UNUSUAL INDAN-1-ONE RING CLOSURE IN A PROJECTED SYNTHESIS OF *o-ar*-JUVABIONE

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Received on April 21, 1973

ABSTRACT

Acid or base hydrolysis of 2-(3-*carbethoxy*-4-*oxo*-6-*methyl*-2-*heptyl*) *benzonitrile* (4) *gave* 3-*methylindanone, instead of the expected benzoic acid corresponding to* o-ar-*juvabione* (Ib). *A mechanism for the ring closure is outlined.*

1. INTRODUCTION

In view of the promising juvenile hormone activity of *ar*-juvabione [1] (1*a*) and other benzoic ester derivatives carrying a similar side chain [2], we recently synthesized [3] a number of analogues of *ar*-juvabione, which exhibited excellent juvenile hormone activity against *Dysdercus koenigii.*

2. PRESENT WORK

A possible scheme for the synthesis of *o-ar*-juvabione (1*b*) involved the

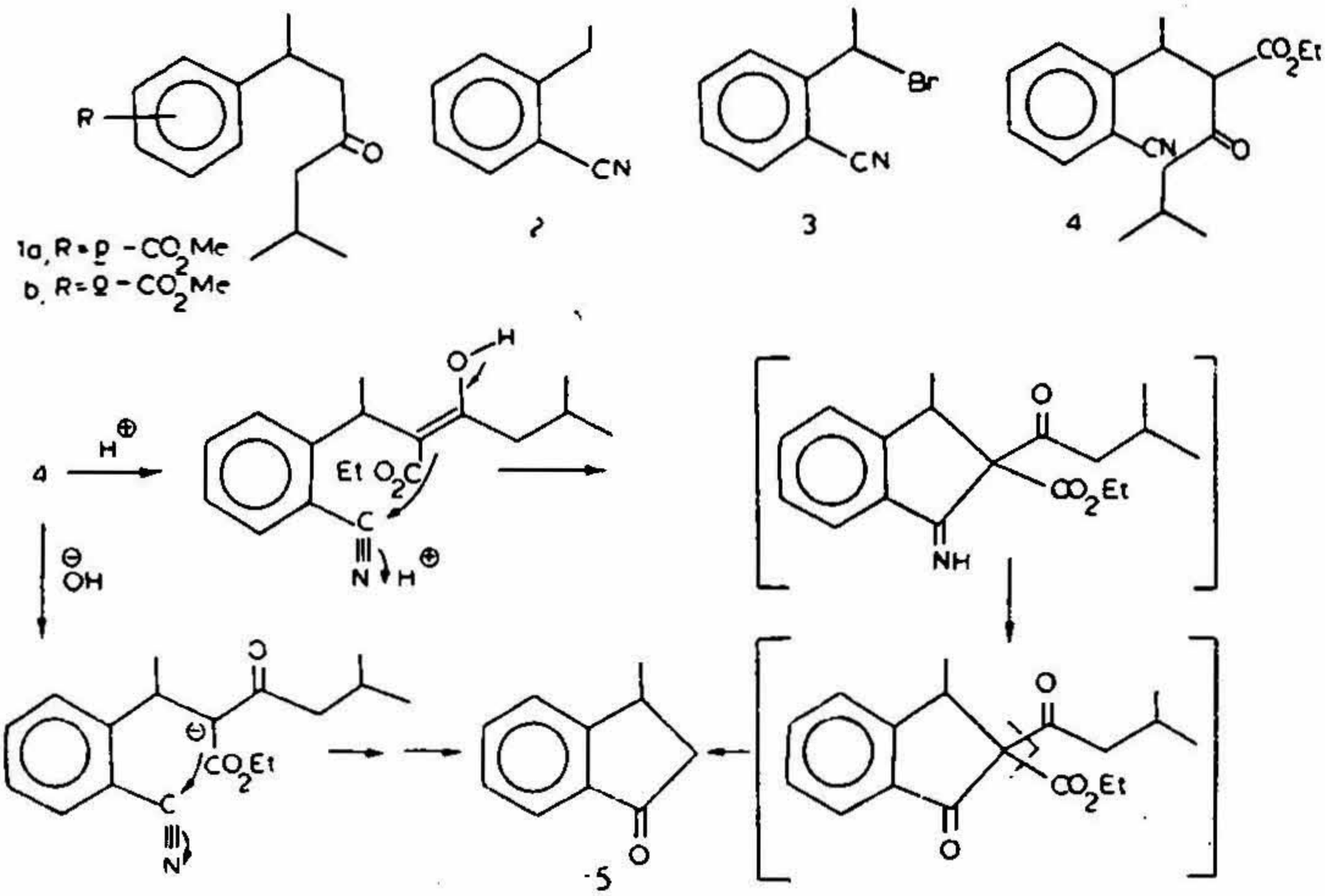
$$H\oplus \text{ or } \overset{\ominus}{O}H$$

sequence: (2) → (3) → (4) → (1*b*). However, in step (4) ⟶ (1*b*) of this scheme, which envisaged the normal hydrolysis and decarboxylation of the β-keto ester (4) with concurrent hydrolysis of the benzonitrile function, we encountered the formation of 3-methylindanone (5) (62%), which was identified by its superimposable infrared spectrum with an authentic specimen and its 2, 4-dinitrophenylhydrazone.

