$$2RCO_2H + BH_3 \xrightarrow[0\,°C]{THF} (RCO_2)_2BH + 2H_2\uparrow$$

R = alkyl or phenyl

We decided to investigate bis(benzoyloxy)borane as a reducing agent because of its ready preparation from benzoic acid.[14] The reduction of tosylhydrazones leads to single hydrocarbon products in high yields. The reaction times vary, generally being from 0.5 to 2 h.[15] Our results are summarized in Table I.

Unsaturated carbonyl derivatives are readily reduced by bis(benzoyloxy)borane. As with catecholborane a regiospecific and stereospecific rearrangement occurs. In previous studies, this rearrangement has permitted the syntheses of thermodynamically unstable materials.[7–9] Our results are summarized in Table II.

In summary, the reduction of tosylhydrazones by bis(benzoyloxy)borane offers a convenient alternative to the Wolff–Kishner and Clemmensen reductions.

Experimental Section

Proton NMR spectra were recorded on a Varian T-60 spectrometer. All chemical shifts are reported in parts per million downfield from Me₄Si.

All carbonyl reagents were obtained commercially and distilled prior to use. The only exception was 6-oxo-15-hexadecenoic acid which was prepared according to a published procedure.[16] Melting points are uncorrected.

Tosylhydrazone Preparation. The tosylhydrazones were prepared by reacting the appropriate ketone with *p*-toluenesulfonhydrazide in ethanol.[8] The melting points of the tosylhydrazones are given in parenthesis following the name of the carbonyl reagent from which they were prepared: decanal (106–108 °C), 2-octanone (96.5–98 °C), 4-*tert*-butylcyclohexanone (149–150 °C), benzaldehyde (127–128 °C), acetophenone (145–146 °C), 6-oxo-15-hexadecenoic acid (82–84 °C), cinnamaldehyde (158–159 °C), (*E*)-4-phenyl-3-buten-2-one (174–175 °C), isophorone (137–138 °C), and 4-phenyl-3-butyn-2-one (164–166 °C).

Reduction of Tosylhydrazones. General Procedure. The reduction of the tosylhydrazone of 6-oxo-15-hexadecenoic acid is representative. Benzoic acid (0.69 g, 5.67 mmol) was placed in a dried, nitrogen-flushed, 25-mL flask fitted with a septum inlet and magnetic stirring bar. Ethanol-free chloroform (5 mL) was added and the mixture cooled to 0 °C. BH₃·THF (1.2 mL of a 2.35 M solution, 2.82 mmol) was added dropwise. (**Caution:** hydrogen evolution.[1]) The clear solution was stirred for 30 min and then the tosylhydrazone of 6-oxo-15-hexadecenoic acid (0.62, 1.42 mmol) was added. The reduction was allowed to proceed for 60 min[15] and then NaOAc·3H₂O (0.46 g, 3.4 mmol) was added and the solution allowed to warm to room temperature.

Pentane (30 mL) was added and the organic layer was separated and washed with 50 mL of a 2% acetic acid solution and then 50-mL portions of warm water (50 °C) (for nonacidic materials, the pentane layer is washed with 5% Na₂CO₃ followed by water). The pentane layer was dried over anhydrous MgSO₄, the solvent removed under reduced pressure, and the product isolated by column chromatography (silica gel using 1:10 ethyl acetate–petroleum ether as eluant): yield 0.347 g (96%); mp 42–43 °C; NMR (CDCl₃) δ 1.21 (m, 22 H, =CHCH₂(CH₂)₁₁CH₂), 1.77–2.07 (m, 2 H, =CHCH₂CH₂), 2.13–2.33 (m, 2 H, CH₂CO₂H), 4.73 (s, 1 H, CH₂=CH), 4.9–5.07 (d, 2 H, CH₂=CH), 11.9 (s, 1 H, CO₂H).

Octane. The tosylhydrazone of 2-octanone (5.34 g, 18.0 mmol) was reduced by using bis(benzoyloxy)borane (36 mmol). Reduction time was 60 min and the yield was 1.89 g (91%) of octane, bp 125 °C (760 mmHg).

