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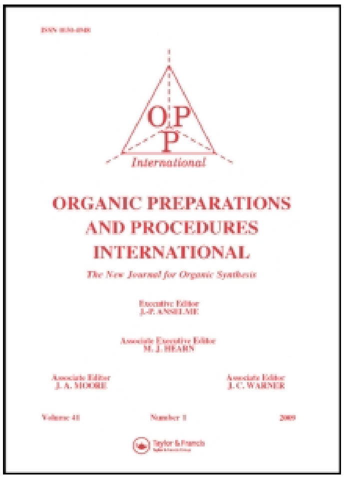

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A CLEAN AND REPRODUCIBLE SYNTHESIS OF 1-BROMO-2-ETHOIYETBANE

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Anal. Calcd. for $C_5H_4N_2O_3$: C, 42.86; H, 2.88; N, 20.00

Found: C, 42.80; H, 2.94; N, 20.35

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A CLEAN AND REPRODUCIBLE SYNTHESIS OF 1-BROMO-2-ETHOXYETHANE

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The first synthesis of 1-bromo-2-ethoxyethene (1) was accomplished by treatment of bromoacetaldehyde diethyl acetal with zinc dust in refluxing ethanol.[1] The discovery that alkyl vinyl ethers could be prepared from alcohols using an alkaline catalyst,[2] made ethyl vinyl ether commercially available at low cost in the mid-1940's. Compound 1 is now most commonly

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produced by a bromination-dehydrobromination[3] sequence first reported by Favorskii from readily available ethyl vinyl ether.[4] The current literature contains numerous accounts of this reaction;[5-9] however, in each case the procedure has been modified because of difficulties encountered in reproducing literature yields. Our original interest in **1** was as a precursor to ethoxyalkynes,[10] a commonly reported use for this compound. Perhaps its greatest synthetic value, however, lies in the use of **1** in coupling reactions[11] where it serves as an acetaldehyde anion equivalent.[9,12] If **1** were more readily available, its utilization in these reactions and in related schemes would be facilitated. Hence, it seemed useful to develop an efficient and reproducible synthesis of this useful but underutilized synthon.

The Favorskii procedure was chosen as the method to be examined in greater detail. Two general modifications of Favorskii's procedure have been reported. In procedure A the dibromide **2**, was heated with an amine as a base while the product was being directly distilled at reduced pressure as it was formed.[6-9] In procedure B, **2** was heated with the amine for a specified period prior to solvent extraction of the mixture thus allowing **1** to be isolated by distillation from the extraction solvent.[2,13]

A repetition of both of these modifications, using an assortment of bases under various conditions, showed that procedure B was much more susceptible to deviation in reaction conditions, product mixture and yield.[14] As noted in earlier work,[7] the yield of **1** decreased markedly by procedure B if the temperature was allowed to rise above 100°; in addition, unreacted dibromide was converted to the byproduct bromoacetaldehyde diethyl acetal upon typical acidic workup procedures.[4] Conversely, procedure A gave reproducible yields and showed no noticeable temperature effects within the

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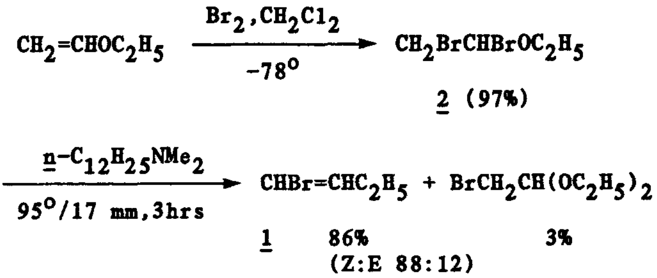
range of 90-130°. Depending on the amine used, yields varied between 19% with quinaldine to 86% with N,N-dimethyldodecylamine. The two most commonly used bases, N,N-diethylaniline (2.5:1 ratio of base to 2) and tributylamine (1:1 ratio) gave yields of 66% and 61% respectively;[14] under these conditions thick, dark solutions were formed and this made distillation of the product difficult and bromoacetaldehyde diethyl acetal was formed as a byproduct in 12-15% yield. The use of N,N-dimethyldodecylamine results in a synthesis of 1 with both high yields (86%) and fewer byproducts. The following scheme summarizes the best conditions found for a clean reproducible synthesis of 1-bromo-2-ethoxyethane (1).



$$CH_2{=}CHOC_2H_5 \xrightarrow[-78^\circ]{Br_2, CH_2Cl_2} \underset{\underline{2}\ (97\%)}{CH_2BrCHBrOC_2H_5}$$

$$\xrightarrow[95^\circ/17\ mm, 3hrs]{\underline{n}-C_{12}H_{25}NMe_2} \underset{\underline{1}\quad 86\%\ (Z{:}E\ 88{:}12)}{CHBr{=}CHC_2H_5} + \underset{3\%}{BrCH_2CH(OC_2H_5)_2}$$

EXPERIMENTAL SECTION

The ^1H-NMR spectra were obtained in CCl_4 on a Perkin Elmer R-24B 60 MHz spectrometer. Chemical shift values are expressed in parts per million (δ) downfield from TMS. The IR spectra were obtained neat on a Beckman Acculab 4 spectrophotometer. Gas chromatography (VPC) identifications and percent yield calculations were made using a Hewlett Packard Model 5791 equipped with an FID and a 50 m HP Ultra cross-linked, methyl silicone wall coated, open tubular, fused silica capillary column. The VPC was programmed to hold at 50° for 8 min and then to increase 4°/min to a maximum of 260°. The ethyl vinyl ether and N,N-dimethyldodecylamine were commercial products of the highest purity available and were distilled and dried over molecular sieves before use. ALL REACTIONS AND WORKUPS SHOULD BE CARRIED OUT IN THE HOOD SINCE THE PRODUCTS AND BYPRODUCTS ARE LACRYMATORY.

