Phase-Transfer Catalysis. I. Heterogeneous Reactions Involving Anion Transfer by Quaternary Ammonium and Phosphonium Salts
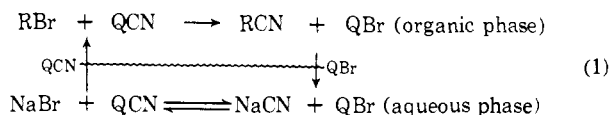
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Abstract: Displacement reactions of alkyl halides in an organic phase with inorganic anions in an aqueous phase that are inhibited because of phase separation may often be strongly catalyzed by adding trace amounts of organic phase soluble tetralkylammonium or tetralkylphosphonium salt. These salts catalyze many other two-phase reactions involving anions, such as dichlorocyclopropanation of alkenes with chloroform and aqueous NaOH, oxidation of alkenes with aqueous $KMnO_4$, deuterium exchange of the active hydrogens of ketones with D_2O, hydrolysis of esters and alkanesulfonyl chlorides with aqueous NaOH, and borohydride reduction of ketones. Catalysis is believed to be due to the ability of the organic-soluble cations to repeatedly bring anions into the organic phase in a form suitable for reaction, and the effect is termed *phase-transfer* catalysis.

Reaction between two substances located in different phases of a mixture is often inhibited because of the inability of reagents to come together. An example is a stirred heterogeneous mixture of 1-bromooctane and aqueous sodium cyanide in which, after 2 weeks at 100°, the only reaction is hydrolysis of NaCN to sodium formate. Traditionally this problem is solved by use of an appropriate mutual solvent.

An alternative solution to the heterogeneity problem, *phase-transfer catalysis*, is introduced here. Reaction is brought about by the use of small quantities of an agent which transfers one reactant across the interface into the other phase so that reaction can proceed. The phase-transfer agent is not consumed but performs the transport function repeatedly. Thus, in the cyanide displacement on 1-bromooctane, a phase-transfer agent may either transport the alkyl bromide into the aqueous phase for reaction, or transport cyanide ion into the organic phase. Organic-soluble quaternary ammonium or phosphonium cations, Q^+, were found to be excellent agents for the transport of anions from aqueous phase to an organic phase. Catalysis of the cyanide displacement on 1-bromooctane by quaternary salt is represented in eq 1. In this way a little organic-

$$RBr + QCN \longrightarrow RCN + QBr \text{ (organic phase)}$$
$$QCN \uparrow \underline{\hspace{5cm}} \downarrow QBr \qquad (1)$$
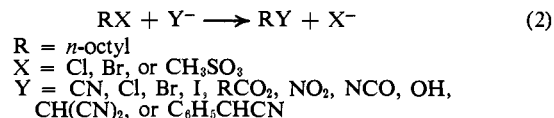$$NaBr + QCN \Longrightarrow NaCN + QBr \text{ (aqueous phase)}$$

soluble quaternary salt dramatically increases the displacement reaction rate. Reaction rates for the displacement shown in the upper step of eq 1 are comparable to those obtained using dimethylformamide as a solvent, and thus the method should become a useful and versatile tool for synthetic organic reactions.

The work discussed in this paper involves use of quaternary salts as catalysts for displacement reactions, preparation of dichlorocyclopropanes from olefins, $CHCl_3$, and aqueous sodium hydroxide, permanganate oxidation of olefins, deuterium exchange of ketones, and other reactions. However, phase-transfer catalysis is actually a general concept; it has been observed that inorganic cations, acids, hydrogen peroxide, and am-

monia can be transported into organic phases for reaction by the use of suitable phase-transfer agents.

