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A SIMPLE METHOD FOR THE PREPARATION OF β-TETRALONE-3-CARBOXYLATES

S. W. Pelletier and P. C. Parthasarathy
Department of Chemistry, The University of Georgia
Athens, Georgia, U.S.A.

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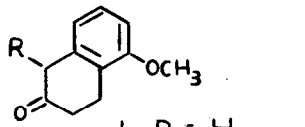
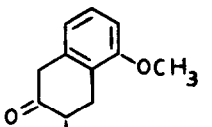
Our recent studies on the carboxylation of β-tetralones have led to unexpected but interesting results. Treatment of 5-methoxytetralone-2 (I)[1] with magnesium methyl carbonate[2,3] gave a β-keto acid[4] in 45% yield, m.p. 153-155°; ν max. (Nujol) 2632, 1661, 1608, 1404 cm.$^{-1}$; the methyl ester showed m.p. 123-124°; ν max. (Nujol) 1672, 1634, 1404 cm.$^{-1}$ λmax. (EtOH) 214mμ (12,900), 262mμ (6,460), 278mμ (3,890); in base: λmax. (EtOH) 225mμ (7,660), 279mμ (11,220), 288mμ (11,480). By analogy with many base-catalysed alkylation reactions of β-tetralones[5], we initially assumed the β-keto acid and ester had structures II and III, respectively. It is known, however, that acylation can occur either at the 1- or 3-position depending on the nature of the acyl group[6]. Thus, formylation occurs at the 1-position (vide infra) while oxalylation occurs at the 3-position[6,7]. Subsequent studies have shown that the structure of the carboxylation product is IV. Thus, this work provides a convenient, one-step method for the preparation of β-tetralone-3-carboxylates. The evidence in favor of the course of this carboxylation reaction is presented below.



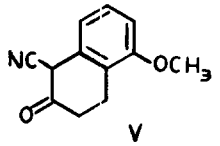
I, R = H
II, R = CO_2H
III, R = CO_2CH_3



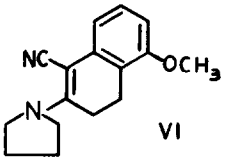
IV

Comparison of the enamine of the keto ester (III or IV) with that of the ketonitrile (V) provided clear evidence in favor of structure IV for the carboxylation

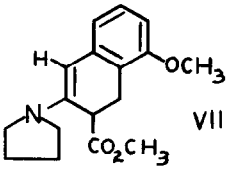
product. The ketonitrile (V) was prepared from I by a conventional procedure[8,9] via the hydroxymethylene derivative, m.p. 107-108°, ν max. (Nujol) 1661 and 1608 cm^{-1}; λ max. (EtOH) 205mμ (9,330), 280mμ (3,980), 308mμ (3,390) and the isoxazole derivative, m.p. 137°, ν max. (Nujol) 1658, 1605, 1580 $cm.^{-1}$; λ max. (EtOH) 274mμ (1,740), 280mμ (1,950). The ketonitrile (V) showed m.p. 175-176°, ν max. (Nujol) 3205, 2212, 1672, 1605, 1590 $cm.^{-1}$; λ max. (EtOH) 272mμ (8320), 278mμ (7590), unchanged with base. The ketonitrile readily afforded a pyrrolidine enamine (VI), m.p. 151-153°, ν max. (Nujol) 2174, 1613, 1582 $cm.^{-1}$; λ max. (EtOH) 214mμ



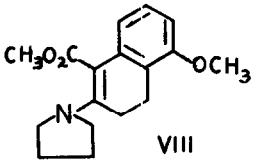
V



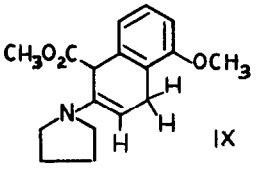
VI



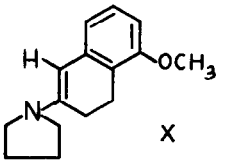
VII



VIII



IX



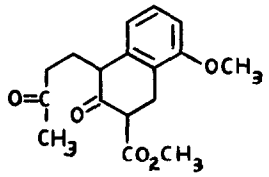
X

(11,750), 280mμ (12,590), 289mμ (13,180). The NMR spectrum of VI showed the absence of a vinyl proton.

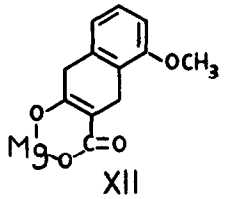
The pyrrolidine enamine of the ketoester, m.p. 109-110°, ν max. (Nujol) 1730, 1613, 1592 $cm.^{-1}$; λ max. (EtOH) 225mμ (8320), 245mμ (8510), 314mμ (11,220) 327mμ (11,480), showed in the NMR spectrum[10] a sharp singlet at 4.75 τ which is consonant with structure VII for the enamine and therefore structure IV for the ketoester. The enamine VIII derived from the alternate structure III has no vinyl proton and the less likely structure IX would not be expected to show an unsplit vinyl proton. It is also pertinent to note that the pyrrolidine enamine X of tetralone, (I), m.p. 81-83°, ν max. (Nujol) 1618, 1597, 1563 $cm.^{-1}$, λ max. (EtOH) 205mμ (10,700), 223mμ (12,000), 245mμ (10,500), 316mμ (14,500), showed a sharp singlet at 4.82 τ.

In agreement with structure IV for the ketoester, the enamine (VII) with methyl vinyl ketone in dioxane afforded XI m.p. 119.5°, ν max. (Nujol) 1706, 1667, 1626 $cm.^{-1}$;

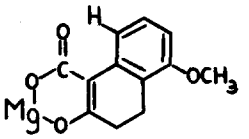
λ max. (EtOH) 260mμ (5570), λ sh. (EtOH) 278mμ (3040), 282mμ (2030), while enamine VI under the same conditions was recovered unchanged.



XI



XII



XIII

The reason for the particular course of this carboxylation reaction is of interest. Since under the conditions used the carboxylation process is reversible, the magnesium salt which results is the one formed at equilibrium[11]. Thus the steric requirement[11] of the chelate salt causes XII to be favored over XIII.

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(6) We thank Dr. M. Stiles for bringing this point and reference 7 to our attention.

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(10) The NMR spectra were measured with a Varian A-60 spectrometer in $CDCl_3$ solution with tetramethylsilane as an internal standard.

(11) M. Stiles, personal communication, April 22, 1963. Dr. Stiles kindly informs us that in their laboratory preliminary carboxylation experiments on β-tetralone led to a complex mixture from which only derivatives of β-tetralone-3-carboxylic acid could be isolated.