The suggested mechanism for the formation of the indanone (5) from (4) is depicted in the scheme. Intramolecular attack on the nitrile is presumed to lead to the observed facile ring closure followed by the predictable removal of the β-keto and ester side chain moieties. Isovaleric acid which distilled off during work-up was detected in the volatile distillate.

From these laboratories we have recently reported similar other less common indene and perhydroindane cyclizations [4] which, like the one dis-

cussed above, may not be synthetically useful, are yet sufficiently obstructive in the achievement of a desired objective.



3. EXPERIMENTAL

All m.ps are uncorrected. Bath temperatures (b.t.) are given for sublimations. After work-ups the solvent extracts were appropriately washed (neutral where necessary) and dried before removal of solvent. The instruments used for the collection of physical data are: IR (Carl-Zeiss UR-10; Perkin-Elmer infracord model 137); UV (Unicam SP-700A).

o-Ethylbenzonitrile (2)

A mixture of *o*-ethylbenzamide [5], m.p. 151–153° (6·0 g), benzene (20 ml) and thionylchloride (8·5 g) was refluxed (8 hr). The cooled reaction mixture was poured into ice-cold water and the benzene phase washed with aqueous sodium hydroxide. Stripping off of solvent and distillation of the residue gave the pure nitrile (4·76 g, 85%), b.p. 70–72°/3 mm. This procedure gave the nitrile in much better yield than the one reported in literature [6].

α-Bromoethyl-o-benzonitrile (3)

A mixture of the above nitrile (5 g), N-bromosuccinimide (7 g) and catalytic amount of benzoylperoxide in carbon tetrachloride (35 ml) was

refluxed (2 hr). The cooled reaction mixture was filtered off from succinimide and the solvent from the filtrate was distilled off giving the crude bromonitrile (8 g).

2-(3-Carbethoxy-4-oxo-6-methyl-2-heptyl) benzonitrile (4)

The crude bromonitrile (8 g) in dimethylformamide (15 ml) was added dropwise with stirring to ethyl 3-oxo-5-methyl hexanoate [7] (8·5 g) in dimethylformamide (25 ml) containing anhydrous potassium carbonate (6 g) [8]. The reaction mixture was stirred at room temperature (48 hr), added to water and acidified. Extraction with ether followed by distillation of the solvent stripped residue gave the keto ester nitrile (4) as a viscous yellow liquid, b.p. 172–174°/2 mm (Found: C, 71·7; H, 7·7; N, 4·9 $C_{14}H_{23}NO_3$ requires C, 71·8; H, 7·6; N, 4·7%). ν_{max} (liquid film) 2229 (C ≡N); 1742 (ester C=O) and 1723 cm^{-1} (ketone C=O).

Hydrolysis of (4) *to* (5)

The above keto ester nitrile (4) (8 g) was refluxed (40 hr) with concentrated hydrochloric acid (30 ml), acetic acid (30 ml) and water (15 ml). The cooled reaction mixture was poured into water (300 ml). Extraction with ether followed by distillation of the solvent stripped residue gave a mobile liquid (2·4 g, 62%), b.p. 90–91°/1·5 mm, identified as 3-methylindanone (5) (Found: C, 81·9; H, 7·0. $C_{10}H_{10}O$ requires C, 82·2; H, 6·9%). λ_{max}^{EtOH} 245 nm (ε 11680), 282 nm (ε 3200) and 292 nm (ε 3113). ν_{max} (liquid film) 1703 (C=O) and 1602 cm^{-1} (aromatic C=C). The infrared spectrum was identical in all respects with that of authentic 3-methyl indanone prepared from benzene by Friedel-Crafts reaction with crotonic acid [9]. Mixture melting point determination of the 2, 4-dinitrophenylhydrazone [m.p. 237–238° (ethyl acetate)] of the hydrolysis product of (4) with that (m.p. 238–239° [10]). of the authentic 3-methylindanone was undepressed and their infrared spectra were identical in all respects.

Hydrolysis of the keto ester nitrile (4) with methanolic sulphuric acid (7 hr) or with aqueous ethanolic sodium hydroxide (5%) (3·5 hr) also resulted in the formation of 3-methylindanone.

ACKNOWLEDGEMENTS

Financial support (Junior Research Fellowship to R. B. M.) from the University Grants Commission of India is gratefully acknowledged.

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