section

Melting points were measured with a Mel-Temp apparatus and are uncorrected. Infrared spectra were obtained using a Perkin-Elmer Model 257 spectrophotometer. Nuclear magnetic resonance spectra were recorded on a Brucker 90 or 270-MHz spectrophotometer; chemical shifts are reported in parts per million downfield from tetramethylsilane and coupling constants are in hertz. Optical rotatory and circular dichroism spectra were recorded with a JASCO-5 and optical rotations at 5461 Å with a Bendix-Ericson Model 987 ETL/NPL polarimeter. Microanalyses were performed by the Beller Laboratories, Göttingen, Germany.

Solvents. Reagent grade tetrahydrofuran (THF) and diethyl ether were distilled from lithium aluminum hydride under nitrogen and stored over 3A molecular sieves. Bulk solvents were distilled before use. Industrial grade dimethylformamide (DMF) was purified by distilling from barium oxide.

Reagents. Organolithium reagents, purchased from Foot Minerals Co., were titrated before use.[35] TMEDA (99%) purchased from Aldrich was kept over solid sodium hydroxide and used with no further purification. DME, triglyme, and crown ethers were passed through activated alumina before use. DME-d_{10} was purchased from Merck and Co., Inc., and was used with no further purification. All other reagent grade materials were purified by distillation.

Deuterium Content Determination. The determination of the ratio of **6** to **8** in a reaction was made as follows. Comparison of the IR and melting point of the isolated product with that of pure **6** was made in each case to rule out the presence of any other product. The NMR spectrum of the mixture was recorded on a Brucker 90 or 270 MHz spectrophotometer. The amount of **6** and thus the ratio of **6** to **8** in the mixture was estimated by comparing the integration of the α-isocyanocyclopropyl proton (3.30–3.50 ppm) with that of the cyclopropyl methylene protons (1.5–1.95 ppm). This determination was checked by comparing the integration of the α-isocyanocyclopropyl proton with that of phenyl protons.

(+)-(*S*)-*N*-(2,2-Diphenylcyclopropyl)formamide. To a mixture of 7.5 g (0.0315 mol) of (*S*)-(+)-2,2-diphenylcyclopropanecarboxylic acid, $[\alpha]^{25.7}{}_{5461}$ +271.9° (*c* 0.74, $CHCl_3$), and 4 g (0.04 mol) of triethylamine dissolved in 100 mL of acetone was added at room temperature 3.81 mL (0.04 mol) of ethyl chloroformate in 15 mL of acetone and the mixture stirred for 1 h. Sodium azide (4.6 g, 0.035 mol) dissolved in 40 mL of water was added and the reaction mixture was stirred for 4 h, to yield upon workup 8 g (0.03 mol) of crude acyl azide. The crude acyl azide was dissolved in benzene and the reaction mixture was refluxed for 7 h to give a quantitative yield of isocyanate. The isocyanate, without isolation, was dissolved in 30 mL of THF and added slowly (1 h), under a nitrogen atmosphere at −13 °C, to a solution of 11.5 g (0.045 mol) of lithium *tert*-butoxyaluminum hydride dissolved in 40 mL of THF. After 2 h of additional stirring, 20 mL of 50% formic acid was added dropwise under rapid stirring (−13 °C). The mixture was extracted with ether, washed with dilute hydrochloric acid and saturated sodium carbonate solution, and dried over anhydrous magnesium sulfate. Evaporation of the solvent gave 6.4 g of the crude formamide which was crystallized from benzene–pentane to yield 4.6 g (0.0195 mol, 65%), mp 140–142 °C. Recrystallization gave the pure formamide: mp 144–146 °C; $[\alpha]^{25.7}{}_{5461}$ +72.6° (*c* 0.69, $CHCl_3$); IR ($CHCl_3$) 3405, 1685 cm^{-1} (s); NMR ($CDCl_3$) δ 1.52–1.57 (m, 2), 3.55–3.75 (m, 1), 5.4–5.8 (broad, 1, NH), 7.1–7.45 (m, 10, aromatic), 7.9 (s, 1, CHO).

Anal. Calcd for $C_{16}H_{15}NO$: C, 80.98; H, 6.38; N, 5.90. Found: C, 81.01; H, 6.40; N, 5.90.

