

A NOVEL DIMERISATION OF 3-BENZOYL 4-PHENYLISOCROTONIC ACID[†]

Janak Singh¹, Kanti P. Agarwal and Gurbakhsh Singh^{*}

Department of Chemistry, Banaras Hindu University, Varanasi-5, India

ABSTRACT: The acid catalized self condensation of 3-benzoyl-4-phenylisocrotonic acid is described.

During the studies in the cyclodehydration of 3-benzoyl 4-phenylisocrotonic acid 1², an interesting dimerisation took place. The structure and the chemistry of this unusual product are described in this communication.

The reaction of the acid 1 with acetylchloride (Scheme-I,A) produced the highly crystalline pseudo-acidchloride 2a, which was thermally unstable and sensitive to moisture, (m.p. 185° d, 40% yield; IR: 1818 cm⁻¹; MS: M⁺ - C1 = 535 & 533 in ratio 1:3)^{3,4}.

Facile elimination of HCl from 2a (Scheme-I,B) resulted in the formation of the monochlorolactone 3 (m.p. 205° d; 75% yield; NMR: δ , 2.08, 2.41, ABq, J = 17 Hz, 2H; 4.07, s, 1H; 4.29, 4.49, ABq, J = 9.5 Hz, 2H; 6.7 - 7.7, m, 20 H; IR: 1818, 1795 cm⁻¹). On refluxing with dry MeOH, the pseudo-acidchloride 3 underwent solvolysis of both the halogen atom and the enollactone functions generating the lactonic ester 4 (m.p. 220 - 22° C; 58% yield; UV: λ max, 243 nm, ϵ 11715; IR: 1805, 1739, 1686 cm⁻¹; NMR: δ , 2.24, 2.38, ABq, J = 17 Hz, 2H; 3.14, s, 3H; 3.35, s, 3H).

The dimer 2a undergoes a thermal ring expansion reaction (Cf. Wagner-Meerwein rearrangement⁵; with loss of 2 HCl and 2H; (Scheme-I,D) to form the orange-yellow dilactone 5 (m.p. 303 - 05° C; 60% yield; NMR: δ , 5.15, s, 1H; 5.97, s, 1H; 7.4, m, 20H; IR: 1767 cm⁻¹, UV: λ max, 267 nm, ϵ 17200, 460 nm, ϵ 11027). On vigorous hydrolysis of 3a (Scheme-I,E) the crystalline diacid 6a was formed (m.p. 304 - 06° C; 40% yield). Treatment of 6a with CH₂N₂ furnished the diester 6b (m.p. 211 - 12° C; 85% yield; NMR: δ , 3.20, s, 3H; 3.38, s, 5H; IR: 1733, 1669 cm⁻¹). Incorporation of two deuterium atoms in the acetate appendage in 6a (at the starred carbon) was observed when D₂O was employed in the hydrolysis. (NMR of 6b: δ , 3.20, s, 3H; 3.38, s, 3H). The doubly vinylogous β -ketoacid salt 7 is probably involved in the deuterium exchange process.

The relative stereochemistry of the two phenyl rings at the contiguous chiral centers in 5 has not been unambiguously established. However, considering the transition state 13, an examination of the molecular models reveals

[†] Dedicated to Professor Gilbert Stork on his sixtieth birthday

that with a β -configuration for the phenyl group at C_2 (vide infra), the other phenyl ring at the site of C-C bond formation is more likely to be oriented trans as shown in 5.

Further evidence of the bislactone functionality in 2a is provided by its hydrolysis (Scheme-I,F) to produce the dicarboxylic acid 8a (m.p. 283-85°C; 73% yield). Reaction of 8a with CH_2N_2 gave the corresponding diester 8b (m.p. 159 - 60°C; 73% yield; NMR: δ , 2.91, s, 3H; 3.12 s, 3H; 3.03, s, 2H; 4.15-4.90, m, 4H).