Results

Displacement Reactions. The displacement reactions shown in eq 2 were run in a heterogeneous system by the use of quaternary salts as anion-transfer catalysts. These experiments were conducted by initially mixing all the reagents except quaternary salts to determine if reaction would go in its absence. Only *n*-octyl methanesulfonate was sufficiently soluble in the aqueous phase for reaction to be detected, and even so the rates at 100° were low and did not hinder observation of the powerful catalytic effect of the quaternary salts. The final reaction products in runs with cyanate,

$$RX + Y^- \longrightarrow RY + X^- \qquad (2)$$
R = *n*-octyl
X = Cl, Br, or CH_3SO_3
Y = CN, Cl, Br, I, RCO_2, NO_2, NCO, OH, $CH(CN)_2$, or C_6H_5CHCN

hydroxide, and malononitrile were the *N,N'*-dialkylurea, the alcohol plus the dialkyl ether, and the dialkylmalononitrile, respectively.

Many types of quaternary ammonium and phosphonium salts were tested. Those most suitable were completely soluble in the organic phase of the reaction mixture and stable under the reaction conditions. A commercially available ammonium salt, "tricaprylylmethylammonium chloride,"[1] and an easily prepared phosphonium salt, hexadecyltributylphosphonium bromide, were suitable for general use and one or the other of these can be used for all experiments described herein. Salts containing phenyl, allyl, and benzyl groups were often unstable under the reaction conditions. Quaternary compounds containing two or three methyl groups and one or two long alkyl groups were difficult to use because they promoted formation of stable emulsions. Phosphonium salts appear to be more stable (up to 200°) than the corresponding ammonium salts (up to 100°) except in systems containing aqueous sodium hydroxide. Tetra-

(1) "Tricaprylylmethylammonium chloride" or "aliquat" 336, from General Mills Co., Kankakee, Ill.

alkylammonium salts were moderately stable in the presence of aqueous alkali at 50°. The reaction between 1-chlorooctane and aqueous sodium cyanide was perceptibly catalyzed by an anionic surfactant (sodium dodecylbenzenesulfonate) and a nonionic surfactant (dodecanol plus tetradecanol treated with 6 mol of ethylene oxide) but the rates were lower by a factor of 100–1000 than when the reaction was quaternary salt catalyzed.
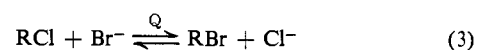
The displacement reactions represented in eq 2 show approximate first-order dependence on quaternary salt concentration and reaction rates can be adjusted to convenient values by changing the catalyst concentration. The initial organic phase usually consisted of 85–90% RX, 1–5% quaternary salt, and ca. 10% of an inert hydrocarbon used as an internal standard for gas chromatographic analysis.

Cyanide displacement was the most thoroughly studied of all reactions. In general, it was found to behave as expected for S_N2 displacements. Reaction is much faster with primary than with secondary alkyl halides; cyclohexyl and tertiary alkyl halides give predominantly elimination products; displacement of d-2-octyl methanesulfonate with cyanide at 100° gave l-2-methyloctanonitrile (inversion product) with a maximum of 30% racemization. At 105° the quaternary salt catalyzed reaction of 2-chlorooctane with aqueous sodium cyanide gave ca. 85–90% displacement product and 10–15% elimination product, comparable to 70% displacement selectivity with NaCN and 2-chlorooctane in dimethyl sulfoxide.[2] At 105° and in the presence of 1% hexadecyltributylphosphonium bromide, more than 95% cyanide displacement was attained in 20 min with n-octyl methanesulfonate, in 90 min with 1-bromooctane, and in 300 min with 1-chlorooctane. When the catalyst level was increased to 5%, runs with the octyl methanesulfonate and 1-bromooctane became uncontrollable because of violent boiling, and the time required for the run with 1-chlorooctane to reach 95% completion was about 1 hr. When either 1-iodooctane or octyl p-toluenesulfonate was used as RX in cyanide displacement, the reaction started well, but after 5–30% conversion, the reaction ceased. If the aqueous phase were replaced by fresh cyanide solution, reaction began only to stop again when the concentration of iodide or tosylate ion in the aqueous phase reached an unfavorable level.