(+)-(*S*)-2,2-Diphenylcyclopropyl Isocyanide (6). Following the procedure developed previously[11b] 4.6 g (0.0195 mol) of optically pure (+)-(*S*)-*N*-(2,2-diphenylcyclopropyl)formamide dissolved in 80 mL of DMF was treated with 2.4 mL (0.033 mol) of thionyl chloride in 10 mL of DMF followed by 7.2 g (0.066 mol) of sodium carbonate. The crude product was purified by column chromatography (neutral alumina) and recrystallized from ether to give 2.65 g (0.012 mol, 60%) of isocyanide: mp 129–131 °C; $[\alpha]^{25.7}{}_{5461}$ +353 ± 2° (*c* 0.43, $CHCl_3$); IR ($CHCl_3$) 2140 cm^{-1} (s); NMR ($CDCl_3$) δ 1.5–1.95 (m, 2), 3.32–3.47 (q, 1, $J_{AB} = 8$, $J_{AB'} = 5$ Hz), 7.2–7.35 (m, 10, aromatic); ORD (*c* 0.05, CH_3OH), 25 °C $[\phi]_{350}$ +6570°, $[\phi]_{272}$ +22 390°, $[\phi]_{269}$ +17 950°, $[\phi]_{264}$ +21 900°, $[\phi]_{261}$ +18 400°, $[\phi]_{253}$ +21 900°, $[\phi]_{250}$ +25 400°, $[\phi]_{240}$ +38 500°; CD (*c* 0.05, CH_3OH), 25 °C $\Delta\epsilon_{350}$ +0.0088, $\Delta\epsilon_{275}$ +0.0044, $\Delta\epsilon_{269}$ +0.5256, $\Delta\epsilon_{265}$ +0.429, $\Delta\epsilon_{261}$ +0.5692, $\Delta\epsilon_{254.5}$ +0.4554, $\Delta\epsilon_{250}$ +0.3167, $\Delta\epsilon_{240}$ +0.1927, $\Delta\epsilon_{234}$ +0.3416, $\Delta\epsilon_{232}$ +0.2365.

Anal. Calcd for $C_{16}H_{13}N$: C, 87.67; H, 5.99. Found: C, 87.63; H, 6.02.

Reaction of 1-Lithio-1-isocyano-2,2-diphenylcyclopropane (5) in THF with Methyl Iodide. In a typical experiment, a THF solution of lithium diisopropylamide (LDA, 6 mmol) kept under a nitrogen atmosphere was cooled to −72 °C and a 5-mL solution of 220 mg (1 mmol) of (+)-(*S*)-2,2-diphenylcyclopropyl isocyanide (optical purity 98 ± 2%) was added over a 10-min period. The reaction mixture was stirred for 30 min and 1.5 g (10 mmol) of methyl iodide in 5 mL of THF was added over a 10-min period. The reaction mixture was allowed to warm to ambient temperature and then poured onto ice water. The ether extract was dried and stripped and the product was purified by column chromatography (neutral alumina) to yield 224 mg (96%) of (+)-(*S*)-1-methyl-2,2-diphenylcyclopropyl isocyanide (**9**), mp 147–151 °C, optical purity 95.4%. IR and NMR spectra were identical with those of an authentic sample.[11b]

In a similar manner, reactions were carried out at −52 ± 1, −25 ± 2, and −5 ± 1 °C.

Reaction of 1-Lithio-1-isocyano-2,2-diphenylcyclopropane (5) in THF with MeOD. In a like manner, 1-lithio-1-isocyano-2,2-diphenylcyclopropane was reacted with MeOD (>99% isotopic purity) at −71 °C to give (+)-(*S*)-1-deuterio-1-isocyano-2,2-diphenylcyclopropane (**8**) in 70% yield: mp 127–129 °C; optical purity 97.5%; NMR ($CDCl_3$) δ 1.67 (d, 1, $J_{AB} = 6$ Hz), 1.89 (d, 1, $J_{AB} = 6$ Hz), 7.21–7.37 (m, 10, aromatic).

Reaction of 1-Lithio-1-isocyano-2,2-diphenylcyclopropane (5) in THF with Ethyl Chloroformate. In a similar manner, 1-lithio-1-isocyano-2,2-diphenylcyclopropane was reacted with ethyl chloroformate at −72 °C to give ethyl (+)-(*S*)-1-isocyano-2,2-diphenylcyclopropylcarboxylate (**10**) in 44% yield: mp 171–173 °C; $[\alpha]^{26}{}_{Hg}$ +146° (*c* 0.3, $CHCl_3$); IR ($CHCl_3$) 2140, 1730 cm^{-1} (s); NMR ($CDCl_3$) δ 1 (t, 3, $J_{AB} = 7$ Hz), 2.2 (d, 1, $J = 6$ Hz, HCHO), 2.6 (d, 1, $J = 6$ Hz, HCH), 3.75–4.2 (m, 2), 7.1–7.65 (m, 10, aromatic).

