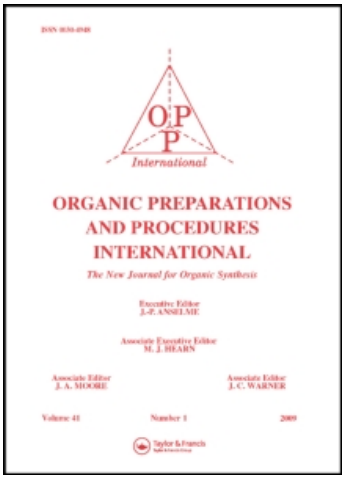

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Melvin S. Newman[a]; Jay R. Geib[a]; Wayne M. Stalick[a]
[a] Evans Chemistry Laboratory, The Ohio State University, Columbus, Ohio

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IMPROVED SYNTHESES OF 1-ETHOXYALKYNES[1]

Melvin S. Newman,* Jay R. Geib, and Wayne M. Stalick[2]

Evans Chemistry Laboratory, The Ohio State University,
Columbus, Ohio 43210

In earlier work, the thermal and boron fluoride catalyzed rearrangements of 1-ethoxyvinyl and 1-ethoxypropenyl esters of a variety of keto acids have been described.[3] The continuation of this study[4] required the synthesis of a number of unbranched 1-ethoxyalkynes from readily available starting materials.

The synthesis of 1-ethoxyalkynes has been previously reported, but usually the preparations have required multi-step sequences resulting in moderate to low overall yields.[5-7] Farnum reported the synthesis of 1-ethoxypropyne from ethoxyacetylene in a 55% yield.[5] Assuming that ethoxyacetylene was obtained by standard procedures,[8] the overall yield becomes about 35%. Many 1-ethoxyalkynes have been prepared according to the following scheme:[6] ethyl vinyl ether → 1,2-dibromoethyl ethyl ether → 2-bromovinyl ethyl ether → 1-ethoxyalkyne. Overall yields of 1-ethoxypropyne (~ 58%), 1-ethoxybutyne (~ 55%), and 1-ethoxyhexyne (~ 56%) have been reported by this method.[7] Two brief reports have been made concerning the direct synthesis of 1-ethoxypropyne (73%, crude),[9] and 1-ethoxyhexyne (58-63%)[10] from chloroacetaldehyde diethyl acetal.

Simplified procedures are described herein for the synthesis of 1-ethoxypropyne, 1-ethoxybutyne, and 1-ethoxyhexyne. Good yields are obtained in a one pot reaction from chloroacetaldehyde diethyl acetal.

Scheme I illustrates the reactions. Minor variations in the general reaction procedure noticeably affect the yields (see Table I).

Scheme I

$$ClCH_2CH(OC_2H_5)_2 \xrightarrow[NH_3]{3NaNH_2} NaC{\equiv}COC_2H_5 + NaCl + NaOC_2H_5 + 3NH_3$$

$$NaC{\equiv}COC_2H_5 + NaOC_2H_5 \xrightarrow{RBr} RC{\equiv}COC_2H_5 + ROC_2H_5 \quad (R = CH_3,\ C_2H_5,\ \underline{n}\text{-}C_4H_9)$$

1-Ethoxypropyne is obtained in good yields when the product is worked up before allowing the ammonia solvent to evaporate (expt 1-5) as the product evidently volatilizes with the ammonia when the solvent is allowed to evaporate (expt 6). A yield of 88% was obtained when the liquid ammonia was dried over calcium hydride for 15 hours before use (expt 7). Of the solvents tried for work-up, bromobenzene and pentane gave the best results. Difficulty in product separation from methylene chloride, tetrachloroethylene, and 1,1,2,2-tetrachloroethane makes these solvents unacceptable. In large scale reactions, the addition of sufficient water to dissolve the ammonia requires very large volumes. If less water is used, continuous bubbling of the ammoniacal layer makes extraction with a solvent lighter than the aqueous phase difficult. The use of bromobenzene avoids the bubbling problem as the product is extracted in the lower layer. Furthermore, the product is easily distilled from this high boiling solvent in the first fraction. However, bromobenzene tends to form emulsions which must be broken up. Pentane shows less tendency to form emulsions but must be removed by fractionation before the product is distilled.

