NMR ($CDCl_3$) δ 8.82 (s, 2 H), 3.88–3.48 (m, 6 H), 2.94–2.67 (m, 2 H), 2.0–1.53 (m, 12 H). Anal. Calcd for $C_{17}H_{23}N_5O_7$: C, 49.88; H, 5.66; N, 17.11. Found: C, 49.8; H, 5.63; N, 17.1.

***cis*-Cycloundecene (3b).** 12,12-Dimorpholino-*cis*-bicyclo-[9.1.0]dodecane[17] (**2b**) (0.36 g, 1.07 mmol) was vaporized at 120 °C within 2 h and pyrolyzed at 650 °C. The condensate was dissolved in pentane (10 mL) and treated with acid ion-exchange resin (0.4 g, Type I, Fa. Merck). Filtration, evaporation of the solvent and distillation in a Kugelrohr apparatus gave **3b** as colorless oil (0.145 g, 89%): bp 25–30 °C (0.01 Torr) [lit.[18] bp 100 °C (12 Torr)]; IR (film, cm^{-1}) 710 (=C—H) (identical with IR spectrum in ref 18); ^1H NMR ($CDCl_3$) δ 5.35 (mc, 2 H), 2.27–2.14 (m, 4 H), 1.55–1.25 (m, 14 H).

***trans*-Cycloundecene (13).** Analogously, 12,12-Dimorpholino-*trans*-bicyclo[9.1.0]dodecane (**12**)[17] (0.96 g, 2.85 mmol; vaporization at 150 °C within 3 h; pyrolysis at 650 °C) yielded **13** (0.40 g, 92%): bp 25–30 °C (0.01 Torr) [lit.[18] bp 88–90 °C (15 Torr)]; IR (film, cm^{-1}) 980 (=C—H) (identical with IR spectrum in ref 19); ^1H NMR ($CDCl_3$) δ 5.45(mc, 2 H), 2.12–1.98 (m, 4 H), 1.50–1.12 (m, 12 H).

2,3,4,5-Tetrahydro-6-pyrrolidinopyridine (6c). A mixture of 6-methoxy-2,3,4,5-tetrahydropyridine (**10**)[20] (4.0 g, 35 mmol) and pyrrolidine (4.75 g, 70 mmol) was stirred for 2 days at 20 °C. Removal of the volatile compounds at 15 Torr and distillation of the residue at 0.01 Torr gave pure **6c** (5.0 g, 94%): bp 60–63 °C (0.01 Torr); IR (film, cm^{-1}) 1620 (C=N); ^1H NMR ($CDCl_3$) δ 3.62–3.19 (m, 6 H), 2.41–2.12 (m, 2 H), 1.98–1.39 (m, 10 H). Anal. Calcd for $C_9H_{16}N_2$: C, 71.00; H, 10.59; N, 18.40. Found: C, 71.4; H, 10.67; N, 18.2. Picrate **8c**: mp 109 °C; for IR and ^1H NMR data, see above.

3,4,5,6-Tetrahydro-7-piperidino-2*H*-azepine (6d). According to a general procedure,[4] caprolactam **9d** (23.0 g, 0.2 mol) was transferred into 7-chloro-3,4,5,6-tetrahydro-2*H*-azepine (**11**) by interaction with phosphoryl chloride (31.0 g, 0.2 mol) in benzene (140 mL, 20 °C, 2 h). Piperidine (17.03 g, 0.2 mol) was added directly to the reaction mixture at 0 °C; after refluxing for 8 h, the usual workup, and distillation at 0.01 Torr pure **6d** (17.7 g, 49%) was obtained. **6d**: bp 56–58 °C (0.01 Torr) [lit.[4] bp 133–134 °C (5 Torr)]; IR (film, cm^{-1}) 1635 (C=N); ^1H NMR ($CDCl_3$) δ 3.53–3.37 (m, 2 H), 3.30–3.09 (m, 4 H), 2.53–2.38 (m, 2 H), 1.88–1.27 (m, 12 H). Anal. Calcd for $C_{11}H_{20}N_2$: C, 73.28; H, 11.18; N, 15.54. Found: C, 73.7; H, 11.34; N, 15.4. Picrate **8d**: mp 118 °C; for IR and ^1H NMR data, see above.