Quaternary salt catalyzed displacement reaction with sodium halides is a choice method for exchange of halogen in alkyl halides, or for the conversion of alcohols, via the methanesulfonate, to alkyl halides. For example, exchange of radioactive ^{36}Cl ion for nonradioactive chloride was accomplished simply by heating under reflux a mixture of alkyl chloride, quaternary salt catalyst, and an aqueous solution of $Na^{36}Cl$. Complete chloride equilibration with 1-chlorooctane was reached after 5 hr at 100°. The corresponding iodide–radioiodide exchange was complete after ca. 5 min at 100° in the presence of quaternary salt catalyst. Alkyl chlorides may be converted to alkyl bromides or vice versa, driving the equilibrium represented by eq 3 in the desired direction by replacing the aqueous phase from the equilibrated system

(2) R. A. Smiley and C. Arnold, J. Org. Chem., 25, 257 (1960).

with fresh sodium halide solution. For the case when

$$RCl + Br^- \underset{}{\overset{Q}{\rightleftharpoons}} RBr + Cl^- \qquad (3)$$

R is octyl, this reaction shows an apparent equilibrium constant of unity.

Alkylation of malononitrile and phenylacetonitrile are different from the other displacement reactions listed in that the displacing anions were generated in situ by treatment with aqueous sodium hydroxide. Alkylation of malononitrile with 1-bromohexane produced only dialkylated product, $(C_6H_{13})_2C(CN)_2$, even when the concentration of alkyl halide was kept extremely low. As in the case of iodide and tosylate reaction with cyanide, the quaternary cation in the organic phase tends, when a choice is available, to be associated with the larger and more organic of two anions, so that $RC(CN)_2^-$ is preferred over $^-CH(CN)_2$. However, alkylation of phenylacetonitrile under mild conditions gave dialkylation with methyl chloride, but only monoalkylation with 1-bromohexane.

Preparation of Dichlorocyclopropanes from an Olefin, Chloroform, and Sodium Hydroxide. The reaction of chloroform, an olefin, and a base to give dichlorocyclopropanes normally requires anhydrous reaction conditions to prevent the rapid hydrolysis of intermediate CCl_3^- anion to carbon monoxide and sodium formate.[3] Thus, addition of chloroform to a mixture of cyclohexene and 25% aqueous NaOH gave less than 5% yield (based on $CHCl_3$) of 2,2-dichlorobicyclo[4.1.0]heptane. However, in the presence of 5% quaternary ammonium catalyst a 60% yield was obtained, comparable to that produced with sodium or potassium alkoxides under anhydrous conditions. The dramatic change in products when the quaternary salt is present suggests that CCl_3^- anion or dichlorocarbene is maintained in the organic phase away from water sufficiently long to undergo reaction with olefin.[4]

Reaction temperatures of 45–55° were required for 1-alkenes, as compared to room temperature for cyclohexene. In reactions with 1-octene and 1-hexene, a product tentatively identified as that expected from dichlorocarbene addition to the 2-alkene was formed in small yield. The unexpected product is evidently formed via an intermediate in the reaction since the starting olefins contained no detectable quantities of 2-alkenes (by nmr) and neither the 1-alkene nor the dichlorocyclopropane undergoes rearrangement under the reaction conditions.

Relative rates for reaction of several isomeric hexenes with chloroform and sodium hydroxide in the presence of quaternary ammonium catalyst, as determined by competition experiments, are shown in Table I. These relative rates are more comparable to those observed in the dichlorocyclopropanation of olefins with the anhydrous $CHCl_3$-$tert$-BuOK system[5] than with C_6H_5-$HgCCl_2Br$.[6] The phase transfer catalyzed reaction

(3) W. Kirmse, "Carbene Chemistry," Academic Press, New York, N. Y., 1964, p 152; S. W. Tobey and R. West, J. Amer. Chem. Soc., 86, 56 (1964).
(4) K. Klamann, M. Fligge, P. Weyerstahl, and K. Ulm (Chem. Ing. Tech., 39, 1024 (1967)) have found that $Et_4N^+Br^-$ is superior to other catalysts including quaternary ammonium tosylates, hydroxide ion, pentacyanopropenide ion, and quaternary phosphonium or arsonium halides for dichlorocyclopropanation of an olefin with $CHCl_3$ and ethylene oxide.
(5) W. von E. Doering and W. A. Henderson, Jr., J. Amer. Chem. Soc., 80, 5274 (1958).

