

minum hydride.²⁶ The product (30 g.) was refluxed for several hours with 47 g. of thionyl chloride in 185 ml. of toluene. After removal of solvent and excess thionyl chloride, the residue was fractionated to yield 18.5 g. (50%) of α -phenethyl- β,β,β - d_3 chloride, b. 60–61° (8 mm.).

A solution of 12 g. of this chloride in 75 ml. of tetrahydrofuran was refluxed for 12 hours with 0.5 g. of lithium aluminum deuteride and 1.5 g. of lithium deuteride. Excess deuteride was destroyed with water and the mixture was taken up in pentane. Washing, drying and distilling gave 7.8 g. (82%) of ethylbenzene- α,β,β,β - d_4 , b. 133–135°, n_D^{25} 1.4918.

(26) We are indebted to G. W. Burton for this preparation.

Kinetics.—Two experiments were performed using the sealed tube procedure (A).⁵ In the first, a mixture of ethylbenzene- α - d and ethylbenzene- α,β,β,β - d_4 was run at 49.9° as a 0.48 *M* solution in cyclohexylamine having a formal concentration of 0.067 *M* in lithium cyclohexylamide. Tubes were removed from the thermostat at intervals and the ethylbenzene was removed, distilled and examined by mass spectral analysis.⁵ The results are given in Table IV.

In the second experiment, a mixture of toluene- α - d and toluene- α,α,α - d_3 was handled in the same way. The results are summarized in Table V. The rate constants obtained as discussed above are given as k_{exp} . The $2b/Q$ correction⁵ has not been applied, since the desired quantities are rate ratios.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF CALIFORNIA, BERKELEY, CALIF.]

Acidity of Hydrocarbons. V. Stereochemistry and Mechanism of the Proton Exchange Reactions of Hydrocarbons in Cyclohexylamine¹

By A. STREITWIESER, JR.,² D. E. VAN SICKLE³ AND L. REIF

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The rate of racemization of optically active ethylbenzene- α - d with lithium cyclohexylamide in cyclohexylamine at 49.9° is 2.8 times the loss of deuterium. This result is analyzed to show that replacement of the α -hydrogen by hydrogen in this system proceeds with 82% net retention of configuration. A mechanism of the exchange reaction is proposed which involves a four-membered ring transition state in which specific asymmetric solvation by individual solvent molecules is not necessary to accommodate the results.

Of especial significance for the elucidation of the mechanism of a reaction is the stereochemistry. Determination of the stereochemistry of a proton exchange reaction can be accomplished in principle by a comparison of a rate of stereochemical change with a rate of isotope exchange; all such procedures require some knowledge of isotope effects. In the present study in which a knowledge of isotope effects is still required, we examine instead the stereochemistry of replacement of an α -hydrogen by hydrogen in optically active ethylbenzene- α - d .

Results and Discussion

Optically active ethylbenzene- α - d^4 was allowed to react with lithium cyclohexylamide in cyclohexylamine at 49.9°. At intervals, aliquots of the hydrocarbon were isolated and examined both for deuterium content and for optical activity. A semi-log plot of optical activity against time gave a satisfactory straight line corresponding to $k_{rac} = 3.0 \times 10^{-5}$ sec.⁻¹, whereas a corresponding plot of deuterium content minus the equilibrium value gives $k_{D,exp} = 1.20 \times 10^{-5}$ sec.⁻¹. The latter value must be corrected for the back reaction as detailed earlier⁵ to give the true pseudo-first-order rate constant for the forward step, $k_D = 1.07 \times 10^{-5}$ sec.⁻¹.⁶

(1) This work was supported by the United States Air Force through the Air Force Office of Scientific Research of the Air Research and Development Command, under contract No. AF 49(638)-105. Reproduction in whole or in part is permitted for any purpose of the United States Government. This paper was presented in part at the Sixteenth National Organic Symposium of the American Chemical Society, Seattle, Wash., June, 1959. A preliminary communication has been published: A. Streitwieser, Jr., D. E. Van Sickle and L. Reif, *J. Am. Chem. Soc.*, **82**, 1513 (1960).

