

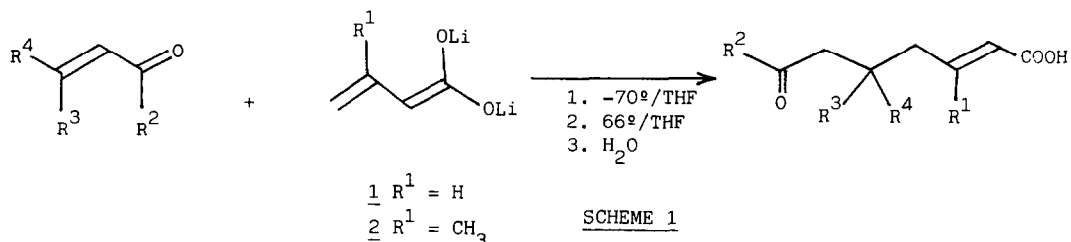
UNSATURATED CARBOXYLIC ACID DIENOLATES. MICHAEL ADDITION TO
ENONES THROUGH TANDEM 1,2-ADDITION - OXY-COPE REARRANGEMENT.

P. Ballester, A. García-Raso, A. Gómez-Solivellas and R. Mestres*

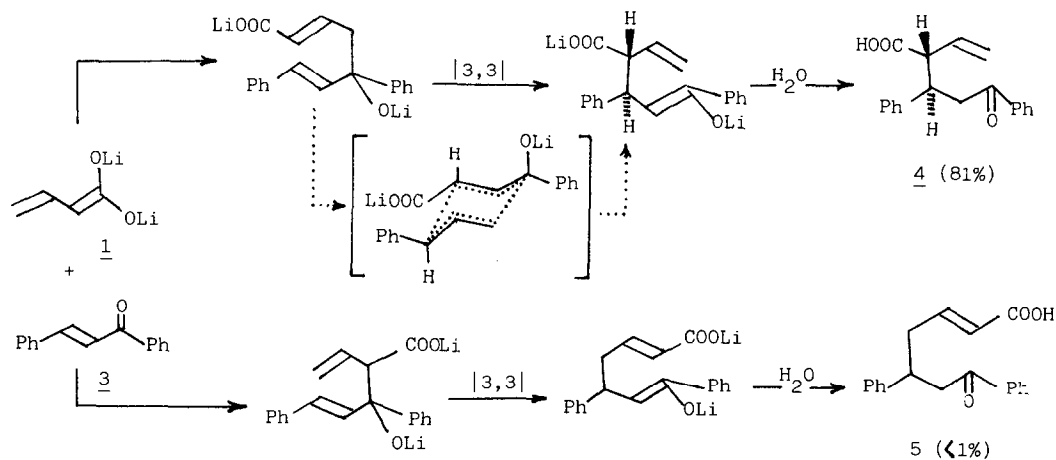
Departamento de Química Orgánica. Facultad de Ciencias. Universidad de
Palma de Mallorca. 07071 Palma de Mallorca. Spain.

Abstract.- Michael addition of the dienolate derived from 2-butenic acid to 1,3-diphenylpro-
penone occurs through a 1,2-addition followed by a [3,3]-sigmatropic rearrangement. α, γ -re-
gioselectivity found for Michael addition to other styryl ketones depends on the steric pa-
rameter of the substituents at the carbonyl group, in agreement with the same tandem addition -
rearrangement mechanism.

In former studies some of us found that complex mixtures of 1,2- and 1,4-adducts were ob-
tained on reaction of dienolates of unsaturated carboxylic acids, namely 2-butenic or 3-me-
thyl-2-butenic acid, with conjugated enones at low temperature. On the contrary, regioelec-
tive Michael addition through the γ -carbon of the dienolates resulted under equilibrating
conditions¹⁻⁵ (Scheme 1). Those observations suggested that the regioselectivity found was
resulting from the reversibility of 1,2- and 1,4- α -additions.