Anal. Calcd for $C_{19}H_{17}NO_2$: C, 78.33; H, 5.88. Found: C, 78.16; H, 5.97.

Reaction of 1-Lithio-1-isocyano-2,2-diphenylcyclopropane (5) in Diethyl Ether. To a stirred solution of LDA (5 mmol) dissolved in diethyl ether at −72 °C under a nitrogen atmosphere was added 220 mg (1 mmol) of (+)-(*S*)-2,2-diphenylcyclopropyl isocyanide (optical purity 94%) dissolved in 3 mL of diethyl ether and 1 mL of THF. The reaction mixture was stirred for a period of 30 min and quenched with an excess of deuterium oxide in 3 mL of THF. The temperature was allowed to rise to 0 °C and the reaction mixture extracted with ether. The purification of the crude product yielded 185 mg (84%) of **8** (90 ± 2% deuterium incorporation), mp 126–129 °C, optical purity 99%.[36]

Reaction of 1-Lithio-1-isocyano-2,2-diphenylcyclopropane (5) in THF–DME Mixture. To a stirred solution of LDA (5 mmol) dissolved in 30 mL of THF at −72 °C under a nitrogen atmosphere was added 220 mg (1 mmol) of (−)-(*R*)-2,2-diphenylcyclopropyl isocyanide (optical purity 98%) dissolved in 2 mL of THF. After the reaction mixture was stirred for 10 min 16 mL of DME was added over a period of 10 min with the temperature being kept at <−70 °C. The reaction mixture was stirred for 20 min and treated with an excess of MeI. The isolated crude product was purified by column chromatography to give 210 mg (91%) of (−)-(*R*)-1-methyl-2,2-diphenylcyclopropyl isocyanide (**9**), mp 145–150 °C, optical purity 98.2%. IR and NMR spectra were identical with those of an authentic sample.[11b]

Effect of the Addition of Sodium *tert*-Butoxide to 5. To a 3 mmol solution of LDA in 30 mL of THF at −72 °C under a N_2 atmosphere was added 220 mg of (+)-(*S*)-2,2-diphenylcyclopropyl isocyanide dissolved in 3 mL of THF. The reaction mixture was stirred for 15 min and 3.5 mmol of freshly prepared sodium *tert*-butoxide in 5 mL of THF was added. After stirring for 30 min, the reaction mixture was treated with an excess of deuterium oxide in THF. Standard isolation procedure yielded 175 mg (78%) of **8**, mp 121–124 °C, optical purity 96%. NMR analysis indicated 98% deuterium content.

Reaction of 1-Lithio-1-isocyano-2,2-diphenylcyclopropane (5) in Pentane in Presence of TMEDA. To a pentane solution of LDA (4.5 mmol) kept under a nitrogen atmosphere at −72 °C was quickly added a mixture of 220 mg (1 mmol) of (−)-(*R*)-2,2-diphenylcyclopropyl isocyanide (optical purity 98%) and 6.5 mmol of TMEDA dissolved in 2 mL of pentane. The heterogeneous reaction mixture was stirred for 30 min and an excess of MeOD was added over a period of 5 min. The reaction mixture was allowed to warm to ambient temperature and poured onto ice water. The ether extract was dried and the crude product obtained after removing the solvent was purified by column chromatography to give 155 mg (70%) of **6** and **8**, mp 122–125 °C, optical purity 93%. NMR analysis indicated the ratio of **6** to **8** as 7:3.

Reaction of 1-Lithio-1-isocyano-2,2-diphenylcyclopropane (5) in THF in Presence of TMEDA. To a THF solution of LDA (5.5 mmol) kept under a nitrogen atmosphere at −72 °C was added 220 mg of (−)-(*R*)-2,2-diphenylcyclopropyl isocyanide (optical purity 98%) dissolved in 3 mL of THF and the reaction mixture was stirred for 10 min. TMEDA (6.5 mmol) dissolved in 5 mL of THF was added and the reaction mixture was stirred for 30 min at −72 °C. Excess of methyl iodide was added, and the product was isolated as before and purified following the usual procedure to give 163 mg (70%) of (−)-(*R*)-1-methyl-2,2-diphenylcyclopropyl isocyanide (**9**), mp 149–151 °C, optical purity ~100%. IR and NMR spectra were identical with those of an authentic sample.