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(17) Vilsmaier, E.; Klein, C. M.; Tröger, W.; Dausmann, D. *Synthesis* **1981**, 724.
(18) Prelog, V.; Boarland, V. *Helv. Chim. Acta* **1955**, *38*, 1776.
(19) Ziegler, K.; Sauer, H.; Bruns, L.; Froitzheim-Kühlhorn, H.; Schneider, J. *Justus Liebigs Ann. Chem.* **1954**, *589*, 122.
(20) Ralls, J. W. *J. Org. Chem.* **1961**, *26*, 66.

A Simple and Convenient Method for the Preparation of *N,N'*-Dibenzyldiaza-crown Compounds

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There has been considerable recent interest in the synthesis of nitrogen-containing crown compounds.[1-8] The aza crown compounds, in some cases, have anion complexation properties that are similar to complexation in certain biological systems.[1,9,10] The diaza-crown compounds have enhanced complexing abilities for ammonium cations in comparison with the all-oxygen crown compounds.[5] In addition, the diaza-crown compounds are important intermediates for the synthesis of the cryptands.[11,12] We now report a convenient two-step synthesis of *N,N'*-dibenzyldiaza-15-crown-5, 18-crown-6, and 21-crown-7.

Many of the previous syntheses of the diaza-crowns have used the reaction of a diamine and a diacid chloride for ring closure, followed by reduction of the resulting diamide to form the diaza-crowns.[11,12] The more recent reports have used the reaction of certain diamines with dihalides, particularly the less available diiodides.[2-4] Okahara and his co-workers[6,7,13] and Oda and his co-workers[14] have used one-step methods to prepare the aza crowns from previously prepared oligoethylene oxide containing diamines. The open-chain diamines, in general, are important intermediates for the synthesis of the diaza-crown compounds.

We have found that *N,N'*-dibenzyldiazaoligoethylene glycols (**1–2** and **6**, Scheme I) can easily be converted in high yields into the *N,N'*-dibenzyldiaza-crown compounds (**7–9**). The diazaoligoethylene glycols were readily prepared by reacting dichlorides **11** or **12** with *N*-benzylethanolamine (or the *N*-ethyl isomer) (see Scheme I). Okahara and his co-workers[6] and Ishidate, Sakurai, and Maruyama[15] have reported similar mono and diaza glycols, but the yields of their reactions were only 20–50%. Diaza compound **1** was also prepared by reacting 1,14-dihydroxy-3,12-diaza-6,9-dioxatetradecane[16] with benzyl bromide.

Secondary diamines **4** and **5** were obtained in good yields by reacting a fourfold excess of the amine with the dichloride in toluene (Scheme I). Generally, these types of diamines have been prepared by various methods, including the Gabriel synthesis,[12,17] the reaction of primary amines with diacid chlorides followed by the reduction of the diamide,[3,18] or the reduction of diazides formed from the reaction of a dichloride with sodium azide.[19] Diamine **4** was also reported by Gokel and co-workers[2] using 1,8-diiodo-3,6-dioxaoctane.