Decane. The tosylhydrazone of decanal (1.34 g, 4.13 mmol) was reduced with bis(benzoyloxy)borane (8 mmol). Reduction time was 30 min and the yield was 0.46 g (78%), bp 174 °C (760 mmHg).

***tert*-Butylcyclohexane.** The tosylhydrazone of 4-*tert*-butylcyclohexanone (2.04 g, 6.34 mmol) was reduced with bis(benzoyloxy)borane (12.68 mmol). Reduction time was 30 min and the yield was 0.733 g (82%) of *tert*-butylcyclohexane: bp 171 °C (760 mmHg); NMR (CDCl₃) δ 0.83 (s, 9 H, C(CH₃)₃), 0.90–1.90 (m, 11 H, CH₂ and CH).

Toluene. The tosylhydrazone of benzaldehyde (5.49 g, 20 mmol) was reduced with bis(benzoyloxy)borane (40 mmol). The reduction time was 70 min and the yield was 1.51 g (82%) of toluene, bp 110 °C (760 mmHg).

Ethylbenzene. The tosylhydrazone of acetophenone (2.89 g, 10 mmol) was reduced with bis(benzoyloxy)borane (20 mmol). The reaction time was 2.5 h and the yield of ethylbenzene was 0.72 g (68%).

3-Phenyl-1-propene. The tosylhydrazone of cinnamaldehyde (5.64 g, 18.8 mmol) was reduced with bis(benzoyloxy)borane (37 mmol). The reduction time was 1 h and the yield of 3-phenyl-1-propene was 1.89 g (85%): bp 156 °C (760 mmHg); NMR (neat) δ 3.22 (d, 2 H, PhCH₂), 4.85 (m, 1 H, PhCH₂CH=CHH), 5.05 (m, 1 H, PhCH₂CH=CHH), 5.52–6.12 (m, 1 H, Ph CH₂CH=CH₂), 7.05 (s, 5 H, **Ph**CH₂).

3,5,5-Trimethylcyclohexene. The tosylhydrazone of isophorone (6.128 g, 20 mmol) was reduced with bis(benzoyloxy)borane (40 mmol). The reaction time was 30 min and the yield was 2.07 g (83%): bp 130 °C (760 mmHg); NMR (CDCl₃) δ 0.90–0.99 (m, 9 H, methyls), 1.0–1.8 (m, 4 H, ring CH₂), 2.17 (br m, 1 H, CHCH₃), 5.50 (s, 2 H, vinyl).

1-Phenyl-1,2-butadiene. The tosylhydrazone of 4-phenyl-3-butyn-2-one (3.89 g, 12.5 mmol) was reduced with bis(benzoyloxy)borane (25 mmol). The reduction time was 66 h and the yield was 0.32 g (21%) of 1-phenyl-1,2-butadiene: bp 200 °C (760 mmHg); IR 1955 cm⁻¹ (C=C=C); NMR (CDCl₃) δ 1.7 (m, 3 H, C=CHCH₃), 5.4 (m, 1 H, C=CHCH₃), 5.95 (m, 1 H, C=CHPh), 7.13 (m, 5 H, C=CHPh).

Polyether-Based Triphase Catalysts. A Synthetic Comparison[1]

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Cross-linked phosphonium and ammonium polymers are receiving considerable attention as triphase catalysts.[3]

(14) The more expensive bis(trifluoroacetoxy)borane also appear to be effective in these reductions.

(15) As in all reductions of tosylhydrazones, the reaction should be quenched as soon as the hydrazone has been reduced to obtain maximum yields. Fortunately the reactions are easily monitored by NMR or TLC.

