Taylor for the infrared measurements, to the Dow Chemical Company for the polystyrene used in most of the experiments, and to the E. I. du Pont de Nemours & Co., Inc. for the sodium oxide.

Department of Chemistry
Massachusetts Institute of Technology
Cambridge 39, Mass.

Preparation of D-Propylene Glycol and Oxide

Nan Shieh and Charles C. Price

Received March 2, 1959

By the reduction of acetol benzoate, readily prepared from chloroacetone and sodium benzoate, with fermenting yeast solution, optically pure D-propylene glycol 1-benzoate was obtained in 65% yield. Saponification produced D-propylene glycol in 60% yield. This contrasts to yeast reduction of acetol itself, which yields L-propylene glycol.[1]

Treatment of the D-glycol with anhydrous hydrogen bromide gave the bromohydrin, $[\alpha]_D^{24}$ +9.90° (in $CHCl_3$), which was converted by alkali to D-propylene oxide, $[\alpha]_D^{21}$ −6.21° (2% in $CHCl_3$).

EXPERIMENTAL

D-*Propylene glycol 1-benzoate.* Into a 3-l. two-necked round-bottomed flask, provided with a gas trap and a mechanical stirrer, a solution of 100 g. of sucrose in 450 ml. of tap water was placed. To this solution, a paste of 40.6 g. of Fleischmann's dry yeast in 140 ml. of tap water was added. The mixture was allowed to stand at room temperature until a lively evolution of gas started. To this vigorous fermenting solution, 4.5 g. of acetol benzoate[2] was added and the mixture was allowed to stand at room temperature until the reaction subsided. The flask was then transferred to an incubator at 32° (or at room temperature for a longer time). The reaction was generally completed when all of the yeast had settled. Most of the clear solution was separated from the yeast by a siphon. The last portion of the solution was filtered. The combined solution was extracted with ether (3 × 150 ml., tech. grade) and the ethereal solution was washed with 3% aqueous sodium carbonate solution, water, and dried. After the removal of the solvent, the yellowish oil was distilled under reduced pressure, b.p. 139–140° (5 mm.). The distillate solidified after cooling. It was recrystallized from ether (Mallinckrodt, anhyd.) as white needles by dissolving the crude product in ether at room temperature and cooling the ethereal solution with an acetone–Dry Ice bath, m.p. 42–42.5°; yield, 64–66%, $[\alpha]_D^{24.2}$ + 21.8° (in $CHCl_3$).

The compound obtained did not give a good analysis, even after it had been purified alternatively by vacuum distillation and recrystallization (each twice).

Anal.: Calcd. for $C_{10}H_{12}O_3$: C, 66.65; H, 6.71. Found: C, 67.17, 67.32, 67.39; H, 6.87, 6.84, 6.77.

D-*Propylene glycol.* Optically-active propylene glycol 1-benzoate (40 g.) was added gradually with constant shaking to 20 g. of 50% alkali solution. An additional 10–15 ml. of water was added and the cakelike sodium benzoate was mashed with a spatula. The reaction mixture was refluxed in an oil bath at 125° for 3 hr. After cooling, 100 ml. of ether was poured in and the mixture was filtered. The precipitate was washed with 10 ml. of absolute ethanol. The filtrate was extracted with ether for 9 hr. The ethereal layer obtained was dried over anhydrous magnesium sulfate and evaporated to yield 10.1 g. (60%) of propylene glycol, b.p. 92° (14 mm.), $n_D^{26.7}$ 1.4334, $[\alpha]_D^{24.2}$ + 30.0° (in $CHCl_3$). (For *l*-propylene glycol, b.p. 86–88° (9–10 mm.), $[\alpha]_D^{24.4}$ −28.6° (in $CHCl_3$); −14.9° (pure state, dm.), d^{24} 1.030, n_D^{24} 1.4355.)