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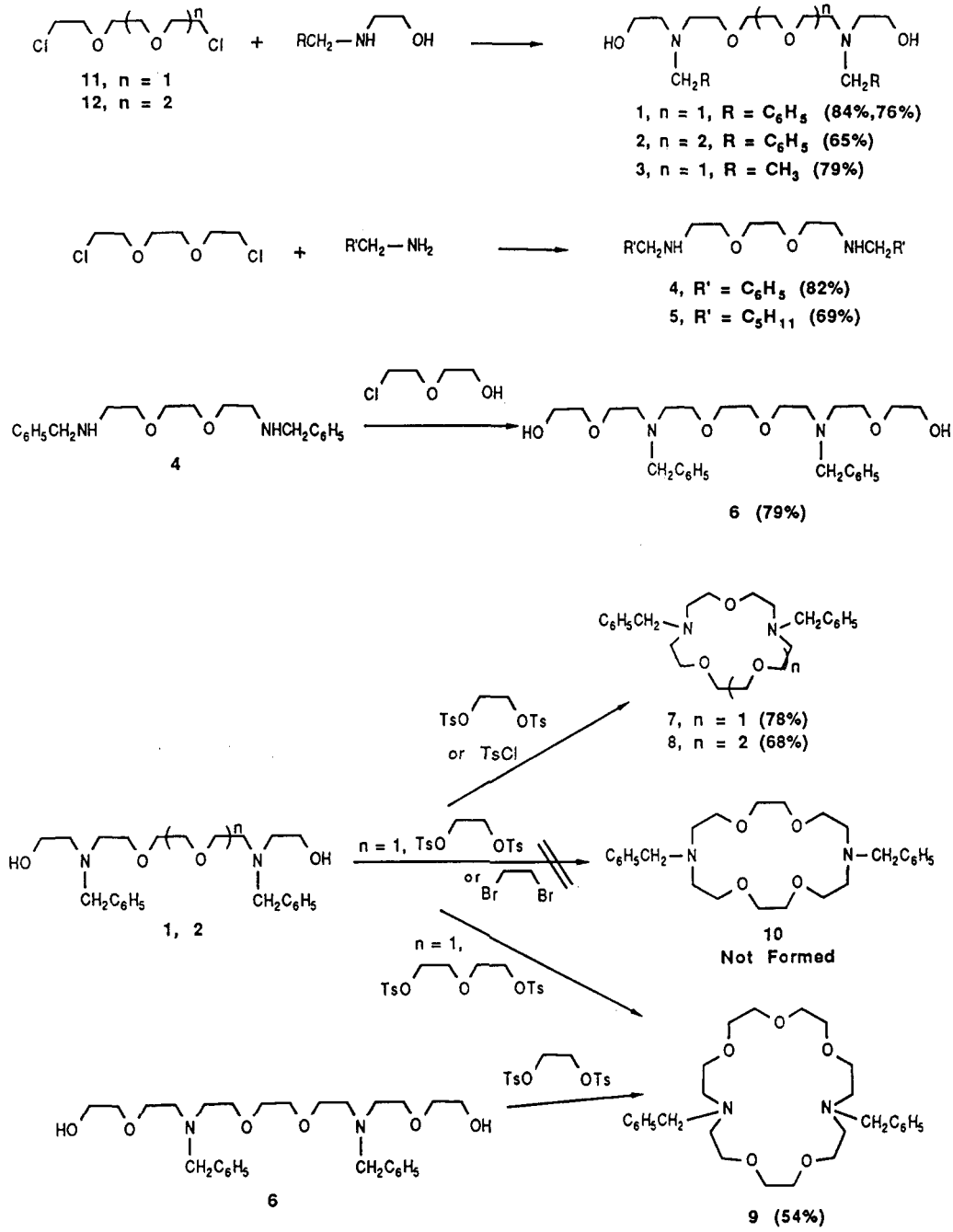
(1) Hosseini, M. W.; Lehn, J. M.; Duff, S. R.; Gu, K.; Mertes, M. P. *J. Org. Chem.* **1987**, *52*, 1662.
(2) Gatto, V. J.; Arnold, K. A.; Viscariello, A. M.; Miller, S. R.; Morgan, C. R.; Gokel, G. W. *J. Org. Chem.* **1986**, *51*, 5373.
(3) Gatto, V. J.; Arnold, K. A.; Viscariello, A. M.; Miller, S. R.; Gokel, G. W. *Tetrahedron Lett.* **1986**, *27*, 327.
(4) Gatto, V. J.; Gokel, G. W., *J. Am. Chem. Soc.* **1984**, *106*, 8240.
(5) Pietraszkiewicz, M.; Jurczak, J. *J. Chem. Soc., Chem. Commun.* **1983**, 132.
(6) Kuo, P.-L.; Miki, M.; Ikeda, I.; Okahara, M. *J. Am. Oil Chem. Soc.* **1980**, 227.
(7) Maeda, H.; Furuyoshi, S.; Nakatsuji, Y.; Okahara, M. *Bull. Chem. Soc. Jpn.* **1983**, *56*, 3073.
(8) Biernat, J.; Luboch, E. *Tetrahedron* **1984**, *40*, 1927.
(9) Lehn, J. M. *Science (Washington, D.C.)* **1985**, *227*, 849.
(10) Yohannes, P. G.; Mertes, M. P.; Mertes, K. B. *J. Am. Chem. Soc.* **1985**, *107*, 8288.
(11) Dietrich, B.; Lehn, J. M.; Sauvage, J. P. *Tetrahedron Lett.* **1969**, 2885.
(12) Dietrich, B.; Lehn, J. M.; Sauvage, J. P. *Tetrahedron* **1973**, *29*, 1629.
(13) Kikui, T.; Maeda, H.; Nakatsuji, Y.; Okahara, M. *Synthesis* **1984**, 74.
(14) Kawaguchi, M.; Ohashi, J.; Kawakami, Y.; Yamamoto, Y.; Oda, J. *Synthesis* **1985**, 701.
(15) Ishidate, M.; Sakurai, Y.; Maruyama, K. *Chem. Pharm. Bull.* **1958**, *6*, 164.
(16) King, A.; Krespan, C. *J. Org. Chem.* **1974**, *39*, 1315.
(17) Krakowiak, K.; Kotelko, B. *Pol. J. Chem.* **1982**, *56*, 1145.
(18) Krakowiak, K.; Kotelko, B. *Acta Polon. Pharm.* **1983**, 313.
(19) Kurlstad, S.; Malmsten, L. A. *Acta Chem. Scand., Ser. B* **1979**, *B33*, 469.