1,3-diphenylpropenone 3 behaved as an exceptional substrate, in that the above dienolates
added regioselectively on heating, but through the α -carbon atom³. We have found now that the
addition of the dienolate of 2-butenic acid to that enone 3 at 66°C leads almost exclusively
to R,R(S,S)-3,5-diphenyl-2-ethenyl-5-oxopentanoic acid 4 in 81% yield^{7,8}, though weak signals
due to the R,S(S,R)-isomer can be observed in the HNMR spectrum of the crude mixture. A small
sample of the diastereoisomer has been obtained by fractionate crystallization, and character-
ized spectroscopically^{3,9}. These features, namely neatly cut inversion of regioselectivity and
high stereoselectivity, would not be expected to result from combined equilibria of reversible
addition, but rather from an oxy-Cope rearrangement of the reversibly formed 1,2-adducts
(Scheme 2). The α orientation of the resulting Michael adduct would imply, according to this
mechanism, that γ attack should predominate in the 1,2-interaction. It has been observed that
on reaction with carbonyl compounds the dienolates of unsaturated carboxylic acids add faster



SCHEME 2

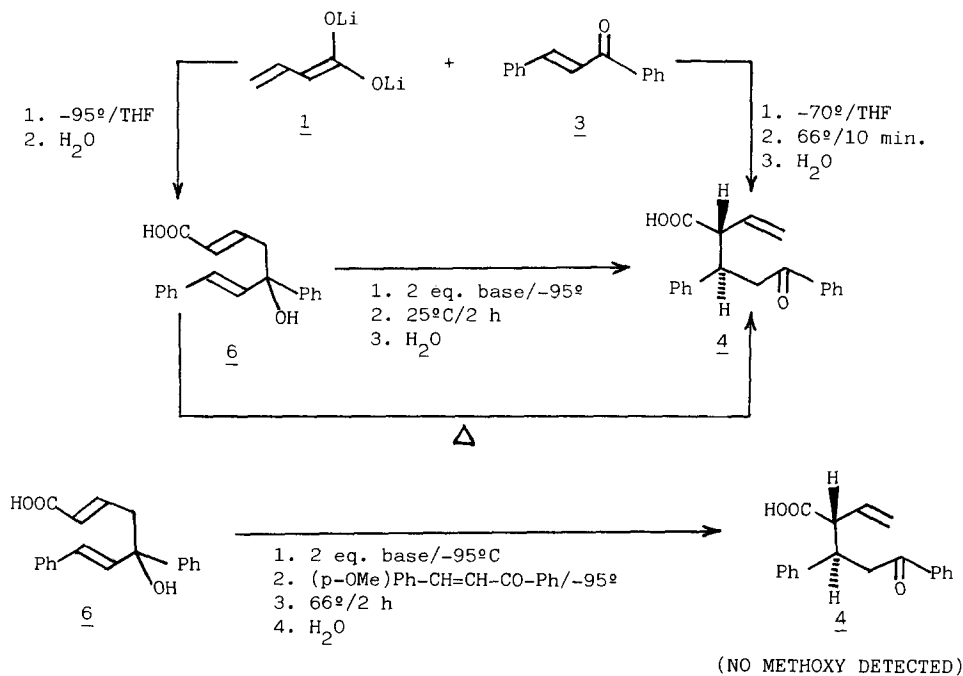
through the α carbon atom. However, the former interaction is easily reversible and sensitive to steric effects^{1,10-12}, and some hindered ketones, like benzophenone, lead to γ -adducts even at -70°C ¹³. The same orientation would not seem unlikely for the present substrate. On the other hand, the R,R(S,S) isomer 4 should result through the accepted chair like transition for the $[3,3]$ -sigmatropic rearrangement¹⁴ of the expected E-1,2- γ -intermediate, whereas the minor R,S(S,R) isomer should derive from the minor Z-1,2- γ -adduct¹⁵.

When addition of 2-butenic acid dienolate to 1,3-diphenylpropenone 3 was performed at -70°C a mixture was obtained, whose HNMR spectrum showed both 1,2- and 1,4-adducts to be present. We hoped that these adducts were the postulated 1,2-intermediate and the final rearranged Michael adduct. To our delight, when the reaction was carried out at -95°C the HNMR of the crude was indicative of the 1,2- γ -adduct as the major product, and the hydroxy acid E,E-5,7-diphenyl-5-hydroxyhepta-2,6-dienoic acid 6 was easily isolated and purified by careful crystallization. The purified acid 6 was converted into the oxo carboxylic acid 4 in 87% yield by deprotonation at low temperature (two equivalents of base), and heating under usual conditions (Scheme 3)¹⁶.

