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A SIMPLE, ONE POT, REGIOSPECIFIC 1,3-DICARBOXY BENZANNULATION OF ACTIVE ACYL SYSTEMS

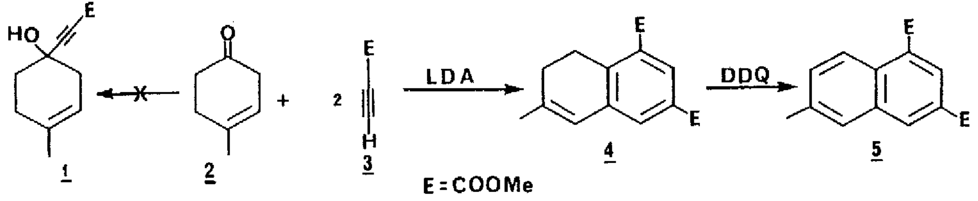
A. Srikrishna* and G. Veera Raghava Sharma
Department of Organic Chemistry, Indian Institute of Science
Bangalore - 560 012 INDIA

Abstract: A simple, one pot 1,3-dicarboxy benzannulation procedure via the sequential Michael-Michael-Aldol and aromatisation reactions of a Michael donor with two equivalents of methyl propynoate (3), is described.

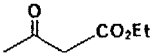
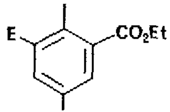
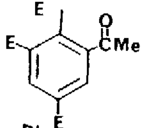
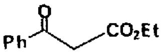
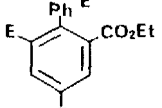
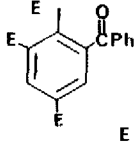
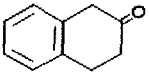
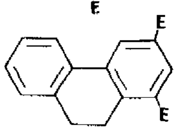
Regiocontrolled formation of several carbon-carbon bonds in one pot is an efficient way of converting simpler molecules into structurally more complex molecules.[1] In our attempt to prepare the tertiary alcohol 1 en-route to andirolactone,[2] we have discovered a novel, one pot benzannulation[3] procedure. This four step, one pot reaction involves sequential Michael-Michael-Aldol-Dehydration reactions of Michael donors with two equivalents of methyl propynoate,[4] which is the subject of this communication.

Reaction of the lithio derivative of the propynoate 3 (LDA, dry THF, -78 °C) with the enone 2 (or alternatively the lithium dienolate of the enone 2 with 3) generated, instead of the expected tertiary alcohol 1, the diester 4, mp. 81 °C, as the sole isolated product of the reaction. The structure of 4 was clearly delineated through its spectral data [UV λ_{max} (MeOH): 236.5(ϵ=21,000),276.5nm(5300); IR (nujol):1730 cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$): δ 8.3(1H,d,J=2Hz), 7.75(1H,d,J=2Hz), 6.28(1H,brs), 3.95(6H,s), 3.28(2H,t,J=7.5Hz), 2.25(2H,t,J=7.5Hz), 1.95(3H,s); ^{13}C NMR (22.5 MHz, $CDCl_3$):167.6(s), 166.5(s), 141(s), 140.3(s), 136.7(s), 129.2(3C,s&d), 128(s), 122.2(d), 52.0(2C,q), 28.1(t), 25.3(t), 23.2(q); HRMS $C_{15}H_{16}O_4$ needs 260.1049, Found 260.1059] in particular the low field ^1H and ^{13}C NMR signals and confirmed through its DDQ oxidation to the naphthalene derivative 5, mp. 127 °C. The formation of 4 can be rationalised as follows; Two sequential Michael additions of the dienolate of 2 with two equivalents of the ester 3 followed by an intramolecular addition of the resultant vinyl anion to the carbonyl group and finally dehydration during work up.[5]

To test its generality, this methodology has been extended to several Michael donors and the results are summarised in the table. In a typical experiment one mmole of the sodium salt of Michael donor was prepared in dry THF (4 ml) at ice temperature and treated with 3 mmole of the ester 3. The reaction mixture was stirred for 14 hr, quenched with dil. HCl, extracted with ether and purified over silica gel column chromatography. In addition



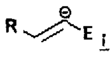
T A B L E

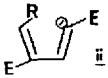
Entry	Michael Donor	Product	% Yield[a]	mp. °C
i	2	4	30	81
ii			32	41
iii			36	b[6]
iv			30	b
v			30	109
vi			32	90

a. Yields refer to isolated and chromatographically pure products. All the products exhibited satisfactory spectral data (IR, NMR, HRMS).
b. Syrapy liquid.

to the benzannulated product varying amounts (0-35%) of trimethyl-1,3,5-benzene tricarboxylate (cyclotrimer of the ester 3) and/or mono Michael addition products were also isolated as bye products. The overall yield of 30% of benzannulated product represents an average yield of 75-80% in each step of the sequence. All our attempts to improve the overall yield by varying conditions (change of counter ion, solvent, temperature, mode of addition) were in vain. In summary, we have described here an easy, one pot procedure for 1,3-dicarboxy benzannulation of acyl systems.

References & Notes: 1. Posner, G.H., Chem. Rev., (1986), 86, 831.
2. Srikrishna, A., Sharma, G.V.R., Tetrahedron Lett., (1988), 29, 6487.
3. Posner, G.H., Canella, K.A., Silversmith, E.F., Pro. Indian Acad. Sci. (Chem. Sci.), (1988), 100, 81 and references cited therein.
4. This procedure is analogous to the (2+2+2) MIMIRC reaction discovered recently by Posner for the construction of cyclohexanoids, Posner, G.H., Webb, K.S., Asirvatham, E., Jew, S., Degl'Innocenti, A., J. Am. Chem. Soc., (1988), 110, 4754, and references cited therein. See also Vernon, J.M., Fouli, F.A., Youssef, A.S.A., Synthesis, (1988), 291.
5. As the Michael addition to propargyl system generates the vinyl anion cis to the added group (as in i), the second Michael generates a system (ii) perfectly suited for cyclisation.





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