(2) Alfred P. Sloan Fellow.

(3) Shell Development Co. Fellow, 1957–1958.

(4) E. L. Eliel, *J. Am. Chem. Soc.*, **71**, 3970 (1949).

(5) A. Streitwieser, Jr., D. E. Van Sickle and W. C. Langworthy, *ibid.*, **84**, 244 (1962).

Racemization under these conditions can result both from replacement of D by H and in part by replacement of H by H. The first case is trivial; we are interested in the fraction, λ , of the latter replacements, k_H , that result in racemization.

$$k_{rac} = k_D + \lambda k_H \quad (1)$$

λ equals 0 for complete retention of configuration, $\lambda = 1$ if each replacement occurs with complete racemization and $\lambda = 2$ for inversion of configuration. The inequality of the experimental k_{rac} and k_D tell us immediately that $\lambda \neq 0$, but a more complete characterization requires a knowledge of k_H . This quantity cannot be measured directly but may be approximated from k_D and the isotope effects. A measurement of the deuterium-tritium isotope effect led to $k_H/k_D = 12 \pm 2$,⁸ in which k_H here refers to ethylbenzene itself. The α -deuterium atom in ethylbenzene- α - d , however, is expected to slow down the rate of replacement of the hydrogen by a factor of 1.14 as estimated from the relative rates of toluene- α - d and toluene- α,α,α - d_3 .⁹ Hence, in the present case, k_H is estimated as $(12 \pm 2)k_D/1.14 = (11 \pm 2) \times 10^{-5}$ sec.⁻¹. Insertion of this value into eq. 1 gives $\lambda = 0.18 \pm 0.03$; *i.e.*, the lithium cyclohexylamide-catalyzed exchange of hydrogen by hydrogen in ethylbenzene- α - d occurs with $82 \pm 3\%$ net retention of configuration.

Previous studies⁸ have demonstrated that the exchange reaction involves an intermediate of the alkyl lithium or carbanion type. We can now eliminate free carbanions as the only intermediates in the reaction since resonance-stabilized benzylic anions are expected to be planar and incapable of supporting asymmetry. The reaction of the alkyl-

(6) This rate constant is included in Table I of ref. 7.

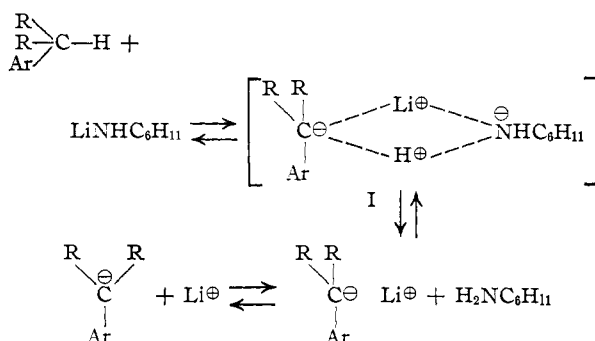
(7) A. Streitwieser, Jr., and D. E. Van Sickle, *ibid.*, **84**, 249 (1962).

(8) A. Streitwieser, Jr., W. C. Langworthy and D. E. Van Sickle, *ibid.*, **84**, 251 (1962).

(9) A. Streitwieser, Jr., and D. E. Van Sickle, *ibid.*, **84**, 254 (1962).

lithium intermediate with solvent is the microscopic reverse of the process for its formation; both could go largely with retention or inversion and account for a net retention. However, a reasonable mechanism for inversion cannot be written that is also consistent with Cram's extensive results on anion cleavage reactions (*vide infra*), whereas, the retention process has several analogies in other reactions of alkyllithium compounds reported to go with retention¹⁰ and the result is readily rationalized.