Table I. Relative Reactivities of Isomeric Hexenes toward Dichlorocyclopropanation with $CHCl_3$ and Aqueous NaOH in the Presence of Tricaprylylmethylammonium Chloride[a]

Hexene	Relative rate of cyclopropanation
2,3-Dimethyl-2-butene	80
2-Methyl-1-pentene	36
cis-4-Methyl-2-pentene	7
Cyclohexene	5
trans-4-Methyl-2-pentene	5
trans-2-Hexene	4
1-Hexene	(1.0)
3-Methyl-1-pentene	0.6

[a] At 30–45°.

does not give hexachlorocyclopropane with tetrachloroethylene, nor does it give addition or insertion products with benzene or toluene. The phase-transfer technique is very convenient and inexpensive for the preparation of large quantities of dichlorocyclopropanes.

Oxidation of Olefins with Potassium Permanganate. Reaction between 1-octene and aqueous neutral $KMnO_4$ was not observed at room temperature, even after vigorous stirring for several hours. Addition of a little quaternary ammonium catalyst caused immediate oxidation of the olefin as shown by precipitation of MnO_2 and by evolution of so much heat that the reaction mixture could not be contained in the flask. When the temperature of the reaction mixture was controlled to 35° by slow addition of 1-octene to a mixture of potassium permanganate, water, and a 5% solution of quaternary ammonium salt in benzene, an essentially quantitative yield of hexanoic acid was obtained. This method is experimentally much easier than permanganate oxidations in the usual solvents. Benzene and toluene are not rapidly attacked by quaternary ammonium permanganate at temperatures below 60°.

Deuterium Exchange of Active Hydrogen Atoms. A convenient procedure for the deuterium exchange of compounds containing active hydrogen atoms was demonstrated with 2-octanone. A solution of 5% NaOD in D_2O was mixed with 5% quaternary ammonium catalyst in neat ketone with magnetic stirring at 30°. Within 0.5 hr complete equilibration of the hydrogen atoms on the 1- and 3-carbons of the ketone had taken place. After two such exchanges with a 10:1 ratio of D_2O per active hydrogen in each exchange, more than 99% of the active hydrogens on the ketone had been replaced by deuterium. In the absence of the quaternary ammonium catalyst less than 5% deuterium exchange had taken place after 3 hr at 30°. In this use of quaternary ammonium catalyst as a phase-transfer agent, D_2O is probably taken into the organic phase as water of hydration on the anion.

Borohydride Reduction. Reduction of 2-octanone (as a 50% solution in benzene) with a solution of $NaBH_4$ in 2 N NaOH was 20–30-fold faster in the presence of quaternary ammonium salt than in its absence. Reduction is still quite slow, however, and the phase-transfer method does not offer any advantages for routine borohydride reductions. However, this

reduction is of considerable interest because of the possibility that optically active quaternary salts may lead to optically selective reductions. The borohydride salts of long-chain quaternary ammonium salts are commercially available[7] and have been used in solvents which are not suitable for $NaBH_4$ reductions.

Ester Hydrolysis. Hydrolysis of esters by aqueous sodium hydroxide is sometimes facilitated by the use of long-chain quaternary ammonium salts. Thus, no hydrolysis of dimethyl adipate by aqueous 50% sodium hydroxide solution is observed when a mixture of the two is stirred at room temperature. However, if a small quantity of quaternary ammonium catalyst is added, reaction begins immediately with evolution of sufficient heat to cause reflux. Hydrolysis is complete in 0.5 hr. If the carboxylic part of the ester has a long organic chain, the quaternary cation will be associated with the carboxylate anion rather than with hydroxide, and its catalytic effect will be destroyed. For example, the catalyzed hydrolysis of methyl tetradecanoate with 50% aqueous sodium hydroxide began rapidly, but as reaction proceeded hydrolysis slowed and had essentially stopped after 35% reaction. Addition of more quaternary ammonium catalyst did not cause the reaction to continue appreciably, indicating that quaternary salt decomposition was not the cause for the reaction to stop. Poly(methyl acrylate) behaved similarly.

