Tetrahedron Letters, Vol. 33, No. 48, pp. 7357-7360, 1992
Printed in Great Britain

0040-4039/92 $5.00 + .00
Pergamon Press Ltd

Asymmetric Vicinal Acylation of Olefins: A New Approach to Enantiomerically Pure γ-Lactones.

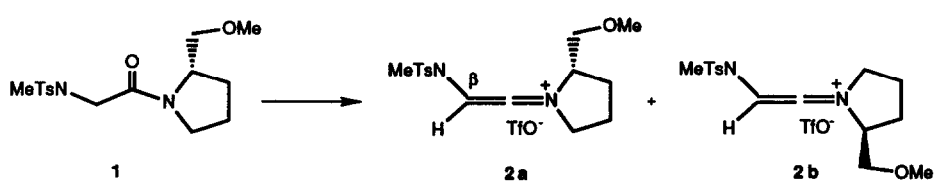
Christophe Genicot and Léon Ghosez*

Laboratoire de Chimie Organique de Synthèse
Université Catholique de Louvain
Place Louis Pasteur, 1, Louvain-la Neuve, B-1348, Belgium

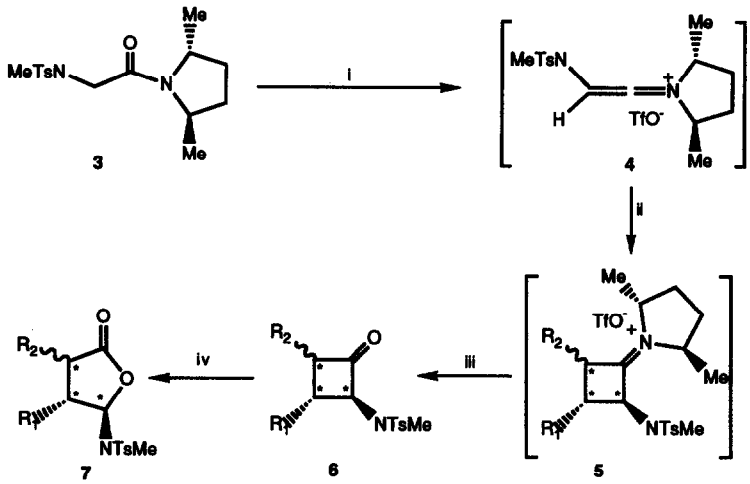
Key Words: keteniminium salts, [2+2] cycloadditions, cyclobutanones, γ-lactones, trans-2,5-dimethylpyrrolidine.

Abstract: *Amide 3 derived from N-tosylsarcosine and (2R,5R)-dimethylpyrrolidine was converted into keteniminium salt 4 which readily cycloadded to olefins. Hydrolysis of the adducts yielded cyclobutanones which were regiospecifically oxidized to γ-lactones 7. High enantioselectivities were observed with 1,2-cis-disubstitued olefins.*

We have recently reported[1] a short and efficient sequence for the regio- and stereocontrolled addition of two different acyl groups on an olefinic double bond. A more ambitious goal was to develop chiral reagents able to "bis-acylated" prochiral olefins with high enantiofacial selectivities. In previous studies[2] we had observed high asymmetric inductions in cycloadditions of olefins with keteniminium salts derived from prolinol methyl ether bearing two identical substituents at the β position . This chiral auxiliary was not expected to give satisfactory facial descrimination in the case of **1**. Amide **1** would probably generate unselectively two diastereoisomeric keteniminium salts **2a** and **2b** which should react with opposite facial selectivities. The obvious solution to this problem was to use a keteniminium salt derived from a C_2 symmetric chiral pyrrolidine[3].



Keteniminium salt **4** was generated by reacting **3** with triflic anhydride and 2,6-ditertbutyl-4-methylpyridine in the presence of an olefin[1,4]. Adducts **5** were directly hydrolysed to the corresponding cyclobutanones, releasing the chiral auxiliary which can be recovered. After flash chromatography, the cyclobutanones were oxidized into the γ-lactones **7**.



Reagents: i: Tf_2O, 2,6-ditertbutyl-4-methylpyridine, dichloroethane, -10°C; ii: olefin, RT; iii: H_2O, CCl_4, RT or Δ; iv: mCPBA, $NaHCO_3$, CH_2Cl_2, 0°C.

The results of the table show that:

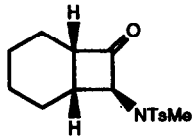
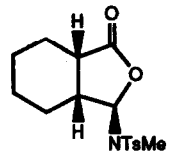
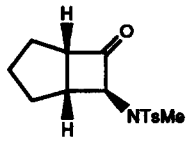
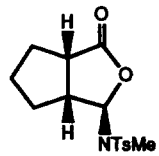
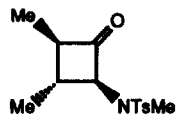
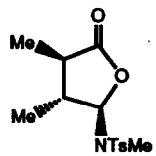
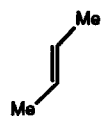
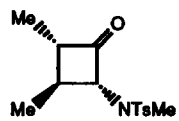
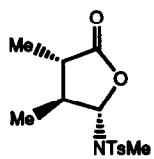
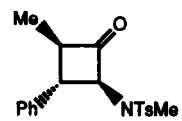
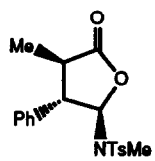
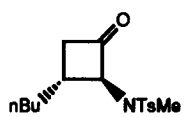
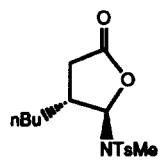
(i) the yields of cycloaddition reactions were always high even in the case of trans-butene which is known as a rather poor ketenophile[5].