The mechanism for the exchange reaction that emerges from the kinetics, substituent effects, isotope effects and stereochemistry is the following: Reaction between lithium cyclohexylamide and hydrocarbon takes place to give a benzyllithium derivative *via* a four-membered transition state, I. The four-membered nature of the transition state is proposed not as a magic consequence of unusual bonding but simply to reduce the electrostatic energy of charge separation in this solvent of low dielectric constant.¹¹ The dotted lines in I represent bonds that may be largely or completely ionic.



The carbanionic character of the hydrocarbon moiety at the transition state accounts for the effect of methyl substituents on rate⁷ and for the β -deuterium isotope effect.⁹ The steric effect of the H^+ and Li^+ in the transition state could be roughly comparable to that of a single bonded hydrogen in the starting hydrocarbon and be consistent with both the absence of a net steric effect when R is methyl⁷ and the α -deuterium isotope effect.⁹ The extreme "looseness" of the migrating proton in this transition state is consistent with the relatively large primary isotope effect observed experimentally.⁸ Retention of configuration is a clear stereochemical consequence of the electrostatic attraction within the benzyllithium derivative formulated here as a "tight" ion-pair. Fluorenyllithium is known to dissociate to some extent in cyclohexylamine¹²; such dissociation before reaction of the alkyllithium with solvent would result in racemization. We suggest that the partial race-

mization observed in the reaction of ethylbenzene- α -*d* is to be attributed to such dissociation.^{10c}

The role played by free ions requires comment. At extremely high dilution all of the ionic species involved would exist as free ions and the exchange reaction would undoubtedly be a true ionic reaction between hydrocarbon and cyclohexylamide ion. In the concentration region used in our experiments ($>10^{-3} M$), the proportion of exchange reaction proceeding *via* free ions is so small that it cannot be detected kinetically. Some portion of the dissociated alkyllithium that racemizes may react as the free carbanion with solvent but from microscopic reversibility, recombination to racemic alkyllithium ion pairs must be more important. In this mechanism, no special role can be given to "solvent separated" ion-pairs. Their presence is not detected in these experiments; however, we might expect that if involved at all, they would contribute to some of the racemization involved. We should point out, however, that separation of two ions by several solvent molecules requires most of the electrostatic energy of total charge separation. Further complete separation requires little additional energy; hence, such species may not be kinetic entities in this system. We suggest that this is the reason that the alkyllithium does not react with solvent with inversion of configuration; this process results in separated ions and requires additional energy. Moreover, the forward step of the exchange reaction would then have to proceed by the microscopic reverse process, a highly improbable reaction. We should note that in this mechanism it is neither necessary nor desirable to attribute a special role to individual solvent molecules, as in some possible forms of "asymmetric solvation."

Cram, Kingsbury and Rickborn¹³ have also reported a predominant net retention of configuration in H-D exchanges in *t*-butyl alcohol with potassium *t*-butoxide. Their interpretation of these results makes use of asymmetric solvation including hydrogen bonding between solvent and the intermediate carbanion. In our solvent system, hydrogen bonding is undoubtedly of minor importance and does not need to be involved to explain our results. It appears to us that the primary difference in interpretation may be stated as follows: In Cram's interpretation of alkoxide catalyzed hydrogen-deuterium exchange with retention, ". . . the active catalytic species are heavily solvated metal alkoxide ion-pairs, and the carbanion-metal cation ion pair produced is heavily solvated on the front side with deuterium donors because of the solvent-orienting power of the metal cation. Thus, deuterium capture from the front is the favored reaction path."^{13b} In our view, reaction occurs frontside because reaction at the rear produces charge separation in a medium of poor ionizing power. At present, we are endeavoring to formulate this distinction in operational terms that may be subject to experimental test.

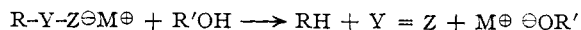
This chemistry is undoubtedly related to anionic cleavage reactions of the type

(13) (a) D. J. Cram, C. A. Kingsbury and B. Rickborn, *J. Am. Chem. Soc.*, **81**, 5835 (1959); (b) **83**, 3688 (1961).

