

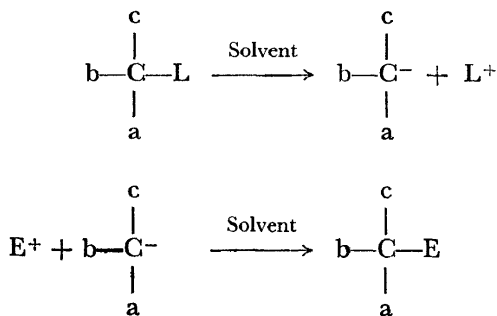
STRUCTURE OF CARBANIONS†

D. J. CRAM

Department of Chemistry, University of California, Los Angeles, U.S.A.

Within the broad theory of organic chemistry, one of the more fundamental problems deals with the constitution of the major reaction intermediates. The detailed structures of carbonium ions have been the subject of many investigations in the last twenty-five years. Less vigorously studied has been the exact constitution of carbon radicals. Carbenes have come under scrutiny only within the last ten years. Although carbanions occupy a central position in synthetic organic chemistry, examination of their intimate geometric character was largely reserved for the last five years. This article is addressed to the problem of the structure of carbanions, particularly with respect to their symmetry properties.

The equations in *Figure 1* illustrate the general approach to the problem. Use of the S_E1 reaction to study carbanions involves three constitutional and one environmental feature. The leaving group (L), the electrophile (E), the substituents (a, b and c) and medium are all subject to wide variation.



Example

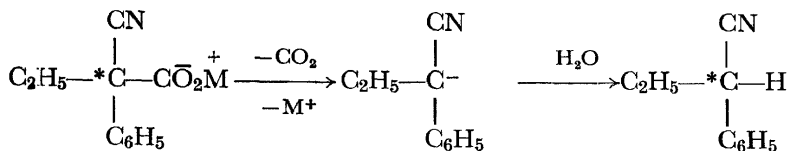


Figure 1

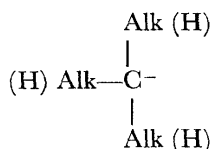
† Parts of this work were supported by grants made by the U.S. Army Research Office (Durham), by the National Science Foundation, and by the Petroleum Research Fund administered by the American Chemical Society. Grateful acknowledgment is made to donors of these funds.

Of the leaving groups for formation of carbanions, those which involve breaking bonds from carbon to hydrogen (deuterium), to carbon, to nitrogen and to oxygen have been employed in the present investigation. Others have studied carbanions formed by the breaking of carbon-metal bonds¹.

A large number of electrophiles are available for the consumption of carbanions. Of these only the proton-donating hydroxyl and ammonium groups have been used in these studies. Proton transfers are among the fastest of all reactions, and in many cases are close to diffusion controlled. Probably many of the observations made with proton donors as electrophiles could not be made with the other electrophiles.

Substituents attached to carbanions play a very important rôle in determining the properties of the intermediates (*Figure 2*). Alkyl and hydrogen groups provide little or no stabilization of charge. Carbonyl-containing groups, and functions such as cyano, nitro and vinyl groups all provide for extensive delocalization of charge into their π -electron systems. The carbanions are thereby stabilized. These anions are ambident, since they react with proton donors at more than one site to give tautomers.

Carbanions not stabilized:



Ambident carbanions stabilized by π -electron delocalization:

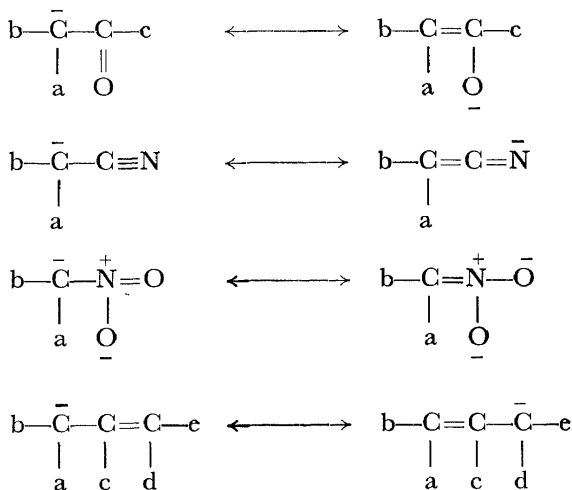


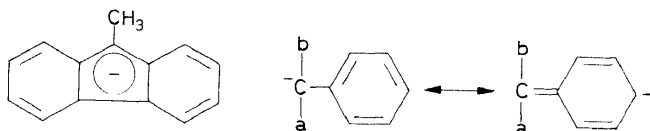
Figure 2

Aryl groups also stabilize carbanions through π -electron delocalization. Such anions are non-ambident, since they usually react only at a single site.

STRUCTURE OF CARBANIONS

Still another class of carbanion-stabilizing substituent contains elements of the second row of the periodic table. Elements such as sulphur, phosphorus, and the halogens (except fluorine) contain *d*-orbitals which are capable of delocalizing and stabilizing negative charge. Examples of such groups are formulated in *Figure 3*.

Non-ambident carbanions stabilized by π -electron delocalization:



Carbanions stabilized by *d*-orbital containing groups:

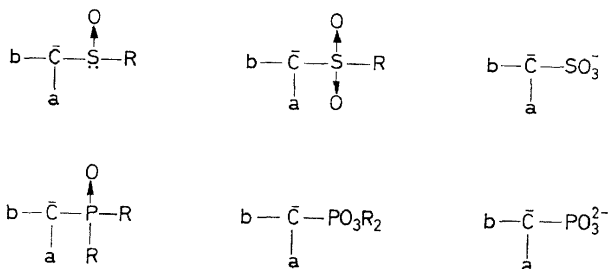
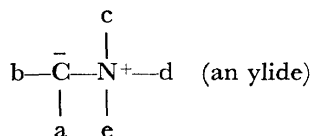


Figure 3

Two other classes of carbanion-stabilizing substituents are known (*Figure 4*). The positive charge on the quaternary ammonium group stabilizes negative charge on adjacent carbon by a combination of inductive and field effects. Halogen atoms attached to carbon bound in turn to carbanions stabilize charge through no-bond resonance.