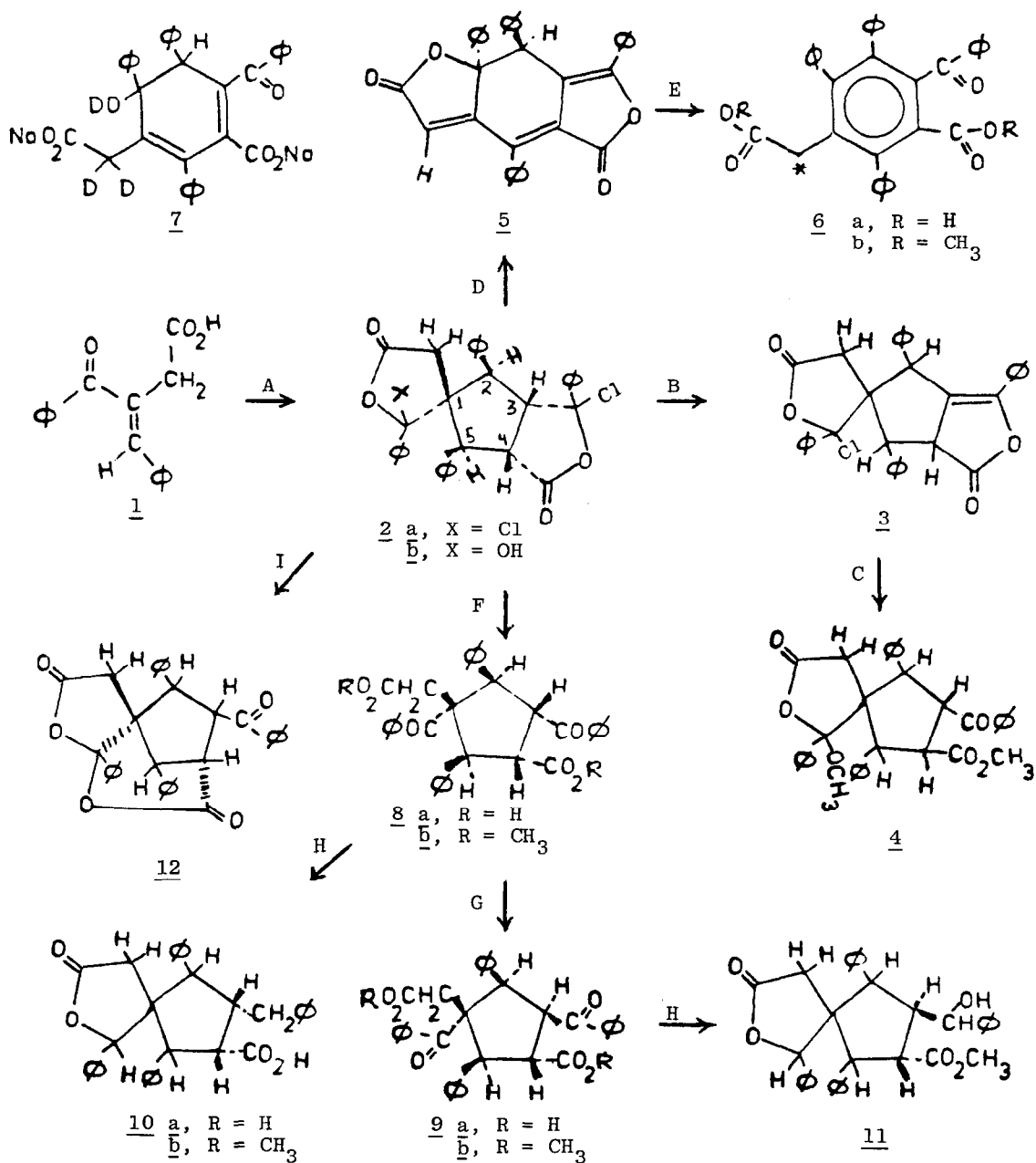
The acid 8a was epimerised at C_3 on treatment with base (Scheme-I,G) to furnish the isomeric acid 9a (m.p. 318-20°C, 80% yield). The reaction of acid 9a with CH_2N_2 afforded the corresponding methyl ester 9b (m.p. 175-77°C; NMR: δ , 2.47, 2.63, ABq, $J = 18$ Hz, 2H; 3.0, s, 3H; 3.5, s, 3H; IR: 1748, 1689 cm^{-1}). The spin-spin coupling of the C_3 and C_4 protons in both cis and trans isomers of this heavily substituted five membered ring are of the same magnitude⁶.

The establishment of the stereochemistry of C_3 and C_4 in esters 8b and 9b is based on the following observations. Catalytic hydrogenation of 8b (Scheme-I,H) results in the formation of the lactonic acid 10a (m.p. 275-77°C), indicating a cis relationship of the substituents at C_3 and C_4 . Esterification of 10a with CH_2N_2 furnished the ester 10b (m.p. 204-06°C; IR: 1785, 1739 cm^{-1} ; NMR: δ , 3.40, s, 3H; 5.50, s, 1H). The trans isomer 9b however, on similar reduction gave rise to the hydroxyester 11 (m.p. 221-22°C; 58% yield; IR: 3597, 1786, 1730 cm^{-1} ; NMR: δ , 5.5, s, 1H).

