An Improved Synthesis of the Ethylene Acetal of 3-Iodopropanal and the Ethylene Ketal of 4-Iodo-2-butanone

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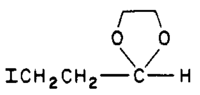
Recently a greatly improved preparation of the ethylene acetal of 3-iodopropanal (1) and the ethylene ketal of 4-iodo-2-butanone (2) on a reasonably large scale was reported.[2] This reaction employs aqueous HI, requires 18 h, and provides **1** in 60% and **2** in 56% yields. We report herein a further improvement in the preparation of these important synthetic reagents.[3]



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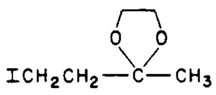
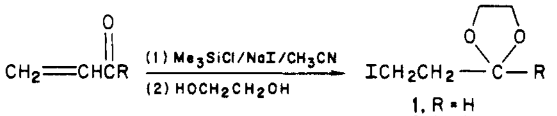


2

Our synthesis, which is similar in concept but simpler in practice to a recent preparation of β-halo acetals,[4] is based on three different reports in the literature: (1) the reported reaction of iodotrimethylsilane with α,β-unsaturated ketones to give 3-iodo enol silyl ethers,[5] (2) the ability to employ chlorotrimethylsilane and sodium iodide in acetonitrile in lieu of the more difficultly handled iodotrimethylsilane,[6] and (3) our report of some years ago that enol silyl ethers react rapidly and cleanly with diols to form the ketals.[7] It therefore seemed to us that the reaction sequence shown in eq 1 should provide a rapid, inexpensive and efficient preparation of **1** and **2**. This is indeed the case.



(1)

1, R = H
2, R = Me

Thus, the rapid, dropwise addition of chlorotrimethylsilane (12 mmol) to a rapidly stirred solution of acrolein (10 mmol) and sodium iodide (12 mmol) in acetonitrile (25 mL) produced an immediate precipitate and a yellow solution, which became dark orange with time.[8] The addition of ethylene glycol and workup gave 2.4 g (105%) of a light yellow liquid whose ^{1}H NMR spectrum was identical with that published[2] except for a small peak at 0.05 ppm for some hexamethyldisiloxane present. Material purified by alumina chromatography[2] with the concentrated material evacuated for 15 min at 1 mmHg gave 1.94 g (85%) of **1**, which showed the expected ^{1}H NMR spectrum with the absence now of the hexamethyldisiloxane peak.

A similar procedure with 3-buten-2-one gave a 62% yield of **2** contaminated with a small amount of hexamethyldisiloxane.[9] This material turns dark within a few minutes at room temperature even when purified chromatographically.

Experimental Section

An oven-dried, standard apparatus under an atmosphere of nitrogen was employed. All reagents were normal commercial grade and were used as received.

2-(2-Iodoethyl)-1,3-dioxolane (1). To a solution of 18 g (120 mmol) of sodium iodide and 5.60 g (100 mmol) of acrolein in 250 mL of acetonitrile was rapidly added with vigorous stirring 15.3 mL (120 mmol) of chlorotrimethylsilane. The resulting suspension was stirred for 5 min and 6.69 mL (120 mmol) of ethylene glycol added rapidly followed by stirring for 5 min, after which time the reaction mixture was poured onto 100 mL of 5% NaHCO$_3$ overlaid with 300mL of pentane. This produced after thorough mixing three distinct liquid phases. The aqueous, undermost layer was removed, and the remaining organic phases were washed with 100 mL of 5% Na$_2$S$_2$O$_3$ and then with 100-mL portions of saturated NaCl until only a single organic phase was evident. This required from eight to ten washes. The pentane layer was dried over K$_2$CO$_3$. Solvent removal at reduced pressure (water aspirator) gave 21.9 g (96%) of **1** as a pale yellow liquid. Chromatography of this material over a 3 × 12 cm alumina column with hexane produced 19.4 g (85%) of **1** whose ^{1}H NMR spectrum was identical with that published as well as with that of the crude material prior to chromatography.

2-Methyl-2-(2-iodoethyl)-1,3-dioxolane (2). In a procedure exactly analogous to that described above 8.3 g (100 mmol) of 3-buten-2-one produced 18.9 g (78%) of crude **2** as a pink liquid containing hexamethyldisiloxane. Alumina chromatography with hexane gave 14.4 g (60%) of **2** as a light yellow liquid whose ^{1}H NMR spectrum corresponded with that published.[10]

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Registry No. 1, 83665-55-8; 2, 53750-51-9; CH$_3$C(O)CH═CH$_2$, 78-94-4; ClSiMe$_3$, 75-77-4; HOCH$_2$CH$_2$OH, 107-21-1; acrolein, 107-02-8.

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(1) Visiting professor at Louisiana State University.

(2) Stowell, J. C.; King, B. T.; Hauck, H. F., Jr. *J. Org. Chem.* **1983**, *48*, 5381.

(3) Consult ref 2 and references therein.

(4) Gil, G. *Tetrahedron Lett.* **1984**, *25*, 3805.

(5) Miller, R. D.; McKean, D. R. *Tetrahedron Lett.* **1979**, 2305.

(6) Olah, G. A.; Narang, S. C.; Gupta, B. G. B.; Malhotra, R. *J. Org. Chem.* **1979**, *44*, 1247.

(7) Larson, G. L.; Hernandez, A. *J. Org. Chem.* **1973**, *38*, 3935.

(8) Experimentation revealed that in the acrolein reaction to form 1 the reaction can be quenched with ethylene glycol within 2 min or as long as 2 h of the addition of chlorotrimethylsilane with essentially the same results.

(9) This reaction mixture turns a dark orange within a few seconds after the addition of the chlorotrimethylsilane. Running the reaction at 0 °C gave comparable results.

(10) Trost, B. M.; Kunz, R. A. *J. Am. Chem. Soc.* **1975**, *97*, 7152. We thank Professor J. C. Stowell for a ^{1}H NMR spectrum of **2**.

Syntheses of α-, β-, and γ-Substituted Carnitines via β-Keto Esters

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Carnitine (1) is extremely important in mammalian systems, where the highest concentrations are found in cardiac and skeletal muscle.[1] In these tissues carnitine

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(1) Bremer, J. *Physiol. Rev.* **1983**, *63*, 1420–1480.