Carbanions stabilized only by inductive effect:



Carbanions stabilized by no-bond resonance:

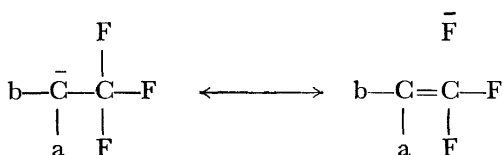


Figure 4

D. J. CRAM

Of the types of substituents listed, we report here on those which produce ambident anions, aryl carbanions, and those anions stabilized by *d*-orbital-containing elements.

The four kinds of solvent systems employed are listed in *Figure 5*. Solvation phenomena play an important rôle in carbanion stabilization. As expected, carbanion structure is seriously effected by the medium.

Dissociating and proton-donating solvents:



Non-dissociating and proton-donating solvents:



Dissociating and non-proton donating solvents:

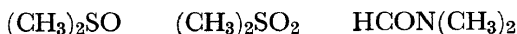


Figure 5

Certain preconceptions about carbanion structure were current at the outset of our work (*Figure 6*). Carbanions with localized charge should be tetrahedral and rapidly inverting. Anions whose charge is extensively delocalized should be planar.

Charge localized-amine, carbanion analogy:

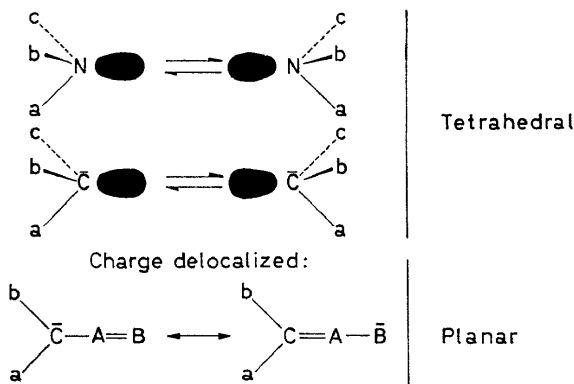
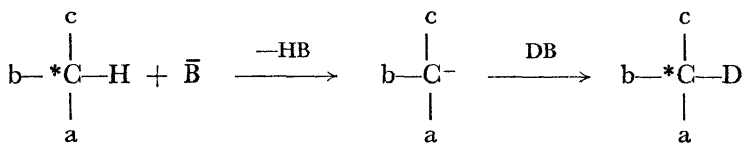


Figure 6

Perhaps the most direct way to probe carbanion structure is through examination of the stereochemistry of the S_E1 reaction. The simplest example is the base-catalysed hydrogen-deuterium exchange reaction at carbon. The steric course of the exchange can be examined purely with kinetic methods as is indicated in *Figure 7*.

STRUCTURE OF CARBANIONS

Stereochemistry of carbon acid-base reactions:



k_e = Rate constant for isotopic exchange

k_α = Rate constant for racemization

k_e/k_α Approaches ∞ as steric course approaches 100% retention

k_e/k_α Approaches 1 as steric course approaches 100% racemization

k_e/k_α Approaches 0.5 as steric course approaches 100% inversion

Figure 7

Since much of the work reported here deals with the stereochemistry of the base-catalysed hydrogen isotopic exchange reaction at carbon, the detailed mechanism of this reaction was examined. From kinetic isotope effect studies², it was concluded that $k_{-a} > k_a$ (see kinetic scheme, Figure 8) if the pK_a of B—H is many units lower than pK_a of C—H.

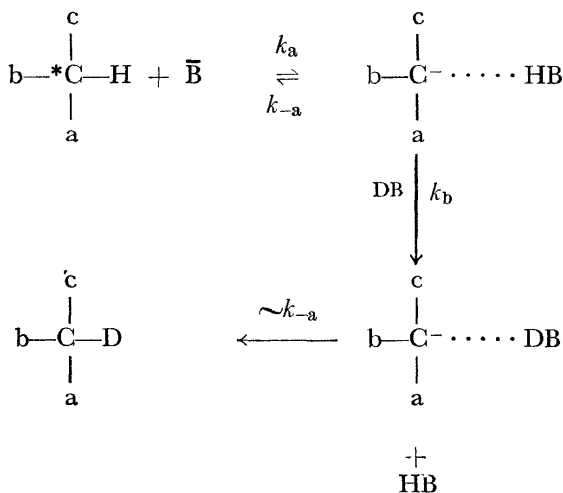


Figure 8

Two systems were devised to detect if indeed $k_{-a} > k_b$. In the first of these, 3-phenyl-1-butene was isomerized to the conjugated *cis*-2-phenyl-2-butene with base. With suitable deuterium labels in the alkene and solvent, the intramolecularity of the reaction was studied³, and Table 1 gives the results.

These data demonstrate the partially intramolecular character of the base-catalysed allylic rearrangement. The simplest mechanism consistent with

the facts involves a bridged "hydrogen bonded" carbanion as intermediate (Figure 9)³. This mechanism is consistent with k_{-a} being greater or of comparable value to k_b in the simple kinetic scheme described earlier.

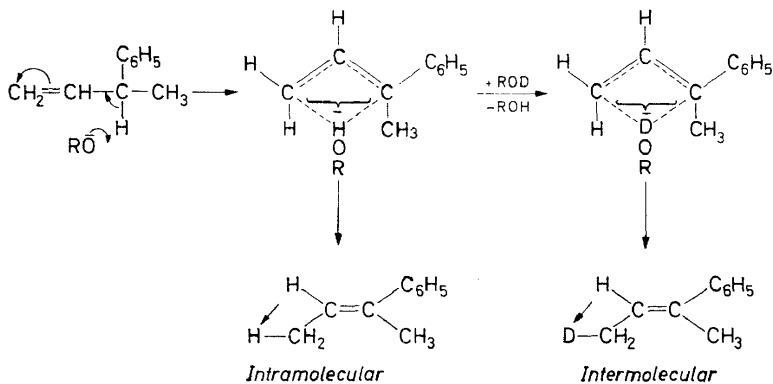
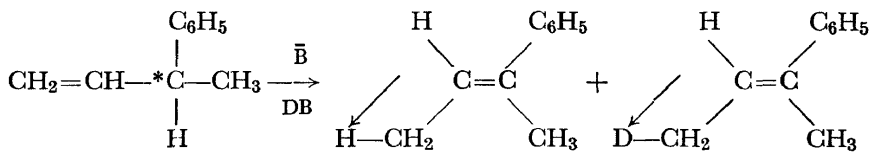


Figure 9

Two other mechanistic schemes, summarized in Figure 10, are entirely inconsistent with the facts of Table 1.

