

DIELS-ALDER REACTIONS OF α -VINYLIDENE- γ -BUTYROLACTONES.

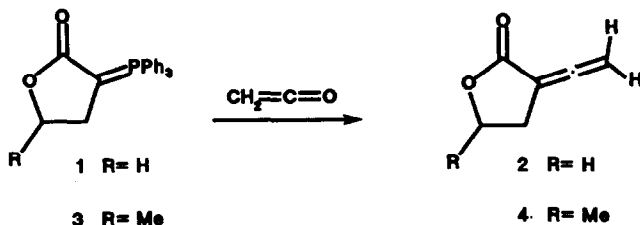
Frédéric FOTIADU, Albert ARCHAVLIS and Gérard BUONO*

Ecole Supérieure de Chimie de Marseille, Laboratoire Associé au CNRS 1410,
Av. Escadrille Normandie Niemen; 13397 MARSEILLE CEDEX 13, France.

Abstract : α -Vinylidene- γ -butyrolactones **2** and **4** are readily prepared via the reaction of ylides **1** or **3** with ketene. Diels-Alder cycloadditions of these compounds with typical dienes are described, addition of **2** to cyclopentadiene giving predominantly the *exo* stereomer.

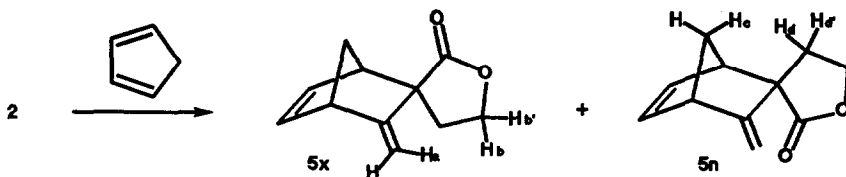
α -Methylene- γ -butyrolactones, which exhibit notable biological activities, are crucial compounds in organic synthesis¹. However, their allenic counterparts, α -vinylidene- γ -butyrolactones, have received poorer attention². Nevertheless, they have been already prepared in moderate yields by Lang and Hansen³ via the Wittig reaction of ylide **1** with acyl chlorides in the presence of triethylamine or, according to Minami et al.⁴, by the condensation of an α -phosphono- γ -butyrolactone carbanion with diphenylketene⁵.

We report herein a convenient synthetic pathway to the simplest α -vinylidene- γ -butyrolactones. Ylides **1** and **3**⁶ in CH_2Cl_2 solution react readily with gaseous ketene to afford α -vinylidene- γ -butyrolactones **2** or **4**⁷ respectively, in high yields.



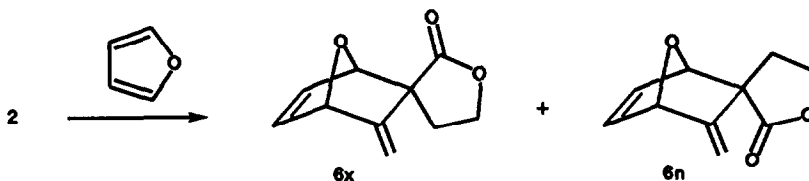
Allenecarboxylates are known to be excellent electron deficient dienophiles in Diels-Alder reactions⁸. We have investigated for the first time the cycloaddition of lactone **2** with cyclopentadiene under thermal and catalytic conditions. In refluxing toluene, the reaction yields 97% of a 12:88 *endo/exo*⁹ ratio mixture of **5a**, **5x**¹⁰. Use of 10% of aluminum chloride at -30°C in dichloromethane results in 74% of **5a**, **5x** in a 13:87 ratio.

Spirotricyclic adducts **5x**, **5m** were separated by chromatography on silicagel and fully characterized¹¹. *Endo* and *exo* structures were unambiguously elucidated from 100 MHz 2D-COSY and C-H CORRD NMR experiments and complete assignment of signals and coupling was done. Moreover, 2D-¹H NOESY let observe a nuclear Overhauser effect between Ha and Hb,b' in the *exo* adduct **5x**, while the *endo* epimer **5m** reveals only one nearness interaction of protons Hc and Hd,d'.

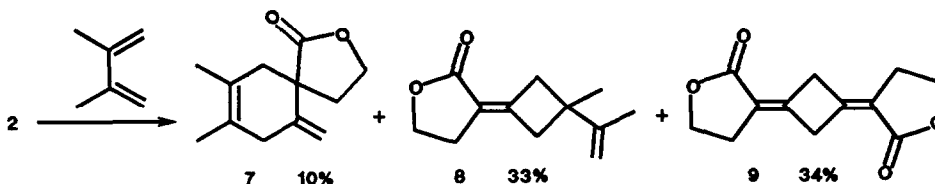


Contrary to α -alkylated allenic esters^{8b}, these reactions exhibit remarkable exoselectivity, in both thermal and catalytic conditions. Furthermore, the major *exo* stereomer was proved to be the kinetic adduct: heating of each pure *endo* **5m**, *exo* **5x** in refluxing toluene for 48 h gave no traces of **5x**, **5m** respectively.