Hydrolysis of Alkanesulfonyl Chlorides. The heterogeneous hydrolysis of long-chain alkanesulfonyl chlorides with aqueous NaOH is difficult to start, although once initiated, the reaction is mildly autocatalytic.[8] Thus, a mixture of isomeric dodecanesulfonyl chlorides in dodecane solution was stirred with 10% NaOH solution for 1 hr at room temperature. No reaction could be detected. However, addition of a little quaternary ammonium catalyst made the hydrolysis essentially instantaneous. In fact, by suitable calibration the temperature increase in this reaction is sharp enough that it can be used for quantitative determination of alkanesulfonyl chlorides in hydrocarbon solution.

Discussion

There are several reports on the use of quaternary ammonium salts as catalyst for heterogeneous reactions in a mode that can be classed as phase-transfer catalysis.[9] However, in these examples moderately low molecular weight quaternary cations were used and either organic solvent was required or the transferred anion was sufficiently organic and hydrophobic that the total quaternary cation plus anion was soluble in the organic phase.

Numerous reports have been published on the kinetic effects of certain surface-active quaternary ammonium salts during micelle formation.[10] Quaternary am-

(6) D. Seyferth, Proc. Robert A. Welch Found. Conf. Chem. Res., 1965, 9, 89 (1966); D. Seyferth and J. M. Builitch, J. Amer. Chem. Soc., 86, 2730 (1964).

(7) Technical Bulletins 6A and 7A, Quaternary Ammonium Borohydrides, Ventron Corporation, Metal Hydrides Division, Beverly, Mass.

(8) J. E. Yates, private communication.

(9) (a) J. Lange, Rocz. Chem., 42, 1619 (1968); Chem. Abstr., 70, 37413 (1969); (b) A. Brandstrom and U. Junggren, Acta Chem. Scand., 23, 2204 (1969); (c) H. B. Copelin and G. B. Crane, U. S. Patent 2,779,-781 (1957); (d) Farbenfabriken Bayer A.G., German Patent 959,497 (1957); Chem. Abstr., 53, 13665 (1959); J. E. Hennis, L. R. Thompson, and J. P. Long, Ind. Eng. Chem., Prod. Res. Dev., 7, 96 (1968).

(10) E. H. Cordes and R. B. Dunlap, Accounts Chem. Res., 2, 329 (1969).

monium salts in use as phase-transfer catalysts have much in common with the surfactant quaternary ammonium salts used in micelle systems, particularly in regard to the types of reaction catalyzed and the inhibiting effects of foreign anions. However, highly effective catalysis by poor surfactants such as tetra-(dodecyl)ammonium salts, the kinetic order (first-order dependence of rate on the concentration of quaternary salt), and the known ability of quaternary ammonium salts to participate in displacement reactions at exceptionally high rates even in nonpolar media,[11] support the belief that the catalysis reported here is not due to micellar effects, but to the cycle represented by eq 1. Details of the kinetics and comparison with micellar systems will be reported subsequently.

It is useful to consider phase-transfer catalysis in terms of the two requirements of the phase-transfer agent. The agent must serve as a vehicle to bring one reactant into the same phase as the second, and the transferred species must be in a suitable environment for reaction.[12] In the example of reaction between 1-bromooctane and aqueous sodium cyanide, the phase-transfer function is represented by eq 4 and the organic displacement reaction by eq 5. Several agents were

$$QBr_{org} + CN_{aq}^- \rightleftharpoons QCN_{org} + Br_{aq}^- \qquad (4)$$

$$QCN + R{-}Br \longrightarrow RCN + QBr \qquad (5)$$

examined that were not capable of both functions. For example, certain metal chelates with large organic ligands were found to be capable of transporting cyanide to the organic phase, but the cyanide was evidently bound so tightly to the cation that a displacement reaction could not occur.

