

FURAN SYNTHESIS BY 1,4 ADDITION OF CARBOETHOXYCARBENE

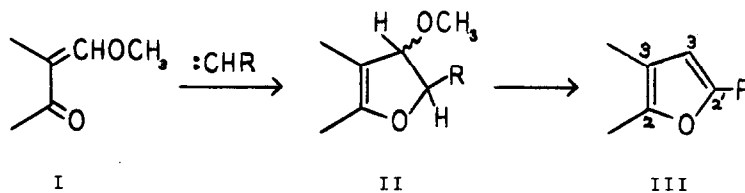
TO  $\alpha$ -METHOXYMETHYLENE KETONES

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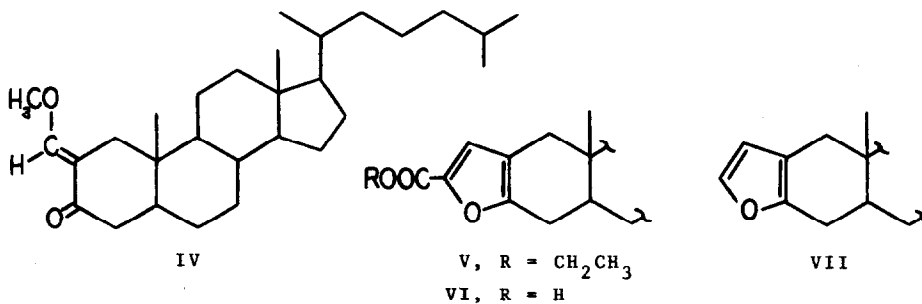
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Our search for an efficient synthesis of furans fused in the 2 and 3 positions to a cyclohexane ring led us to investigate the reaction of  $\alpha$ -methoxymethylene ketones (I) with carbenoid reagents bearing at least one hydrogen. If the product of 1,4 addition (II) were obtained, spontaneous elimination of methanol to afford the aromatic system (III) might be anticipated. During the course of these studies, Fried reported<sup>(2)</sup> that "difluoromethylene" reacts with a steroidal  $\alpha$ -methoxymethylene ketone to afford 1,4 addition products (epimeric 2',2'-difluoro-3'-methoxy-2',3'-dihydrofurans). We now report realization of the scheme represented by I  $\rightarrow$  III in the reaction of 2-methoxymethylenecholestanone-3 (IV) with ethyl diazoacetate in the presence of copper sulfate.



Starting material IV, m.p. 151.0-152.5°, <sup>(3,4)</sup> was prepared from the corresponding 2-hydroxymethylene derivative <sup>(5)</sup> by treatment with sodium methoxide and dimethyl sulfate in methanol (95% yield of material with m.p. 128-132°). When IV was treated with four equivalents of ethyl diazoacetate in a nitrogen atmosphere at 160° in the presence of a trace of copper sulfate, the major product was the furan carboxylic ester V, m.p. 145.0-145.5°, obtained pure in 29% yield. The structure of the product was suggested by its spectral properties:  $\lambda_{\max}^{\text{hexane}}$  221 ( $\epsilon$  13,000), 261 ( $\epsilon$  18,000), 266 ( $\epsilon$  21,000), 271 ( $\epsilon$  22,000), 277 ( $\epsilon$  19,000) and 283  $\mu$  ( $\epsilon$  13,000);  $\lambda_{\max}^{\text{KBr}}$  5.78, 6.50, and 6.80  $\mu$ ;  $\delta_{\text{TMS}}^{\text{CDCl}_3}$  0.6-3.0 broad multiplet (47H), 4.30 (2H, q, J=7 Hz), and 6.95 ppm (1H, s).

Furoic ester V was converted in excellent yield to the parent furan VII by saponification to acid VI, m.p. 252.5-253.0°, in essentially quantitative yield, followed by decarboxylation of VI at its melting point in the presence of copper to VII, m.p. 102.0-102.5°, which was conveniently isolated in 92% yield by sublimation as it was formed. Furan VII showed  $\lambda_{\max}^{\text{hexane}}$  228  $\mu$  ( $\epsilon$  4200);  $\lambda_{\max}^{\text{KBr}}$  6.63, 7.00, and 11.15  $\mu$ ;  $\delta_{\text{TMS}}^{\text{CDCl}_3}$  0.6-3.0 broad multiplet (44H), 6.12 (1H, d, J=2 Hz) and 7.21 ppm (1H, d, J=2 Hz).



Isolation of 1,4 addition products from carbenoid reactions is extremely rare. Aside from the present work and the closely analogous difluoromethylene case,<sup>(2)</sup> the only known example is the isolation in very small yield of cyclopentene from the reaction of 1,3-butadiene with photolytically generated methylene.<sup>(6)</sup> Any speculation about mechanism is better deferred until investigations into the scope and limitations of this type of reaction are reported in a full paper.

#### References

- (1) Support of this research by an Alfred P. Sloan Foundation Research Fellowship to T.A.S. and by PHS Grant AM-05014 is gratefully acknowledged.
- (2) P. Hodge, J.A. Edwards, and J.H. Fried, Tetrahedron Letters, 5175 (1966).
- (3) Satisfactory elemental analyses have been obtained for all new compounds reported.
- (4) The 151.0-152.5<sup>o</sup> compound is assigned structure IV, with the methoxyl group trans to the carbonyl group, on the basis of its nmr spectrum [ $\delta_{\text{TMS}}^{\text{CDCl}_3}$  3.83 (3H, s) and 7.30 ppm (1H, broad s)] by comparison with nmr data on the 4:1 mixture of geometrical isomers obtained by Hodge, Edwards, and Fried (ref. 2) in the case of their steroidal  $\alpha$ -methoxy-methylene ketone. We thank Dr. Edwards for providing us with this information.
- (5) C. Djerassi, N. Finch, R.C. Cookson, and C.W. Bird, J. Am. Chem. Soc., 82, 5488 (1960).
- (6) (a) V. Franzen, Chem. Ber., 95, 571 (1962).  
(b) B. Grzybowska, J.H. Knox, and A.F. Trotman-Dickenson, J. Chem. Soc., 3826 (1962).