Reaction of 1-Lithio-1-isocyano-2,2-diphenylcyclopropane (5) in THF in Presence of Triglyme. To a THF solution of LDA (3 mmol) kept under a nitrogen atmosphere at −72 °C was added 220 mg of (+)-(*S*)-2,2-diphenylcyclopropyl isocyanide (optical purity 96%) dissolved in 3 mL of THF and the solution was stirred for 10 min. Triglyme (1.1 g, 6 mmol) dissolved in 1 mL of THF was added and the reaction mixture was stirred for 30 min at −72 °C. Excess of D_2O was added and the crude product was purified to yield 184 mg (84%) of (+)-(*S*)-1-deuterio-2,2-diphenylcyclopropyl isocyanide (**8**), mp 128–129 °C, optical purity 99% (90% deuterium incorporation). IR and NMR spectra were identical with those of an authentic sample.

Reaction of 1-Lithio-1-isocyano-2,2-diphenylcyclopropane (5) in THF in Presence of HMPA. To a THF solution of LDA (5 mmol) kept under a nitrogen atmosphere at −72 °C was added 260 mg of (−)-(*R*)-2,2-diphenylcyclopropyl isocyanide (optical purity 96%) dissolved in 3 mL of THF. After 15 min 3.6 g (20 mmol) of HMPA in 3 mL of THF was added. The reaction mixture was stirred for 30 min at −72 °C and quenched with an excess of MeOD. Purification of the crude product gave 210 mg (80% yield) of (−)-(*R*)-1-deuterio-2,2-diphenylcyclopropyl isocyanide (**8**) (90% deuterium incorporation), mp 128–130 °C, optical purity >99%. IR and NMR spectra were identical with those of an authentic sample.

Reaction of 1-Lithio-1-isocyano-2,2-diphenylcyclopropane in Presence of 1 Equiv of Crown Ether. To a stirred solution of LDA (2.5 mmol) in 30 mL of THF under a nitrogen atmosphere at −72 °C was added a mixture of 220 mg (1 mmol) of (+)-(*S*)-2,2-diphenylcyclopropyl isocyanide (optical purity 100%) dissolved in 3 mL of THF. The reaction mixture was stirred for 5 min and 3 mmol of dicyclohexyl-18-crown-6 dissolved in 5 mL of THF was added at a temperature of <−70 °C. After stirring for 0.5 h the reaction mixture was treated with an excess of MeI, allowed to warm to ambient temperature, and poured onto ice water. The ether extract was dried and the crude product obtained was purified by column chromatography to give 182 mg (79%) of (+)-(*S*)-1-methyl-2,2-diphenylcyclopropyl isocyanide (**9**), mp 148–152 °C, optical purity 101%. IR and NMR spectra were identical with those of an authentic sample.

Reaction of 1-Lithio-1-isocyano-2,2-diphenylcyclopropane in Presence of 2 Equiv of Crown Ether. To a 3-mmol solution of LDA in 30 mL of THF at −72 °C under a nitrogen atmosphere was added 220 mg (1 mmol) of (−)-(*R*)-2,2-diphenylcyclopropyl isocyanide (optical purity 100%) dissolved in 3 mL of THF to give a light yellow solution. The reaction mixture was stirred for 5 min and 6 mmol of dicyclohexyl-18-crown-6 dissolved in 5 mL of THF was added slowly at a temperature of <−70 °C and the color of the solution changed from yellow to dark brown. The clear solution was stirred for an additional 30 min and reacted with an excess of methyl iodide. The crude product isolated as above was purified by column chromatography to give 170 mg (77%) of **6**, mp 125–127 °C, optical purity 92%.

Effect of Successive Addition of Dicyclohexyl-18-crown-6 and DME-d_{10} to 5. In a similar manner, to a solution of **5** in THF at −72 °C under a nitrogen atmosphere was added 1 equiv of dicyclohexyl-18-crown-6, followed by 5 equiv of DME-d_{10} in 15 min, and finally, after stirring for a period of 0.5 h, the reaction mixture was treated with an excess of MeI. Standard workup and purification of the reaction product gave **6** in 88% yield, mp 122–124 °C, optical purity 88 ± 2%.

Effect of Successive Addition of TMEDA and 15-Crown-5 to 5. An identical reaction as above was carried out first by adding 1 equiv of TMEDA to **5**, followed by 1 equiv of 15-crown-5 in 20 min and working up the reaction with an excess of MeOD after stirring the reaction mixture for 30 min. Standard workup and purification of the reaction product resulted in the isolation of **6** in 86% yield with 97% optical purity.