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Scheme I
Hydroxymethyl-18-Crown-6

Scheme II
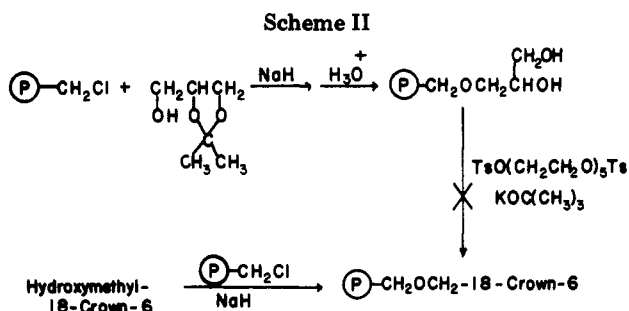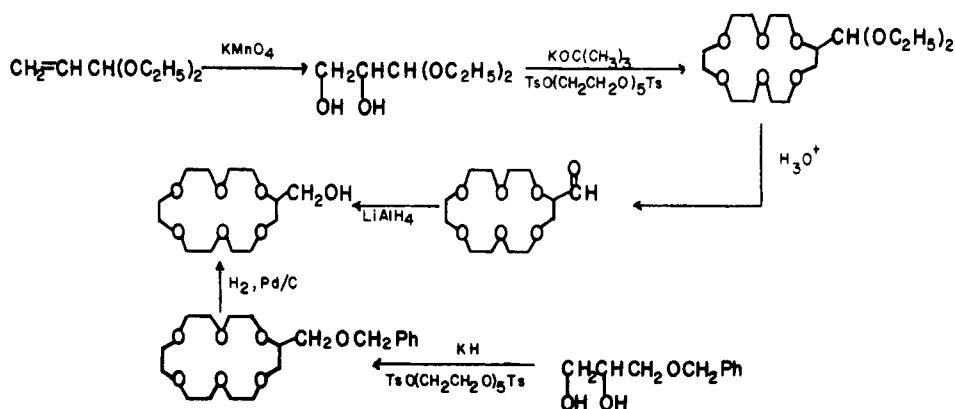
Because of their susceptibility toward dequaternization, however, all practical applications based on their use are limited to relatively mild reactions and conditions.[3,4] Insoluble polyethers avoid this problem and, in principle, should become the catalysts of choice in many instances. Surprisingly, there is very little information available concerning the efficacy of such resins. Only two types of polyethers have been employed in triphase reactions (cross-linked polystyrene bearing pendant crown ethers or polyglymes) and no synthetic comparisons have been made between them.[5-10] In this note we report (1) an improved synthesis of hydroxymethyl-18-crown-6 (1a)[5] and (2) an operational comparison between triphase catalysts derived from 1a, poly(ethylene glycol monomethyl ether), and dibenzo-18-crown-6 for cyanide, iodide, and phenoxide displacement on 1-bromooctane. Results presented herein demonstrate that pendant 18-crown-6 offers no special advantage over polyglymes and that polymerized forms of dibenzo-18-crown-6 have remarkably high activity.[11]

Two successful routes to 1a are outlined in Scheme I.

Cyclization of pentaethylene glycol ditosylate with 1,2-dihydroxy-3,3-diethoxypropane afforded a 42% yield of diethoxymethyl-18-crown-6. Subsequent hydrolysis and reduction produced 1a in 32% overall yield. Analogous cyclization using 1,2-dihydroxy-3-benzyloxypropane followed by hydrogenolysis yielded 1a in two steps (24%). Covalent attachment of 1a to cross-linked polystyrene was effected by reacting its sodium salt with a chloromethylated form of the copolymer, yielding 2a and 2b (Scheme II). Attempted preparation of identical crown ether polymers by cyclization of glycerol-modified[12] cross-linked polystyrene proved unsuccessful.[13] Resins 2c, 2d, 3a, and 3b were prepared by using procedures similar to those described in the literature.[11,14]
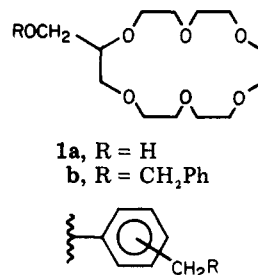
1a, R = H
b, R = CH₂Ph

functionalized microporous polystyrene-
  1% divinylbenzene
  2a, R = OCH₂-18-crown-6; percent ring substitution
    (prs) = 5
  b, R = OCH₂-18-crown-6; prs = 20
  c, R = O(CH₂CH₂O)₇CH₃; prs = 17
  d, R = O(CH₂CH₂O)₁₆CH₃; prs = 17
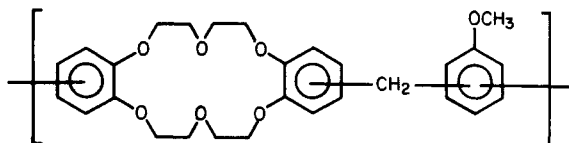
3a, 0% anisole
b, anisole/dibenzo-18-crown-6 = 10/1 (mol ratio of monomers)

In Table I we present an operational comparison between the triphase catalysts for iodide, cyanide, and

(2) On leave from (a) Kyoto University of Industrial Arts and Textile, Kyoto, Japan, (b) Silesian University, Katowice, Poland.