(10) (a) R. L. Letsinger, *J. Am. Chem. Soc.*, **72**, 4842 (1950); (b) H. M. Walborsky and F. J. Impastato, *ibid.*, **81**, 5835 (1959); (c) D. Y. Curtin and W. J. Koehl, Jr., *Chemistry & Industry*, 262 (1960); (d) D. E. Applequist and A. H. Peterson, *J. Am. Chem. Soc.*, **83**, 862 (1961).

(11) Estimated dielectric constant of cyclohexylamine at 50° is ~4; at -21°, the dielectric constant is reported to be 5.4: A. H. White and W. S. Bishop, *J. Am. Chem. Soc.*, **62**, 8 (1940).

(12) Dissociation of ionic compounds is slight in cyclohexylamine; however, fluorenyllithium is orders of magnitude more dissociated than lithium cyclohexylamide or lithium perchlorate (unpublished results of W. M. Padgett).



which, for some years, have been the subject of an extensive and detailed investigation by Cram, *et al.*¹⁴ Such reactions differ in principle from the proton exchange reactions because an additional leaving group, $Y = Z$, is involved. Without reviewing Cram's extensive and pioneering stereochemical studies, suffice it to say that solvents are classifiable experimentally as "inversion" or "retention" depending on the predominant stereochemistry of the product, RH. Glycols are in the inversion class; amines and higher alcohols are in the retention class. To the extent that these reactions are related to the simple proton exchanges, our present results find a prior analogy to Cram's "retention" solvents.

(14) D. J. Cram, J. Allinger and A. Langemann, *Chemistry & Industry*, 919 (1955); D. J. Cram, A. Langemann, J. Allinger and K. R. Kopecky, *J. Am. Chem. Soc.*, **81**, 5740 (1959); and numerous papers following.

TABLE I

| Time, min. | α_D | $10^4 k_{\text{exp}}$, min. ⁻¹ | $\log I_0/I$ | $10^4 k_{D,\text{exp}}$, min. ⁻¹ |
|------------|------------|--|--------------|--|
| 0 | 0.405° | | 0.619 | |
| 150 | .330 | 14 | .559 | 6.1 |
| 450 | .172 | 19 | .461 | 6.8 |
| 800 | .102 | 17 | .376 | 6.7 |
| 1330 | .036 | 18 | .269 | 7.1 |
| 7500 | .002 | | .052 | |

Experimental

Kinetics.—Optically active ethylbenzene- α -d⁴ was allowed to exchange at 49.9° as a 0.71 *M* solution in cyclohexylamine, 0.049 *M* in lithium cyclohexylamide according to procedure (A) described previously.⁵ Samples of ethylbenzene were isolated at intervals, distilled and examined for deuterium (infrared) and polarimetrically (1-dm. semi-micro tube). The results are summarized in Table I. Although more accurate rate constants are determined graphically, the instantaneous constants obtained by the usual first-order equation are given in Table I to illustrate the quality of the data.

[CONTRIBUTION FROM THE DANIEL SIEFF RESEARCH INSTITUTE, THE WEIZMANN INSTITUTE OF SCIENCE, REHOVOTH, ISRAEL]

Unsaturated Macrocyclic Compounds. XXI.¹ The Synthesis of a Series of Fully Conjugated Macrocyclic Polyene-polyynes (Dehydro-annulenes) from 1,5-Hexadiyne

