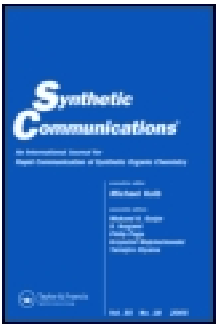

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A SHORT AND SIMPLE SYNTHESIS OF KETENE ACETALS

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Abstract: A novel and convenient synthesis of ketene acetals **1a-g** in moderate to good yield has been achieved starting from acetonitrile by using Pinner reaction approach.

Ketene acetals type-**1** constitute a class of compounds of great interest in organic synthesis as well as in polymer science. In organic synthesis various ketene acetals have been employed as a key intermediate, especially in cycloaddition reaction,[2] and ester and lactone formation reaction.[3] A systematic study of reactions of different ketene acetals with acyl halides,[4] methyl chloroformate[5] and organometallic compounds,[6] like borohydride and organolithium, has been reported in the literature. In the field of polymer science, Bailey *et al.* have extensively used various ketene acetals and similar compounds as a versatile monomer for the ring opening polymerization *via* a radical mechanism to obtain industrially valuable polymers.[7,8]

Several methods are known in the literature for the synthesis of ketene acetals.[2a,9-13] The methods reported by McElvain and coworkers are centered around the dealcoholysis of orthoesters by means of pyrolysis,[10] Grignard reagent (MesMgBr),[11a] bases like ethyl sodium[11a] and sodium ethoxide,[11b] and Lewis acids,

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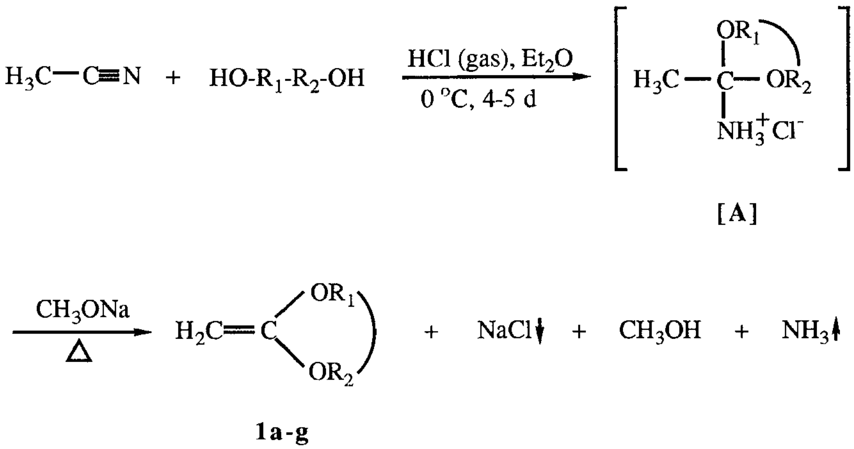
such as aluminum *tert*-butoxide,[12b] to obtain the corresponding ketene acetals. Similarly the dehydrohalogenation of 2-haloketals by means of potasium *tert*-butoxide is known to give the corresponding ketene acetals.[2a,13] In all these strategies, either orthoesters or 2-haloketals have been exploited as key intermediates.

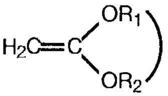
Most of the methods for the preparation of ketene acetals by dealcoholysis have had limited success and are accompanied by side reactions. To ovecome the drawback, we wish to report a new, short and simple synthetic strategy for the synthesis of various ketene acetals **1a-g** starting from commercially available chemicals.

Scheme-1



Pinner reaction[14] of nitriles with 3 mole equivalents of alcohol is known to give the corresponding orthoesters. In the course of this investigation of a new synthetic strategy, we attempted the reaction of acetonitrile with 2 mole equivalents of alcohols or 1 mole equivalent of diols in the presence of anhydrous hydrogen chloride gas at 0 °C, and found that the resulting intermediate salt [A][15] upon treatment with