0022-3263/88/1953-1808$01.50/0

Scheme I. New Diaza Compounds



Cyclization of the *N,N'*-dibenzyldiaza glycols was carried out by using tosyl chloride or ethylene glycol ditosylate. The Tosyl chloride initiated cyclization of various oligoethylene glycols to form the crown ether compounds was first reported by Okahara and his co-workers.[20] It is interesting to note that the reaction of the *N,N'*-dibenzyldiazaoligoethylene glycols with the ditosylate of ethylene glycol did not yield the typical 1:1 condensation product but caused the glycol to cyclize in the same manner as tosyl chloride does. Thus, diaza glycol **1**, when treated with ethylene glycol ditosylate, gave compound **7**, a 15-crown-5, rather than **10**, an 18-crown-6. We are not sure why this unusual reaction occurred; however, Reinhoudt and co-workers[21] and Chenevert and Plante[22] also reported that crown compounds could not be prepared by using ethylene glycol ditosylate. No cyclocondensation product was obtained when 1,2-dibromoethane was reacted with **1**. In this case, only starting materials were recovered. Diethylene glycol ditosylate, on the other hand, did react with **1** to form cycloaddition product **9**, a 21 crown-7, in a good yield.

Experimental Section

Infrared (IR) spectra were obtained on a Beckman Acculab 2 spectrometer. The proton nuclear magnetic resonance (NMR) spectra were obtained on a JEOL FX-90 Q spectrometer. Elemental analyses were performed by MHW Laboratories, Phoenix, AZ. Molecular weights were obtained by mass spectrometry on a Finnigan 8430 high resolution mass spectrometer. Starting materials were purchased from Aldrich or Parish Chemical Companies.

(20) Kuo, P.; Miki, M.; Ikeda, I.; Okahara, M. *Tetrahedron Lett.* **1978**, 4273.

(21) de Jang, F.; van Zan, A.; Reinhoudt, D.; Tovey, G.; Tourassau, H. *Recl. Trav. Chim Pays-Bas* **1983**, *102*, 164.

(22) Chenevert, R.; Plante, R. *Synthesis* **1983**, 847.

1,14-Dihydroxy-3,12-dibenzyl-3,12-diaza-6,9-dioxatetradecane (1). A mixture of 18.7 g (0.1 mol) of **11**, 32 g (0.21 mol) of *N*-benzylethanolamine, and 25 g of anhydrous sodium carbonate was stirred in 200 mL of xylene under reflux for 3 days on a Dean–Stark apparatus to remove water. The insoluble inorganic salts were filtered and the filtrate was evaporated under reduced pressure. The residue was distilled to give 35 g (84%) of product, bp 233–236 °C/0.5 mm; ^{1}H NMR ($CDCl_3$) δ 2.76 (m, 8 H), 3.2 (s, 2 H), 3.55 (m, 12 H), 3.72 (s, 4 H), 7.24 (s, 10 H); IR 3460, 1100, 730, 690 cm^{-1}; MS, *m/z* (relative intensity) 540, 91 (100). Anal. Calcd for $C_{24}H_{36}N_2O_4$: C, 69.20; H, 8.71. Found: C, 68.98; H, 8.62.

Compound **1** was also prepared by refluxing a mixture of 1.18 g (0.005 mol) of 1,14-dihydroxy-3,12-diaza-6,9-dioxatetradecane,[16] 2.5 g (0.011 mol) of benzyl bromide, and 5 g of potassium carbonate in 100 mL of toluene for 20 h on a Dean–Stark apparatus to remove water. The product was isolated as above to give a 76% yield of **1**.

