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THE FACILE SYNTHESIS OF A LARGE RING LACTONE BY ACID-CATALYSED CYCLISATION OF AN (Z)-ENE-DIYNE HYDROXY ACID PRECURSOR.

Danielle GUILLERM and Gérard LINSTRUMELLE
E.R.12 du CNRS, Laboratoire de Chimie, Ecole Normale Supérieure,
24, rue Lhomond, 75231 PARIS CEDEX 05 - FRANCE.

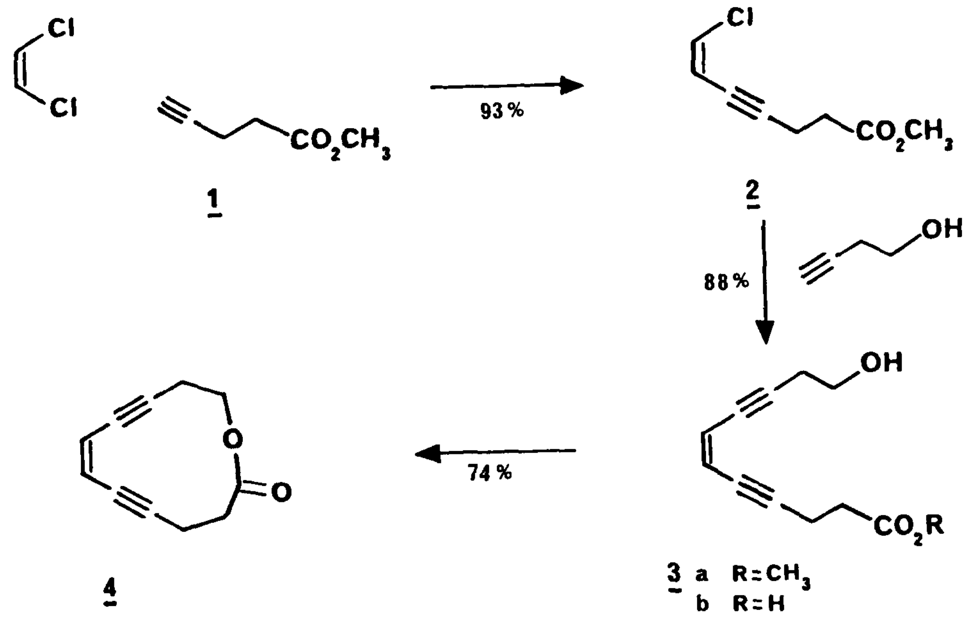
ABSTRACT : *A large ring lactone is obtained in good yield by acid catalysed cyclisation of the ω-hydroxy acid precursor.*

The direct cyclisation of long-chain hydroxy acids usually cannot be easily realised and necessitates sophisticated methods involving activation of one or both of the two functional groups 1). However, we herein report a facile synthesis of an enediyne 12-membered ring lactone by simple acid-catalysed lactonisation of the corresponding hydroxy acid precursor.

We have previously reported that (E) and (Z)-dichloroethylenes are monosubstituted in high yield by palladium-copper catalysed reaction with terminal acetylenes 2). The chloroenynes can react further with another acetylenic compound to generate unsymetrical enediynes with net retention of the double bond geometry.

Thus, when treated with methyl pentynoate 1 (1eq) in the presence of palladium tetrakis (triphenylphosphine)(0.05 eq), copper iodide (0.05 eq) and n-butylamine (2 eq) at room temperature for 6h, (Z)-1,2-dichloroethylene (2 eq) gave pure chloroester 2 in 93 % yield 3,4). Under the same experimental conditions, stoichiometric reaction between chloroester 2 and 3-butyn-1-ol led to pure hydroxyester 3a 5) in 88 % yield. Hydroxy acid 3b was quantitatively obtained by saponification with lithium hydroxide in ethanol-water.

When treated with a catalytic amount of p-toluene sulphonic acid in refluxing benzene, hydroxy acid 3b gave, after flash chromatography on silica gel (elution methylene chloride), pure lactone 4 6,7) in 74 % yield. Catalytic hydrogenation (platinum oxide, ethyl acetate) of lactone 4 furnished (85 %) 11-undecanolide which was identical to an authentic sample 8).



The efficient lactonisation reported here is attributable to the rigidity of the (Z)-ene-diyne structure which enables cyclisation to compete successfully with intermolecular esterification. The easy preparation of (Z)-ene-diyne compounds from (Z)-1,2-dichloroethylene might thus provide a convenient access to other large ring compounds. Further applications are in progress.

NOTES AND REFERENCES

1) T.C. BACK, Tetrahedron, 1977, 33, 3041 ; K.C. NICOLAOU, Tetrahedron, 1977, 33, 683.

2) V. RATOVELOMANANA and G. LINSTRUMELLE, Tetrahedron Lett., 1981, 22, 315 ; ibid., 1984, 25, 6001.

3) All products were purified by flash chromatography on silica gel.

4) ^{1}H NMR($CDCl_3$) : 2.66(4H,m) ; 3.72(3H,s) ; 5.9(2H,dt,J=7.5Hz,J=2Hz) ; 6.4 (2H,d, J=7.5Hz)ppm.

5) ^{1}H NMR($CDCl_3$) : 2.7(6H,m) ; 3.72(3H,s) ; 3.78(2H,t,J=6Hz) ; 5.80(2H,s)ppm.

6) mp 67°C ; ^{1}H NMR($CDCl_3$) : 2.62(2H,m) ; 2.78(4H,m) ; 4.38(2H,t,J=5.5Hz) ; 5.80 (2H,s)ppm ; ^{13}C NMR($CDCl_3$) : 16.60 ; 20.36 ; 33.75 ; 61.20 ; 80.04 ; 80.49 ; 93.50 ; 95.38 ; 119.91 ; 120.17 ; 171.44ppm. C.I.M.S.: m/e=192$(M+NH_4)^+$; I.R. : 3030, 2200, 1730, 1560 cm^{-1}.

7) The corresponding lactide which was also formed in 12% yield was easily separated by further elution, mp 96°C ; ^{1}H NMR($CDCl_3$) : 2.68(2H,m) ; 2.78(4H,m) ; 4.30(2H,t, J=6.5Hz) , 5.78(2H,s)ppm ; ^{13}C NMR($CDCl_3$) : 15.89 ; 20.45 ; 33.72 ; 62.46 ; 78.71 ; 79.36 ; 93.02 ; 95.57 ; 118.91 ; 119.36 ; 170.95.

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