Besides, **2** reacts with furan at reflux, affording in 86% yield a 90:10 mixture of diastereomeric adducts **6x** and **6m**, which structure were established from NMR data¹¹. However, their respective *endo* or *exo* stereochemistry could not yet be elucidated as for **5x** and **5m**, NOESY 2D-NMR experiments being useless in absence of the methylene bridge in the diene moiety¹².

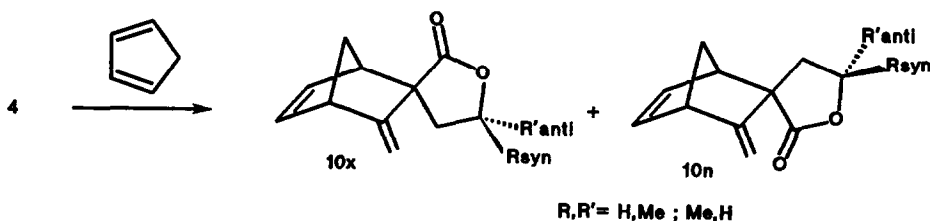


When 2,3-dimethyl-1,3-butadiene was used, the expected [4+2] cycloadduct **7** and compound **8**, resulting from an unusual regioselective [2+2] cycloaddition¹³, were isolated, as well as the starting lactone dimer **9**¹¹.



It is noticeable that, contrary to α -vinylidene cyclanones, isoprene¹⁴, 2,5-dimethyl-2,4-hexadiene and anthracene failed to give adducts with **2** and led only to polymeric material.

Finally, we reacted racemic α -vinylidene- γ -valerolactone **4** with cyclopentadiene in toluene at reflux. One major stereomer was formed among the four predicted adducts **10** (in 18:68:4:10 ratios by GC, 85% yield). Obviously the methyl group is effective in directing the steric course of the attack to some degree. In fact, if this was not the case, we would have observed equal ratios of *syn* and *anti* epimers¹⁶ for each the *endo* **10n** and *exo* **10x** adducts¹⁶.



In conclusion, Diels-Alder reactions of allenic lactone **2** with cyclopentadiene give rise to new spirotricyclic lactones with high exoselectivity. This feature has attracted our attention and we will try to clear up this point in the following communication.

Acknowledgement : We thank C. Santier who took a great part in experimental work.

References and Notes :

- (1) (a) Grieco, P. A. *Synthesis* 1975, 67. (b) Hoffmann, H. M. R.; Robe, J. *Angew. Chem., Int. Ed. Engl.* 1985, 24, 94. (c) Sarma, J. C.; Sharma, R. P. *Heterocycles* 1986, 24, 441 and references therein.
- (2) Schuster, H. F.; Coppola, G. M. "Allenenes in Organic Synthesis"; Wiley-Interscience : New York, 1984. Carbonyliron and carbonylcobalt complexes of substituted allenic lactones were found to undergo isomerization, affording 2-vinylbutenolides : Trifonov, L. S.; Orahovats, A. S.; Heimgartner, H. *Helv. Chim. Acta* 1987, 70, 1070. Trifonov, L. S.; Orahovats, A. S.; Prewo, R.; Heimgartner, H. *Helv. Chim. Acta* 1988, 71, 551.
- (3) Lang, R. W.; Hansen, H.-J. *Helv. Chim. Acta* 1980, 63, 1204.
- (4) Minami, T.; Niki, I.; Agawa, T. *J. Org. Chem.* 1974, 39, 3236.
- (5) It has been shown in an earlier study that α -allenic esters result from the action of dibromo-triphenylphosphorane on β -keto esters but this method fails when starting from α -acetyl- γ -butyrolactone; Buono, G. *Tetrahedron Lett.* 1972, 3257.
- (6) Ylides **1** and **2** are easily obtained as follows : the corresponding bromide is reacted with PPh_3 (1 equiv.) in refluxing THF for 24h. The resulting phosphonium salt in CH_2Cl_2 solution is then treated by 10% aqueous NaOH under phase transfer conditions : the reaction is achieved in a few minutes (90% overall yield).