Table 1. Allylic carbanion provides partially intramolecular proton transfer

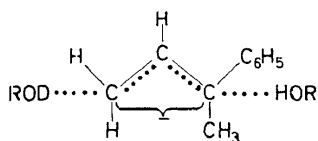


Starting material	Solvent	Base	% Intra-molecular
R—H	(CH ₃) ₃ COH	(CH ₃) ₃ COK	53
R—D	(CH ₃) ₃ COH		24
R—H	(CH ₃) ₃ COH	(CH ₃) ₄ N ⁺ OH ⁻	62
R—D	(CH ₃) ₃ COH		38
R—H	DOCH ₂ CH ₂ OD	HOCH ₂ CH ₂ OK	33
R—D	HOCH ₂ CH ₂ OH		12
R—D	(CH ₃) ₂ SO—CH ₂ OH		CH ₃ OK

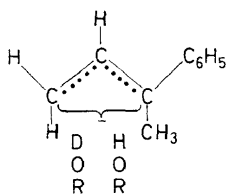
In a second test of a carbanion's ability to recapture its proton, the stereochemistry of the base-catalysed deuterium-hydrogen exchange of a fluorene system was studied ($pK_a \sim 23$)⁴. Table 2 records the results.

The data indicate that in a non-dissociating solvent (tetrahydrofuran) deuterium-hydrogen exchange occurs with high retention. Clearly the ammonium ion of the ammonium carbanion ion-pair (formed as intermediate) rotates and collapses to give a product faster than the ion-pair

STRUCTURE OF CARBANIONS



Predicts no intramolecular
proton transfer



Predicts same isotopic distribution
with either $R-H + DOR$ or $R-D + HOR$

Figure 10

dissociates. In terms of the mechanistic scheme formulated in Figure 11, k_e and $k_c \gg k_d$. The geometry of the ion-pairs formed are undoubtedly maintained through "hydrogen bonds" to a planar carbanion.

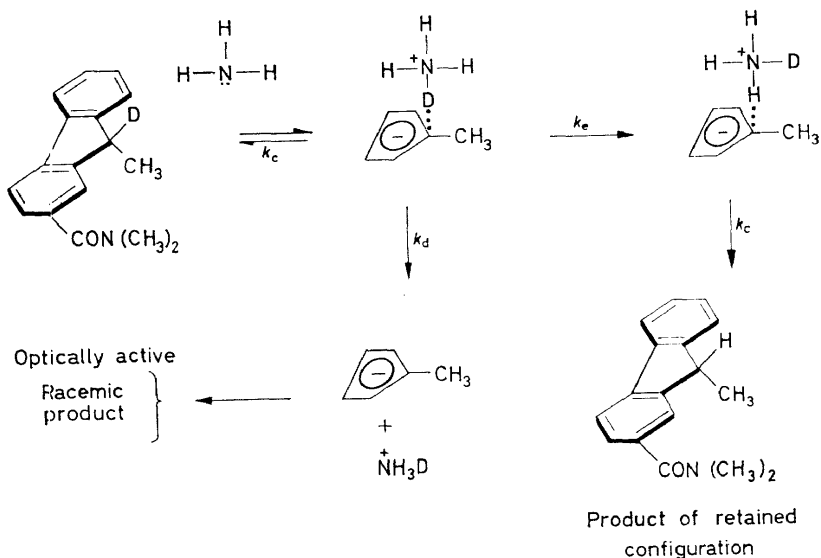
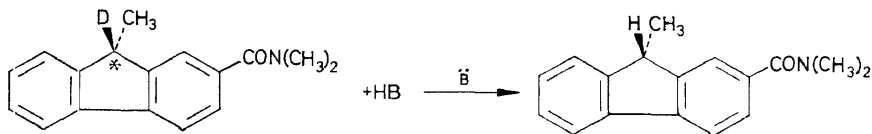


Figure 11

Table 2. Stereochemistry of base-catalysed deuterium-hydrogen exchange of fluorene system ($pK_a \sim 23$)



Solvent	Base	k_e/k_x	Stereochemistry
$(CH_2)_4O$ $(CH_3)_2SO$ CH_2OH	NH_3 NH_3 $(n-C_8H_7)_2N$	~ 300 1 0.65	High retention Racemization Inversion

In dimethyl sulphoxide as solvent, $k_e/k_\alpha = 1$, or racemization was the steric result. In this good dissociating solvent ion-pair dissociation is faster than rotation and collapse of the ion-pair. In such a medium, the planar carbanion was probably longer lived, passed into a symmetric solvent shell and, therefore, gave only the racemic product (*Figure 12*).