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(13) Reactions were carried out with ratios of 1:1 or 1:10 of diol–ditosylate and *N,N*-dimethylformamide as solvent. In both cases, the infrared spectrum of the recovered resin was identical with that of the starting polymeric diol. However, these polymers did show activities for iodide displacement equaling 38 × 10⁻⁵ and 8 × 10⁻⁵ s⁻¹ g⁻¹, respectively.

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Table I. Triphase Catalytic Displacement
on 1-Bromooctane[a]

	activity, $10^5 k_{obsd}/g$, s^{-1} g^{-1}		
catalyst	KI	KCN	KOPh
poly(ethylene glycol)[b]	15	1	11
dibenzo-18-crown-6[c]	18	4	14
1b	632	5	4
2a	14	2	4
2b	207	5	17
2c	16	1	2
2d	116	1	1
3a	5	55	9
3b	37	2	12

[a] Reaction of 3.0 mL of 0.125 M 1-bromooctane in toluene containing 0.178 mmol of n-dodecane (internal standard) with 5.0 mL of saturated aqueous potassium iodide (cyanide) solution or 5.0 mL of 0.75 M aqueous potassium phenoxide at 90 °C catalyzed by 0.02 g of cross-linked polymer or 0.04 mmol of soluble catalyst; k_{obsd} = observed pseudo-first-order rate constant obtained from vigorously stirred reactions. All polymers were conditioned by heating for 15 h under triphase conditions at 90 °C. In the absence of catalyst, yields of 1-iodooctane, 1-cyanooctane and 1-octyl phenyl ether were 7, 7, and 14%, respectively, after 4 days. [b] 0.04 mmol (0.0606 g) of ethylene oxide units were used (mol wt 20 000). [c] A precipitate was also present.

phenoxide displacement on 1-bromooctane. Also included are data for analogous soluble phase-transfer catalysts. In all cases, activity is expressed as k_{obsd} per gram of catalyst. For iodide displacement, polymers **2b** and **2d** exhibited high activity, comparing favorably with the most active soluble catalyst **1b**. Surprisingly, **3b** having the crown moiety as an integral part of the polymer backbone, also showed significant activity.[15] Results obtained for cyanide displacement were in sharp contrast to those of the halogen exchange reaction. Here, only the dibenzo-18-crown-6 polymer **3a** showed reasonable activity. When phenoxide was used as the nucleophile, **2b** and **3b** were the most active catalysts.

The large variation in catalyst performance for these displacement reactions is puzzling and will require careful mechanistic examination for clarification. Nonetheless, from a synthetic standpoint, these results establish that *pendant crown ether groups are not essential for high activity in polyether-based triphase catalysts.* The ready availability and low cost of polymerized benzo crown compounds and polyglyme graft copolymers should make them attractive for many synthetic applications.

Experimental Section

General Methods. Unless stated otherwise, all reagents and chemicals were obtained commercially and were used without further purification. Toluene was dried by distillation from sodium and benzophenone under a nitrogen atmosphere. Deionized water was distilled from $KMnO_4/Ba(OH)_2$. The temperature of the oil bath used for triphase reactions was controlled (±0.5 °C) with the aid of a Therm-O-Watch electronic controller Model L6-1000 (I^2R Co., Cheltenhan, PA) attached to a thermometer. Product mixtures were analyzed by GLC on a Hewlett-Packard Model 5830 A flame-ionization instrument (6 ft × 0.125 in. 10% QF1 column). All ^1H NMR, IR, and mass spectra were recorded by using Varian A-60, Beckman Acculab 7, and Finnigan 4000 GC/MS spectrometers, respectively. Chemical shifts were taken in $CDCl_3$ in δ from internal tetramethylsilane. 1,2-Dihydroxy-3,3-diethoxypropane was prepared from acrolein diethyl acetal (Aldrich Chemical Co.) by using established procedures.[16] 1,2-Dihydroxy-3-(benzyloxy)propane was prepared

as described in the literature.[17] Pentaethylene glycol ditosylate was prepared from pentaethylene glycol (Columbia Organics) by using standard methods.[18] Poly(ethylene glycol monomethyl ether) was grafted to polystyrene by using established procedures.[19]

