expulsion of a partly protonated amine, the nonconcerted mechanism ($k_1 - k_{-1}$) will be the lowest energy path in both directions. General base catalysis has not been reported for the addition of basic amines to simple carbonyl compounds and even for the addition of 2-methylthiosemicarbazide ($pK_a(RNH_3^+) = 1.2$) the Brønsted plot is nonlinear, suggesting a stepwise mechanism.[10]

(b) Base catalysis of two-step acyl aminolysis reactions will ordinarily proceed through a stepwise mechanism. Although proton transfer is required in the overall reaction to form a stable product, the difference in pK between the addition intermediate $T^\pm$ and the catalyzing base is generally small so that concerted catalysis is not expected. Thus, the rule provides an explanation for the nonlinear Brønsted plots observed for several such reactions, as described in the preceding communication.[11] In the case of methyl formate aminolysis[12] the leaving group is sufficiently poor that the expulsion of methoxide ion from T^-, the immediate product of the proton abstraction step, becomes rate-determining when the pH is decreased. The rule requires amplification of a previously proposed concerted mechanism for catalysis[12] into a fast amine addition and a rate-determining proton transfer step; the "water" reaction may be assigned to a proton switch in $T^\pm$ to form the neutral addition intermediate.

(c) The addition of hydrogen peroxide to the carbonyl group gives an extremely unstable initial product, $H_2O_2^+{-}CR_2{-}O^-$, so that concerted general base catalysis by weak bases is possible; however, catalysis by strong bases is not expected because of the favorable equilibrium to form the hydroperoxide anion ($pK_a(HOOH) = 11.6$). In general, when the pK of the catalyst is changed so that the requirements of the rule are no longer met, a concerted will change to a stepwise mechanism of catalysis; this may appear as a positive deviation of the "water" or "hydroxide-catalyzed" point in a Brønsted plot. The observed[13] β value of 0.66 for catalysis by carboxylate ions of hydrogen peroxide addition and the positive deviation of the "hydroxide" point, interpreted as an uncatalyzed attack of HOO^-, agree with these predictions. Base catalysis by hydroxide ion of other addition reactions of ROH is likewise expected to involve specific base catalysis.

(d) "Acid catalysis" by water of addition reactions to the carbonyl group and, in the reverse reaction, hydroxide ion catalysis of the breakdown of addition compounds $HOCR_2X$ involve a small or unfavorable ΔpK and does not occur through a simple concerted mechanism.

(e) Fully concerted bifunctional acid-base catalysis is rare or nonexistent because of the improbability of meeting the conditions of the rule simultaneously at two sites on the reactant and catalyst. Enhanced reactivity of bifunctional catalysts may represent proton transfer alone[14] or a mechanism in which a separate proton transfer step permits product formation, but need not be rate determining, as suggested for catalysis by carboxylic acids of hydrogen peroxide addition to aldehydes.[13]

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[10] J. M. Sayer and W. P. Jencks, *J. Amer. Chem. Soc.*, **94**, 3262 (1972).

[11] J. P. Fox, M. I. Page, A. Satterthwait, and W. P. Jencks, *ibid.*, **94**, 4729 (1972); see also references therein.

[12] G. M. Blackburn and W. P. Jencks, *ibid.*, **90**, 2638 (1968).

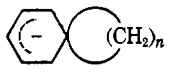
[13] E. Sander and W. P. Jencks, *ibid.*, **90**, 4377 (1968).

[14] R. E. Barnett and W. P. Jencks, *ibid.*, **91**, 2358 (1969). Other examples may be interpreted in the same way; *e.g.*, B. A. Cunningham and G. L. Schmir, *ibid.*, **88**, 551 (1966).