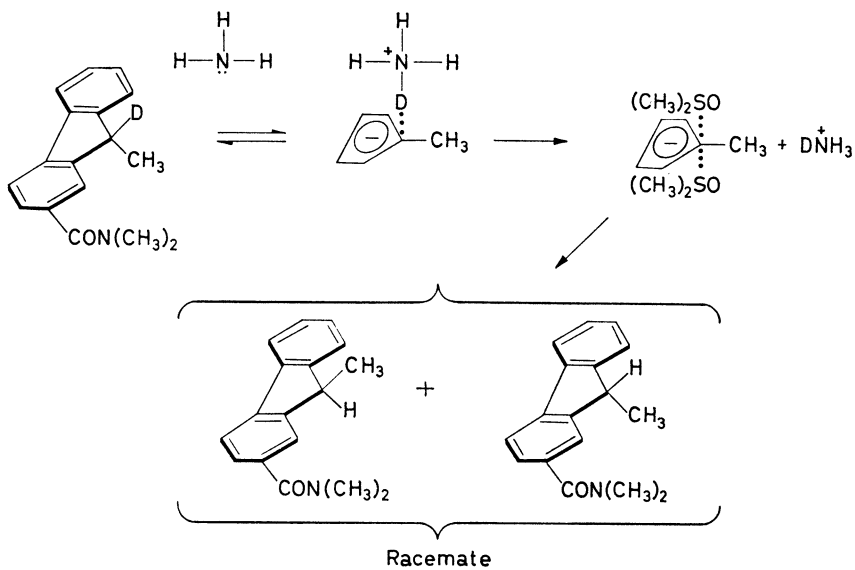


Figure 12

In methanol with tri-*n*-propylamine as solvent, $k_e/k_\alpha = 0.6$, or high net inversion of configuration was found. This solvent is acidic enough to "hydrogen bond" at the "rear" of the carbanion, and the base does not possess proton donors (*Figure 13*). Collapse of the ion-pair formed gives back the starting material by the process described by k_c . Collapse of the carbanion by proton abstraction from methanol gives inverted material (k_a). Ion-pair dissociation gives a racemic product (k_e). The results suggest that k_c and $k_a > k_e$.

The results obtained with the allylic and florenyl systems indicate that in certain solvents with certain bases, carbanions can recapture their protons faster than their solvation shells are reshuffled. Strikingly different results are observed as the solvent is changed. This effect is visible in the patterns of results obtained with the systems discussed below, in which the carbanion stabilizing substituents are systematically varied.

Many years ago, Wilson and Ingold found that k_e/k_α was equal to unity in the base-catalysed exchange and racemization of 2-methyl-1-phenyl-1-butanone⁵ in deuterium oxide-dioxane mixtures (*Figure 14*). A similar result was observed in our work with an optically active nitrile, an amide and an ester in a variety of solvents⁶. These results point to carbanions which are planar, and which live long enough to pass into symmetric solvent envelopes. Negative charge is probably more distributed on the more

STRUCTURE OF CARBANIONS

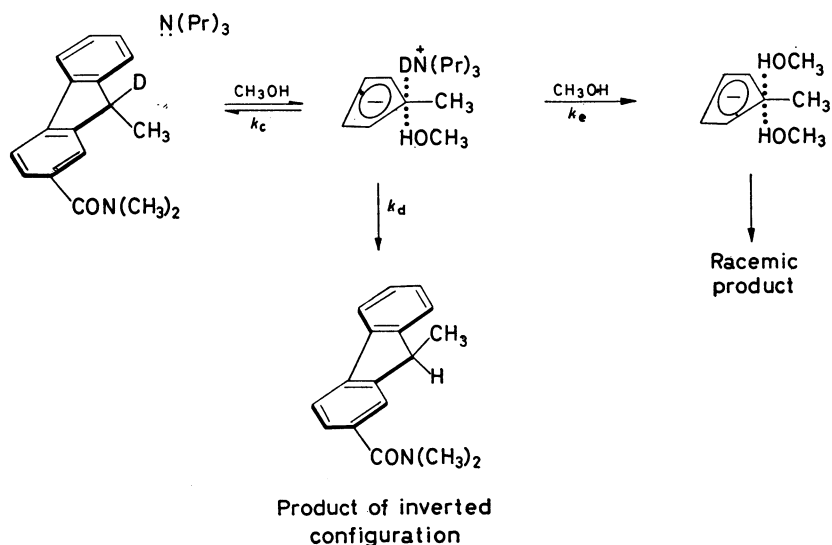


Figure 13

electronegative elements (oxygen or nitrogen), and protonation there occurs at least part of the time to give tautomers incapable of optical activity. Subsequent equilibration returns these tautomers to their more stable keto or nitrile forms.

Ambident anion systems:

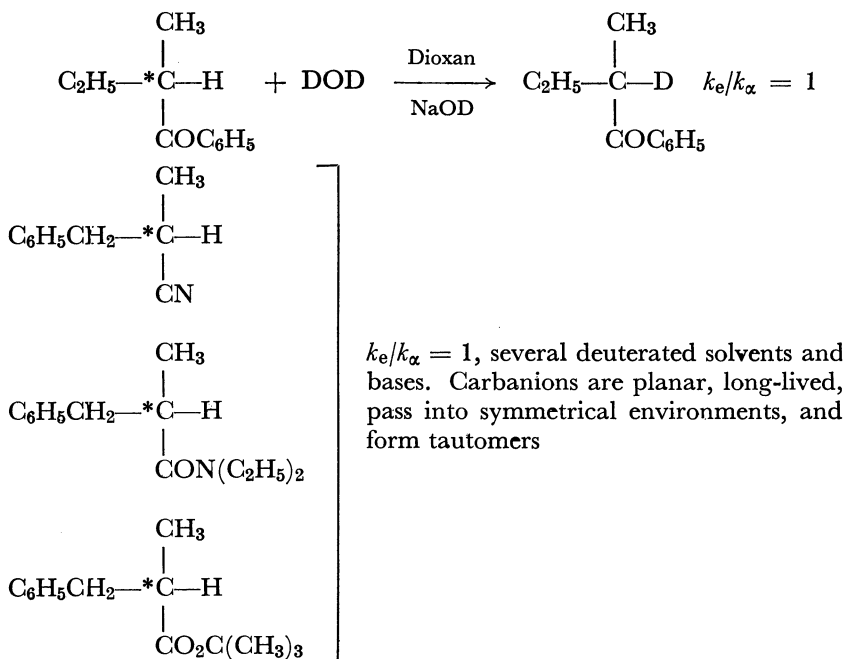
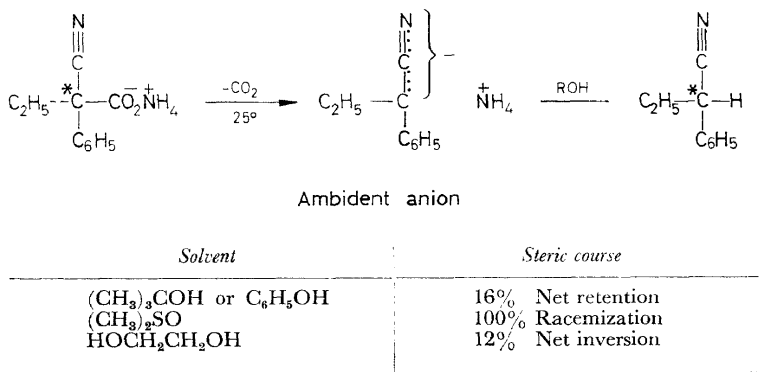


Figure 14

D. J. CRAM

Low orders of stereospecificity were observed when cyano carbanions were formed by a decarboxylation reaction (carbon dioxide as leaving group). The data in *Table 3* indicate that in non-dissociating solvents, the ammonium salt of an α -cyanoacetic acid decarboxylates to give low net retention. In dimethyl sulphoxide, a dissociating and non-proton donating solvent, the result is racemization. In ethylene glycol, which is both proton donating, and dissociating, net inversion is observed irrespective of cation character⁷.