D-*Propylene oxide.* Levene's synthesis[3] for L-propylene oxide was used. D-Propylene bromohydrin was prepared by passing dry hydrogen bromide through D-propylene glycol at 0°; yield, 60%, b.p. 57–58° (19 mm.), n_D^{25} 1.4765 $[\alpha]_D^{24}$ +9.90° (in $CHCl_3$). (For L-propylene bromohydrin, n_D^{25} 1.4775, $[\alpha]_D^{24}$ −10.53° (in $CHCl_3$) or −3.37° (pure bromohydrin), $d^{24.5}$ 1.541.)

The D-propylene bromohydrin was then cyclized to D-propylene oxide with 45% (by weight) aqueous potassium hydroxide, b.p. 35°, $[\alpha]_D^{21}$ −6.21° (2% in $CHCl_3$). [*l*-Propylene oxide, $[\alpha]_D^{21}$ +7.05° (2% in $CHCl_3$); +14.5° (38% in ether)].

Department of Chemistry
University of Pennsylvania
Philadelphia 4, Pa.

---

(1) The reduction of the benzoate in the opposite sense to the glycol was predicted by Dr. V. Prelog (private communication).

(2) For the preparation of acetol benzoate, Adams and Govindacharis' procedure was followed [*J. Am. Chem. Soc.*, **72**, 158 (1950)] with the following modification. The combined ethereal solution was washed with ice-cold 3% sodium carbonate solution, water, and dried. It is very important that no trace of benzoic acid remain in the acetol benzoate. Otherwise the yeast will be killed during the fermentation.

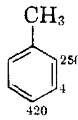
(3) P. A. Levene and A. Walti, *J. Biol. Chem.*, **68**, 415 (1926).

Relative Reactivities of Toluene and Toluene-*α,α,α-d*$_3$ in Hydrogen-Deuterium Exchange

W. M. Lauer and C. B. Koons[1]

March 2, 1959

Recent exchange studies[2] carried out in this laboratory have led to the following values for the partial rate factors for hydrogen-deuterium exchange in the case of toluene:



These exchange studies were conducted at 70° in a trifluoroacetic acid medium. Under these conditions, exchange occurs only in the aromatic nucleus. This fact was demonstrated by oxidizing a sample of randomly deuterated toluene to benzoic acid with aqueous alkaline permanganate. There was no loss of deuterium in this transformation. Infrared absorption studies, though less sensitive, also indicated the absence of side-chain deuterium in the randomly deuterated toluene samples. These

---

(1) Abstract of part of Ph.D. thesis submitted to the University of Minnesota, June 1958.

(2) W. M. Lauer, G. Matson, and G. Stedman, *J. Am. Chem. Soc.*, **80**, 6433, 6437, 6439 (1958).

circumstances made it feasible to include the study of the deuteration of toluene-α,α,α-d_3, since determination of the deuterium content of the benzoic acid produced on oxidation provides a comparison of the relative rates of nuclear deuteration of toluene and toluene-α,α,α-d_3.

Several interesting studies dealing with secondary isotope effects have been reported.[3] These studies have shown that a measurable secondary isotope rate effect is transmitted across the aromatic nucleus. Thus, for example, p-$CD_3C_6H_4CH(Cl)C_6H_5$ and p-$CH_3C_6H_4CH(Cl)C_6H_5$ manifest slightly different solvolysis rates; the introduction of deuterium into the p-methyl group definitely slows the rate of solvolysis. However, only the work of Swain and his co-workers dealt directly with the secondary isotope effect in nuclear substitution. These investigators found that the secondary isotope effects on the rates of nuclear nitration, mercuration and bromination due to isotopic substitution for hydrogen in the methyl group of toluene are 3% per deuterium atom or less. Our results showed that the substitution (90%) of deuterium for the three hydrogens in the methyl group of toluene decreased the nuclear deuterium-hydrogen exchange rate approximately 5% or about 2% per deuterium atom. The size of this effect is dependent upon the detailed mechanism of the process and since it is intermediate between the values found by Swain, Knee, and Kresge for nitration and bromination in 85% acetic acid, it may perhaps be concluded that deuteration in trifluoroacetic acid follows an intermediate course. On the other hand, these differences in the secondary isotope effect between various electrophilic aromatic substitution reactions are quite small and may be without mechanistic significance.

