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DIANION OF DIETHYL SUCCINATE: REACTIONS WITH ALKYLATING AGENTS AND CARBONYL COMPOUNDS

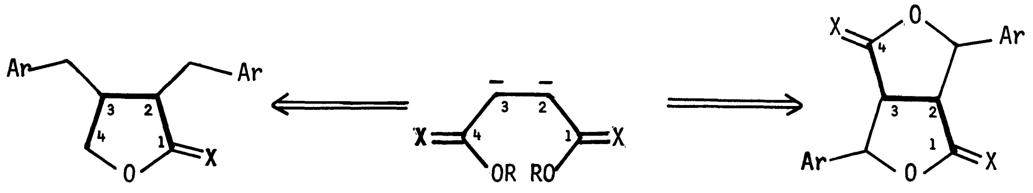
Manat POHMAKOTR,* Vichai REUTRAKUL, Tipparat PHONGPRADIT, and Arayan CHANSRI

Department of Chemistry, Faculty of Science, Mahidol University, Rama VI Road, Bangkok 4, Thailand

Dianion of diethyl succinate reacted readily with alkylating agents and carbonyl compounds to give α,β-dialkylsubstituted diethyl succinate and paraconic esters respectively. The conversion of some paraconic esters into 4-carboethoxy-cyclopentenones was also demonstrated.

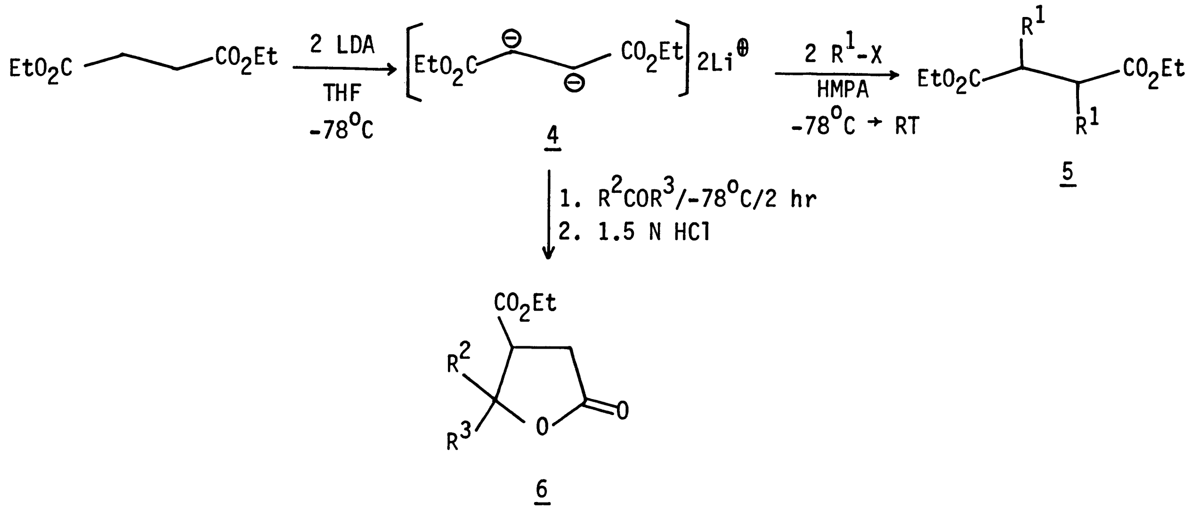
Dianions of numerous classes of organic compounds have been reported and these species played important roles in organic syntheses due to their high regioselectivity with electrophiles.[1] Recently, P.J. Garatt and co-workers indicated that vicinal dianions of α,β-disubstituted succinic esters could undergo addition reactions with various electrophiles.[2] In the course of our exploration of synthetic pathways to lignan systems of types 1 and 2, which are classes of natural products exhibiting interesting biological activities,[3] we needed a synthetic equivalent containing four-carbon unit of type 3 which possesses nucleophilic sites at C-2 and C-3, as shown in Scheme I.

Scheme I



1, X = O or H_2 3, X = O; R = H,CH_3CH_2,etc.
X = H_2: R = H 2, X = O, or H_2

Recent report by M.W. Rathke[4] on the alkylation of the dianion 4 with alkyl halides prompted us to report our results in this area. The reaction of one equivalent of 4 with two equivalents of halides, aliphatic aldehydes and ketones at -78°C gave good yields of alkylated products 5 and paraconic esters 6 respectively. The use of excess aldehydes or ketones in the reaction gave no diadduct and only the paraconic esters 6 could be isolated. The sequential treatment of the dianion 4 with cyclohexanone (or acetone) (1 equiv.) and methyl iodide (or allyl bromide) (1 equiv.) gave only trace amount of the expected diadduct, the major product being the paraconic esters.



The reaction of 4 with aryl aldehydes under standard conditions gave trace amount of the expected paraconic esters of the type 6. However, upon addition of equivalent of 1M THF solution of $ZnCl_2$ at -78° to the reaction mixture resulted in moderate yields of the expected paraconic esters. The results are summarized in Table I.