Table 3. Decarboxylation gives low order stereospecificity that varies with solvent



Three mechanisms based on carbanion structure provide explanations for these results (*Figure 15*). In non-dissociating solvents, the ion-pair decarboxylates to give an ammonium carbanide ion-pair, held together partially by "hydrogen bonds". A small amount of tetrahedral character is probably induced in this carbanion by specific solvation at the front. Collapse of this species competes with dissociation, and net retention is observed. In dimethyl sulphoxide, dissociated anion decarboxylates, the anion becomes symmetrically solvated by non-proton donating solvent molecules, and ultimate reaction with proton donors gives racemic material. In ethylene glycol, again carbon dioxide leaves from a dissociated anion, but the solvent

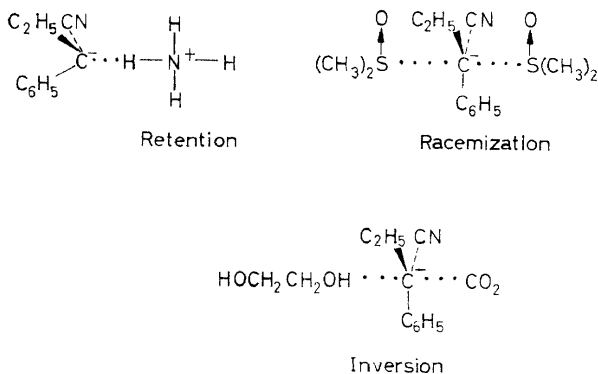


Figure 15

STRUCTURE OF CARBANIONS

participates from the side remote from the leaving group. A planar carbanion results, which is hydrogen bonded at the back, and coordinated at the front with the leaving group, which momentarily blocks attack at the front by solvent. Inversion of configuration results.

Systems capable of generating the 2-phenyl-2-butyl anion were selected for study of the effect of aryl on carbanion structure. This anion is not ambident since it captures protons exclusively at the benzyl position. Four different leaving groups were used to generate this anion (*Figure 16*). Similar stereochemical results were observed when hydrogen, carbon, nitrogen or oxygen bonds were cleaved. In general, the stereochemical fate of the 2-phenyl-2-butyl anion is independent of the leaving group.

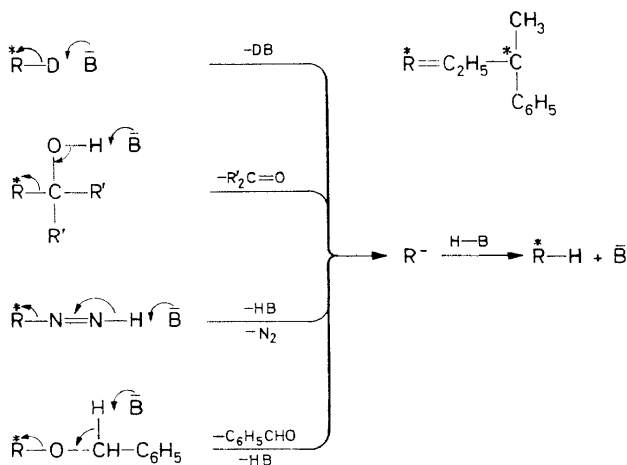


Figure 16

With deuterium as leaving group, k_e/k_α can be varied from 10 (retention) to 1 (racemization) to 0.7 (inversion), depending on the solvent (*Table 4*)⁸.

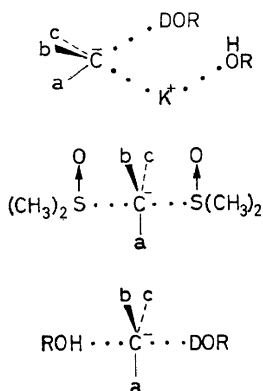
Table 4. Deuterium as leaving group

$\text{C}_2\text{H}_5-\overset{\text{CH}_3}{\underset{\text{C}_6\text{H}_5}{\overset{*}{\text{C}}-\text{D}}} + \text{HOR} \xrightarrow{\text{ROK}} \text{C}_2\text{H}_5-\overset{\text{CH}_3}{\underset{\text{C}_6\text{H}_5}{\overset{*}{\text{C}}-\text{H}}} + \text{DOR}$		
<i>Solvent</i>	k_e/k_α	<i>Steric course</i>
(CH ₃) ₃ COH	10	Retention
(CH ₃) ₂ SO·(CH ₃) ₃ COH	1	Racemization
O(CH ₂ CH ₂ OH) ₂	0.7	Inversion

The carbanion structures envisaged for each of these three stereochemical results are formulated in *Figure 17*. In non-dissociating solvents, a solvated ion-pair is formed which induces substitution with retention. In dimethyl

D. J. CRAM

sulphoxide, a poor proton-donating solvent, the carbanion lasts long enough to pass into a symmetrical solvent environment. In ethylene glycol, a good dissociating and proton-donating medium, the solvent participates in carbanion formation from the back side, and net inversion is observed.



Non-dissociating solvents induce front-side solvation, slight carbanion asymmetry, and substitution with retention

Dissociating and non-proton donating solvents induce symmetrically solvated planar carbanion, and substitution with racemization

Dissociating and proton-donating solvents provide asymmetrically solvated but planar carbanion, and substitution with inversion

Figure 17

Use of nitrogen as leaving group depends on generation of a transitory alkyl diimide. Three methods of accomplishing the reaction were developed (Figure 18). The fact that the same steric results were obtained from each of three different starting materials points to the alkyl diimide as a common intermediate⁹.