1-Ethoxybutyne, like 1-ethoxypropyne, is obtained in a good yield if the product is worked-up before the ammonia is allowed to evaporate. A

TABLE I

EFFECT OF REACTION CONDITIONS ON PRODUCT YIELDS

Expt. No.	Ratio of RBr/ $ClCH_2CH(OC_2H_5)_2$	Product $R\text{-}C{\equiv}COC_2H_5$	Procedure[a]	Isolated Yield (%)
1-3	3.0/2.0	$CH_3\text{-}C{\equiv}COC_2H_5$	A	66-72
4-5	3.0/2.0	$CH_3\text{-}C{\equiv}COC_2H_5$	A[b]	70-77
6	2.5/2.0	$CH_3\text{-}C{\equiv}COC_2H_5$	B	21
7	3.0/2.0	$CH_3\text{-}C{\equiv}COC_2H_5$	A[c]	88
8-9	1.3/1.0	$C_2H_5\text{-}C{\equiv}COC_2H_5$	A	53-55
10-11	2.2/1.0	$C_2H_5\text{-}C{\equiv}COC_2H_5$	A	75-77
12	1.3/1.0	$C_2H_5\text{-}C{\equiv}COC_2H_5$	B	38
13-14	1.3/1.0	$\underline{n}\text{-}C_4H_9\text{-}C{\equiv}COC_2H_5$	A	60-67[d]
15	3.2/1.0	$\underline{n}\text{-}C_4H_9\text{-}C{\equiv}COC_2H_5$	A	65[e]
16-17	1.3/1.0	$\underline{n}\text{-}C_4H_9\text{-}C{\equiv}COC_2H_5$	B	60-62

[a]In procedure A, a saturated salt solution is added to the reaction flask and work-up with pentane is made before ammonia evaporates. Procedure B allows the ammonia to evaporate before regular work-up. [b]Bromobenzene used in work-up in place of pentane. [c]Ammonia was predried over calcium hydride; bromobenzene was used as a work-up solvent. [d]A 21% yield of butyl ethyl ether was isolated as a co-product. [e]A 75% yield of butyl ethyl ether was isolated as a co-product.

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two fold excess of ethyl bromide is required to obtain good yields since elimination apparently competes with alkylation (compare expt 8-9 with 10-11).

<u>1-Ethoxyhexyne</u> is sufficiently non-volatile that evaporation of ammonia does not noticeably decrease the yield (expt 16-17). A by-product of all the alkylation reactions described is the ether formed by the attack of sodium ethoxide on the alkyl bromide (Scheme I). If a stoi-

chiometric amount of n-butyl bromide is used as the alkylating agent (expt 13-14), a 21% yield of butyl ethyl ether is isolated. When the amount is more than doubled, the yield of butyl ethyl ether increases to 75%, but the yield of 1-ethoxyhexyne remains unchanged (expt 15). Thus ether formation must not be a serious competitor to 1-ethoxyalkyne formation under the reaction conditions employed.

EXPERIMENTAL[11]

1-Ethoxypropyne (Procedure A - Bromobenzene Solvent). - To a suspension of 6.6 mole of sodium amide[12] in 2.5 ℓ of liquid ammonia in a 5 ℓ three-necked round-bottomed flask fitted with a mechanical stirrer and Dry Ice condenser (see Figure 1 for all-glass condenser)[13] is added 305.2 g (2 mole) chloroacetaldehyde diethyl acetal (Aldrich, used as obtained) over a period of 30 min.[14] After about 1 hr, gaseous methyl bromide (290 g, 3 mole) is added during 1-2 hr. About 45 min later, 500 ml of a saturated sodium chloride solution is added as rapidly as allowed by the reflux condenser. Bromobenzene (200 ml) is stirred into the flask, the contents are transferred to a separatory funnel, and the lower organic layer is removed.[15] The aqueous layer is extracted with three 100-ml portions of bromobenzene. The combined organic layers are extracted with three 100-ml portions of water to remove the salt. The emulsion between layers is collected with the organic layer each time. After the third extraction the emulsion is filtered through fast-flow filter paper or coarse $CaCl_2$ supported on glass wool. All organic layers are combined and dried over Na_2SO_4 in a refrigerator. The dried organic layer is decanted and the Na_2SO_4 is washed three times. Distillation is performed at 150 mm[16] through a 8" x $^3/_4$" column packed with glass beads and topped with a fractionating head cooled by circulating ice water. Collection