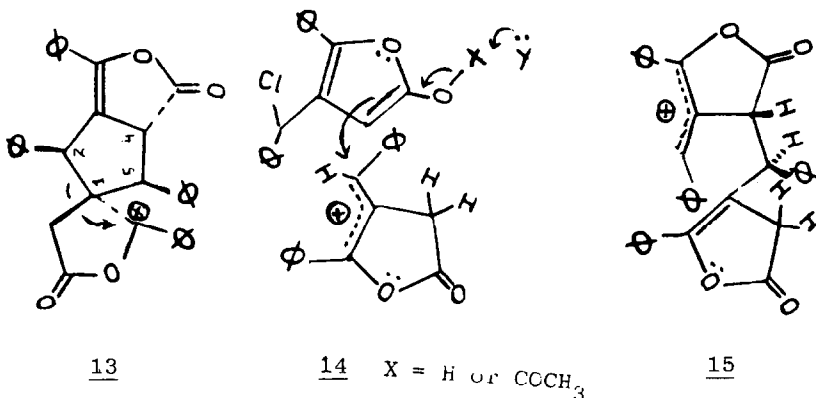
The relative orientation of C_1 and C_4 functionalities became apparent from the following experiment. Treatment of pseudo-acidchloride 2a with reagent grade pyridine (Scheme-I,I) formed, probably through the intermediacy of the hydroxylactone 2b, the spirobislactone 12 (m.p. 238-40°C; 60% yield; IR: λ max 248 nm, ϵ 13100; IR: 1808, 1783, 1684 cm^{-1} ; NMR of C_2 , C_5 dideuterated isomer of 12⁷: δ , 2.67, s, 2H; 3.96, d, $J = 6$ Hz, 1H, 5.03, d, $J = 6$ Hz, 1H). This transformation implies a cis relationship of the benzoate group at C_1 and the carbomethoxyl at C_4 .

The mechanism for the formation of the dimer 2a and the relative stereochemistry of the remaining two centers (phenyl rings at C_2 and C_5) are not elucidated at this stage. It is envisaged that the intermediates of the type 14 may be involved in the initial C-C bond formation⁸. On the basis of the assumption that allylic cation 15 is the intermediate during the cyclization process, the molecular models appear to favor the transition state that leads to the two phenyl groups at C_2 and C_5 cis to each other. Ring closure of 15 followed by addition of Cl^- and HCl would give rise to the dimer 2a⁹.

SCHEME - I



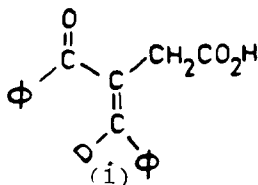
A: CH₃COCl, RT; B: C₆H₆, Δ; C: CH₃OH, Δ; D: 260°C/0.001mm.; E: 1. KOH - EtOH, Δ, 2. CH₂N₂, F: 1. CH₂Cl₂ - H₂O, RT, 2. CH₂N₂; G: 1. NaOH - H₂O, Δ, 2. CH₂N₂; H: H₂, Pd/C, CH₃OH, 60 psi; I: C₅H₅N - H₂O, RT.



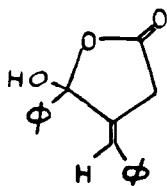
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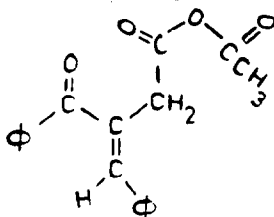
1. The correspondence regarding this work may be addressed to this author: Department of Chemistry, Columbia University, New York, New York 10027.
2. W. Borsche, Chem. Ber., 47, 1108, (1914).
3. The dimerisation also takes place with TFAc₂O, (COCl)₂, and SOCl₂. A full account of this investigation shall be reported elsewhere.
4. The NMR spectrum of the pseudo-acidchloride 2a was not obtained because of its insolubility.
5. A. Nickon, R.C. Weglein, J. Am. Chem. Soc., 97, 1271, (1975) and references therein.
6. L.E. Erickson, J. Am. Chem. Soc., 87, 1867, (1965).
7. The deuterated acid (i) was used to prepare the deuterioisotopomers at C₂ and C₅ positions of the dimeric products. It was synthesised by the condensation² of 2-benzoylpropionic acid with C₆H₅CDO (D. seeback, B.W. Erickson, G. Singh, J. Org., Chem., 31, 4303, (1966).



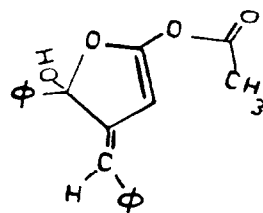
8. These intermediates may arise from the tautomeric lactol forms (ii) and (iv) of the parent acid 1 and its mixed anhydride (iii) respectively.



(ii)



(iii)



(iv)

9. All compounds gave satisfactory mass spectra (EI) and elemental analyses.