Effect of Successive Addition of DME-d_{10} and 15-Crown-5 to 5. To a stirred solution of LDA (3 mmol) in THF under a nitrogen atmosphere at −72 °C was added 150 mg of (+)-(*S*)-2,2-diphenylcyclopropyl isocyanide dissolved in 3 mL of THF. After stirring for 10 min, 15 mmol of DME-d_{10} was added and the reaction mixture was stirred for 15 min at −72 °C to give a pale yellow solution. As 3.2 mmol of 15-crown-5 in 2 mL of THF was added, the color of the reaction mixture changed from yellow to a dark color. The solution was stirred for 25 min at −72 °C and an excess of MeI was added. The temperature was allowed to rise to 0 °C and the reaction mixture was poured onto ice water. Standard workup and purification yielded 130 mg (86%) of **6**, mp 124–126 °C, optical purity 88 ± 2%.

Experiment to Show That Diisopropylamine Does Not React with 5 in THF in Presence of 2 Equiv of 15-Crown-5. To a THF solution of LDA (3 mmol) at −72 °C under a nitrogen atmosphere was added 220 mg of (+)-(*S*)-1-deuterio-2,2-diphenylcyclopropyl isocyanide (61% optical purity, 88% deuterium content) dissolved in 3 mL of THF. After 15 min, 1.45 g (7 mmol) of 15-crown-5 was added and stirring was continued for 30 min. The reaction mixture was treated with an excess of MeI. The crude product was purified by column chromatography to yield 170 mg (77%) of (+)-(*S*)-2,2-diphenylcyclopropyl isocyanide (59% optical purity, 5% deuterium), mp 96–112 °C. IR and NMR spectra were identical with those of an authentic sample.

Reaction of 1-Lithio-1-isocyano-2,2-diphenylcyclopropane (5) in THF-d_8 in Presence of 2 Equiv of 15-Crown-5. To a THF-d_8 solution of LDA (prepared from 1 mmol of diisopropylamine and 1.32 mmol of *n*-butyllithium) kept under nitrogen atmosphere at −72 °C was added 55 mg of 2,2-diphenylcyclopropyl isocyanide dissolved in 1 mL of THF-d_8. After stirring for a period of 30 min 0.61 g (2.8 mmol) of 15-crown-5 dissolved in 1 mL of THF-d_8 was added. The reaction mixture was stirred for 30 min and treated with an excess of MeI. NMR analysis of the crude product indicated the absence of methylated product. The product was purified using column chromatography and NMR spectrum analysis showed the amount of deuterium incorporation to be 28.6%.

(+)-(*R*)-*N*-(1-Benzylethyl)formamide. A solution of 27 g (0.2 mol) of (−)-(*R*)-1-phenyl-2-aminopropane in 100 mL of ethyl formate was refluxed in the presence of a trace of *p*-toluenesulfonic acid for 24 h. Evaporation of solvent and vacuum distillation yielded 26 g (0.16 mol) of formamide, bp 146–147 °C (1.75 mm), mp 48–52 °C. Recrystallization from an ether–petroleum ether mixture gave pure formamide: mp 51–53 °C; $[\alpha]^{25}{}_{5461}$ +21.87° (*c* 2.8, $CHCl_3$); IR (CCl_4) 3410, 1695 cm^{-1} (s); NMR ($CDCl_3$) δ 1.07 (d, 3, J_{AB} = 7.25 Hz), 2.4–3.0 (m, 2), 4.0–4.4 (m, 1), 7.1 (s, 5, aromatic), 7.3–7.7 (1, -NH-), 7.9 (s, 1, O=CH).

Anal. Calcd for $C_{10}H_{13}NO$: C, 73.61; H, 8.05; N, 8.59. Found: C, 73.74; H, 8.03; N, 8.52.

(−)-(*R*)-1-Phenyl-2-isocyanopropane. Following the procedure developed earlier,[11b] 24 g (0.15 mol) of optically pure (+)-(*R*)-*N*-(1-benzylethyl)formamide dissolved in 200 mL of DMF was treated with 12.8 mL (0.175 mol) of thionyl chloride dissolved in 50 mL of DMF followed by 37.1 g (0.35 mol) of sodium carbonate. The crude product was distilled to give 12.4 g of pure isocyanide in 60% yield: bp 76 °C (1.25 mm); $[\alpha]^{24.5}{}_{5461}$ −57.2° (*c* 1.855, $CHCl_3$); IR (CCl_4) 2140 cm^{-1}; NMR ($CDCl_3$) δ 1.2–1.36 (m, 3), 2.7–2.9 (m, 2), 3.15–4.0 (m, 1), 7.22 (m, 5, aromatic).

Anal. Calcd for $C_{10}H_{11}N$: C, 82.7; H, 7.63. Found: C, 82.74; H, 7.58.