of the fractions is made by immersing the receiver in a Dry Ice-acetone bath while keeping two Dry Ice traps between the distillation apparatus and the vacuum source. The pure 1-ethoxypropyne (114 g, 68%) is collected at 45-48°/150 mm as a clear colorless liquid. The lower and higher boiling fractions are combined with the material removed from the Dry Ice traps and redistilled at atmospheric pressure to yield (15 g, 9%) pure 1-ethoxypropyne at 89-92° (lit[17] bp 88-90.5°). Isolated yields total 70-77% by this method.

1-Ethoxybutyne (Procedure A - Pentane Solvent). - Chloroacetaldehyde diethyl acetal (76.1 g, 0.5 mole) is added over a period of 20 min to a suspension of 1.56 mole sodium amide in 600 ml of liquid ammonia.[14] After 1 hr, 120 g (1.1 mol) freshly distilled ethyl bromide is rapidly added through an addition funnel. The solution is stirred vigorously for 2.5 hr before 30 ml of a saturated NH_4Cl solution is added. This is followed by 120 ml of pentane and an additional 470 ml of the saturated salt solution. The contents of the flask are transferred to a separatory funnel, where the lower aqueous layer is removed and extracted with three 50-ml portions of pentane.[15] Any emulsion formed is easily dissipated by filtering through fast-flow filter paper. The organic layers are combined and quickly filtered through $MgSO_4$ supported on fast-flow filter paper. After the pentane is removed by distillation at atmospheric pressure, the residue is distilled at reduced pressure[16] using the same apparatus described for 1-ethoxypropyne. The pure 1-ethoxybutyne (30 g, 62%) is collected at 43-45°/50 mm (lit[18] 112.5-113°/750 mm). A lower boiling fraction collected at 20-42°/50 mm can be combined with any material removed from the gas traps and redistilled to yield additional product (7 g, 14%). Total yields of 75-77% are obtained.

1-Ethoxyhexyne (Procedure B). - Chloroacetaldehyde diethyl acetal (76.1 g, 0.5 mole) is added over a 20 min period to a suspension of 1.64 mole sodium amide in 600 ml of liquid ammonia.[14] After 1 hr, 89 g (0.65 mole) of freshly distilled n-butyl bromide is added (~ 20 min). After a short time the reaction solution develops distinct layers, a white salt layer that settles to the bottom, an oily grayish-brown band around the flask, and the yellow ammonia solution throughout. At this time, the addition funnel is replaced by a water condenser and the ammonia is allowed to evaporate overnight. The flask, containing a solid residue, is immersed in an ice bath and 500 ml of water is slowly added with stirring. The mixture is worked up as given in the preceding example. After a low boiling fraction is removed, the pure 1-ethoxyhexyne (35 g, 56%) is collected as a clear colorless liquid at 48-49°/10 mm (lit[10] 47-51°/9 mm). The lower boiling fraction can be redistilled to yield pentane, n-butyl ethyl ether, and some additional 1-ethoxyhexyne (4 g, 6%). Total yields of 1-ethoxyhexyne by this method are 60-62%.

REFERENCES

1. This research was supported in part by Grant 12445 of the National Science Foundation.

2. Ohio State University Postdoctoral Fellow 1971.

3. (a) M. S. Newman and Z. U. Din, J. Org. Chem., 36, 2740 (1971). (b) M. S. Newman and S. Gupte, ibid., 35, 4176 (1970).

4. M. S. Newman and W. M. Stalick, in preparation.

5. D. G. Farnum, M. A. T. Heybey, and B. Webster, J. Amer. Chem. Soc., 86, 673 (1964).

6. L. Brandsma, H. J. T. Bos, and J. F. Arens, "Acetylenic Ethers and Thioethers," in "Chemistry of Acetylenes," H. G. Viehe, Ed., Marcel Dekker, Inc., New York, N.Y., 1969, pp 754-758 and 826-828, and references cited therein.