The phase-transfer function represented by eq 5 is a known[13] equilibrium between anions in an aqueous phase and anions associated with quaternary cations in an organic phase. Quaternary cations in a nonpolar environment preferentially associate with large and minimally hydrated anions and also with anions having considerable organic structure. This selectivity is important to the reaction step since, in anion-transfer reactions, it dictates which anion will predominate in the organic phase. The CN^-/Br^- partitioning is so balanced that sufficient QCN is present in the 1-bromooctane phase to allow displacement to proceed readily to completion (provided NaCN was used in at least 20 mol % excess). This is evidently not true in NaCN reaction with alkyl iodides, wherein anion-partitioning selectivity by the quaternary cation for iodide ion is much greater than for cyanide ion. Anion-partitioning selectivity can also account for the greater ease in

displacement reactions of alkyl methanesulfonates relative to alkyl tosylates, exclusive dialkylation of malononitrile, and the reluctance of quaternary salts to catalyze displacement reactions with bisulfite and thiosulfate anions.

The remarkable ability of anions associated with quaternary cations in nonpolar media to undergo displacement reactions[11] is particularly suited to the requirement that the phase-transfer agent bring the transferred species in a reactive form. Uglestad, et al.,[11] suggests that in nonpolar media the ion-pair form of the quaternary salt is the reactive entity, and that the abnormal activity is explained by a reduced cation–anion interaction energy. However, an alternate possibility is the formation of a weak complex in which the alkyl halide penetrates deeply into the web of alkyl groups around the quaternary nitrogen or phosphorus atom. Such complex formation is favored not only by Coulombic ion–dipole attractions, but also by van der Waals attraction between the alkyl groups of quaternary cation and that of the alkyl halide. From such a complex a "push-pull" transition state, as described by Swain,[14] can be readily formed, although in this case it is not necessary that the displacing anion be separated from the cation (ionized).

Experimental Section

"Tricaprylylmethylammonium chloride" or "aliquat" 336 was obtained from General Mills Company, Chemical Division, Kankakee, Ill. The alkyl groups are a mixture of C_8-C_{12} straight chains with an average of ten carbon atoms. Molecular weight by titration of the chloride was 507.

Hexadecyltributylphosphonium bromide was prepared by heating equimolar quantities of 1-bromohexadecane and tributylphosphine at 65° for 3 days. The solid product was recrystallized from hexane and vacuum dried to give the phosphonium salt, mp 54°, in 68% yield. Anal. Calcd for $C_{28}H_{60}PBr$: Br, 15.77. Found: 15.8.

Displacement Reactions. These reactions were normally run by heating and stirring a mixture of alkyl halide, an inert hydrocarbon (as glc internal standard), and an aqueous solution of the inorganic reagent to 100–105°. After 3–4 hr a sample of the organic phase was analyzed to determine if any reaction had taken place. In reactions with halooctanes no reaction could be detected until the quaternary salt was added. Addition of catalyst caused the reaction to start promptly. Normally the inorganic reagent was used in two-threefold excess over that required in order to offset the partition effect of the displaced anion. Saturated solutions of the inorganic reagent in water were normally used but little change in rate was observed when dilute solutions were employed provided that an excess of reagent was present. The organic phase usually was made up of 80–90% alkyl halide, 10% inert hydrocarbon, and 1–10% quaternary salt catalyst. In most experiments the reaction products were separated by distillation from the quaternary salt under reduced pressure. The quaternary salt may also be separated by precipitation with several types of anions, such as phosphotungstate or perchlorate (n-hexane was sometimes required to cause precipitation).