Evidence for the intramolecular nature of the rearrangement was obtained by a crossover experiment in the presence of 3-(p-methoxyphenyl)-1-phenylpropenone. This enone was allowed to react first with the dienolate of 2-butenic acid at both -95°C and 66°C . Entirely similar behaviour and reactivity to that found for the unsubstituted diphenyl enone was observed, and the corresponding E-1,2- γ - and 1,4- α -adducts were obtained. When E,E-5,7-diphenyl-5-hydroxyhepta-2,6-dienoic acid 6 was ionized and heated in the presence of the above methoxy enone, a crude was obtained whose HNMR spectrum was superimposable to that of the oxo carboxylic acid 4, no signal for any ether methoxy group being found.

Furthermore, the hydroxy acid 6 rearranged into the oxo carboxylic acid 4 on heating in refluxing xylene, though the rearrangement was accompanied now by dehydration and other side processes.

On reaction of 2-butenic acid dienolate with several styryl ketones mixtures have been obtained whose composition (HNMR and GLC¹⁷) strongly suggest that the addition-rearrangement



SCHEME 3

mechanism is operative for these substrates as well. We have found that α/γ ratios increase along with the Taft steric parameter of the substituent at the carbonyl group (see Table). This trend is indicative of regioselectivity being established by interaction of the dienolate with the carbonyl group. Conversion into the final Michael adduct should then occur as a second step through an irreversible intramolecular process, or otherwise regioselective character of the addition would not be preserved. A high (low) α/γ ratio for the 1,2-intermediates, as it would be expected for small (large) substituents at the carbonyl group, would yield a low (high) α/γ ratio for the final 1,4-adducts, in agreement with the present findings.

Table. Regioselectivity for the Michael addition

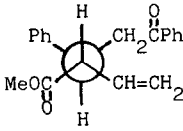
Ph-CH=CH-CO-R	CRUDE YIELD (%)	1,4 α : 1,4 γ	E_s^{18}
R = Ph	81	100:0	-2.55
t-Bu	92	85:15	-1.54
i-Bu	71	55:45	-0.93
i-Pr	70	47:53	-0.47
n-Pr	87	36:61	-0.36
Me	93	20:80	0.00

A tandem addition-rearrangement mechanism for conjugate addition of allylic carbanions to enones is within expectancy and might be widely operative, although we have not found it referred in the literature^{14,19-21}, except for some sulfonyl-allyl carbanions reported by Hirama²². It is noteworthy that the present intermediate alkoxides and those reported by Hirama rearrange under much milder conditions than those described for other base accelerated oxy-Cope rearrangements.

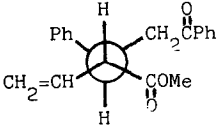
Work is currently done in order to establish the scope of the 1,2-addition - oxy-Cope mechanism, and to find out the influence of co-solvents on the course of the additions of the dienolates.

ACKNOWLEDGEMENTS: The present work has been financed by Comisión Asesora de Investigación Científica y Técnica (Project No. 1238/81). One of us (P.B.) acknowledges a grant by Ministerio de Educación y Ciencia.