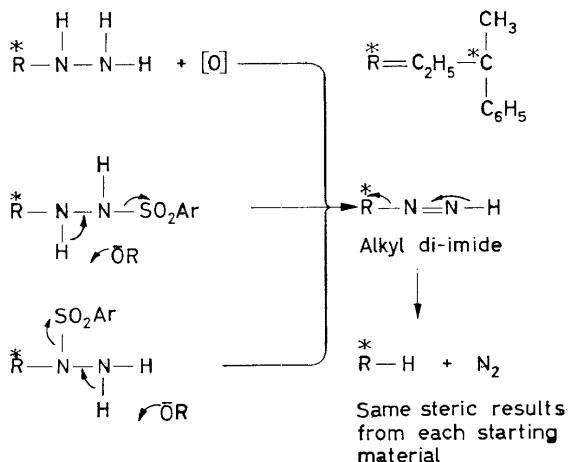


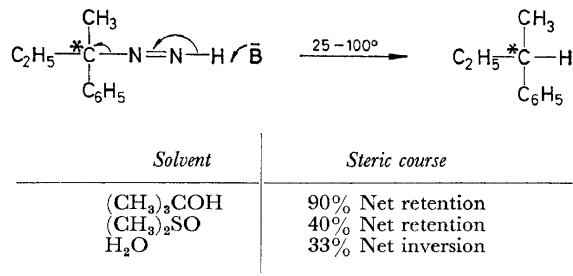
Figure 18

As with hydrogen, nitrogen as leaving group can give either retention or inversion, depending on solvent (see Table 5). Generation of a proton donor

STRUCTURE OF CARBANIONS

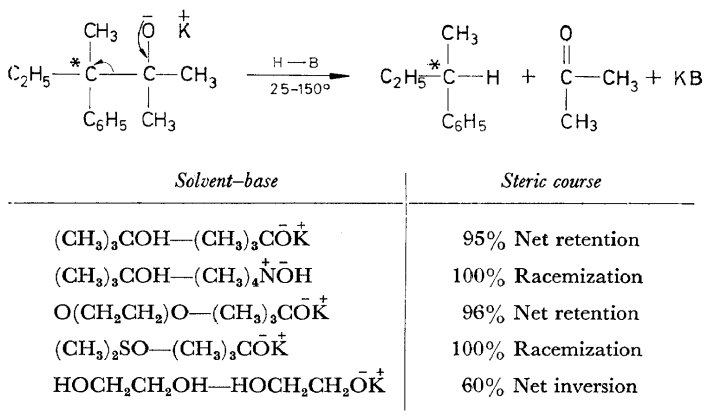
at the front of the carbanion predisposes the system towards retention, as is shown by the fact that dimethyl sulphoxide as solvent gives retention of configuration.

Table 5. Nitrogen as leaving group



Carbon as leaving group gives results completely analogous to those obtained with hydrogen as leaving group. The data are summarized in Table 6. That potassium ion is responsible for the high retention observed in t-butyl alcohol is shown by the fact that substitution of quaternary ammonium for potassium ion reduces the stereochemical result from 95 per cent net retention to 100 per cent racemization. Clearly, the coordinating ability of the potassium ion is a necessary feature of asymmetric solvation from the front side. The 60 per cent net inversion observed in ethylene glycol probably involves the ability of the leaving group to act as a shield at the front while proton-donating solvent attacks the incipient carbon on the side remote from the leaving group¹⁰. Analogies to carbonium ion mechanisms are visible in these results.

Table 6. Carbon as leaving group



D. J. CRAM

Four systems were used for the study of carbanions stabilized by *d*-orbital containing groups (Figure 19). Three of them were subjected to base-catalysed deuterium-hydrogen exchange, and one to decarboxylation experiments.

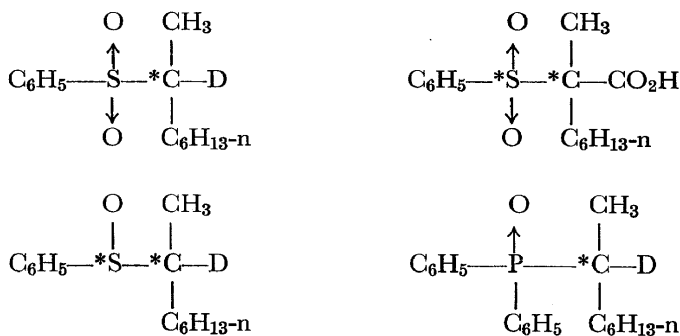
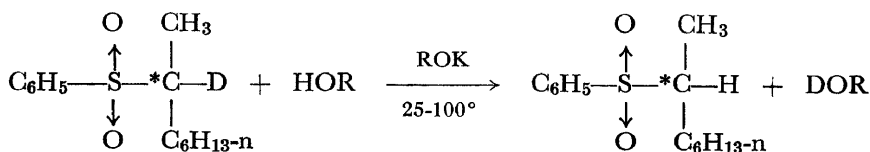


Figure 19

In Table 7 are listed the results obtained with the sulphonyl carbanion as intermediate. Although the ratios of k_e/k_α varied by as much as a factor of 200 with changes in solvent, high retention was observed for all solvents. This strongly suggests that asymmetric solvation effects are superimposed on carbanions which are themselves asymmetric².

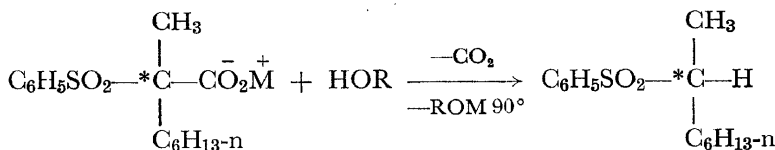
Table 7. Stereochemistry of base-catalysed isotopic exchange reaction with phenylsulphonyl as carbanion-stabilizing group



Solvent-base	k_e/k_α
$(\text{CH}_3)_3\text{COH}-(\text{CH}_3)_3\text{COK}$	140-2000
$(\text{CH}_3)_3\text{COH}-(\text{CH}_3)_4\text{NOH}$	22-64
$(\text{CH}_3)_2\text{SO}-\text{CH}_3\text{OK}$	10
$\text{CH}_3\text{OH}-\text{CH}_3\text{OK}$	10
$\text{HOCH}_2\text{CH}_2\text{OH}-\text{HOCH}_2\text{CH}_2\text{OK}$	32

The same sulphonyl carbanion was generated by both the decarboxylation and alkoxide cleavage reactions with similar stereochemical results¹¹ (Figure 20).