Table



1a-g

No	R_1	R_2	Yields (%) [a]	^1H NMR δ ppm [b]
1a	$-CH_3$	$-CH_3$	52	3.04 (s, 2H,=CH_2); 3.40 (s, 6H, 2 x-OCH_3).
1b	$-C_2H_5$	$-C_2H_5$	55	1.30 (t, 6H, 2 x -CH_3); 3.03 (s, 2H, =CH_2); 3.68 (q, 4H, 2 x -OCH_2-).
1c	--$(CH_2)_2$--		61	3.20 (s, 2H, =CH_2) ;3.95 (s, 4H, $(OCH_2)_2$-).
1d	--$(CH_2)_3$--		64	1.95 (m, 2H, -CH_2-); 3.20 (s, 2H, =CH_2), 3.95 (m, 4H, 2 x -OCH_2-).
1e	--$(CH_2)_4$--		68	1.75 (m, 4H, -$(CH_2)_2$); 3.20 (s, 2H ,=CH_2); 3.75(m, 4H, 2 x -$(OCH_2)_2$).
1f	--(CH-$(CH_2)_2$-- CH_3		67	1.30 (d, 3H,-CH_3); 2.20 (m, 2H, -CH_2-,-CH_2-); 3.20 (dd,2H,=CH_2); 3.70(m, 3H,-OCH_2- and -OCH-).
1g	--$(CH_2)_6$--		63	1.70-1.90 (m, 8H, -$(CH_2)_4$-); 3.25 (s, 2H,=CH_2); 3.85 (m,4H, 2 x -$OCH_2)_2$).

[a] Isolated yield after distillation, and [b] ^1H NMR spectra were recorded in CCl_4 using TMS as internal standard.

2.5 mole equivalents of anhydrous sodium methoxide resulted in the formation of the corresponding ketene acetals **1a-g** in moderate to good yields (scheme-1). The formation of **1a-g** from the respective intermediates [A] could be explained by the simultaneous formation of sodium chloride and methanol moieties with the elimination of gaseous ammonia. In this procedure the formation of **1a-g** from the corresponding salts [A] shows the deamination to proceed preferentially over the dealcoholysis.

In this study different alcohols (R_1OH or R_2OH) like methanol and ethanol as well as diols (HOR_1R_2OH) such as 1,2-ethane-; 1,3-propane-; 1,3-butane-; 1,4-butane-; and 1,6-hexane- diols were studied and the resulting products were isolated by distillation under reduced pressure.[16] The structures of **1a-g** were assigned and confirmed on the basis of ^1H NMR, IR[17] and boiling points, which were in agreement with that of reported in the literature.[16] ^1H NMR spectra were recorded on a Jeol-60 MHz spectrophotometer using CCl_4 as a solvent. The chemical shifts are in δ values relative to that of TMS.

Preparation of Ketene Acetals 1a-g: The following procedure for the preparation of ketene dimethyl acetal **1a** is representative. In a 100-mL reaction flask, equipped with a rubber septum and a magnetic stirring bar was placed 4.1 g (0.1 mol) of acetonitrile, 6.4 g (0.2 mol) of methanol and 50-mL of anhydrous ethyl ether (Et_2O). To this reaction mixture, 8.8 g (0.25 mol) of anhydrous hydrogen chloride gas was absorbed at 0 °C under stirring. After keeping it at 0 °C for 4-5 days, a colorless solid obtained was isolated after removing the supernatant liquid by means of a double ended needle under a static pressure of nitrogen. The resulting colorless solid of the corresponding salt [A] was dried under reduced pressure (20 mm of Hg), and stirred with 13.25 g (0.25 mol) of anhydrous sodium methoxide at room temperature for 30-40 min. The desired product, ketene dimethyl acetal **1a** formed was isolated in 52% yield (4.5 g) after distillation at 87 °C. (lit.[16] bp 88-89 °C/760 torr); IR (neat):

1585 and 1065 cm^{-1} and ^{1}H NMR (CCl_4): δ ppm 3.04 (s, 2H, $=CH_2$), 3.40(s, 6H, 2 x $-OCH_3$).

However away from our desired program, the formation of acetamide (CH_3CONH_2), mp 79 °C (lit.[18] mp 79-81 °C) and diethyl ether (R_1OR_2, where $R_1 = R_2 = Et$), bp 34 °C, (lit.[19] bp 34.6 °C) by simply heating the salt [**A**] in absence of any base was observed.

This short synthetic strategy involves a facile deamination which favours the formation of ketene acetals and differs from the standard dealcoholysis step.[10-12] In order to make use of chiral ketene acetals as novel monomers for the preparation of chiral biodegradable polymers *via* a free radical poymerization approach, the synthesis of chiral ketene acetals by this method is in progress. Thus the present preparation method of ketene acetals is novel, attractive and has bright scope.

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