BY FRANZ SONDSHEIMER AND REUVEN WOLOVSKY

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The oxidative coupling of 1,5-hexadiyne (I) with cupric acetate in pyridine yields the cyclic trimer II, tetramer III, pentamer IV, hexamer V and heptamer X. The cyclic trimer is rearranged smoothly by means of potassium *t*-butoxide in *t*-butyl alcohol to the fully conjugated eighteen-membered ring monocyclic hexaene-triynene XIII (tridehydro-[18]annulene), a reaction which also produces some triphenylene. Similar rearrangements of III, IV and V give rise to the corresponding conjugated monocyclic polyene-polyynes tetradecahydro-[24]annulene, pentadecahydro-[30]annulene and hexadecahydro-[36]annulene (XIV, XV and XVI, or isomers), respectively. The synthesis of these conjugated substances is carried out most conveniently by the coupling of 1,5-hexadiyne followed by direct rearrangement, without isolation of intermediates. The properties of the novel conjugated polyene-polyynes are discussed briefly, especially in relation to their possible aromatic nature.

Introduction.—Completely conjugated monocyclic large-ring systems are of very considerable interest from a theoretical as well as possibly from a practical standpoint. In Part XIX of this series² we described an attempt to prepare such systems making use of the fact that the oxidative coupling of aliphatic α,ω -diacetylenes may give rise to large-ring poly-acetylenes^{3,4} and that the prototropic rearrangement of linear 1,5-enynes with potassium *t*-butoxide in *t*-butyl alcohol produces the corresponding conjugated polyenes.⁵ It was anticipated that large-ring hydrocarbons made up of 1,5-enyne units could be constructed by the coupling of a suitable α,ω -diacetylene and that subsequent rearrangement would then lead to completely conjugated cyclic polyenes. In the event, the desired prototropic shifts did not proceed smoothly and no clear-cut results were obtained.²

It has been shown by us that linear 1,5-diyne are rearranged by means of potassium *t*-butoxide to conjugated polyen-yne,⁶ a reaction which is analogous to the rearrangement of 1,5-enynes to polyenes but which proceeds with considerably greater facility. An alternative approach to completely conjugated monocyclic systems therefore appeared to involve the synthesis of large-ring compounds consisting of 1,5-diyne units through oxidative coupling of an appropriate α,ω -diacetylene, followed by prototropic rearrangement. This type of approach has been found to be realizable in practice, and in this paper we describe by its use the synthesis of fully conjugated macrocyclic polyene-polyynes containing 18, 24, 30 and 36 carbon atoms in the ring.^{7,8}

Nomenclature.—The work described in this and subsequent papers⁹⁻¹⁰ has made available a con-

(1) For Part XX, see F. Sondheimer and Y. Gaoni, *J. Am. Chem. Soc.*, **83**, 1259 (1961).

(2) F. Sondheimer, R. Wolovsky and D. A. Ben-Efraim, *ibid.*, **83**, 1686 (1961).

(3) (a) F. Sondheimer and Y. Amiel, *ibid.*, **75**, 5817 (1957); (b) F. Sondheimer, Y. Amiel and R. Wolovsky, *ibid.*, **79**, 6263 (1957); (c) F. Sondheimer, Y. Amiel and R. Wolovsky, *ibid.*, **81**, 4600 (1959).

(4) G. Eglington and A. R. Galbraith, *J. Chem. Soc.*, 889 (1959).

(5) F. Sondheimer, D. A. Ben-Efraim and R. Wolovsky, *J. Am. Chem. Soc.*, **83**, 1675 (1961).

(6) F. Sondheimer, D. A. Ben-Efraim and Y. Gaoni, *ibid.*, **83**, 1682 (1961).

(7) For preliminary communications, see (a) F. Sondheimer, Y. Amiel and R. Wolovsky, *ibid.*, **79**, 4247 (1957); (b) F. Sondheimer and R. Wolovsky, *ibid.*, **81**, 1771 (1959); (c) F. Sondheimer and R. Wolovsky, *ibid.*, **81**, 4755 (1959); (d) F. Sondheimer, R. Wolovsky and Y. Gaoni, *ibid.*, **82**, 754 (1960).

(8) For the synthesis of related compounds by use of the same type of approach, see F. Sondheimer and Y. Gaoni, Part XXV, *ibid.*, in press (for preliminary communications, see footnotes 1 and 7d).