Reaction of 1-Chlorooctane with Sodium Cyanide. A mixture of 100 g (0.67 mol) of 1-chlorooctane, 100 g (2.0 mol) of NaCN, 25 ml of H_2O, and 25 ml of decane was heated to 105° for 3 hr. After this time a sample of the organic phase of the reaction mixture was analyzed by gas chromatography and found to be identical with a sample of the organic phase before heating. The mixture was cooled to 50° and 5 g (0.01 mol) of hexadecyltributylphosphonium bromide was added. The mixture was heated rapidly to the reflux temperature (105°). After 1 hr the reaction was 89% complete. After 1.8 hr the reaction was 99% complete. The organic phase of the reaction mixture was passed through a short residence time wiped-film evaporator at 140° and 1 mm pressure

(11) J. Uglestad, T. Ellingsen, and A. Berge, *Acta Chem. Scand.*, 20, 1593 (1966).

(12) Phase-transfer agents need not participate in the reaction. For example, addition of copper(I) chloride to two-phase mixtures of 1-decene, formaldehyde, and aqueous HCl markedly catalyzes the Prins reaction. In this case it is believed that catalysis results from formation of a weak, aqueous phase soluble complex between alkene and cuprous ion. Alternatively, the phase-transfer agent may combine with the organic reagent, followed by transfer of this product to the aqueous phase for reaction. This sequence is believed to occur in the strong catalysis observed on addition of a large (C_{32}) "oil-soluble" alkanesulfonic acid to 1-cyanododecane for hydrolysis with aqueous HCl at 60°.

(13) (a) I. M. Ivanov, L. M. Gindin, and G. N. Chicaqova, *Izv. Sib. Otd. Akad. Nauk SSSR, Ser. Khim. Nauk*, 100 (1967); *Chem. Abstr.*, 69, 13377 (1968); (b) F. G. Seeley and D. J. Crouse, *J. Chem. Eng. Data*, 11, 424 (1966); (c) E. Cerai, *Chromatog. Rev.*, 6, 154 (1964); G. Scibona, J. F. Byrum, K. Kimura, and J. W. Irvine, *Solvent Extr. Chem. Proc. Int. Conf.*, 398 (1965); *Chem. Abstr.*, 69, 30827 (1968).

(14) C. G. Swain, *J. Amer. Chem. Soc.*, 70, 1119 (1958); C. G. Swain and C. B. Scott, *ibid.*, 75, 141 (1953).

to give 98.4 g of distillate. Analysis of this material by gas chromatography showed it to contain 90.6% 1-cyanooctane corresponding to a 95% yield.

When the reaction was repeated in the absence of decane, a 94% yield of 1-cyanooctane was obtained in 97% purity.

Reaction of Chloroform with 1-Octene with Sodium Hydroxide. Chloroform (37.5 g, 0.31 mol) was added dropwise to a stirred mixture of 75 g (0.67 mol) of 1-octene, 140 g of 50% NaOH solution (1.75 mol of NaOH), and 5.0 g (0.01 mol) of "tricaprylylmethylammonium chloride" at such a rate that the temperature was maintained at 45–50° (*ca.* 0.5 hr). After the addition was complete, the reaction mixture was stirred at room temperature for 1 hr. The organic layer was separated and washed with H_2O (two 200-ml portions); the last wash gave an emulsion which was broken by the addition of 10 ml of saturated NaCl solution). Analysis of the organic layer by glc showed it to contain 59% 1-octene, 9.6% chloroform, and 31% products. Distillation through a 12-in. vacuum-jacketed Vigreux column gave 28 g of product fraction, bp 49° (0.2–0.5 mm), and was shown by glc analysis to contain two components. These were separated by preparative glc. The major component (93%) was the expected 2-hexyl-1,1-dichlorocyclopropane as shown by comparison of its ir and nmr spectra and its glc retention time with those of a sample prepared by the method of Weinberg.[15] The minor component

(7%) was identified by its nmr and mass spectra as 2-pentyl-3-methyl-1,1-dichlorocyclopropane. The isolated yields of the two products were 60 and 4%, respectively, based on unrecovered chloroform.