Generation of a Stable Spiro Dihydroaromatic Anion

Sir:

While the intermediacy of bridged arylalkyl cations in rearrangement reactions is well established[1] and stable salts of such cations have been prepared and studied,[2,3] the corresponding anions (**1**) have been comparatively neglected. Such anions have been implicated in the rearrangements of polyarylethyl metal compounds.[4,5]

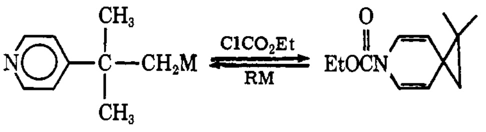


1

2

Herein we describe the preparation and properties of several stable spiro aromatic organometallic compounds and show how 4-(4-pyridyl)butyl metal compounds exist in the 4,4-spirodihydropyridine structure rather than the open form as is the case for 2-(4-pyridyl)-2-methylpropyl metal compounds.[6]

Pyridylalkyl metal compounds are more likely to exist in the spiro structure (**2**) due to the great electron-withdrawing power of the pyridine ring. We have already reported how 2-(4-pyridyl)-2-methylpropyl metal compounds (**3**) close to the spirourethane (**4**)



(1)

3 **4**, M = Li, Na, K, MgCl

with ethyl chloroformate. We have now synthesized two new *N*-carbethoxydihydropyridines and converted them to organometallic compounds by a reaction analogous to eq 1, right to left.

Conversion of dimethyl 3,3-tetramethyleneglutarate *via* the acyloin[7] reaction to 4,4-tetramethylene-2-hydroxycyclopentanone (**5**), bp 85–86° (0.17 mm), $M^+ = 154$, followed by sodium borohydride reduction gave *trans*-1,2-dihydroxy-4,4-tetramethylenecyclopentane (**6**), mp 102–103°, $M^+ = 156$. The diol **6** was cleaved with aqueous sodium metaperiodate to give 3,3-tetramethyleneglutaraldehyde (**7**). Treatment of the dried ether extract of this reaction mixture with dry gaseous ammonia at 0° afforded 4,4-tetramethylene-1,4-dihydropyridine (**8**), as evidenced by nmr analysis,

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[1] D. J. Cram, *J. Amer. Chem. Soc.*, **71**, 3863, 3875, 3883 (1949); **74**, 2159 (1952); **86**, 3767 (1964).

[2] L. Eberson and S. Winstein, *ibid.*, **87**, 3506 (1965).

[3] G. Olah, E. Namanworth, M. Comisarow, and B. Ramsey, *ibid.*, **89**, 711 (1967).

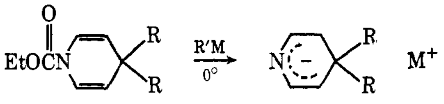
[4] H. E. Zimmerman and F. J. Smentowski, *ibid.*, **89**, 5455 (1957); H. E. Zimmerman and E. Zweig, *ibid.*, **83**, 1196 (1961).

[5] E. Grovenstein, Jr., *ibid.*, **79**, 4895 (1957); E. Grovenstein, Jr., and G. Wentworth, *ibid.*, **85**, 3305 (1963); **89**, 1852, 2348 (1967).

[6] G. Fraenkel and J. W. Cooper, *ibid.*, **93**, 7228 (1971).

[7] H. Kwart and J. A. Ford, *J. Org. Chem.*, **24**, 2060 (1959). This procedure is the fastest and most efficient of several tried.

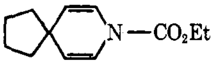
Table I. Dihydropyridine Anions Reaction Conditions and Nmr Data



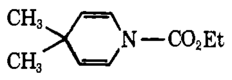
Reagent		Solvent	R,R	$\tau_{2,6}$[b]	$\tau_{3,5}$	$J_{2,3}$Hz
12		THF	CH_3, CH_3[a]	3.26	5.27	8.0
14a	*n*-BuLi	Hexane	CH_3, CH_3	3.75	5.70	6.5
14b	*n*-BuLi	Hexane and TMEDA	CH_3, CH_3	4.04	6.10	7.2
14c	*n*-BuMgBr	THF	CH_3, CH_3	4.00	*c*	7.4
14d	*n*-BuNa	Pentane	CH_3, CH_3	*d*	*d*	*d*
14e	*n*-BuK	Hexane + crown ether, 1:1	CH_3, CH_3	4.10	*c*	7.2
9		THF	$(CH_2)_4$[a]	3.34	5.27	8.5
13a	*n*-BuLi	Hexane	$(CH_2)_4$	3.75	5.62	7.6
13b	*n*-BuLi	Hexane + TMEDA	$(CH_2)_4$	3.97	6.02	7.6
13c	$(n\text{-Bu})_2Mg$	THF	$(CH_2)_4$	3.70	5.72	7.7
13d	*n*-BuK	Pentane	$(CH_2)_4$	*d*	*d*	*d*