1,17-Dihydroxy-3,15-dibenzyl-3,15-diaza-6,9,12-trioxaheptadecane (2). A mixture of 11.55 g (0.05 mol) of **12**, 16 g (0.11 mol) of *N*-benzylethanolamine, and 13 g of anhydrous sodium carbonate was reacted as above for **1**. The residue was chromatographed on a short alumina column and then on a silica gel column (ethyl acetate/ethanol/triethylamine, 95:4:1) to give 15 g (65%) of an oil: ^{1}H NMR δ 2.72 (m, 8 H), 3.0 (s, 2 H), 3.54 (m, 16 H), 3.68 (s, 4 H), 7.28 (s, 10 H); IR 3400, 1100, 705, 670 cm^{-1}. Anal. Calcd for $C_{26}H_{40}N_2O_5$: C, 67.80; H, 8.75. Found: C, 67.89; H, 8.78.

1,14-Dihydroxy-3,12-diethyl-3,12-diaza-6,9-dioxatetradecane (3). A mixture of 18.7 g (0.1 mol) of **11**, 20 g (0.22 mol) of 2-(ethylamino)ethanol, and 25 g of anhydrous potassium carbonate was reacted as above for **1**. The residue was distilled to give 23 g (79%) of **3** as an oil, bp 140 °C/0.05 mm: ^{1}H NMR δ 1.0 (t, 6 H), 2.63 (m, 12 H), 3.5 (m, 14 H); IR 3400, 1100 cm^{-1}. Anal. Calcd for $C_{14}H_{32}N_2O_4 \cdot {}^1/_2H_2O$: C, 55.79; H, 11.03. Found: C, 56.04; H, 10.51.

1,10-Dibenzyl-1,10-diaza-3,7-dioxadecane (4). To a solution of 50 g (0.47 mol) of benzylamine and 25 g of sodium carbonate in 100 mL of toluene under reflux was added 23.0 g (0.12 mol) of **11** over a 5-h period. The mixture was refluxed for 20 h on a Dean–Stark apparatus to remove the water. The insoluble inorganic salts were filtered and the filtrate was evaporated. The residue was distilled twice (bp 183–185 °C/0.1 mm) to give 33 g (82%) of **48** which was identical with that reported.[2]

7,16-Diaza-10,13-dioxadocosane (5). Compound **11** (25.7 g, 0.14 mol) was slowly added to a refluxing solution of 50.6 g (0.5 mol) of hexylamine and 10 g of sodium hydroxide in 100 mL of toluene over a 5-h period. The mixture was refluxed for 10 h on a Dean–Stark apparatus, cooled, and filtered and the filtrate was evaporated. The residue was dissolved in 100 mL of chloroform, and the organic layer was washed twice with 50-mL portions of water. The water was extracted with 100 mL of chloroform. The combined chloroform layers were dried over anhydrous magnesium sulfate and evaporated and the residue was distilled to give 29.9 g (69%) of **5**, bp 135–140 °C/0.1 mm: ^{1}H NMR δ 0.86 (t, 6 H), 1.22 (m, 18 H), 2.56 (m, 8 H), 3.48 (m, 8 H); IR 3520, 1100 cm^{-1}. Anal. Calcd for $C_{18}H_{40}N_2O_2$: C, 68.30; H, 12.74. Found: C, 68.12; H, 12.57.

1,20-Dihydroxy-6,15-dibenzyl-6,15-diaza-3,9,12,18-tetraoxaicosane (6). A mixture of 3.28 g (0.01 mol) of **4**, 4 g (0.032 mol) of 2-(2-chloroethoxy)ethanol, 5 g of sodium carbonate, and 100 mL of xylene was reacted as above for **1**. The low boiling material of the residue was distilled (to 200 °C/0.01 mm) and the resulting residue was chromatographed first through a small alumina column and then through silica gel, using ethyl acetate/ethanol/triethylamine (95:4:1) as eluant, to give 4.0 g (79%) of **6** as an oil: NMR δ 2.76 (m, 8 H), 2.95 (s, 2 H), 3.6 (m, 24 H), 7.28 (s, 10 H); IR 3600, 1100, 715, 680 cm^{-1}; MS, *m/z* (relative intensity) 504, 429 (100). Anal. Calcd for $C_{28}H_{44}N_2O_6$: C, 66.64; H, 8.79. Found: C, 66.42; H, 8.74.