(ii) Baeyer-Villiger oxidations proceeded regiospecifically to provide high yields of the lactones **7**.

(iii) facial selectivities were high for cyclic and 1,2-disubstitued olefins. The corresponding γ-lactones could be obtained enantiomerically pure after one recrystallisation without much loss of material. Interestingly, cis-butene and cis-β-methylstyrene afford respectively the trans adduct **6c** and **6e** (for cis-butene, 5% of the cis-adduct was detected by ^1H NMR spectroscopy). This can be accounted for by a fast base-catalysed epimerization of the cis-3,4-disubstitued-cyclobutaniminium salts **5c** and **5e** to the most stable trans isomers under the reaction conditions.

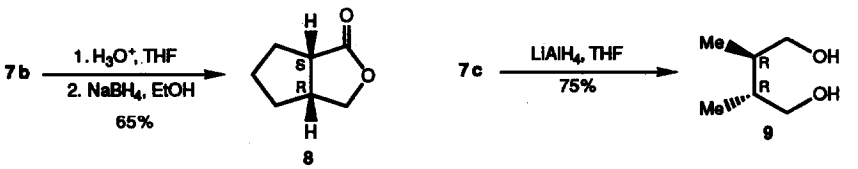
(iv) in all cases, the bulky NTsMe group was trans with respect to the vicinal alkyl group. This also resulted from an epimerization during the reaction.

Table: Asymmetric Synthesis of Cyclobutanones 6 and γ-Lactones 7

	Olefins	Cyclobutanones[a]	Yields[b], %	γ-Lactones[a]	Yields[c], %	e.e.[e], %
a			81		93	93
b			75		95 (78)[d]	91(>98)[d]
c			73		96(86)[d]	96(>98)[d]
d			51		96	61
e			74		92(70)[d]	86(98)[d]
f			70		95	48

a: All products have been fully characterized by IR, ^1H and ^{13}C NMR spectroscopy, by mass spectrometry and elemental analysis. b: After purification by flash chromatography. c: Yields obtained after standard work-up. d: After one recrystallisation in hexane-ethanol. e: Determined on the lactones by HPLC on a Daicel AD column.

The absolute configurations of **7b** and **7c** were established by chemical correlation with the known compounds **8**[6] and **9**[7]. The transformation of **7c** confirms our earlier observation that the NTsMe group can be exchanged for an OR group.



In conclusion keteniminium salt **4**, which is accessible in both enantiomeric forms[8], is a unique and efficient reagent for the asymmetric vicinal acylation of cyclic and cis-1,2-disubstitued olefins. Studies aiming at the generalisation of this methodology to other types of olefins are currently underway.

Acknowledgments: Christophe Genicot thanks the "Institut pour l'encouragement de la Recherche Scientifique dans l'Industrie et l'Agriculture" for a Ph.D. fellowship. The work was generously supported by the "Ministère de l'Education et de la Recherche Scientifique de la Communauté Française de Belgique (Action Concertée 86/91-84) and the "Fonds National de la Recherche Scientifique".

References.

1. Genicot, Ch.; Gobeaux, B.; Ghosez, L. *Tetrahedron Lett.* **1991**, *32*, 3827-3830 and references cited therein.
2. (a) Houge, C.; Frisque-Hesbain A-M.; Mockel, A.; Ghosez, L.; Declercq, J.P.; Germain, G.; Van Meerssche, M. *J. Am Chem. Soc.* **1982**, *104*, 2920-2921. (b) Saimoto, H.; Houge, C.; Frisque-Hesbain, A-M.; Mockel, A.; Ghosez, L. *Tetrahedron Lett.* **1983**, *24*, 2251-2254.
3. (a) Chen, L-Y.; Ghosez, L. *Tetrahedron Lett.* **1990**, *31*, 4467-4470. (b) Ghosez, L.; Chen, L.-Y.; Gobeaux, B.; Houge, C.; Marko, I.; Perry, M.; Saimoto, H. in *"Strain and its Implications in Organic Chemistry"*, A. de Meijere and S. Blechert (Eds.), Kluwer Academic Publishers **1989**, 235-254.
4. (a) Falmagne, J.B.; Escudero, J.; Taleb-Sahraoui, S.; Ghosez, L. *Angew. Chem. Int. Ed. Engl.* **1981**, *20*, 879-880. (b) Schmit, C.; Falmagne, J.B.; Escudero, J.; Vanlierde, H.; Ghosez, L. *Org. Synth.* **1990**, *69*, 199-204.
5. Huisgen, R.; Mayr, H. *Tetrahedron Lett.* **1975**, 2965-2968 and 2969-2972.
6. Jakovac, I.J.; Goodbrand, H.B.; Lok, K.B.; Jones, J.B. *J. Am. Chem. Soc.* **1982**, *104*, 4659-4665.
7. Mc Cosland, G.E.; Proskow, S.J. *J. Am. Chem. Soc.* **1956**, *88*, 5646-5651.
8. Masamune, S.; Kennedy, M.; Short, P.J. *J. Org. Chem.* **1989**, *54*, 1755-1756.

(Received in France 11 September 1992)