REFERENCES AND NOTES

- (1) I. Casinos, and R. Mestres, *J.C.S. Perkin Trans I*, 1978, 1651
 - (2) I. Casinos, R. Mestres, and M. Valero, *An. Quim.*, 1980, 76C, 70
 - (3) I. Casinos, and R. Mestres, *An. Quim.*, 1982, 78C, 368
 - (4) Generation of unsaturated carboxylic dienolates by the lithium naphthalenide-diethylamine system, as well as addition conditions and working up has been described in above references. See as well reference 6.
 - (5) N. Petragnani, and M. Yonashiro, *Synthesis*, 1982, 521
 - (6) P. Ballester, A. García-Raso, and R. Mestres, *Synthesis* (in press)
 - (7) Satisfactory analytical values were obtained for all new compounds.
 - (8) Selected HNMR data (δ (CDCl₃) as methyl esters):
 R,R(S,S)-3,5-diphenyl-2-ethenyl-5-oxopentanoic acid: 3.39 (m, 3H, PhCO-CH₂ and MeOOC-CH), 3.42 (s, 3H, COOCH₃), 3.78 (m, 1H, Ph-CH), 5.19 (d, 1H, J=15 Hz, CH=CH-H), 5.21 (d, 1H, J=9 Hz, CH=CH-H), 5.90 (m, 1H, CH=CH₂), 7.22 (s, 5H, Ph), 7.79 (m, 5H, CO-Ph).
 R,S(S,R)-3,5-diphenyl-2-ethenyl-5-oxopentanoic acid: 3.40 (d, 2H, J=6Hz, PhCO-CH₂), 3.54 (m, 1H, MeOOC-CH), 3.70 (s, 3H, COOCH₃), 3.93 (m, 1H, Ph-CH), 4.98 and 5.10 (m, 2H, CH=CH₂), 5.80 (m, 1H, CH=CH₂), 7.30, 7.50, and 7.95 (m, 10H, Ph and CO-Ph).
 E-5,7-diphenyl-5-oxo-2-heptenoic acid: 2.56 (d, 1H, J=7.1 Hz, MeOOC-CH=CH-CH-H), 2.65 (d, 1H, J=6.4 Hz, MeOOC-CH=CH-CH-H), 3.28 (d, 1H, J=7.8 Hz, Ph-CO-CH-H), 3.29 (d, 1H, J=5.5 Hz, Ph-CO-CH-H), 3.58 (m, 1H, Ph-CH), 3.66 (s, 3H, COOCH₃), 5.75 (d, 1H, J=15 Hz, MeOOCCH=CH), 6.80 (m, 1H, MeOOCCH=CH), 7.24 (s, 5H, Ph), 7.86 and 7.40 (m, 5H, Ph-CO).
 E,E-5,7-diphenyl-5-hydroxyhepta-2,6-dienoic acid: 2.91 (d, 1H, J=7.3 Hz, HOC-CH-H), 2.92 (d, 1H, J=7.4 Hz, HOC-CH-H), 3.67 (s, 3H, COOCH₃), 5.86 (d, 2H, J=13.5 Hz, MeOOC-CH), 6.40 (d, 1H, J=15.2 Hz, -CH=), 6.61 (d, 1H, J=15.2 Hz, -CH=), 6.85 (m, 1H, MeOOC-CH=CH), 7.30, and 7.46 (m, 10 H, Ph and CO-Ph).
 - (9) About 0.3 ppm downfield and 0.25 ppm upfield relative shifts for ethylenic and methoxy protons respectively are found in the spectrum of the methyl ester of the adduct when compared to that of the minor isomer. These shifts are, no doubt, due to the anisotropic effect by the phenyl group, and allow the above R,R(S,S) and R,S(S,R) assignments, as predominance of conformers *anti* for both diastereoisomers should be expected.
- 

R,R(S,S)



R,S(S,R)
- (diastereoisomers)
- (10) P.E. Pfeffer, L.S. Silbert, and E. Kinsel, *Tetrahedron Lett.*, 1973, 1163
 - (11) C.A. Henrick, W.E. Willy, D.R. McKean, E. Baggiolini, and J.B. Siddal, *J. Org. Chem.*, 1975, 40, 8.
 - (12) G. Cainelli, G. Cardillo, M. Contento, G. Trapani, and A. Umani-Ronchi, *J.C.S. Perkin Trans I*, 1973, 400
 - (13) I. Casinos, and R. Mestres, *An. Quim.*, 1982, 78C, 364
 - (14) D.A. Evans, and J.V. Nelson, *J. Am. Chem. Soc.*, 1980, 102, 774
 - (15) On γ -interaction with ketones 2-butenic acid leads to E-adducts, though along with small amounts of Z-isomers.
 - (16) Traces of the R,S(S,R) diastereoisomer were not found in the HNMR spectrum of the crude.
 - (17) GLC conditions: packed column of SE-30 (1%) - CHROMOSORB W-HP, 80-100 mesh (2 ft x 1/8"). Injector and detector temperature: 250°C. Column temperature: 170°C. Carrier gas: nitrogen (23 ml/min).
 - (18) T.H. Lowry, and K.S. Richardson, "Mechanism and Theory in Organic Chemistry", 2nd Ed. Harper & Row, Pub., New York, 1981, p. 138
 - (19) Y. Yamamoto, H. Yatagai, Y. Saito, and K. Maruyama, *J. Org. Chem.*, 1984, 49, 1096
 - (20) M.R. Binns, R.K. Haynes, T.L. Houston, and W.R. Jackson, *Tetrahedron Lett.*, 1980, 573
 - (21) D.E. Evans, D.J. Baillargeon, and J.V. Nelson, *J. Am. Chem. Soc.*, 1978, 100, 2242
 - (22) M. Hirama, *Tetrahedron Lett.*, 1981, 1905

(Received in UK 27 March 1985)