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An Efficient Method for the Vicinal Acylation of Unactivated Olefins Using Keteniminium Salts Derived from Protected α-Hydroxy- or α-Aminoacids.

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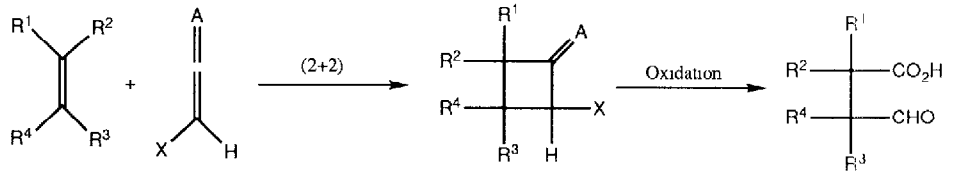
Abstract: Keteniminium salts derived from O-methylglycolic or N-tosylsarcosine amides cycloadd to olefins to give good yields of the corresponding cyclobutanones which undergo regiospecific Baeyer-Villiger oxidation to form γ-butyrolactones

A short sequence leading to the regio- and stereoselective addition of two different acyl groups to an olefinic double bond should be synthetically useful[1] This might be achieved by a strategy involving the cycloaddition of ketenes or keteniminium salts at the appropriate oxidation level followed by a regiospecific oxidation of the adduct (scheme 1)[2].

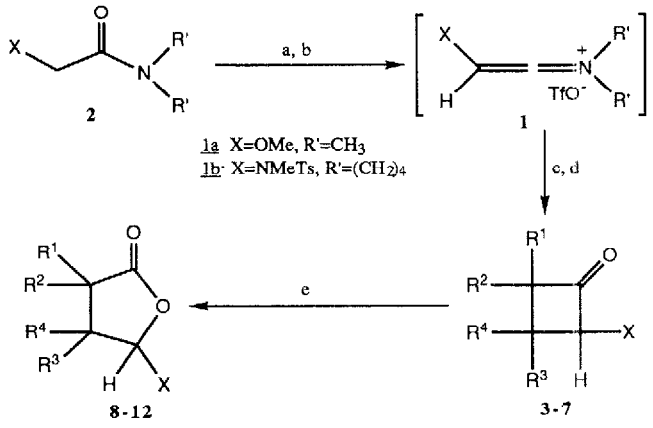


A = $NR'_2{}^{+}$, X = OR, NR_2

Scheme 1.

Functionnalised keteniminium salts **1** should be suitable reagents for the sequence[3,4]: (a) they are more reactive than ketenes and are expected to cycloadd readily even with unactivated olefins, (b) they bear an electron-donating substituent at C-2 which will provide the required oxidation level and control the regioselectivity of the oxidation step, (c) they should readily allow an extension to an asymmetric version of the sequence.

Keteniminium salts **1** were generated from the reaction of amides **2** with triflic anhydride in the presence of collidine or 2,6-ditertbutyl-4-methylpyridine and reacted *in situ* with olefins (scheme 2)[5].



Reagents a Tf_2O b collidine or 2,6-ditertbutyl-4-methylpyridine, 1,2-dichloroethane c $R^1R^2C{=}CR^3R^4$ d CCl_4/H_2O e. mCPBA/$NaHCO_3$, CH_2Cl_2

Scheme 2.

When X=NMeTs, the ketenimmium salt **1b** is more electrophilic and readily reacts at room temperature. Much better yields were obtained with 2,6-ditertbutyl-4-methylpyridine[6] than with collidine By contrast, the reaction with **1a** took place at 80°C but, in this case, collidine could be used as well as 2,6-ditertbutyl-4-methylpyridine. The resulting cyclobutaniminium salts were directly hydrolysed to the corresponding cyclobutanones **3-7**[7].

