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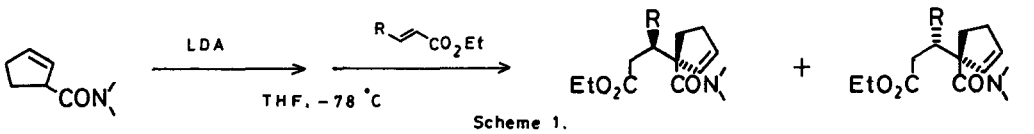
A STEREOSELECTIVE CONSTRUCTION OF THE ADJACENT TERTIARY AND QUATERNARY CARBONS BY THE MICHAEL ADDITION

Masahiko Yamaguchi,* Michiyuki Hamada, Hisataka Nakashima, and Toru Minami
Department of Industrial Chemistry, Kyushu Institute of Technology, Sensui-cho, Tobata, Kitakyushu 804, Japan

Abstract: The stereocontrolled construction of the adjacent tertiary and quaternary asymmetric centers was performed by using the stereoselective Michael addition of amide dienolates to α,β-unsaturated esters.

In the previous letter,[1] we have shown that the lithium dienolates derived from unsaturated amides reacted regio- and stereoselectively with α,β-unsaturated esters to give β-alkyl-α-vinylglutarates —— a stereocontrolled formation of the adjacent tertiary chiral centers not attached to heteroatoms. As a further advance of the methodology, we now wish to present the stereoselective Michael addition of α-alkyl substituted dienolates, which allows the stereocontrolled construction of the adjacent tertiary and quaternary carbons.

After the examination of the reaction conditions, the Michael reaction of lithiated N-(2-cyclopentenecarbonyl)piperidine to β-substituted unsaturated esters was found to proceed highly stereoselectively in THF at -78 °C (Scheme 1). The use of the β,γ-unsaturated amides was important, and the reaction of 1-cyclopentene carboxamides in THF-HMPA at -78 °C resulted in lower yield. Also noted was the low selectivity with pyrrolidine amide (Table 1).



Scheme 1.

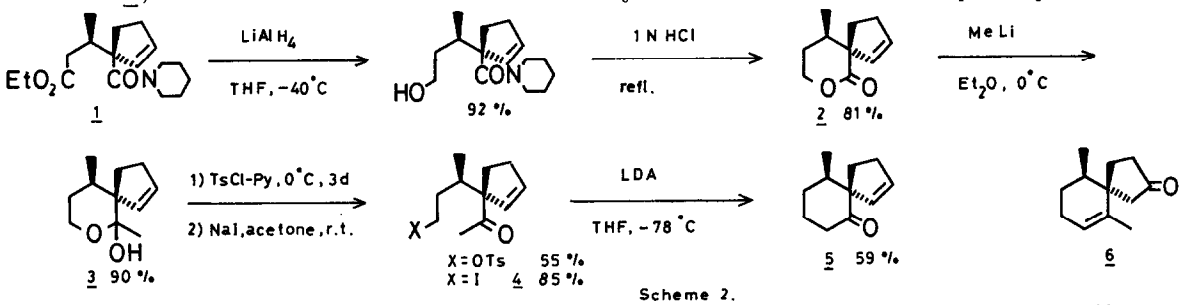
Table 1. The Michael Addition of Cyclopentenecarboxamides.

-N<	R	Yield/%[a]	ratio
-N⟨ ⟩	CH_3	80	> 20 : 1
	CH_3	0[b]	
	n-C_7H_{15}	80	> 20 : 1
-N⟨ ⟩	n-C_7H_{15}	93	1 : 1
	n-C_7H_{15}	61[b]	1 : 1

[a] All the products gave satisfactory ^{1}H-, ^{13}C-NMR, and IR spectra.
[b] 1-Cyclopentenecarboxamides were reacted in THF-HMPA (4:1) at -78 °C.

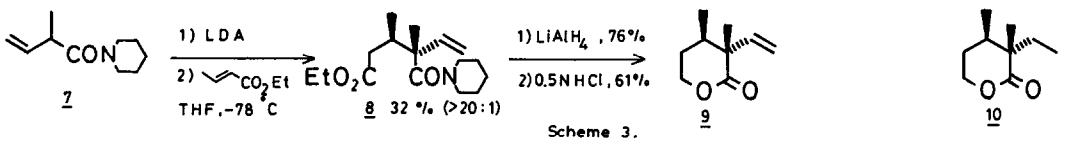
In order to determine the stereochemistry of the adducts, 1 was related to the known spirocompounds (Scheme 2). Selective reduction of the ester group followed by the acid-treatment gave the lactone 2,[2] which was transformed to lacto

3 with methyllithium. Then, 3 was converted to iodoketone 4 by a two-steps procedure, and subjected to the intramolecular alkylation with LDA in THF at -78 °C to afford spiroketone 5, whose ^{1}H-NMR and IR spectra agreed well with the authentic compound.[3] By employing the Piers's method,[3], 5 was further transformed to cyclopentanone 6, an active intermediate for the synthesis of several sesquiterpenes.[4]



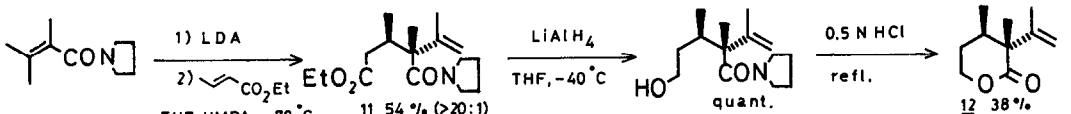
Scheme 2.

The reaction of dienolate derived from 2-methyl-3-butenamide 7 also gave the adduct 8 highly selectively (Scheme 3). Similar to the cyclopentenecarboxamides, the use of pyrrolidine amide resulted in low selectivity.[1] Adduct 8 was converted to lactone 10 by the hydrogenation of vinyllactone 9.[2] The ^{13}C-NMR spectra of 10 agreed well with the known compound.[5]



Scheme 3.

Different phenomena were observed with 2,3-dimethyl-2-butenamide: Pyrrolidine amide dienolate showed a high stereoselectivity, and the use of piperidine amide gave a complex mixture. The adduct 11 was converted to the 2-propenyllactone 12,[2] whose stereochemistry was determined by ^{13}C-NMR assuming a similar conformation with 9 (Scheme 4).



Scheme 4.

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References

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2 The selected ^{13}C-NMR data in ppm ($CDCl_3$-CCl_4): 2; 15.5. The stereoisomer of 2; 16.5. 9; 15.9, 20.5. The stereoisomer of 9; 15.5, 22.4. 12; 16.3, 19.9. 3 E. Piers, C. K. Lau, and I. Nagakura, Can. J. Chem., 61, 288 (1983). 4 C. Iwata, Y. Ida, K. Miyashita, T. Nakanishi, and M. Yamada, Chem. Pharm. Bull., 30, 2738 (1982); and references cited therein. 5 K. Tomioka, K. Yasuda, H. Kawasaki, and K. Koga, Tetrahedron Lett., 27, 3247 (1986).

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