STRUCTURE OF CARBANIONS



98% Net retention with 5 extreme solvent types and bases

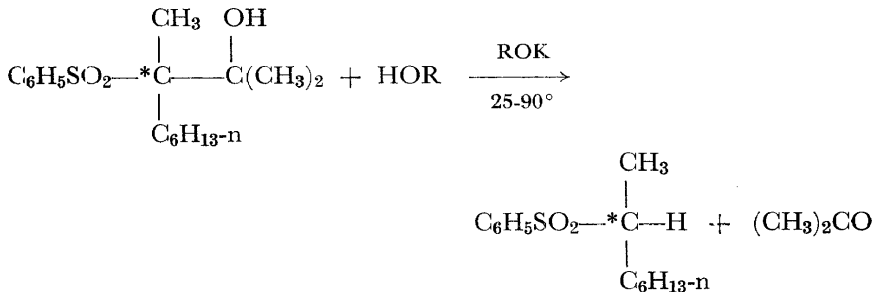
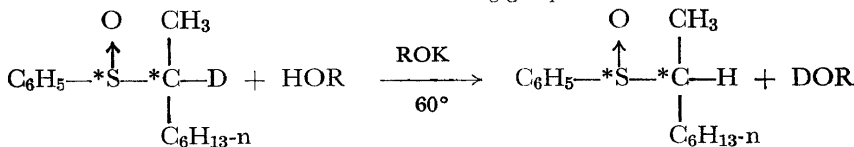

 98–100% Net retention in $(\text{CH}_3)_3\text{COH}$ and $\text{HOCH}_2\text{CH}_2\text{OH}$

Figure 20

In contrast to the sulphonyl carbanion, the sulphinyl carbanion appears to be symmetric. Only asymmetric solvation effects are in evidence from the data of *Table 8*¹².

Table 8. Stereochemistry of base-catalysed isotopic exchange reaction with phenylsulphinyl as carbanion-stabilizing group



Solvent-base	k_e/k_a
$(\text{CH}_3)_3\text{SO}-\text{CH}_3\text{OK}$	0.58–1.4
$(\text{CH}_3)_3\text{COH}-(\text{CH}_3)_3\text{COK}$	1.2–3.6

The diphenylphosphinoxy carbanion resembles the sulphinyl carbanion, and only asymmetric solvation effects are visible in the results¹³ (*Table 9*).

Table 9. Stereochemistry of base-catalysed isotopic exchange reaction with diphenylphosphinoxy as carbanion-stabilizing group



Solvent-base	k_e/k_a
$(\text{CH}_3)_3\text{COH}-(\text{CH}_3)_3\text{COK}$	3.3
$(\text{CH}_3)_2\text{SO}-\text{CH}_3\text{OK}$	1.0
$\text{CH}_3\text{OH}-\text{CH}_3\text{OK}$	1.1
$\text{HOCH}_2\text{CH}_2\text{OH}-\text{HOCH}_2\text{CH}_2\text{OK}$	1.3

The conclusions about the symmetry properties of the *d*-orbital containing systems are summarized in *Figure 21*.

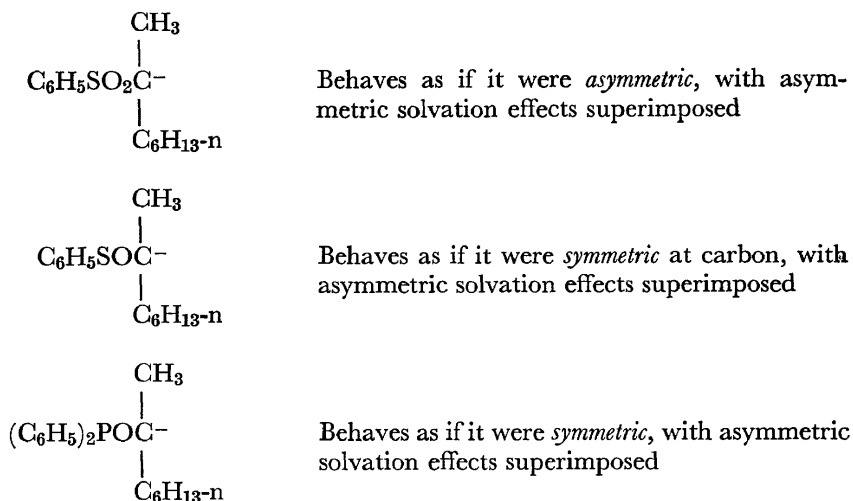


Figure 21

The question arises as to why the sulphonyl carbanion should be intrinsically asymmetric, and the other two symmetric. A number of possible explanations are available, but have not yet been experimentally differentiated.

These conclusions indicate that carbanion structure is subject to considerable variation. Solvent and substituent effects on geometry are the most prominent, but the nature of the cation and leaving group play an important rôle in some systems.

Dramatic solvent effects were encountered in these studies. For example, the rates of acid-base reactions were found to vary by as much as nine powers of ten by simply changing solvent⁶ (*Table 10*).