α-Metalation of (−)-(*S*)-2-Methyl-3,3-diphenylpropionitrile[3a] with LDA in THF Solvent. To a THF solution of LDA (5 mmol) at −70 °C under a nitrogen atmosphere was added 220 mg (1 mmol) of (−)-(*S*)-2-methyl-3,3-diphenylpropionitrile dissolved in 3 mL of THF. The reaction mixture was stirred for 30 min and treated with an excess of D_2O at −72 °C. Standard workup yielded 135 mg (60% yield) of racemic 2-deuterio-2-methyl-3,3-diphenylpropionitrile (95% deuterium incorporation), mp 57–61 °C. IR and NMR spectra were identical with those of an authentic sample.[3a]

α-Metalation of (−)-(*R*)-1-Phenyl-2-isocyanopropane by Lithium 2,2,6,6-Tetramethylpiperidide in THF. To a solution of 6 mmol of lithium 2,2,6,6-tetramethylpiperidide in THF at −72 °C under a nitrogen atmosphere was added a solution of 365 mg (2.5 mmol) of (−)-(*R*)-1-phenyl-2-isocyanopropane (100% optical purity) dissolved in 4 mL of THF. The clear green solution was stirred for 30 min at −72 °C and quenched with an excess of MeOD. After the temperature was raised to 0 °C the reaction mixture was poured onto ice water. The ether extract was dried ($MgSO_4$), the solvent evaporated, and the residue purified by column chromatography on alumina to give 53 mg (14%) of racemic 1-phenyl-2-isocyanopropane which had no deuterium incorporated. The IR and NMR spectra were identical with those of an authentic sample.

α-Metalation of (−)-(*R*)-1-Phenyl-2-isocyanopropane by Lithium Diisopropylamide in THF. In a similar manner to that described above but using lithium diisopropylamide as the base a quantitative yield of starting material was recovered with no deuterium incorporation. The optical purity was 67%. A similar result was obtained when the reaction was allowed to proceed for 1.5 h. No deuterium incorporation was observed and the products were ~68% optically pure.

α-Metalation of (−)-(*R*)-1-Phenyl-2-isocyanopropane by LTMP in Methylcyclohexane Solvent in Presence of an Excess of TMEDA. To 6 mmol of lithium 2,2,6,6-tetramethylpiperidide dissolved and kept in methylcyclohexane at −72 °C under a nitrogen atmosphere was added 365 mg (2.5 mmol) of (−)-(*R*)-1-phenyl-2-isocyanopropane (optical purity 100%) in 4 mL of 1:1 mixture of methylcyclohexane and TMEDA. The colloidal reaction mixture was stirred for 30 min at −72 °C and was quenched with an excess of MeOD. The temperature was allowed to rise to 0 °C and the mixture was poured onto ice water. The ether extract was dried over anhydrous $MgSO_4$, solvent evaporated, and the residue purified by column chromatography to give 255 mg (70% yield) of 1-phenyl-2-deuterio-2-isocyanopropane

(100% D incorporated), optical purity 0%. IR and NMR spectra were identical with those of an authentic sample.

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References and Notes

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(2) (a) M. Szwarc, Ed., "Ions and Ion Pairs in Organic Reactions", Vol. 1, Interscience, New York, N.Y., 1972; (b) J. Smid, *Angew. Chem., Int. Ed. Engl.*, **11**, 112 (1972); (c) N. E. Howe, E. W. Yankee, and D. J. Cram, *J. Am. Chem. Soc.*, **95**, 4230 (1973); (d) H. M. Walborsky and M. S. Aronoff, *J. Organomet. Chem.*, **51**, 31, 55 (1973), and references cited therein; (e) H. L. Elbe and G. Kobrich, *Tetrahedron Lett.*, 2557 (1974); (f) E. Grovenstein Jr., and J. U. Rhee, *J. Am. Chem. Soc.*, **97**, 769 (1975), and references cited therein; (g) F. Guibe and G. Bram, *Bull. Soc. Chim. Fr.*, 933 (1974).

(3) (a) H. M. Walborsky and J. M. Motes, *J. Am. Chem. Soc.*, **92**, 2445, 3697 (1970); (b) H. M. Walborsky and L. M. Turner, *ibid.*, **94**, 2273 (1972); (c) J. F. Arnett and H. M. Walborsky, *ibid.*, **94**, 3678 (1972).

(4) (a) D. A. Jaeger, M. D. Broadhurst, and D. J. Cram, *J. Am. Chem. Soc.*, **95**, 7526 (1973), and references cited therein; (b) J. Almy, D. H. Hoffman, K. C. Chu, and D. J. Cram, *ibid.*, **95**, 1185 (1973).