7,13-Dibenzyl-7,13-diaza-1,4,10-trioxacyclopentadecane (7). Tosyl chloride (1.95 g, 0.01 mol) in 125 mL of dioxane was added to a mixture of 300 mL of *tert*-butyl alcohol, 0.82 g (0.02 mol) of potassium metal, and 4.16 g (0.01 mol) of **1** during a 5-h period at 60 °C. The mixture was refluxed for 12 h. The mixture was then filtered and evaporated and the residue was passed through an alumina column (toluene/ethanol, 60:1) to give 3.1 g (78%) of compound **7** as an oil. The NMR and IR spectra were the same as reported by Gokel and co-workers.[2]

The above reaction was repeated except 3.70 g (0.01 mol) of ethylene glycol ditosylate was used instead of tosyl chloride. The product, 2.9 g (73%), proved to be compound **7**.

10,16-Dibenzyl-10,16-diaza-1,4,7,13-tetraoxacyclooctadecane (8). To a solution of 1.12 g (0.02 mol) of powdered potassium hydroxide and 2.3 g (0.005 mol) of **2** in 200 mL of dioxane at 60 °C was slowly added 0.95 g (0.005 mol) of tosyl chloride in 100 mL of dioxane over a 3-h period. The mixture was stirred for 12 h and then filtered and the solvent was evaporated. The residue was passed through an alumina column using toluene/ethanol (60:1) as eluant to give 1.5 g (68%) of **8** as an oil: ^{1}H NMR δ 2.80 (t, 8 H), 3.64 (m, 20 H), 7.28 (s, 10 H); IR 2860, 1100, 730, 695 cm^{-1}; MS, *m/z* (relative intensity) 442, 351 (100). Anal. Calcd for $C_{24}H_{38}N_2O_4$: C, 70.56; H, 8.65. Found: C, 70.56; H, 8.58.

10,19-Dibenzyl-10,19-diaza-1,4,7,13,16-pentaoxacyclohenicosane (9). A mixture of 0.9 g of metallic cesium and 1 g (0.002 mol) of **6** in 100 mL of *tert*-butyl alcohol was slowly added to 0.74 g (0.002 mol) of ethylene glycol ditosylate in 50 mL of dioxane at 60 °C during a 3-h period. The mixture was refluxed for 18 h and then filtered and evaporated. The residue was chromatographed on alumina (toluene/ethanol, 50:1) to yield 0.52 g (54%) of **9** as an oil: ^{1}H NMR δ 2.82 (t, 8 H), 3.65 (m, 24 H), 7.32 (s, 10 H); IR 1120, 735, 695 cm^{-1}; MS, *m/z* (relative intensity) 486, 395 (100). Anal. Calcd for $C_{28}H_{42}N_2O_5 \cdot {}^1/_4H_2O$: C, 68.43; H, 8.71. Found: C, 68.37; H, 8.71.

Compound **9** was also prepared by adding 2.13 g (0.005 mol) of **1** to a mixture of 0.41 g (0.01 mol) of potassium metal dissolved in 200 mL of *tert*-butyl alcohol. Diethylene glycol ditosylate (2.12 g, 0.005 mol) in 125 mL of dioxane was added to the above mixture over a 5-h period at 60 °C. The resulting mixture was refluxed for 5 h and a small portion of product **9** was isolated as above. No yields were obtained for this reaction.

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Registry No. 1, 113585-52-7; 2, 113585-53-8; 3, 113585-54-9; 4, 66582-26-1; 5, 105399-99-3; 6, 113585-55-0; 7, 94195-16-1; 8, 105399-96-0; 9, 94195-17-2; 11, 112-26-5; 12, 638-56-2; *N*-benzylethanolamine, 104-63-2; 1,14-dihydroxy-3,12-diaza-6,9-dioxatetradecane, 50977-92-9; 2-(ethylamino)ethanol, 110-73-6; benzylamine, 100-46-9; hexylamine, 111-26-2; 2-(2-chloroethoxy)ethanol, 628-89-7; diethylene glycol ditosylate, 7460-82-4.

Why Are Carboxylic Acids and Phenols Stronger Acids than Alcohols?

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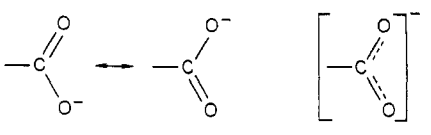
Carboxylic acids and phenols are relatively strong acids, e.g., stronger than simple alcohols, both in the gas phase and in solution. In contemporary textbooks the difference is attributed to a low energy content of the anions. In terms of organic chemistry it is said that these anions are stabilized by conjugation or by mesomeric (resonance) interaction as pictured by the formulas **1** ↔ **2** or by **3** in the case of carboxylate anion, and by similar well-known formulas for phenolate anion.



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