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ANOTHER NOVEL FURANOID PRODUCT FROM THE REACTION OF A 2-METHOXYMETHYLENE KETONE WITH CARBOETHOXYCARBENE

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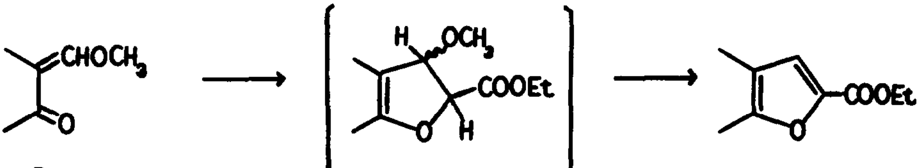
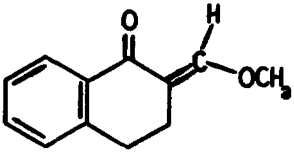
Previous communications from this laboratory have described a synthesis of furans involving the net 1,4 addition of carboethoxycarbene to 2-methoxymethylene ketones (as shown in I → → II)(2), and the use of this procedure in the total synthesis of the diterpene methyl vinhaticoate(3).



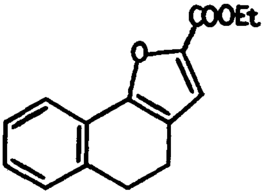
I

II

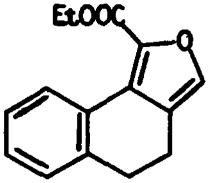
We now wish to report the formation of a different type of furan when this method was applied to 2-methoxymethylene-1-tetralone (III)(4). Treatment of III with five equivalents of ethyl diazoacetate in boiling 1,1,2,2-tetrachloroethane in the presence of copper sulfate afforded a 48% yield of "furanoid" material, which could be separated by chromatography and crystallization into 17% of the expected furan IV, mp 68-69°, and 20% of the isomeric furan V, mp 54-55°(5).



III



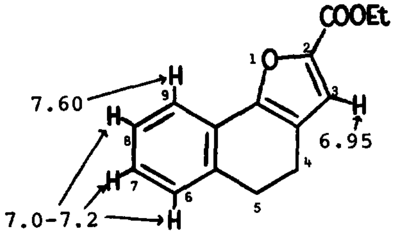
IV



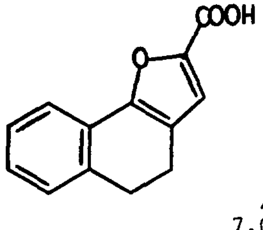
V

The structural assignments to IV and V are based largely on analysis of the aromatic proton regions of the nmr spectra of these two furans and derived substances. Compound IV displayed a one-proton (1-H) singlet at 6.95 ppm(6), a 3-H complex multiplet centered at 7.1 ppm, and a 1-H multiplet at 7.60 ppm. The assignment of these resonances to particular protons of IV is shown by arrow in the figure below, and this same method of summarizing nmr data is used for the other substances discussed. Saponification of IV afforded 91% of furoic acid VI, mp 205-208°, and copper-catalyzed decarboxylation of VI in boiling dimethylacetamide afforded oily furan VII. As expected for this compound lacking the C2 carboethoxyl group, its C3 proton appeared as a doublet (J=1.9 Hz) at 6.23 ppm, a chemical shift consistent with a proton β, but not α, to the furan oxygen(7).

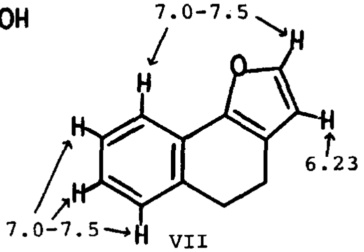
A clearer demonstration of the furan substitution pattern of IV was achieved by dehydrogenation of IV over palladium-on-carbon at 210° to VIII, which was saponified to IX and decarboxylated to X(8). In the nmr spectrum of X two doublets (at 7.40 and 6.51 ppm, J=2.1 Hz) for the protons at C2 and C3 could readily be discerned. Final confirmation that the 6.95 ppm singlet displayed by IV was due to a β furan proton was obtained by lithium aluminum hydride reduction of IV to XI, which showed, as expected, a 1-H singlet shifted upfield (to 6.09 ppm).