[a] Starting material. [b] 60-MHz spectra. [c] Resonance obscured by other absorption. [d] Compound insoluble.

at τ 4.19 (AB), and τ 5.79 (J = 5.5 Hz).[8] Though stable in solution, compound **8** was not isolated but acylated with ethyl chloroformate to give the stable colorless urethane, 1-carbethoxy-4,4-tetramethylene-1,4-dihydropyridine (**9**), in 13% yield based on diol **6**:



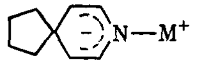
9



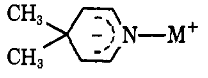
12

bp 105° (0.11 mm); M+ = 207; ir 5.9 μ; nmr see Table I.

In a similar procedure to that for **9**, *trans*-1,2-dihydroxy-4,4-dimethylcyclopentane, prepared as described by Kwart and Ford,[7] was converted *via* 3,3-dimethylglutaraldehyde (**10**) to 1-carbethoxy-4,4-dimethyl-1,4-dihydropyridine (**12**): bp 153–154° (0.4 mm); mp 84.5°; M+ = 153; ir 5.8, 5.9 μ; nmr see Table I.

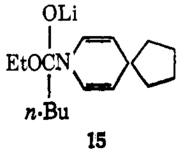


13



14

In contrast to the cleavage reactions of the spirocyclopropyl derivative **4** to the *open-chain* organometallics **3**,[6] both urethanes **9** and **12** underwent cleavage to the corresponding dihydropyridine anions with a variety of organometallic compounds of sodium, potassium, lithium, and magnesium, giving deep red stable solutions (see Table I). For instance, when spirourethane **9** was treated with a 3.5 molar excess of *n*-butyllithium in hexane-*N*,*N*,*N'*,*N'*-tetramethylethylenediamine, at 0°, the olefinic resonance was first replaced by another AB multiplet at τ 3.48 and 5.17, which in turn changed to one at τ 3.97 and 6.02 (**13b**). The former resonance is ascribed to an intermediate in the cleavage reaction **15**.



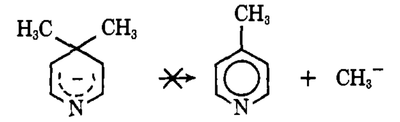
15

When lithium compound **13a** was treated with methyl choroformate, methylspirourethane ensued. The latter procedure was used to prove cleavage in those cases where the organometallic product was insoluble (**13d** and **14d**).

From the results described above together with the similarity of the chemical shifts to values for adducts of *n*-butyllithium and pyridines,[9] it is clear that the cleavage products **14a–e** and **13a–d** (Table I) are salts of dihydropyridines.

These salts of dihydropyridines are unusually stable to heat and do not undergo the aromatization reactions common to dihydropyridines.

The potassium salt of 4,4-dimethyl-1,4-dihydropyridine (**14e**) in hexane with 1 equiv of dicyclohexyl-18-crown-6 is stable for months at room temperature. The lithium salt **14a** only decomposes after 6 hr of reflux at 100°. There is no evidence that salts such as **14a** can behave as methyl anion donors (eq 2) nor do



(2)

they rearrange to lutidine. Further, among the spirodihydropyridine anions, the magnesium salt **13e** was unchanged after 18 days at 85°. The open-chain forms of the reagents (**16**) could not be detected by nmr or chemical means.