Diethoxymethyl-18-crown-6. Pentaethylene glycol ditosylate (5.9 g, 0.011 mol) dissolved in 20 mL of dry THF was added dropwise to 100 mL of THF containing 1.61 g (0.01 mol) of 1,2-dihydroxy-3,3-diethoxypropane and 2.4 g (0.022 mol) of potassium *tert*-butoxide. The mixture was stirred under a nitrogen atmosphere at room temperature for 12 h, refluxed for 4 h, cooled to room temperature, and filtered, and the solvent was then distilled. The crude residue (8.0 g) was chromatographed on neutral alumina, using ether–dichloromethane (1:1) as eluant, to give 2.1 g (42%) of diethoxymethyl-18-crown-6 as a viscous reddish brown oil. Refluxing an ether solution of this oil over neutral Norit decolorizing carbon for 1 h followed by filtration and solvent evaporation afforded a colorless product: ^1H NMR ($CDCl_3$) 4.45 (d, 1, $CH(OC_2H_5)_2$), 3.3–4.0 (m, 27, CH_2O), 1.22 (t, 6, CH_3); IR (neat) ν_{C-O-C} 1120 cm^{-1}. Anal. Calcd for $C_{17}H_{34}O_8$: C, 55.92; H, 9.31. Found: C, 55.95; H, 9.20.

18-Crown-6-carboxaldehyde. Diethoxymethyl-18-crown-6 (1.0 g, 2.74 mmol) was refluxed in a solution of 40 mL of 1 M H_2SO_4 plus 10 mL of acetone for 45 min. The product mixture was cooled to room temperature, extracted with chloroform (5 × 25 mL), and dried ($MgSO_4$) and the solvent evaporated, affording 0.6 g (76%) of the aldehyde as a colorless oil: ^1H NMR ($CDCl_3$) 9.97 (s, 1, CHO), 3.4–4.0 (br m, 23, CH_2O); IR (neat) $\nu_{C=O}$ 1730, ν_{C-O-C} 1120 cm^{-1}. Anal. Calcd for $C_{13}H_{24}O_7$: C, 53.42; H, 8.22. Found: C, 52.19; H, 8.53.

Hydroxymethyl-18-crown-6. 18-Crown-6-carboxaldehyde (3.7 g, 12.7 mmol) dissolved in 100 mL of anhydrous ethyl ether was added slowly to a suspension of $LiAlH_4$ (0.14 g, 3.5 mmol) in 150 mL of dry ethyl ether. After addition, the product mixture was stirred for 3 h at room temperature, refluxed for 1 h, cooled to room temperature, and treated with 5 mL of ice–water followed by 10 mL of 5% H_2SO_4 (with cooling, 0 °C). Extraction with $CHCl_3$ (50 × 10 mL) followed by drying ($MgSO_4$) of the combined organic layer and solvent evaporation afforded 3.7 g (99%) of hydroxymethyl-18-crown-6 as a colorless oil: ^1H NMR ($CDCl_3$) 3.4–4.0 (br s, 25, CH_2O), 3.18 (br, 1, OH); IR (neat) ν_{OH} 3300, ν_{C-O-C} 1120 cm^{-1}; mass spectrum, m/e 294 (M^+). Anal. Calcd for $C_{13}H_{26}O_7$: C, 53.06; H, 8.84. Found: C, 52.71; H, 8.99.

