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DECARBETHOXYLATION OF β-KETO ESTERS: FORMATION OF THERMODYNAMICALLY STABLE ENOLS[+]

V. Dabral, H. Ila and Nitya Anand*

Central Drug Research Institute,
Lucknow, India

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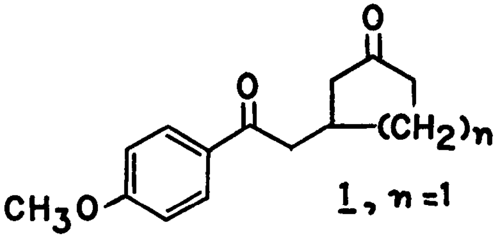
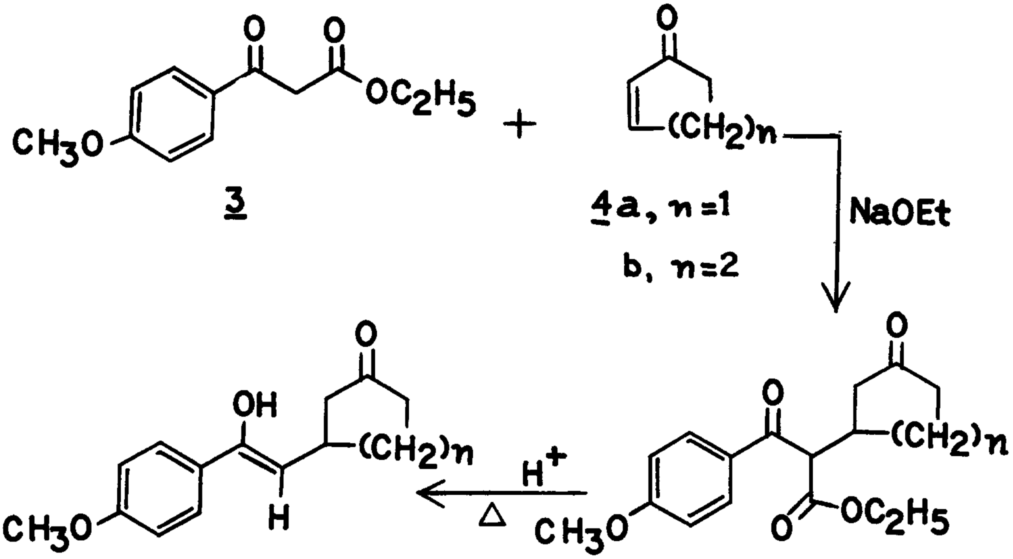
In the course of a study directed towards the synthesis of some derivatives of B,C-disecoestrone, diketones 1 and 2 were required as intermediates. Since 1 and 2 were not described earlier, their synthesis was planned by decarbethoxylation of β-keto esters 5 and 6, which were conveniently prepared in excellent yields by Michael addition of α-carbethoxy-p-methoxyacetophenone (3) to the enones 4a and 4b respectively. Decarbethoxylation of 5 and 6 was carried out in acidic conditions instead of alkaline media, since the latter would promote retro-Michael cleavage.[1] Thus 5 was refluxed in 8% HCl for 18 hr, work up of the mixture followed by chromatography of the residue over silica gel (1:3 EtOAc-hexane) gave a colourless solid, mp 128-130° (68 %) which was not the expected diketone 1, but was characterised as the enol 7 on the basis of following spectroscopic evidences, $C_{14}H_{16}O_3$ (232): M^+ 232, λ_{max} (ethanol) 266 nm (logϵ, 4.09). The IR spectrum ($CHCl_3$) of 7 showed broad band between 3000-3500 cm^{-1} (enolic OH) and a sharp peak at 1705 cm^{-1} (ring -C=O); in the nmr spectrum ($CDCl_3$) of 7, a broad peak was present at δ 5.95 (1H, olefinic) and a downfield signal (exchangeable with D_2O) at δ 11.1 (1H) indicating the presence of an enolic OH group. Decarbethoxylation of 6 similarly gave 8 under identical conditions, colourless solid, mp 112-114° (71 %), $C_{15}H_{18}O_3$ (246): M^+ 246; uv λ_{max} (methanol) 257 nm (logϵ, 4.13); ir ν_{max}($CHCl_3$) cm^{-1}: 3000-3500 (broad, enolic OH) and 1705 (ring C=O); nmr ($CDCl_3$): δ 6.03 (bs, 1H, olefinic), 11.5 (bs, 1H, enolic OH).