Table I

Reactions of the dianion 4 with alkylating agents and carbonyl compounds

Alkylating agents or carbonyl compounds	Products	Yields (%)[a]	Diastereomeric ratio[b]
CH_3I	5a, $R^1 = CH_3$	85	-[c]
$CH_2{=}CHCH_2Br$	5b, $R^1 = CH_2{=}CHCH_2$	80	-[c]
$C_6H_5CH_2Br$	5c, $R^1 = C_6H_5CH_2$	84	-[c]
CH_3CHO	6a, $R^2 = H$; $R^3 = CH_3$	61	1:1.3[d]
n-C_3H_7CHO	6b, $R^2 = H$; $R^3 =$ n-C_3H_7	59	1:2[d]
n-$C_6H_{13}CHO$	6e, $R^2 = H$; $R^3 =$ n-C_6H_{13}	58	1:1[d]
CH_3COCH_3	6d, $R^2 = R^3 = CH_3$	86	-
$CH_3COCH_2CH_3$	6e, $R^2 = CH_3$; $R^3 = CH_3CH_2$	83	-
Cyclopentanone	6f, R^2-$R^3 = -(CH_2)_4-$	81	-

Table I (cont.)

Alkylating agents or carbonyl compounds	Products	Yields (%)[a]	Diastereomeric ratio[b]
Cyclohexanone	6g, R^2-R^3 = $-(CH_2)_5-$	84	-
Cyclooctanone	6h, R^2-R^3 = $-(CH_2)_7-$	59	-
p-$CH_3OC_6H_4CHO$	6i, R^2 = H; R^3 = p-$CH_3OC_6H_4$	70	1:1.5[e]
m-$CH_3OC_6H_4CHO$	6j, R^2 = H; R^3 = m-$CH_3OC_6H_4$	43	1:1.5[e]

a. Isolated yields by preparative layer chromatography (PLC).

b. The structure of diastereomers were determined by ^{1}H-NMR[8].

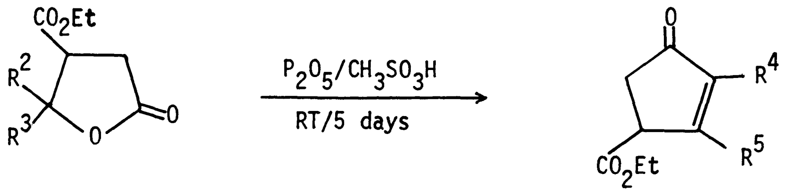
c. Ratio could not be determined either by PLC or ^{1}H-NMR.

d. Ratio was determined by PLC separation.

e. Ratio was determined by ^{1}H-NMR.

Our results demonstrated the synthetic potential of the dianion 4 for the preparations of disubstituted succinic esters and paraconic esters. These types of paraconic esters are of special interest due to their versatile utility as intermediates in the synthesis of natural products.[5,7] Thus, the lactones 6e-h had been converted into cyclopentenone derivatives 7a-d by treating with phosphorus pentoxide/methanesulfonic acid mixture.[6] The results are summarized in Scheme II. Compound 7a was an important synthetic intermediate for the preparation of (±)-Methylenomycin A, an antibiotic from the culture filtrate of a streptomycete, which had previously been reported.[7]

Scheme II



6e, R^2 = CH_3; R^3 = CH_2CH_3
6f, R^2-R^3 = $-(CH_2)_4-$
6g, R^2-R^3 = $-(CH_2)_5-$
6h, R^2-R^3 = $-(CH_2)_7-$

7a, R^4 = R^5 = CH_3 (86%)
7b, R^4-R^5 = $-(CH_2)_3-$ (75%)
7c, R^4-R^5 = $-(CH_2)_4-$ (81%)
7d, R^4-R^5 = $-(CH_2)_6-$ (67%)

Further exploratory investigations including the syntheses of the lignans types 1 and 2 are now in progress.

REFERENCES

1. See for examples: E.M. Kaiser, J.D. Petty, and P.L.A. Knutson, Synthesis, 509 (1981); D. Seebach and M. Pohmakotr, Tetrahedron, 37, 4147 (1981); D. Seebach, M. Pohmakotr, Ch. Schregenberger, B. Weidmann, R.S. Mali, and S. Pohmakotr, Helv.Chim.Acta, 65 (1982); R.S. Mali, M. Pohmakotr, B. Weidmann, and D. Seebach, Liebigs Ann. Chem. 2272 (1981).
2. K.G. Bilyard, P.J. Garatt, and R. Zahler, Synthesis, 389 (1980) and references cited therein; C.W. Doecke and P.J. Garatt, J.C.S. Chem.Comm., 873 (1981); K.G. Bilyard and P.J. Garratt, Tetrahedron Lett., 22, 1755 (1981).
3. P. Brownbridge and T.H. Chan, Tetrahedron Lett., 21, 3427 (1980); A. Pelter, P. Satyanarayana, and R.S. Ward, ibid., 22, 1549 (1981) and references cited therein.
4. N.R. Long and M.W. Rathke, Synth. Comm., 11, 687 (1981).
5. S. Kano, S. Shiyuya, and T. Ebata, Heterocycles, 14, 661 (1980) and references cited therein.
6. P.E. Eaton, G.R. Carlson, and J.T. Lee, J.Org.Chem., 38, 4071 (1973).
7. J. Jernow, W. Tautz, P. Rosen, and J.F. Blout, J. Org. Chem., 44, 4210 (1979); Y. Takahashi, K. Isobe, H. Hagiwara, H. Kosugi, and H. Uda, J.C.S. Chem.Comm., 714 (1981).
8. L.M. Jackman and S. Sternhell, Application of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry, Pergamon Press, London, 1969.

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