(Benzyloxy)methyl-18-crown-6. To a solution of 9.11 g (0.05 mol) of 1,2-dihydroxy-3-benzyloxypropane in 500 mL of THF was added 34.5 g of KH oil dispersion (23.8% KH in oil) at room temperature. After the mixture was allowed to react overnight under a nitrogen atmosphere, a solution of pentaethylene glycol ditosylate (27.4 g, 0.05 mol) in 100 mL of THF was added over a period of 1 h with stirring. The mixture was stirred for an additional 1 h at room temperature, refluxed for 24 h, cooled to room temperature, and quenched with 20 mL of water at 0 °C. The volatile solvents were removed by distillation under reduced pressure and the residue was dissolved in 300 mL of water. Residual oil remaining from the KH dispersion floated above the aqueous layer and was removed. The aqueous phase was then extracted with $CHCl_3$ (5 × 50 mL), and the extract washed with saturated NaCl solution (2 × 100 mL), dried ($MgSO_4$), and concentrated to give 20 g of a brown residue. Half of this residue was extracted with cyclohexane (5 × 100 mL) and the solvent was then evaporated, leaving 6 g of crude product. Chromatography on neutral alumina (200 g), using cyclohexane and cyclohexane–chloroform (1:10) as eluants, followed by treatment with Norit decolorizing carbon, afforded 2.42 g (25%) of (benzyloxy)-methyl-18-crown-6 as a colorless oil: ^1H NMR ($CDCl_3$) 7.26 (s, 5, Ph), 4.51 (s, 2, $PhCH_2O$), 3.63 (br s, 25, CH_2O); IR (neat) ν_{C-O-C} 1120 cm^{-1}; mass spectrum, m/e 384 (M^+). Anal. Calcd for $C_{20}H_{33}O_7$: C, 62.48; H, 8.39. Found: C, 62.32; H, 8.13.

Hydrogenolysis of (Benzyloxy)methyl-18-crown-6. A solution of (benzyloxy)methyl-18-crown-6 (2.45 g, 6.4 mmol) in

(15) Previous studies have indicated that separation of a crown ether moiety from the polymer backbone is important for high activity.[7]

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ethanol (200 mL) was stirred under 1 atm of hydrogen in the presence of 10% palladium on activated carbon (Aldrich Chemical Co.) for 48 h at room temperature. Thin-layer chromatography (alumina, using EtOAc–CH₃OH (10:1) as the eluant) indicated the complete disappearance of starting material. The product mixture was filtered and concentrated, yielding hydroxymethyl-18-crown-6 (1.76 g, 94%) as a colorless oil having IR and ^{1}H NMR spectra identical with those of an authentic sample.

Hydroxymethyl-18-crown-6 Grafted to Cross-linked Polystyrene. Hydroxymethyl-18-crown-6 (0.76 g, 2.58 mmol) dissolved in THF (40 mL) was stirred with 0.19 g (4.1 mmol) of sodium hydride under a nitrogen atmosphere at room temperature for 1 h. Chloromethylated polystyrene (1.00 g, 1% divinyl-benzene–microporous, 1.76 mmol of chlorine (20% ring substitution), 20–40 mesh) was then added to the solution and the mixture refluxed without stirring for 24 h under a nitrogen atmosphere. The product mixture was cooled to room temperature and 5 mL of methanol was added. The resin was filtered, washed successively with THF (5 × 10 mL), THF–water (1:1, 3 × 10 mL), water (2 × 20 mL), and THF (10 mL) and dried under reduced pressure [12 h, 56 °C (0.1 mm)], yielding 1.400 g of polymer. For quantitative replacement of chlorine by the crown ether, the theoretical expected weight of the product is 1.462 g. The IR spectrum of the resulting resin showed a strong C–O–C band at 1200 cm⁻¹ and the complete disappearance of the H–C–Cl bending vibration at 1260 cm⁻¹. Procedures similar to the above were used to graft hydroxymethyl-18-crown-6 onto a 5% ring-substituted microporous polymer.