1, $n = 1$

2, $n = 2$



3

4a, $n = 1$

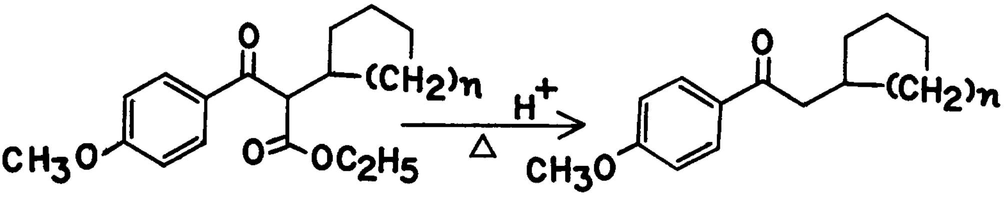
b, $n = 2$

7, $n = 1$

8, $n = 2$

5, $n = 1$

6, $n = 2$



9, $n = 1$

10, $n = 2$

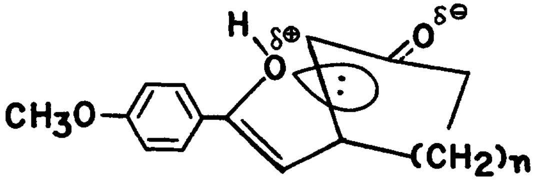
11, $n = 1$

12, $n = 2$

Attempts to reverse the equilibrium from the enolate ion to the ketone 1 or 2 were not successful, even when the enols 7 or 8 were left for 10 days in dilute alkaline solution. However, the ketone 2 could be prepared in 50 % yield by Friedel-Crafts acylation of anisole using 3-oxocyclohexyl acetyl chloride and $AlCl_3$ at 0° in carbon disulfide, colourless solid, mp 82-83°, ir $\nu_{max}(CHCl_3)$ cm^{-1}: 1715 (ring -C=O) and 1675 (aromatic -C=O); uv λ_{max} (methanol): 273 nm (log ε, 4.27); nmr $(CDCl_3)$: δ 2.9 (d, 2H, $-\overset{O}{\overset{\|}{C}}-CH_2$); M^+ (mass) 246. The ketone 2 remained unchanged when left at room temperature either in dilute alkaline or acidic media, however, when refluxed in 8 % HCl, it was slowly tautomerised to the enol 8 in nearly quantitative yields (superimposable ir and nmr spectra).

The compound 1,2-dimesityl-1-propen-1-ol is the only example of thermodynamically stable enol reported in the literature.[2] Thus, the rather unusual stability of enols 7 and 8 is interestingly significant and must be due to some interaction[3] which prevents its ketonization. Dreiding models of the enol 7 and 8 indicate that the nonbonding orbital of enolic oxygen is in close proximity, so as to interact with the carbonyl group as shown in 13. This interaction is supported by the lower wavelength shift of ring carbonyl frequencies to 1705 cm^{-1} in 7 and 8.[4] That this interaction plays an important role for the stability of enols 7 and 8, is further supported by the fact that the β-keto esters 9 and 10 having no ring carbonyl group give the ketones 11 and 12 respectively[5] (aromatic -C=O at 1675 cm^{-1}) when refluxed in 8 % HCl for 18 hr and no traces of respective enols could be isolated. Similarly ketones 11 and 12 remain unchanged in refluxing HCl.

This, we understand, is one of the rare examples of formation of stable enols due to neighbouring group participation.



13, n = 1 or 2

REFERENCES

[+] CDRI Communication No. 2092.

1. In another experiment, ester 5 was stirred at room temperature with dil NaOH solution under N_2 atmosphere and the mixture was treated with dil H_2SO_4 and refluxed for 15 hr. Work-up of the reaction mixture gave enol 7 and *p*-methoxyacetophenone formed by the decarbethoxylation of retro-Michael product 3. Decarbethoxylation under neutral conditions using DMSO, NaCl and H_2O[6] also yielded similar type of products.
2. R.C. Fuson, J. Corse and C.H. McKeever, J. Am. Chem. Soc., 62, 3250 (1940).
3. Stability of enols 7 and 8 due to intramolecular hydrogen bonding was ruled out, as enolic hydrogen and carbonyl oxygen were not present in the bonding distance.
4. The normal position of cyclopentanone and cyclohexanone carbonyl frequencies are 1740 and 1715-1720 cm^{-1} respectively. There was no significant shift of the carbonyl frequencies when the ir spectra of 7 and 8 were taken in KBr.
5. The structures of 9-10 and 11-12 were confirmed by spectral and analytical data.
6. A.P. Krapcho and A.J. Lovey, Tetrahedron Letters, 957 (1973).