Permanganate Oxidation. 1-Decene (28 g, 0.2 mol) was added to a stirred mixture of 50 ml of benzene, 5 g (0.01 mol) of "tricaprylylmethylammonium chloride," 125 g (0.8 mol) of $KMnO_4$, and 100 ml of H_2O at such a rate that the temperature was maintained at 40–45° (0.5 hr). After addition was complete the mixture was stirred for an additional 0.5 hr. Excess permanganate was destroyed by addition of sodium sulfite solution. The reaction mixture was filtered to remove MnO_2 and acidified with dilute HCl. The MnO_2 was washed with 100 ml of benzene, which was also used to wash the aqueous phase of the filtrate. The combined benzene solutions were shaken with 100 ml of 10% NaOH solution. The aqueous alkaline phase was washed with ether and then acidified with hydrochloric acid. The carboxylic acid which was separated was taken up in 100 ml of ether, and the ethereal solution was dried (Na_2SO_4). Evaporation of ether left 29 g (91%) of nonanoic acid (98% purity by glc).

(15) H. E. Weinberg, *J. Org. Chem.*, 24, 264 (1959).

Carbon-13 Nuclear Magnetic Resonance Studies of Heterogeneous Systems. Amino Acids Bound to Cationic Exchange Resins[1]

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Abstract: The ^{13}C nmr spectra of several protonated and deuterated amino acids bound to cationic exchange resins (cross-linked polystyrenes with sulfonic acid groups) have been measured using pulsed Fourier transform techniques. In many cases narrow, 1–10-Hz wide ^{13}C resonances were observed for the amino acids in this heterogeneous system. In those cases where they were measured accurately Overhauser enhancement factors of about 3 were obtained for the protonated amino acids. Large differences between T_2 (transverse relaxation time) and T_1 (spin–lattice relaxation time) were observed. T_2 was considerably shorter than T_1 and was sensitive to the degree of cross-linking in the resin, whereas T_1 was insensitive to the degree of cross-linking. Deuterium-decoupled, deuterated amino acids on the resins often showed ^{13}C line widths which were three–four times narrower than those from proton-decoupled, protonated amino acids. These observations are discussed in terms of an anisotropic model for the resin-bound amino acids which assumes a nonzero time-averaged dipolar interaction. The resin method is shown to have particular value in (1) shortening the T_1 values of quaternary carbons and other carbons that do not have hydrogens bonded to them, thus facilitating their detection by pulsed Fourier transform techniques, and (2) distinguishing these carbons from carbons which are bonded to hydrogens.

There is presently considerable interest in using ^{13}C nmr for organic and bioorganic investigations. Instrumental advances based on pulsed Fourier transform techniques[2–4] have provided significant signal-to-noise improvement per unit time relative to conventional continuous-wave nmr. Measurements are now possible

which could not readily be done in the past. However, carbons that are not bonded to hydrogens remain difficult to detect because of their relatively long spin–lattice relaxation (T_1) times.[2,4,5] The driven equilibrium Fourier transform (DEFT)[5,6] and modifications thereof[7] represent instrumental methods for circumventing the low signal-to-noise ratios which are often characteristic of carbons that have long T_1 values. The instrumentation required, however, is more complex than that needed for pulsed Fourier transform.

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(1) A preliminary report was presented April 1970 to the Eleventh Experimental Nuclear Magnetic Resonance Conference, Mellon Institute, Pittsburgh, Pa.

(2) R. R. Ernst and W. A. Anderson, *Rev. Sci. Instrum.*, 37, 93 (1966).

(3) R. R. Ernst, *Advan. Magn. Resonance*, 2, 1 (1966).

(4) D. Jones, Ph.D. Thesis, The University of California, Berkeley, Calif., 1970.

(5) E. D. Becker, J. A. Ferretti, and T. C. Farrar, *J. Amer. Chem. Soc.*, 91, 7784 (1969).

(6) R. L. Streever and H. Y. Carr, *Phys. Rev.*, 121, 20 (1961).

(7) J. Waugh, to be published.