Poly(dibenzo-18-crown-6). The procedure used for preparing poly(dibenzo-18-crown-6) was identical with that previously reported.[11]

Poly(dibenzo-18-crown-6-anisole). A solution of paraformaldehyde (3.3 g, 0.11 mol) in 30 mL of formic acid was added in one portion to a stirred solution of dibenzo-18-crown-6 (0.9 g, 2.5 mmol) and anisole (2.71 g, 25.1 mmol) in 80 mL of formic acid maintained at 60 °C. The mixture was refluxed for 5 h and the resulting gel poured into 100 mL of water, filtered, and washed with water until all traces of acid were removed. The brownish polymer was extracted (Soxhlet) for 3 days with methanol and then dried [12 h, 56 °C (0.1 mm)], affording 2.84 g of dry polymer.

Kinetic Methods. Kinetic methods used to analyze the activity of the various soluble and insoluble catalysts were similar to those previously described.[19] Culture tubes (50-mL, Corning no. 9826), containing a Teflon-coated magnetic stirring bar ($^1/_2 × ^5/_{16}$ in. octagonal bar with pivot ring), were used in all experiments. Pseudo-first-order rate constants were calculated from the disappearance of 1-bromooctane in the organic layer. A minimum of four aliquots was taken per reaction, and the kinetics was generally followed for at least three half-lives.

Deuterium Isotope Effects in Carbon-13 Nuclear Magnetic Resonance Spectroscopy. Investigation of Tautomeric Equilibria in Enamino Ketone Systems

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We have developed a new method by which carbon-13 NMR spectroscopy can be used to yield a qualitative picture of tautomeric equilibria. This simple-to-use procedure involves application of deuterium isotope effects.[1]

The deuterium isotope effect can be manifested in several ways. The most easily recognized effects are signal broadening caused by residual C–D coupling, reduction of signal intensity by deuterium quadrapole relaxation, and deuterium isotope induced shifts.[2]

The nature of the experiment involves the examination of the sample in a coaxial NMR tube to which D₂O was added to half the solution and H₂O to the other as described by Pfeffer et al.[3] The resulting spectrum can be analyzed readily and by consideration of the deuterium isotope effects previously mentioned, information concerning the position of the deuterium can be evaluated.

We have been interested in the tautomeric properties of enamino ketones. These compounds can exist as one or some combination of the three potential tautomers shown.
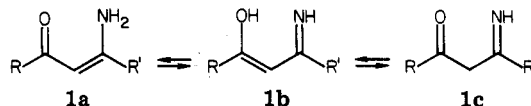
The determination of this type of tautomeric equilibria has been extensively studied by proton NMR with ^{15}N-labeled compounds.[4] No evidence for tautomer **1c** has ever been observed. The obvious drawback of this procedure does not allow for routine use of this method. We decided to see if deuterium isotope effects could be of some use to gain an understanding of the position of equilibrium in these systems. The three compounds studied (**2–4**) are shown below.
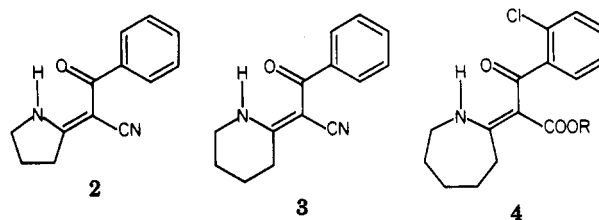
The results of our deuterium isotope effect investigation are exemplified by the observations given in Figures 1 and 2. Shown in Figure 1 is the deuterium isotope induced shifted spectrum of the low-field region for **3**. Isotope shifts are observed for both of the low-field resonances which can be assigned to C_1 and C_2.[5] (An isotope shift is also seen for the aliphatic carbon α to nitrogen.) Since deuterium isotope induced shifts are operative over only three bonds, the interpretation of the results is straightforward; both tautomeric forms similar to **1a** and **1b** are present in equilibrium.[2] In Figure 2 the results of the deuterium isotope effect of reduced signal intensity are obvious for carbons C_1, C_2, and C_4, due to quadrupolar and reduced dipole–dipole relaxation.[2d] This result nicely complements the isotope-shifted spectrum, confirming the tautomeric equilibrium.

A similar result was obtained for **4**. However, for **2** deuterium isotope effects were observed only for carbons C_2 and C_4, and the carbon atom α to nitrogen, strongly indicating that for **2** no tautomeric equilibrium exists. This

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