Since chemical shifts in conjugated ions are related to the charge distribution,[10] the similarities among the ring shifts (Table I) for the open (**14**) and spiro (**13** anions, respectively, argue strongly for similar electronic structures. Thus, the spiro anions should be regarded as conjugated azacyclohexadienylic systems (five orbitals, six electrons) with little interaction with the spiro ring. Analysis of the shifts[10] shows about 25% of the negative charge to be located at the 3 and 5 positions, respectively, and the rest on nitrogen.

Recently, Grovenstein, Akabori, and Rhee reported how reduction of 4-chloro-1-*p*-biphenylylbutane with

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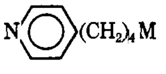
(8) M. Saunders and E. Gold, *J. Org. Chem.*, 27, 1849 (1962).

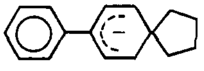
(9) G. Fraenkel and J. W. Cooper, *Tetrahedron Lett.*, 1825 (1968).

(10) G. Fraenkel, R. E. Carter, A. D. McLachlan, and J. Richards, *J. Amer. Chem. Soc.*, **82**, 5840 (1960).

excess Cs–K–Na eutectic at −70° gives a solution containing spiro anion **17**.[11]



16



17

Thus, while 4-phenylbutyl metal compounds exist mainly in the open form, the substitution of the para carbon by nitrogen or the substitution of the para hydrogen by phenyl provides sufficient conjugation to stabilize the spiro anions.

Acknowledgment. This research was supported by National Science Foundation Grants GP-8567 and GP-16402.

[11] E. Grovenstein, S. Akabori, and J-U Rhee, *J. Amer. Chem. Soc.*, **94**, 4734 (1972).

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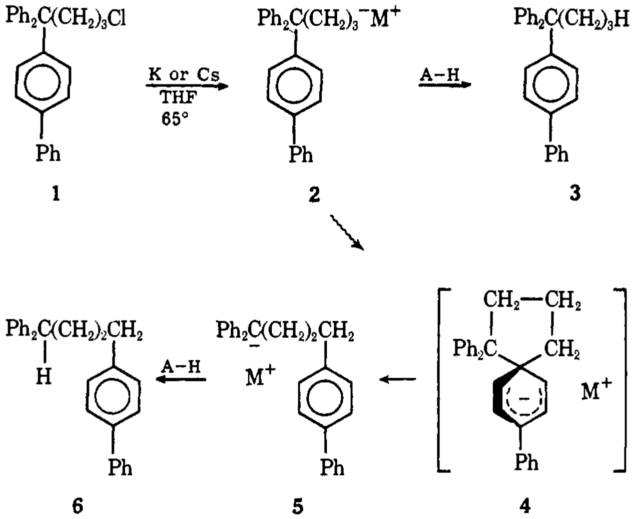
Carbanions. XIII. 1,4 Migration of the *p*-Biphenylyl Group. Formation of an Intermediate Spiro Anion

Sir:

Whereas 1,4 migration of the phenyl group occurs only as a minor process in the reaction of 4-chloro-1,1,1-triphenylbutane with alkali metals,[1] 1,4 migration of the *p*-biphenylyl group is now found to be the major process in similar reactions of 4-chloro-1-*p*-biphenylyl-1,1-diphenylbutane (**1**). The chloride[2] (**1**), mp 99–100°, was prepared by reaction of *p*-biphenylyldiphenylmethylsodium[3] with excess of 1-bromo-3-chloropropane. Addition of **1** over a 10-min period to finely divided potassium (in a Morton high-speed stirring apparatus) in boiling tetrahydrofuran (THF) gave a dark red solution which, upon carbonation, yielded 5-*p*-biphenylyl-2,2-diphenylpentanoic acid, mp 191–192°, or upon decomposition with methanol gave 4-*p*-biphenylyl-1,1-diphenylbutane (**6**), mp 81–82°, containing only some 1% of 1-*p*-biphenylyl-1,1-diphenylbutane (**3**), mp 94.5–95°.[4] Reaction of **1** with finely divided cesium over a 4-min period in boiling THF gave the same rearranged carbanion according to analysis of the products from carbonation and protonation. These results may be explained according to Scheme I.

