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A NEW CYCLOPENTANONE ANNULATION OF α-BROMOMETHYLACRYLATES

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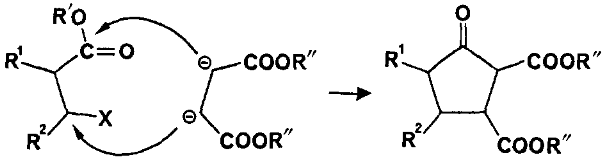
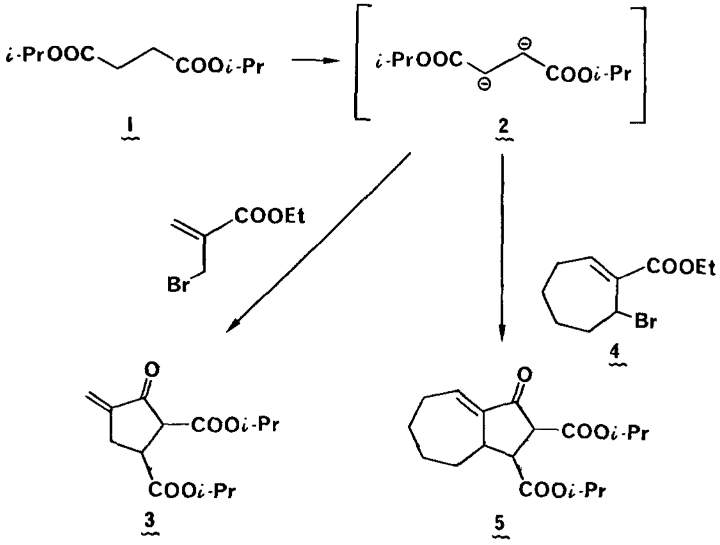
Summary: Direct couplings of the α-bromomethylacrylates and the doubly charged succinate ion are described.

For a number of years we have been interested in the development of new annulation which would afford five-membered rings via direct coupling of the β-haloesters and the doubly charged succinate ions.[1] Conceptually, this approach should result in the one-pot construction of cyclopentanones with a variety of side chains at the desired positions.[2] The obvious drawback of the methodology is the lack of regio- and stereoselectivities,[3] and an attractive solution to this problem is reported in this and the following papers.



The readily available diisopropyl succinate (1)[4] in dry tetrahydrofuran (THF), on exposure at -78°C with 2.1 equiv of lithium diisopropylamide (LDA) for 1 h, undergoes facile metallation to give a pale yellow solution of the dianion 2; treatment of this solution at -78°C for 20 min with 1 equiv of ethyl α-(bromomethyl)acrylate in hexamethylphosphoric triamide (HMPA) gave on aqueous work-up and chromatography on silica gel[5] the cyclopentanone 3[6] in 56% yield. Attention was then turned to the application of the method to annulation which was simply effected by reaction of 2 with the olefinic bromoester 4: reaction in THF-HMPA at -78°C for 1 h and 0°C for 1 h, followed by usual work-up gave the bicyclic ketone 5[7] in 88% yield. The preparation of 4 was readily accomplished from ethyl 2-oxocycloheptanecarboxylate in three steps: (1) hydrogenation (PtO_2, 88%);[8] (2) selenation (LDA, PhSeBr)-deselenation (H_2O_2) sequence (58%);[9] (3) bromination (PBr_3, 95%).



Condensation reaction of ethyl 3-bromopropionate was also investigated, but it was soon ascertained that the desired coupling was not promoted selectively under a variety of conditions. In all these instances the regioisomeric products (2,4-isomers) predominated.[3,10] Thus, it is clear from this fact that the proton exchange process seems to be considerably fast even under the carefully controlled conditions.

References and Notes

1. (a) For dianion of succinate ester: P. J. Garratt, R. Zahler, J. Am. Chem. Soc., 100, 7753 (1978); (b) K. G. Bilyard, P. J. Garratt, R. Hunter, E. Lete, J. Org. Chem., 47, 4731 (1982); (c) C. Girard, R. Bloch, Tetrahedron Lett., 23, 3683 (1982); (d) K. K. Mahalanabis, M. Mumtaz, V. Snieckus, ibid., 23, 3971, 3975 (1982); (e) P. D. Noire, R. W. Franck, ibid., 23, 1031 (1982).
2. For other cyclopentane syntheses using dianions, see (a) M. Koreeda, Y. Liang, H. Akagi, J. Chem. Soc., Chem. Commun., 449 (1979); (b) K. Kojima, K. Sakai, Tetrahedron Lett., 3337 (1972); (c) R. Mitschka, J. M. Cook, U. Weiss, J. Am. Chem. Soc., 100, 3973 (1978); (d) R. W. Weber, J. M. Cook, Can J. Chem., 56, 189 (1978).
3. Dieckmann cyclization of 1,2,4-tricarbethoxybutane was reported to give a mixture of 2,3- and 2,4-dicarbethoxycyclopentanones in the ratio of *ca* 3:1, see J. P. Schaefer, J. J. Bloomfield, Org. React., 15, 1 (1967).
4. The use of dimethyl succinate is sharply limited by its insolubility in THF after treatment with LDA. We also have found the readily availabe diisopropyl ester is superior to diethyl or dibenzyl derivative, both of which gave the lower yield of the coupling products.
5. The product 3 decomposes gradually on chromatographic purifiction. Column chromatography on silanized silica gel (Merck 7719) gave the satisfactory results.
6. ^{1}H NMR (CDCl$_3$, 200 MHz)δ1.26 (m, 12H), 2.59 (d, 17 Hz, 1H), 2.91 (ddt, 17, 8.4, 2.1 Hz, 1H), 3.64 (dd, 3.6, 8.4 Hz, 1H), 5.00, 5.12 (2 sept, 6.2 Hz, 1H each), 5.20 (t, 2.1 Hz, 1H), 5.58 (t, 2.1 Hz, 1H), 10.18 (s, 1H); IR (CCl$_4$) 2990, 2950, 1740, 1670, 1610, 1470 cm^{-1}.
7. Dealkoxycarbonylation of 5 (DMSO-H$_2$O-NaCl, 120°C, 2 h, 97%) gave an isomeric mixture of ketones.
8. G. Bernáth, M. Svobada, Tetrahedron, 28, 3475 (1972).
9. H. J. Reich, J. M. Renga, I. L. Reich, J. Am. Chem. Soc., 97, 5434 (1975).
10. The ratio of the two isomers was inconsistent and varies significantly (1:1~3:1) depending upon the reaction conditions and the structure of esters.

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