1,2-Dibromoethoxyethane(2).- A 1-L 3-neck round-bottom flask equipped with a mechanical stirrer, a pressure-equalizing addition funnel, and a condenser topped with a drying tube ($CaCl_2$), was half-immersed in a Dry Ice-acetone bath after the addition of 90 g (1.25 mol) ethyl vinyl ether and 300 ml of dry CH_2Cl_2. The addition funnel was filled with a solution of 200 g (125 mol) bromine in 150 ml of dry CH_2Cl_2, and addition was started and continued at the rate of 2-3 drops/sec until all the solution was added in about 2 hrs. The reaction mixture remained colorless until the last 15 min at which time it became clear red-orange. The flask was removed from the Dry Ice bath and stirring stopped as the solution was allowed to stand overnight at room temperature. The resulting clear yellow liquid was concentrated by rotary evaporation in a bath maintained at 35-40°. The crude dibromide, 282.8 g (97%), was a clear deep yellow oil. Product purity was determined by ^1H NMR (CCl_4) [δ 5.99 (t, 1H), 3.87 (d, 2H), 3.69 (t, 2H), 1.32 (t, 3H)]; to a peak at δ 5.32 indicated the CH_2Cl_2 impurity of about 2%. Distillation of 1,2-dibromoethoxyethane can be performed at reduced pressure to give a clear, colorless, fuming liquid, bp. 44-47°/1.8 mm, lit.[4] 76°/16 mm, usually in about 90% yield.[15]

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1-Bromo-2-ethoxyethane (1).- The reaction apparatus consisted of a 2-L 3-neck round-bottom flask equipped with a mechanical vacuum stirrer assembly, a 500 mL pressure-equalizing addition funnel, and a simple vacuum distillation apparatus connected through a Claisen adapter thus allowing the insertion of a thermometer to measure the pot temperature. To the flask was added 665.6 g (3.12 mol) of dried, distilled N,N-dimethyldodecylamine. The crude 1,2-dibromoethoxyethane [282.8 g, 1.22 mol] produced in the previous step was added to the addition funnel before the preheated oil bath was raised. The temperature of the oil bath was adjusted to 110-120° so as to maintain a pot temperature close to 100° throughout the course of the reaction and a vacuum of 30mm was applied. When the pot temperature reached 97°, the addition of the dibromide was started at 2-3 drops/sec and the solution turned from yellow to brown.[16] Within 0.5 hr., a colorless product began distilling at 49°/30 mm which was collected in a receiver cooled in a dry ice-isopropanol bath. The pressure was lowered to 20 mm as the addition was completed within 1.5 hr. The reaction was allowed to proceed for an additional 1.5 hr before the final amounts of product were brought over by dramatically increasing the stirrer speed and by heating the pot and head with a heat gun until no more liquid distilled. The main fraction, 168.3 g, and a small amount collected in the gas trap, were analyzed by VPC and shown to be almost pure 1-bromo-2-ethoxyethane (1) in a crude yield of 90%. The combined fractions were redistilled through a 30 cm Vigreux column to give the following fractions: 21.4 g, bp. 50-62°/46 mm (Z:E = 73:27), 99.2 g, bp. 62-66°/43 mm (Z:E = 89:11), and 35.8 g, bp. 66-78°/45 mm (Z = 89%, acetal = 11%), lit.[7] bp. 28-47°/12 mm. The combined weight of the clear, colorless distilled fractions was 156.3 g (83%) based on the starting ethyl vinyl ether. Separation of pure isomers was accomplished by VPC and their identities were confirmed by ^{1}H NMR (CCl_4); Z isomer: δ 6.65 (d, 1H), 5.10 (d, 1H), 4.02 (q, 2H), 1.36 (t, 3H); E isomer: δ 6.78 (d, 1H), 5.38 (d, 1H), 3.82 (q, 2H), 1.31 (t, 3H).[17]

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15. A series of bromination was carried out and gave the following distilled yields: 1 mole runs: 210 g (91%) and 202 g (87%); 2 mole runs: 418g (90%) and 385 g (83%); 2.5 mole runs: 544 g (94%) and 545 g (94%).

16. When freshly distilled 1,2-dibromoethoxyethane (2) is used, a clear solution with an orange precipitate results.

17. It is possible to recover a good portion of the N,N-dimethyldodecylamine which is used in excess to keep all of the salts of reactions dissolved. Recovery is best accomplished by first acidifying the reaction mixture to remove the intractable greasy residues before basification of the mixture. Extraction of the basified mixture with ether followed by drying ($MgSO_4$) and distillation yields a clear, colorless liquid, bp. 104-105°/1.2 mm, which can be reused when the reaction is repeated.

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