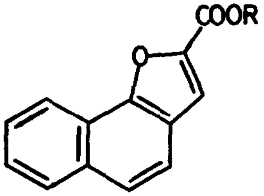
IV



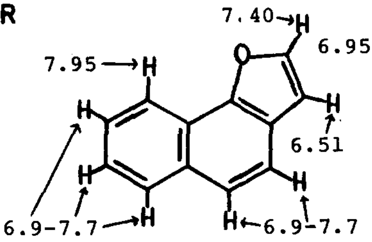
VI



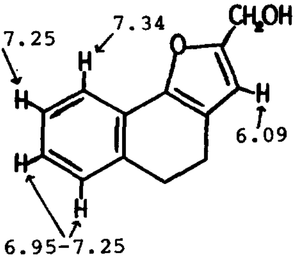
VII



VIII,R=Et
IX,R=H



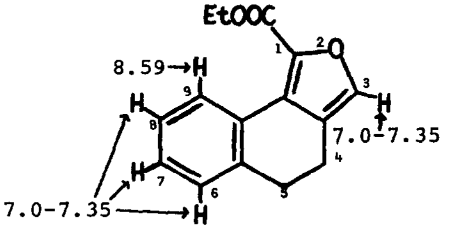
X



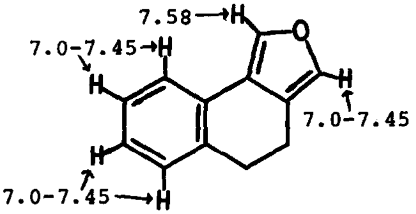
XI

No such evidence for the presence of a β furan proton could be found for V. Saponification and decarboxylation of V led to oily, unstable XII which was characterized as its maleic anhydride adduct XIII, mp 169-170° (dec). No aromatic proton appeared at a higher field than 6.9 ppm in XII, or in alcohol XIV, prepared by reduction of V. A doublet at 7.58 ppm (J = 1.4 Hz)(9) in the spectrum of XII is assigned to the C1 proton, deshielded by the benzene moiety.

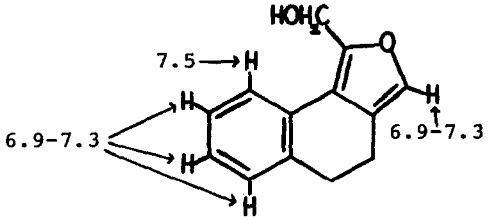
The marked deshielding of the 1-H multiplet at 8.59 ppm in the spectrum of V can only easily be explained as being caused by the proximity of the C9 aromatic proton to the ester carbonyl. Removal of this carbonyl group by conversion to XII or XIV effects an upfield shift of about 1 ppm for the multiplet. This observation establishes the position of the carboethoxyl group as C1.



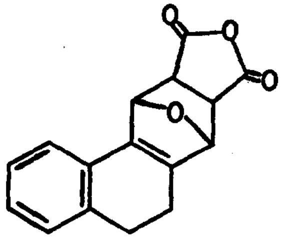
V



XII

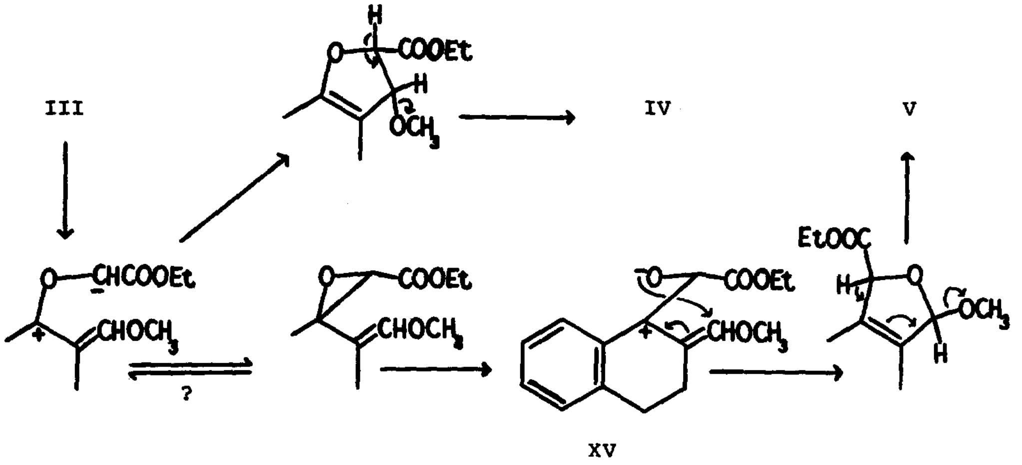


XIV



XIII

The formation of IV and V can be economically envisaged as occurring by a pathway involving initial attack of the copper-carbenoid reagent on the carbonyl oxygen of III(10), as shown on the next page. The presence of the benzene ring in III would help to stabilize zwitterion XV and thus possibly account for the isolation of V in the present case. However, it should be emphasized that no definitive evidence pertaining to the mechanism of the formation of either type of furan has been obtained. Efforts in this direction are in progress.



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(3) T.A. Spencer, R.M. Villarica, D.L. Storm, T.D. Weaver, R.J. Friary, J. Posler, and P.R. Shafer, J. Am. Chem. Soc., 89, 5497 (1967).

(4) cf., D. Nasipuri and K.D. Biswas, Tetrahedron Letters, 2963 (1966). The nmr spectrum of our 2-methoxymethylene-1-tetralone indicates it has the stereochemistry shown in III [cf. ref. (4) cited in ref. (2) above].

(5) Satisfactory ir, uv, and nmr spectral properties were observed for all new compounds; satisfactory elemental analyses have been obtained for all compounds for which a melting point is given.

(6) Nmr spectra were all run in CCl_4; chemical shifts are relative to TMS.

(7) Nmr spectrum no. 125 of methyl α-furoate in the Varian Nmr Spectra Catalog, Vol. 1, Varian Associates, Palo Alto, California, 1962, illustrates the essence of all these chemical shift arguments; also, cf. ref. (2).

(8) Compound X has previously been reported by R. Stoermer, Ann., 312, 237 (1900).

(9) cf., R.J. Abraham and H.J. Bernstein, Can. J. Chem., 39, 909 (1961), for α,α' furan proton coupling constants of 1.5 and 1.6 Hz.

(10) cf., M.S. Kharasch, T. Rudy, W. Nudenberg, and G. Buchi, J. Org. Chem., 18, 1030 (1953).