Scheme I



In view of the fact that phenyl groups are known to undergo 1,4 migrations in free radicals,[5] to establish Scheme I it is necessary to show that formation of carbanion **2** precedes rearrangement of the *p*-biphenylyl group. In experiments designed to trap the intermediate anion **2**, the chloride **1** was allowed to react at 65° in THF with increments of potassium and *tert*-butyl alcohol, the latter always in slight excess. Analysis of the reaction mixture at intervals revealed that 1-*p*-biphenylyl-1,1-diphenylbutane (**3**) was an initial product of reaction; the maximum yield of **3** was some 18%, but this product largely disappeared with continued reduction by excess potassium. The final product consisted of 3% of **3**, 90% of 1-(*p*-cyclohexylphenyl)-1,1-diphenylbutane[2] (**7**) (mp 100.5–102°), and 6% of an unknown **8**. Compound **8** is evidently a 1,4-dihydro derivative of **3** since (unlike **7** which was unaffected) it gave **3** upon treatment with 5% Pd/C at 100°. The structure of **7** was confirmed by its mass spectrum (peaks at *m/e* 368 and 325). Since alkyl radicals are very similar to hydrogen atoms in their rate of abstraction of hydrogen atoms from organic compounds and since hydrogen atoms abstract hydrogen from THF more than 150 times more readily than from *tert*-butyl alcohol,[6] the intermediate trapped by addition of small amounts of *tert*-butyl alcohol in our experiments must be the carbanion **2**, as shown in Scheme I, rather than the corresponding free radical.

Reaction of the chloride **1** with potassium in the more acidic solvent dioxane at 101°, rather than THF at 65°, gave the rearranged hydrocarbon **6** (75% yield) and no detectable **3**; however, repetition with sodium in place of potassium gave an 8:92 ratio of rearranged to nonrearranged hydrocarbons (**6**:**3**). These reactions in the solvent dioxane confirm the conclusions derived from work in THF and show moreover that the rate of rearrangement of the organopotassium compound **2** greatly exceeds that of the corresponding organosodium compound. The inequality of rate between sodium and potassium compounds in carbanion rearrangements has not been previously observed, although it has been known for some time that organolithium compounds rearrange more slowly than organosodium or organopotassium compounds.[7]

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[1] E. Grovenstein, Jr., J. A. Beres, Y.-M. Cheng, and J. A. Pegolotti, *J. Org. Chem.*, **37**, 1281 (1972).

[2] All new compounds gave elemental analysis and nmr spectra consistent with the assigned structures.

[3] This reagent was prepared in ether by reaction of sodium amalgam with *p*-biphenylyldiphenylchloromethane [for the latter see N. N. Lichtin and H. Glazer, *J. Amer. Chem. Soc.*, **73**, 5537 (1951)].

[4] Cleavage of 4-*p*-biphenylyl-1,1-diphenylbutyl methyl ether (mp 137–138°) with potassium in boiling THF gave a deep red anion which, upon carbonation or protonation, gave rise to the same major carboxylic acid or hydrocarbon as obtained from chloride **1**.

[5] S. Winstein, R. Heck, S. Lapporte, and R. Baird, *Experientia*, **12**, 138 (1956); W. H. Starnes, *J. Amer. Chem. Soc.*, **85**, 3708 (1963); H. Sakurai and A. Hosomi, *ibid.*, **93**, 7507 (1970); M. Julia and B. Malassiné, *Tetrahedron Lett.*, 987 (1971).

[6] W. A. Pryor and R. W. Henderson, *J. Amer. Chem. Soc.*, **92**, 7234 (1970); W. A. Pryor and J. P. Stanley, *ibid.*, **93**, 1412 (1971); W. A. Pryor, *Chem. Eng. News*, 42 (June 7, 1971).

[7] (a) E. Grovenstein, Jr., and L. P. Williams, Jr., *J. Amer. Chem. Soc.*, **83**, 412 (1961); (b) H. E. Zimmerman and A. Zweig, *ibid.*, **83**, 1196 (1961).