EXPERIMENTAL

Toluene-α,α,α-d_3 (2.7 D) was prepared according to the procedure of Renaud and Leitch.[4] Acetic anhydride (3.0 moles) was heated with magnesium turnings (10 g.) under reflux for 24 hr. The anhydride was then decanted and treated with powdered zinc (10 g.), carbon tetrachloride (10 ml.), and phosphorus pentoxide (0.1 g.). Deuterium oxide (99.5%, 3.2 moles) was added slowly during a period of 1.5 hr. The mixture was then stirred mechanically for 3 hr. at 60°. Fractional distillation yielded acetic acid-d (b.p. 116–118°, n_D^{25} 1.3706, 250 g.). A mixture of anhydrous ether (600 ml.), acetic acid-d (170 g., 2.78 moles), and zinc dust (110 g.), cooled to 3°, was then treated with freshly distilled benzotrichloride (90 g.) dissolved in dry ether (300 ml.). The time of addition was 3 hr. and after the addition was complete stirring was continued for 3 hr. A white precipitate formed in the reaction flask. Water (500 ml.) was added and the reaction mixture was filtered. The ether layer was washed with water (300 ml., 3×), aqueous sodium bicarbonate (10%; 250 ml., 2×), and finally with water (300 ml.). The ether solution on distillation yielded toluene-α,α,α-d_3 (b.p. 109–110°, n_D^{25} 1.4929, 29%). A deuterium assay indicated 2.70 atoms of deuterium per molecule. An alkaline permanganate oxidation gave benzoic acid containing only the normal level of deuterium per molecule.

The infrared Spectrum (Perkin-Elmer model 21) showed no absorption for ring deuterium in the 2245–2285 cm.$^{-1}$ region. In addition, there is no absorption at 617, 640, and 830 cm.$^{-1}$ which are characteristic of ortho, meta, and para deuterotoluenes, respectively.

Determination of deuterium. The toluene samples were oxidized with alkaline permanganate and the benzoic acid obtained was burned in a stream of oxygen. The water produced was passed over hot zinc and the gas was analyzed using a mass spectrometer.[5] It had been shown earlier that toluene deuterated in the ring is oxidized in the presence of alkali to benzoic acid without the loss of any deuterium.

Calculations. At the temperature of the reduction (zinc), the equilibrium constant for the following reaction is approximately 4.

$$H_2 + D_2 \rightleftarrows 2HD$$

$$(a - x) \quad (b - x) \; 2x$$

At equilibrium

$$\frac{(2x)^2}{(a - x)(b - x)} = 4 \text{ and } x = \frac{ab}{a + b}$$

The HD/H_2 ratio, $R = 2x/(a - x)$ and $x = aR/(R + 2)$; consequently $b = aR/2$. The mole fraction of deuterium X_D in the deuterated compound may be expressed by the following equation:

$$X_D = \frac{D}{D + H} = \frac{2x + 2(b - x)}{2x + 2(b - x) + 2x + 2(a - x)} = \frac{b}{a + b} = \frac{R}{R + 2}$$

Since the mole fraction of deuterium of an unchanged sample is 0.00015, the mole fraction of deuterium introduced becomes $R/(R + 2) - 0.00015$. It is often convenient to express the amount of deuterium introduced as the mole fraction of monodeuterated compound formed, ArD/(ArD + ArH). Thus, in the case of monodeuterobenzoic acid, C_6H_4DCOOH, the mole fraction of deuterium is $^1/_6$. An HD/H_2 value of 0.01522 yields a value $6/1[R/R + 2 - 0.00015]$ or 0.045; *i.e.*, $C_6H_{4.955}D_{0.045}COOH$.