- (7) Buono, G. *Thesis* 1977, Marseille. A typical procedure for such a reaction is : gaseous ketene from acetone pyrolysis is bubbled in a solution of ylide 1, 3 (27.8g, 28.8g; 80 mmol) in 100 ml anhydrous CH_2Cl_2 at 0°C . The reaction is monitored by ^{31}P NMR or IR. When no more ylide is detected, the solution is concentrated to one fourth on rotary evaporator. Triphenylphosphine oxide formed is precipitated with 150 ml of ether-pentane 1:1 and filtered off. Concentration and flash chromatography on silicagel with ether afford pure allenic lactone 2, 4 (7.9 g, 90%; 7.5 g, 76%). Spectroscopic data for 2 are consistent with those cited earlier³. Compound 4 : 100 MHz ^1H NMR (CDCl_3) δ ppm : 1.43 (d, $J = 5.2$ Hz, 3 H), 2.64 (m, 1 H), 3.20 (m, 1 H), 4.71 (m, 1 H), 5.35 (t, $J = 4.3$ Hz, 2 H); 25 MHz ^{13}C NMR (CDCl_3) δ ppm : 21.78 (CH_3), 33.82 (CH_2), 74.86 (CH), 81.83 ($=\text{CH}_2$), 94.45 (C=), 169.72 (C=O), 209.03 ($=\text{C}$). IR (KBr) cm^{-1} 1980, 1760, 1200.
- (8) (a) Jones, E. H. R.; Mansfield, G. H.; Whiting, M. C. *J. Chem. Soc.* 1956, 4073. (b) Ismail, Z. M.; Hoffmann, H. M. R. *J. Org. Chem.* 1981, 46, 3549 and references therein. Adduct of 2-methyl-2,3-butadienoate with cyclopentadiene has been elegantly used in the synthesis of racemic β -santalene : (c) Bertrand, M.; Monti, M.; Huong, K. C. *Tetrahedron Lett.* 1979, 15. The (-) enantiomer has been obtained starting from a chiral allenic ester : (d) Oppolzer, W.; Chapuis, C.; Dupuis, D.; Guo, M. *Helv. Chim. Acta* 1985, 68, 2100. (e) Kozikowski, A.; Ames, A. *J. Am. Chem. Soc.* 1981, 103, 3923. (f) Fink, M.; Gaier, H.; Gerlach, H. *Helv. Chim. Acta* 1982, 65, 2563. (g) Jung, M. E.; Node, M.; Pflugler, R. W.; Lyster, M. A.; Lowe, J. A. III *J. Org. Chem.* 1982, 47, 1150. (h) Gandhi, R. P.; Ishar, M. P. S.; Wali, A. *J. Chem. Soc., Chem. Commun.* 1988, 1074. (i) Gandhi, R. P.; Ishar, M. P. S. *Indian J. Chem.* 1989, 28B, 287.
- (9) *Endo* and *exo* notations refer to the carboxy group stereochemistry.
- (10) Yield and products ratio are determined by GC on a CP-WAX 51 column ; *exo* adduct 5x having the shorter retention time.
- (11) Spectral data and elemental analyses for new compounds are consistent with the proposed structural formulae.
- (12) Stereoselectivities in cycloadditions of furan with allenic esters have been elucidated through evidence based on ^1H nOe and $J_{\text{LR}}(^1\text{H}, ^1\text{H})$ which involved an hydrogen atom on the carbon bearing the ester group (the stereogenic carbon of the dienophile)⁸¹. This methodology is invalid for the case of α -alkylated dienophiles, such as lactone 2. Works are in progress to assign stereochemistry of cycloadducts 6m, 6x by chemical correlations.
- (13) 2,3-Butadienoic esters are known to undergo such stereospecific addition with olefins at the terminal allene double bond with Lewis acid catalysts to give cyclobutylidene derivatives : (a) Snider, B. B.; Spindell, D. K. *J. Org. Chem.* 1980, 45, 5017. (b) Hoffmann, H. M. R.; Ismail, Z. M.; Weber, A. *Tetrahedron Lett.* 1981, 22, 1953.
- (14) Gras, J.-L.; Guerin, A. *Tetrahedron Lett.* 1985, 26, 1781.
- (15) As shown in the reaction scheme, the *syn* and *anti* descriptors refer to the relative position of the methyl group and the exocyclic methylene bond.
- (16) Steric control of the molecular approach has been demonstrated in a 95% π -face selective cycloaddition to cyclopentadiene : Mattay, J.; Mertes, J.; Maas, G. *Chem. Ber.* 1989, 122, 327, and in reactions of chiral butenolides : Batllori, R.; Font, J.; Monsalvatje, M.; Ortuno, R. M.; Sanchez-Ferrando, F. *Tetrahedron* 1989, 45, 1833.