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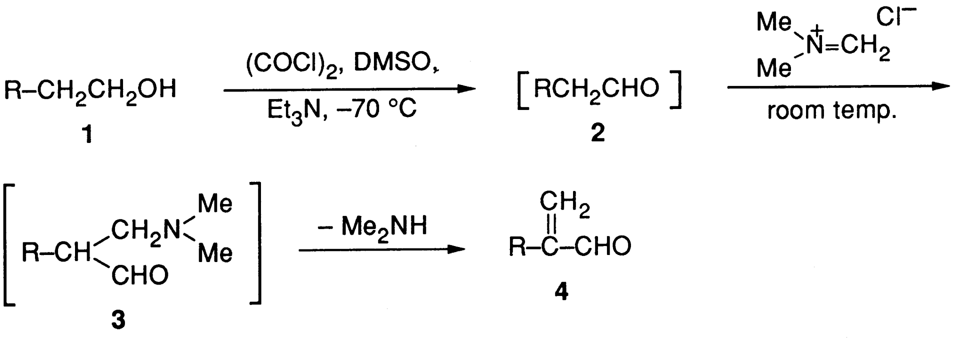
A Convenient One-flask Synthesis of α-Methylenealdehydes from Primary Alcohols

Seiichi TAKANO,* Kohei INOMATA, Kiyohiro SAMIZU, Shun'ichi
TOMITA, Masashi YANASE, Mahito SUZUKI, Yoshiharu IWABUCHI,
Takumichi SUGIHARA, and Kunio OGASAWARA
Pharmaceutical Institute, Tohoku University, Aobayama, Sendai 980

A convenient one-flask synthesis of α-methylenealdehydes from primary alcohols has been established.

In relation to the ongoing project, we required an efficient construction of certain α-methylenealdehydes.[1)] We report here a convenient one-flask synthesis of α-methylenealdehydes from the primary alcohol precursors.

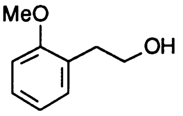
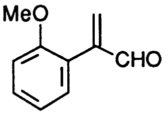
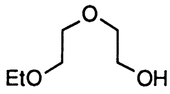
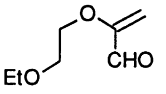
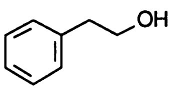
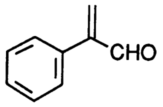
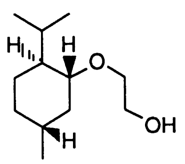
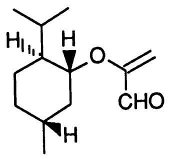
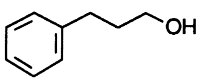
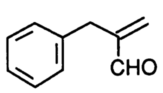
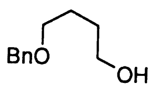
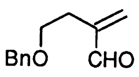
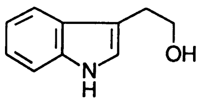
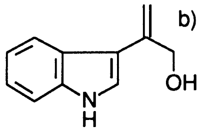
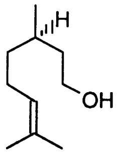
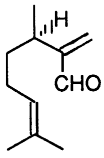
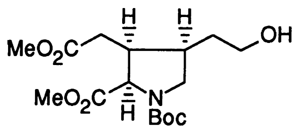
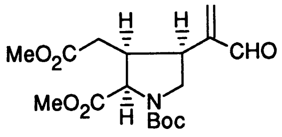
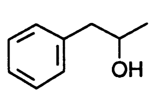
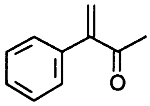
The reaction could be simply carried out by treating a primary alcohol with oxalyl chloride, triethylamine, and dimethyl sulfoxide,[2)] followed by methylene-N,N-dimethylammonium chloride[3)] in the same flask to give an α-methylenealdehyde presumably via the sequence of reactions shown in Scheme 1. Generally, secondary alcohols did not form the corresponding α-methyleneketones except 3-phenyl-2-propanol[4)] (entry 10).



Scheme 1.

A typical procedure is as follows: To a stirred solution of oxalyl chloride (0.52 ml, 6.0 mmol) in dichloromethane (15 ml) is added dimethyl sulfoxide (0.58 ml, 12.0 mmol) dropwise at -70 °C, and after 15 min, 2-(2-methoxyphenyl)ethanol (304 mg, 2.0 mmol) followed by triethylamine (3.1 ml, 22.4 mmol) are added at the same temperature. After having stirred at room temperature for 15 min, methylene-N,N-dimethylammonium chloride (376 mg, 4.0 mmol) is added to the mixture and the stirring is continued for 15 h at the same temperature. The mixture is taken up into dichloromethane (30 ml), washed (sat. $NaHCO_3$ then sat. NaCl), dried ($MgSO_4$), and purified (SiO_2 column) to give 2-(2-methoxyphenyl)acrylaldehyde (302 mg, 93%) (entry 1).

Table 1. One-flask Synthesis of α-Methylenealdehydes from Primary Alcohols

Entry	Substrate	Product$^{a)}$	Yield/%	Entry	Substrate	Product$^{a)}$	Yield/%
1			93	6			72
2			60	7			45
3			72	8			64
4		 b)	52	9			78
5			62	10			65

a) All new compounds were fully characterized by elemental (combustion and/or high resolution mass) and spectral (IR, ^{1}H-NMR, and mass) analyses.

b) Since the aldehyde was too unstable to isolate, the crude product was reduced directly with $NaBH_4$-$CeCl_3$.

References

1) A direct synthesis of -methyleneketones from ketone precursors, see: J. -L. Gras, Tetrahedron Lett., 1978, 2111, 2955.

2) Cf. A. J. Mancuso and D. Swern, Synthesis, 1981, 165.

3) G. Kinast and L. -F. Tietze, Angew. Chem., 88, 261 (1976).

4) Secondary alcohols (1-phenylethyl alcohol, cyclopentanol, cyclohexanol, trans-4-methylcyclohexanol) afforded exclusively the corresponding ketones in excellent yield under these conditions without incorporation of methylene group.

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