Deuteration studies. The deuterating reagent was prepared as follows: Deuterium oxide (99.7%, 5 g., 0.2497 mole) was diluted to 100 ml. with trifluoroacetic acid (Eastman Kodak Co., White Label).

Toluene (1.38 g., 0.0150 mole) or toluene-α,α,α-d_3 (2.7 D) (1.43 g., 0.0150 mole) was dissolved in the deuterating agent (3.00 ml.). Solutions were prepared in glass ampoules (10 ml.), which were sealed immediately and placed in a bath maintained at a temperature of 70.0 ± 0.1°. Deuterations were carried out for 25, 50, 72, and 98 hr. At the end of these periods, the ampoules were opened and the contents poured into ice and water. The hydrocarbon layer was then separated and washed twice with aqueous potassium hydroxide solution (10%, 5 ml.).

The hydrocarbon samples were then oxidized by means of an aqueous alkaline permanganate solution. Dr. Gale Matson of this laboratory found that there was no loss of deuterium

---

(3) E. S. Lewis and C. E. Boozer, *J. Am. Chem. Soc.*, **74**, 6306 (1952); **76**, 791, 794 (1954). E. S. Lewis and G. M. Coppinger, *J. Am. Chem. Soc.*, **76**, 4495 (1954). V. J. Shiner, Jr., *J. Am. Chem. Soc.*, **75**, 2925 (1953); **76**, 1603 (1954); **78**, 2653 (1956); V. J. Shiner, Jr. and C. J. Verbanic, *J. Am. Chem. Soc.*, **79**, 373 (1957). A. Streitweiser, Jr., R. H. Jagow, and S. Suzuki, *J. Am. Chem. Soc.*, **80**, 2326 (1958). C. G. Swain, T. E. C. Knee, and A. J. Kresge, *J. Am. Chem. Soc.*, **79**, 505 (1957).

(4) R. Renaud and L. Leitch, *Can. J. Chem.*, **34**, 98 (1956).

(5) We are indebted to Prof. A. O. C. Nier and his colleagues of the department of physics for the determination of the HD/H_2 ratios.

in this process. This statement is based on the finding that a sample of randomly deuterated toluene HD/H_2 ratio of 0.00862; $C_6H_{4.967}D_{0.033}CH_3$ gave benzoic acid HD/H_2 ratio of 0.0114; $C_6H_{4.967}D_{0.033}COOH$ on oxidation under these conditions.

An analysis of the samples of benzoic acid obtained in the present study follows:

Time, Hr.	Toluene		Toluene-α,α,α-d_3 (2.7 D)	
	HD/H_2	$C_6H_{(5-n)}D_nCOOH$, n	HD/H_2	$C_6H_{(5-n)}D_nCOOH$, n
25	0.01522	.044	0.01424	.042
50	0.02837	.083	0.02684	.078
72	0.03899	.113	0.03747	.109
98	0.05078	.148	0.04843	.141

Acknowledgment. This work was supported by the Atomic Energy Commission, Contract AT(11-1) 478.

SCHOOL OF CHEMISTRY
UNIVERSITY OF MINNESOTA
MINNEAPOLIS 14, MINN.

Solubility Classification Test for the Differentiation of Strong and Weak, Water-insoluble Organic Bases

ANTHONY E. PETRARCA

Received March 4, 1959

Solubility classification tests for the differentiation of strong and weak, water-insoluble acids have long been a part of the customary procedure for identification of organic compounds; however, similar tests for the differentiation of strong and weak, water-insoluble organic bases are not described in the most recent editions of several widely adopted texts for qualitative organic analysis.[1-3] The absence of such tests probably is due to the lack of a simple suitable reaction solvent which would be capable of differentiating bases in a manner analogous to the differentiation of acids by sodium bicarbonate solution.