(5) W. A. Bernett, *J. Chem. Educ.*, **44**, 17 (1967); L. N. Ferguson, *ibid.*, **47**, 46 (1970); H. M. Walborsky, *Rec. Chem. Prog.*, **23**, 75 (1962).

(6) (a) H. M. Walborsky and F. J. Impastato, *J. Am. Chem. Soc.*, **81**, 5835 (1959); (b) H. M. Walborsky and A. E. Young, *ibid.*, **83**, 2595 (1961); (c) H. M. Walborsky, F. J. Impastato, and A. E. Young, *ibid.*, **86**, 3283 (1964).

(7) J. B. Pierce and H. M. Walborsky, *J. Org. Chem.*, **33**, 1962 (1968).

(8) H. M. Walborsky, L. E. Allen, H. J. Traenkner, and E. J. Powers, *J. Org. Chem.*, **36**, 2937 (1971).

(9) H. M. Walborsky and F. M. Hornyak, *J. Am. Chem. Soc.*, **77**, 6026 (1955).

(10) (a) G. Kobrich and D. Merkel, *Justus Liebigs Ann. Chem.*, **761**, 50 (1972); (b) G. Kobrich, D. Merkel, and K. Imkampe, *Chem. Ber.*, **106**, 2017 (1973).

(11) (a) H. M. Walborsky, G. E. Niznik, and M. P. Periasamy, *Tetrahedron Lett.*, 4965 (1971); (b) H. M. Walborsky and G. E. Niznik, *J. Org. Chem.*, **37**, 187 (1971); (c) G. E. Niznik, W. H. Morrison III, and H. M. Walborsky, *ibid.*, **39**, 600 (1974); (d) N. Hirowatari and H. M. Walborsky, *ibid.*, **39**, 604 (1974); (e) G. E. Niznik and H. M. Walborsky, *ibid.*, **39**, 608 (1974); (f) M. P. Periasamy and H. M. Walborsky, *ibid.*, **39**, 611 (1974).

(12) For a preliminary communication see H. M. Walborsky and M. P. Periasamy, *J. Am. Chem. Soc.*, **96**, 3711 (1974).

(13) (a) H. M. Walborsky and C. G. Pitt, *J. Am. Chem. Soc.*, **84**, 4831 (1962); (b) W. Klyne and J. Buckingham, "Atlas of Stereochemistry", Oxford University Press, London, 1974.

(14) E. Grovenstein, Jr., and R. E. Williamson, *J. Am. Chem. Soc.*, **97**, 646 (1975).

(15) (a) L. Lochmann and D. Lim, *J. Organomet. Chem.*, **28**, 153 (1971); (b) L. Lochmann, J. Pospisil, and D. Lim, *Tetrahedron Lett.*, 257 (1966); (c) W. J. Trepka, F. A. Faure, and R. E. Sonnenfeld, *J. Organomet. Chem.*, **55**, 221 (1973).

(16) E. J. Panek, B. L. Neff, H. Chu, and M. G. Panek, *J. Am. Chem. Soc.*, **97**, 3996 (1975).

(17) R. A. Olofson and C. M. Dougherty, *J. Am. Chem. Soc.*, **95**, 582 (1973).

(18) E. P. Kyba, *J. Am. Chem. Soc.*, **97**, 2554 (1975).

(19) (a) J. R. Murdock and A. Streitwieser, Jr., *Intra-Sci. Chem. Rep.*, **7**, 45 (1973); (b) J. Plodinec and T. E. Hogen-Esch, *J. Am. Chem. Soc.*, **96**, 5262 (1974); (c) R. H. Cox and H. W. Terry, Jr., *J. Magn. Reson.*, **14**, 317 (1974).

(20) (a) T. E. Hogen-Esch and J. Smid, *J. Am. Chem. Soc.*, **88**, 307 (1966); (b) J. B. Grutzner, J. M. Lawlor, and J. M. Jackman, *ibid.*, **94**, 2306 (1972).

(21) E. J. Panek and T. J. Rodgers, *J. Am. Chem. Soc.*, **96**, 6921 (1974).

(22) (a) H. O. House, A. V. Prabhu, and W. V. Phillips, *J. Org. Chem.*, **41**, 1209 (1976); (b) E. S. Gore and H. S. Gutowsky, *J. Phys. Chem.*, **73**, 2515 (1969).