7. L. Brandsma, "Preparative Acetylenic Chemistry," Elsevier Publishing Co., New York, N.Y., 1971, pp. 38, 41, 46, and 191.

8. E. R. H. Jones, G. Eglinton, M. C. Whiting, and B. L. Shaw, "Organic Synthesis," Coll. Vol. 4, 404 (1963).

9. H. J. Alkema and J. F. Arens, Rec. Trav. Chim. Pays-Bas, 79, 1257 (1960).

10. J. R. Nooi and J. F. Arens, ibid., 81, 517 (1962).

11. All boiling points are uncorrected. Infrared spectra were recorded on a Perkin-Elmer Infracord and nmr spectra on a Varian A-60 instrument. All compounds had ir (neat) and nmr (CCl_4, TMS standard) spectra consistent with the assigned structures.

12. Prepared as described by K. W. Greenlee and A. L. Henne, Inorg. Syn., 2, 128 (1946).

13. For a description of an efficient all metal condenser for large scale work with liquid ammonia see M. S. Newman, "An Advanced Organic Laboratory Course," p. 146, Macmillan Co., New York, N.Y., 1972.

14. During any addition, excessive foaming may occur. This may be diminished by using larger amounts of ammonia for the reaction, by interrupting the addition of reagent with a subsequent increase in the speed of stirring or by immersion in a Dry Ice-acetone bath for a few seconds.

15. Since the 1-ethoxyalkyne formed is very volatile, extreme care should be taken during the work-up to minimize loss of product.

16. Distillations should be made at reduced pressure since 1-ethoxyalkynes are known to dimerize at temperatures of 90° or higher; see J. Nieuwenhuis and J. F. Arens, Rec. Trav. Chim. Pays-Bas, 77, 761 (1958).

17. J. F. Arens, ibid., 74, 275 (1955).

18. J. Ficini, Bull. Soc. Chim. Fr., 1367 (1954).

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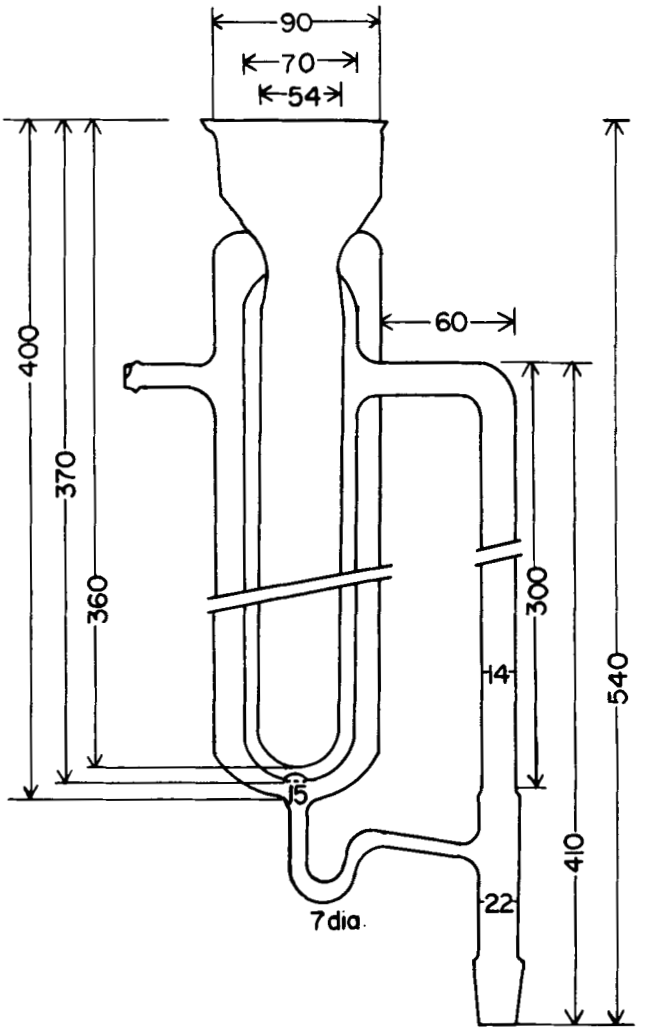

Fig. 1 - All glass liquid ammonia reflux condenser
All measurements o.d. in mm.