Table 10. Changes in solvent drastically effect kinetic basicity of alkoxide anions toward carbon acids

$\text{C}_6\text{H}_5\text{CH}_2-\overset{\text{CH}_3}{\underset{\text{CN}}{\text{C}}}-\text{H} \xrightarrow[25^\circ]{k_x} \text{C}_6\text{H}_5\text{CH}_2-\overset{\text{CH}_3}{\underset{\text{CN}}{\text{C}}}-\text{H}$		
Optically pure		Racemic
<i>Solvent</i>	<i>Base</i>	<i>Relative rate</i>
CH_3OH $(\text{CH}_3)_2\text{SO}$ $(\text{CH}_3)_3\text{COH}$ $(\text{CH}_3)_2\text{SO}$	CH_3OK CH_3OK $(\text{CH}_3)_3\text{COK}$ $(\text{CH}_3)_3\text{COK}$	1 $\sim 10^9$ 10^6 10^{12}

STRUCTURE OF CARBANIONS

This effect is interpreted as reflecting the importance of "hydrogen bonding" and "ion pairing" an anion activity (*Figure 22*). In dimethyl sulphoxide, the potassium alkoxide ion-pair is dissociated, and the alkoxide anion is not "hydrogen bonded". The resulting anion is highly reactive.

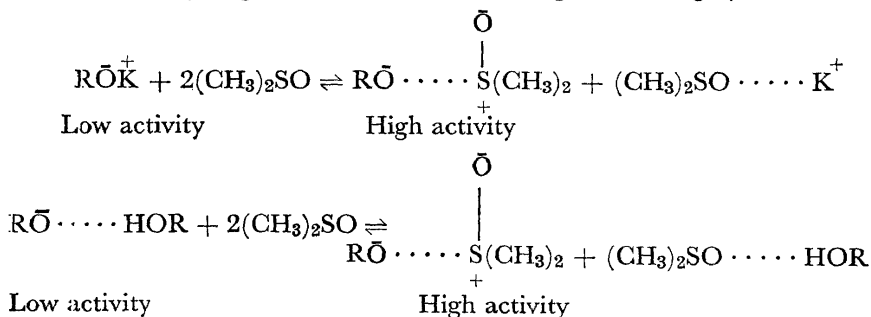
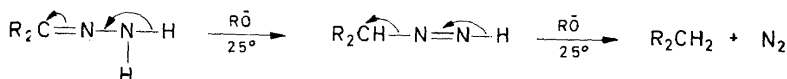
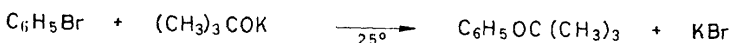


Figure 22

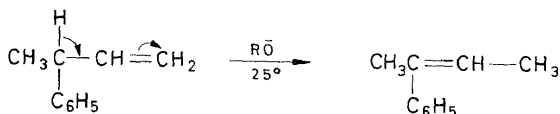
Wolff-Kishner reduction¹⁴:



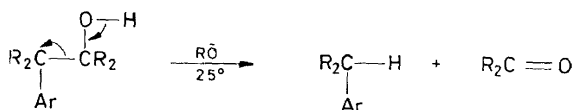
Nucleophilic-aromatic substitution¹⁵:



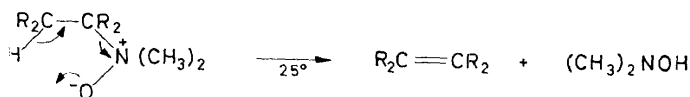
Allylic rearrangement³:



Cleavage of alcohols¹⁰:



Cope elimination¹⁶:



E₂ reaction¹⁷:

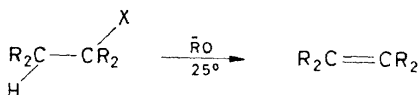


Figure 23

Six reactions are listed in *Figure 23*, the rates of which are enhanced by about six powers of ten by substitution of dimethyl sulphoxide for hydroxylic or non-dissociating solvents.

The importance of carbanions as intermediates is self evident. Less obvious is the fact that the complete constitution of charged species must include an intimate description of the solvation shell. Without such details, interpretations pertaining to their ease of formation, symmetry properties, and reactivities are superficial.

References

- ¹ For general reviews, see G. Kobrich. *Angew. Chem. Intern. Ed. Engl.* **1**, 382 (1962); O. A. Reutov. *Record Chem. Progr.* **22**, 1 (1961).
- ² D. J. Cram, D. A. Scott, and W. D. Nielsen. *J. Am. Chem. Soc.* **83**, 3696 (1961).
- ³ D. J. Cram and R. T. Uyeda. *J. Am. Chem. Soc.* **84**, 4358 (1962), and unpublished results by the same authors.
- ⁴ D. J. Cram and L. Gosser. Unpublished results.
- ⁵ C. K. Ingold. *Structure and Mechanism in Organic Chemistry*, p. 570, Cornell University Press, New York (1953).
- ⁶ D. J. Cram, B. Rickborn, C. A. Kingsbury, and P. Haberfield. *J. Am. Chem. Soc.* **83**, 3678 (1961).
- ⁷ D. J. Cram and P. Haberfield. *J. Am. Chem. Soc.* **83**, 2354, 2363 (1961).
- ⁸ D. J. Cram, C. A. Kingsbury, and B. Rickborn. *J. Am. Chem. Soc.* **83**, 3688 (1961).
- ⁹ D. J. Cram and J. S. Bradshaw. *J. Am. Chem. Soc.* **85**, 1108 (1963).
- ¹⁰ D. J. Cram, J. L. Mateos, F. Hauck, A. Langemann, K. R. Kopecky, W. D. Nielsen, and J. Allinger. *J. Am. Chem. Soc.* **81**, 5774 (1959).
- ¹¹ D. J. Cram and A. S. Wingrove. *J. Am. Chem. Soc.* **85**, 1100 (1963).
- ¹² D. J. Cram and S. H. Pine. *J. Am. Chem. Soc.* **85**, 1096 (1963).
- ¹³ D. J. Cram and R. D. Partos. *J. Am. Chem. Soc.* **85**, 1093 (1963).
- ¹⁴ D. J. Cram, M. R. V. Sahyun, and G. R. Knox. *J. Am. Chem. Soc.* **84**, 1734 (1962).
- ¹⁵ D. J. Cram, B. Rickborn, and G. R. Knox. *J. Am. Chem. Soc.* **82**, 6412 (1960).
- ¹⁶ M. R. V. Sahyun and D. J. Cram. *J. Am. Chem. Soc.* **85**, 1263 (1963).
- ¹⁷ D. J. Cram and A. S. Wingrove. Unpublished results.