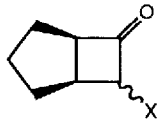
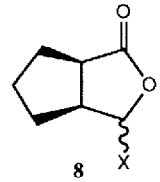
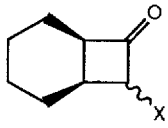
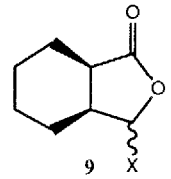
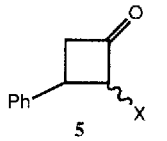
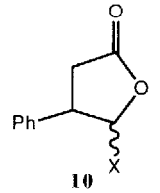
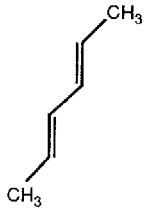
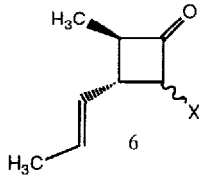
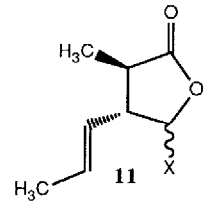
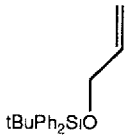
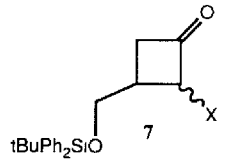
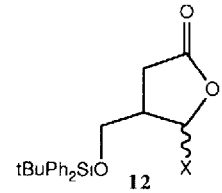
In a typical experiment, 0.5 g (1.69 mmol, 1 equiv) of amide **2b** dissolved in 5 mL of 1,2-dichloroethane was added to a solution of 0.34 mL (2.03 mmol, 1.2 equiv) of triflic anhydride in 10 mL 1,2-dichloroethane at 0°C After 5 min , the mixture was treated with a solution of 0 38 g (1 85 mmol, 1.1 equiv) of 2,6-ditertbutyl-4-methylpyridine and 0.683 mL (6.76 mmol, 4 equiv) of cyclohexene in 5 mL of 1,2-dichloroethane. After 5 hours at room temperature, the solvent was removed and the solid residue was taken up in 10 mL of water and 10 mL of carbon tetrachloride. After 4 hours at room temperature, the two phases were separated and the aqueous phase was extracted with carbon tetrachloride (3x10 mL). The combined organic phases were dried over magnesium sulfate and concentrated.The product was purified by flash chromatography (silicagel, petr.ether/ethyl acetate· 85/15, Rf· 0 2)

Representative results are summarised in Table 1. Mixtures of stereoisomers were obtained from **1a** while with **1b** only one stereoisomer was obtained where the NMeTs group was always trans with respect to the neighbouring substituent. This did not reflect kinetic preferences since the carbon atom bearing the X group has been shown to epimerise under the reaction conditions

Cyclobutanones could be readily converted into the corresponding γ-lactones by treatement with mCPBA at room temperature. The ring expansion was totally regiospecific[8], even when X=NMeTs, showing that the nitrogen atom had retained some of its electron donating character in spite of the presence of the sulphonyl group

In conclusion, a practical method for the acylation of unactivated olefins is now available. This method should be applicable to a wide range of olefins. An asymmetric version of the sequence using N-tosylsarcosine amides derived from chiral pyrrolidines will be shortly disclosed.

Table 1: Results of Scheme 2.

Olefins	Cycloaddition			Oxidation		
	Products[a]	Yields[b] (exo/endo)[d]		Products[a]	Yields[c] (exo/endo)[d]	
		X=OMe[e]	*X=NMeTs*		*X=OMe*	*X=NMeTs*
	 **3**	71%	64% (100/0)	 **8**	82% (47/53)	80% (100/0)
	 **4**	81%	74% (100/0)	 **9**	79% (85/15)	92% (100/0)
	 **5**	82%	76% (100/0)	 **10**	81% (91/9)	93% (100/0)
	 **6**	39%	78% (100/0)	 **11**	78% (72/28)	84% (100/0)
	 **7**	68%	70% (100/0)	 **12**	80% (83/17)	93% (100/0)

a: All products were characterised by ^{1}H and ^{13}C NMR spectroscopy, IR and mass spectrometry.

b: Isolated yields based on the amide **2** c: Yields of pure products after silicagel chromatography

d Exo/endo ratios were determinated by ^{1}H NMR spectroscopy

e After addition of the mixture of collidine and olefin, the solution was heated to 80°C.

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