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A DIRECT THREE-CARBON ANNELATION TO CYCLOPENTENONE DERIVATIVES

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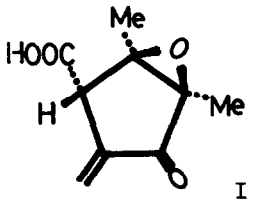
Summary: Cyclopentenone derivatives were prepared by three-carbon alkylation followed by cyclisation of the ester.

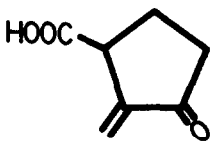
Numerous reports have appeared in the literature concerning the synthesis of the cyclopentenone nucleus, a significant unit found in many naturally occuring compounds. Although the existing methods[1] are still widely used with great success several alternative approaches have been presented recently. Examples are the rearrangement method,[2] acylation-cyclisation by the use of vinyltrimethylsilane,[3,4] the retro Diels-Alder reaction,[5,6] 2+2 cycloaddition reaction followed by ring enlargement,[7] and the use of 3-bromo-2-methoxy-1-butene as a three-carbon annelation reagent.[8]

During our study towards the syntheses of the antibiotics methylenomycin A I[9,10] and sarkomycin II[11,12] we found that allylation of the ester III could be achieved under normal alkylation conditions. Thus when lithiumdiisopropylamide (LDA) was used as the base in THF/HMPA (10/1) the reaction went smoothly at 0° to give cleanly the expected product IV. However, the use of excess LDA with longer reaction time and higher temperature (eg.overnight, room temperature) gave a mixture of products from which IV and cyclopentenone V were isolated togetherwith several unidentified products, the cyclopentenone V apparently arising from the intra-molecular attack of the allyl anion VI on the ester group followed by double bond isomerisation.

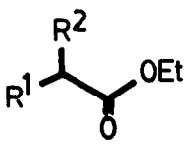
We have proved this sequence to be of general application which thus provides a convenient and direct three-carbon annelation that promises to be an excellent alternative method for the synthesis of cyclopentenone derivatives. In view of its simplicity, it is in fact surprising that the reaction should have hitherto gone unexploited.



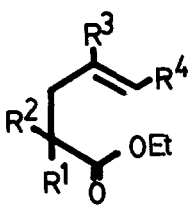
I



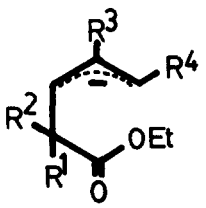
II



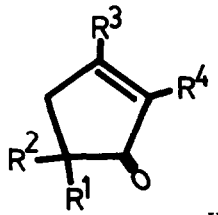
III



IV



VI



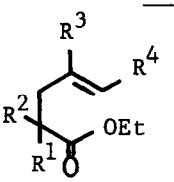
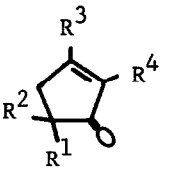
V

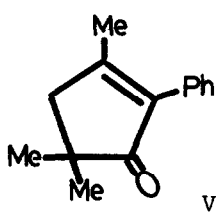
Unsaturated ester IV a-h were prepared by direct allylation of III with the required allylic halides.[13] The corresponding cyclopentenones V a-h were obtained when IV was allowed to react with LDA(1.5eq.) in THF/HMPA (10/1) solution (20 ml of solvent for 1 mmole of reactant) at room temperature overnigh The crude products were purified by preparative TLC using chloroform/hexane (40/60) as eluent and yields shown in the Table were not optimised.

From the Table it can be seen that yields are generally high with the exception of IV a when $R^4 \neq$ Aryl. In the case of IV h two products V h_1 and V h_2 were isolated in a ratio 3:2. Identification of these two products was possible from their spectroscopic data; the nmr spectrum of V h_1 (m/e 200, ir. 1705cm^{-1}) displaying singlets at δ1.18(6H), 2.16(3H), 2.54(2H), and 7.35(5H), while that of V h_2 (m/e 200, ir.1708cm^{-1}) showing five signals at δ1.07(6H), 2.43(2H), 3.70(2H), 5.83(1H), and 7.29(5H). These two products probably arise from anions of the type VI h_1 and VI h_2 respectively. Attempted one-pot alkylation-cyclisation of the ester III without isolation of IV posed some technical difficulty in purification of the final product, and therefore we preferred, in all cases, the stepwise process.

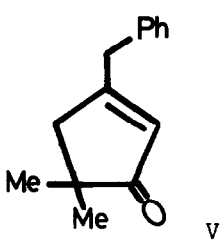
Further progress in this field will be reported.

TABLE

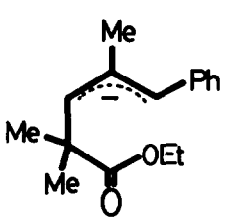
REACTANT IV	% PRODUCT V	
		
a. R^1=Ph, R^2=Me, R^3=R^4=H	45	(semi-solid)
b. R^1=R^4=Ph, R^2=Me, R^3=H	78	(mp.84-84.5°)
c. R^1=R^4=Ph, R^2=R^3=Me	84	(mp.89-89.5°)
d. R^1=Ph, R^2=Me, R^3=H, R^4= o-OMe-C_6H_4	80	(mp.78-79°)
e. R^1=Ph, R^2=Me, R^3=H, R^4= m-OMe-C_6H_4	78	(semi-solid)
f. R^1=R^3=R^4=Ph, R^2=Me	78	(mp.104-105°)
g. R^1=R^2=Me, R^3=H, R^4=Ph	73	(semi-solid)
h. R^1=R^2=R^3=Me, R^4=Ph	79	(two products both semi-solid, see text)[14]



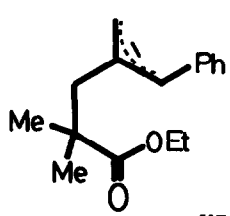
V h_1



V h_2



VI h_1



VI h_2

References and Notes

1. R.A.Ellison, Synthesis, 397 (1973).
2. H.Ogawa, Y.Taketugu, and T.Imoto, Tetrahedron Lett., 3457 (1979), see also von M.Karpf and A.S.Dreiding, Helv.Chim.Acta, 62, 852 (1979).
3. F.Cooke, J.Schwindeman,and P.Magnus, Tetrahedron Lett., 1995 (1979)
4. W.E.Fristad, D.S.Dime, T.R.Bailey, and L.A.Paquette, Tetrahedron Lett., 1999 (1979).
5. N.E.Schore, Synthetic Communications, 9, 41 (1979).
6. R.Bloch, Tetrahedron Lett., 3945 (1979).
7. A.E.Greene and J.P.Deprès, J.Amer.Chem.Soc., 101, 4003 (1979).
8. R.M.Jacobson, A.Abbaspour, and G.P.Lahm, J.Org.Chem., 43, 4650 (1978).
9. U.Hornemann and D.A.Hopwood, Tetrahedron Lett., 2977 (1978).
10. R.M.Scarborough,Jr., A.B.Smith,III, J.Amer.Chem.Soc., 99, 7085 (1977).
11. R.K.Hill, P.J.Foley,Jr., and L.A.Gardella, J.Org.Chem., 32, 2330 (1967).
12. J.N.Marx and G.M.Minaskanian, Tetrahedron Lett., 4175 (1979).
13. From our experience, allylation reactions occur only in a direct S_N2 fashi All compounds are fully characterised. We thank Mrs.P.Poochaiwattananon, Mrs.J.Udcharchon, and Miss.A.Srisuthtiprut for spectroscopic, MS, and analytical services.
14. Only one product (V c) was obtained from the cyclisation of IV c.

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