(23) (a) L. L. Chan and J. Smid, *J. Am. Chem. Soc.*, **89**, 4547 (1967); (b) P. M. Atlani, J. F. Biellmann, S. Dube, and J. J. Vicens, *Tetrahedron Lett.*, 2665 (1974); (c) J. F. Biellman and J. J. Vicens, *ibid.*, 2915 (1974); (d) A. W. Langer, Ed., "Polyamine-Chelated Alkali Metal Compounds", American Chemical Society, Washington, D.C., 1974.

(24) (a) C. J. Peterson and H. K. Frensdroff, *Angew. Chem., Int. Ed. Engl.*, **11**, 16 (1972); (b) L. F. Kindoy, *Chem. Soc. Rev.*, **4**, 421 (1975); (c) G. W. Gokel and H. D. Durst, *Synthesis*, 168 (1976).

(25) (a) C. L. Liotta and H. P. Harris, *J. Am. Chem. Soc.*, **96**, 2250 (1974); (b) D. J. Sam and H. E. Simmons, *ibid.*, **96**, 2252 (1974); (c) J. San Filippo, Jr., C. I. Chern, and J. S. Valentine, *J. Org. Chem.*, **40**, 1678 (1975); (d) C. Cambillau, P. Sarthou, and G. Bram, *Tetrahedron Lett.*, 281 (1976).

(26) K. H. Wong, G. Konizer, and J. Smid, *J. Am. Chem. Soc.*, **92**, 666 (1970).

(27) Ting-Pol and E. Grunwald, *J. Am. Chem. Soc.*, **96**, 2879 (1974).

(28) J. A. Orvik, *J. Am. Chem. Soc.*, **98**, 3322 (1976).

(29) H. K. Frensdroff, *J. Am. Chem. Soc.*, **93**, 600 (1971).

(30) (a) E. Clementi and D. Klint, *J. Chem. Phys.*, **50**, 4899 (1969); (b) L. C. Snyder and H. Basch, "Molecular Wave Functions and Properties", Wiley, New York, N.Y., 1972, p T172; (c) T. K. Ha, *J. Mol. Struct.*, **11**, 185 (1972); (d) G. H. Loew and S. Chang, *Tetrahedron*, **27**, 3069 (1971).

(31) S. N. Ghosh, R. Trambarulo, and W. Gordy, *J. Chem. Phys.*, **21**, 308 (1953).

(32) (a) D. Holtz, *Prog. Phys. Org. Chem.*, **8**, 1 (1971); (b) K. J. Klabunde and D. J. Buron, *J. Am. Chem. Soc.*, **94**, 5985 (1972); (c) A. Streitwieser, Jr., and F. Mares, *ibid.*, **90**, 2444 (1968).

(33) (a) S. J. Brois, *J. Am. Chem. Soc.*, **90**, 508 (1968); (b) D. Felix and A. Eschenmoser, *Angew. Chem., Int. Ed. Engl.*, **7**, 224 (1968); (c) S. J. Brois, *J. Am. Chem. Soc.*, **92**, 1079 (1970); (d) J. B. Lambert, *Top. Stereochem.*, **6**, 19 (1971).

(34) R. W. Stephany, Thesis, University of Utrecht, Utrecht, 1973, p 68.

(35) R. L. Epplex and J. A. Dixon, *J. Organomet. Chem.*, **8**, 176 (1967).

(36) The optical purity reported here and in subsequent experiments is based on the optical purity of the starting material and adjusted to 100%.

Radical Detection in Benzylic Halide–Aromatic Radical Anion Reactions by Continuous Flow Electron Spin Resonance Spectroscopy

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Abstract: An apparatus for the study of radical intermediates in the reaction of sodium naphthalene with organic halides in tetrahydrofuran by the continuous flow ESR method is described. The successful detection of bis(3,5-di-*tert*-butylphenyl)methyl radicals, **2**, from bis(3,5-di-*tert*-butylphenyl)methyl bromide has provided direct physical evidence for the existence of radical intermediates in reductions of halides by aromatic radical anions.

The reaction of aromatic radical anions with alkyl halides is believed to produce radical and carbanion intermediates sequentially as precursors to products.[2a-c] The currently accepted mechanistic scheme is shown in schematic form in eq 1.

$$RX + NaC_{10}H_8 \rightarrow R\cdot \xrightarrow{NaC_{10}H_8} R{:}^- \rightarrow \text{products} \qquad (1)$$

The evidence for the existence of radicals as intermediates comes from CIDNP records of associated radical pairs,[2d,3] from kinetic and product analyses of the 5-hexenyl halide sodium-naphthalene system,[4] as well as from a comparative study of the 3,5-cyclocholestan-6-yl chloride system's rearrangement behavior with sodium biphenyl- vs. triphenyltin hydride.[9]