A reaction solvent that has been found suitable for such a differentiation of bases is a sodium acetate–acetic acid solution buffered at a *p*H of 5.5. Aliphatic amines (K_b 10^{-3} to 10^{-5}) are soluble in this solution, but aromatic amines and other weak bases (K_b about 10^{-10}) are not. Thus, by a simple extension of the solubility classification tests now commonly used, basic compounds may be separated into two classes by reference to their solubilities in this reagent, class B_1 to include those that are soluble and class B_2 those that are insoluble. A series of water-insoluble bases whose classifications have been determined on this basis are listed in Table I.

TABLE I

SOLUBILITIES* OF WATER-INSOLUBLE BASES IN 5% HCL AND NAOAC-HOAC BUFFER[b]

Base	5% HCl	NaOAc–HOAc	Class
Tri-*n*-butylamine	+	+	B_1
N,*N*-dibenzylamine[c]	+	+	B_1
N-methyl-3-piperidylphenylcarbinol[d,e]	+	+	B_1
N-benzyl-4-piperidylphenylcarbinol[d]	+	+	B_1
N-methyl-3-benzyl-1,2,5,6-tetrahydropyridine[d]	+	+	B_1
Aniline	+	−	B_2
N,*N*-dimethylaniline	+	−	B_2
p-toluidine	+	−	B_2
p-anisidine	+	−	B_2
4-benzoylpyridine	+	−	B_2

* 0.2 ml. of liquids and 0.1 g. of solids in 3 ml. of solvent. [b] 2.0*M*. in NaOAc and 0.4*M*. in HOAc. [c] Insoluble salts precipitated from the reaction solvents. [d] Obtained through the courtesy of Glenn H. Warner, Teaching Fellow, Univ. of New Hampshire. [e] Although most of this material dissolved in NaOAc-HOAc buffer, a small quantity remained undissolved.

This same reaction solvent is also useful for the separation of a mixture of aromatic and aliphatic amines. In connection with a separate study where such mixtures are usually encountered,[4] a procedure utilizing sodium acetate–acetic acid buffer for the separation of α-*p*-methoxyphenylethylamine from *N*-ethyl-*p*-methoxyaniline was found to be more satisfactory than one previously employed.[5,6]

EXPERIMENTAL

Preparation of sodium acetate–acetic acid buffer. A solution of the desired *p*H (5.5) was prepared by dissolving 164 g. (2 moles) of anhydrous sodium acetate and 24 g. (0.4 mole) of acetic acid in sufficient water to make 1 liter of solution.

Solubility classification tests. The limits of solubility used were those described by Shriner, Fuson, and Curtin.[7] The tests were performed by placing 0.2 ml. of the amine (0.1 g. of solids) in 3 ml. of the appropriate reaction solvent, followed by vigorous shaking of the mixture. If the amine dissolved completely or was found to be appreciably more soluble than in water alone it was recorded as soluble.

Separation of mixtures of aliphatic and aromatic amines. A 50-ml. sample of a solution of α-*p*-tolylethylamine and *N*-ethyl-*p*-toluidine in ether, on titration by potentiometric techniques, was found to contain 0.78 m.equiv. of the former

---

(1) N. D. Cheronis and J. B. Entrikin, *Semimicro Qualitative Organic Analysis*, 2nd ed., Interscience Publishers, Inc., New York, 1957.

(2) R. L. Shriner, R. C. Fuson, and D. Y. Curtin, *The Systematic Identification of Organic Compounds*, 4th ed., John Wiley and Sons, Inc., New York, 1956.

(3) S. M. McElvain, *The Characterization of Organic Compounds*, 2nd ed., The MacMillan Co., New York, 1953.

(4) A. E. Petrarca, PhD. thesis, University of New Hampshire (1959).

(5) R. E. Lyle and H. J. Troscianiec, *J. Org. Chem.*, **20**, 1757 (1955).

(6) D. Smith, M. Maienthal, and J. Tipton, *J. Org. Chem.*, **17**, 294 (1952).

(7) Ref. 2, pp. 65–7.