QUININDINES

IV.* SYNTHESIS AND PROPERTIES OF 3-ACYL DERIVATIVES OF 4-METHYL-1,2-DIHYDRO-4H-β-QUININDINES

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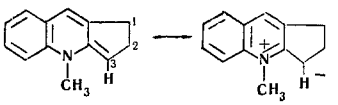
3-Acyl-4-methyl-1,2-dihydro-4H-β-quinindines (VI and III) were obtained by acylation of 1,2-dihydro-4H-β-quinindine (I), obtained from β-quinindane methiodide (IV) by the action of alkali with acid chlorides or anhydrides. The IR and UV spectra of these ketones were studied. Quaternary salt V is formed by treatment of I with excess aliphatic acid anhydride.

We have previously studied the acylation of β-quinindane through the 3-lithio derivative [2]. This communication is devoted to the synthesis and study of the properties of several 3-acyl derivatives of 4-methyl-1,2-dihydro-4H-β-quinindines. Formally speaking, 4-methyl-1,2-dihydro-4H-β-quinindine (I) has seven 2pz electrons in the pyridine ring and, to achieve the aromatic sextet, one electron should be withdrawn at the $C_{(3)}$ atom (I ⇌ II), which leads to the significant contribution of structure II. This is apparently the fundamental reason for the high reactivity (the ease of oxidation, polymerization, and electrophilic substitution at the 3 position) and the well-known instability of I [3]. The introduction of electron-accepting substituents in the 3 position should stabilize the compound as a whole.



I II

In this connection, we have obtained 3-aroyl derivatives of 4-methyl-1,2-dihydro-4H-β-quinindine (III) by the action of aroyl chlorides on I.

Starting compound I, obtained by treatment of methiodide IV with excess aqueous alkali, was extracted with ether and, without isolation, subjected to the action of acid chlorides in the presence of aqueous alkali. In the process, the 3-aroyl derivatives (IIIa-e) precipitated immediately. IIIa was also obtained by using benzoic anhydride as the acylating agent. The ketones formed are brightly colored (from yellow to dark-red), completely stable, and easily purifiable compounds (Table 1).

A reaction with the acid chloride of a fatty acid (undecanoyl chloride) was carried out since the reaction of this acid chloride with water proceeds slowly. This reaction yielded a crystalline, salt-like compound with empirical formula $C_{35}H_{54}INO_2$. The IR spectrum of this compound contained bands from the ester carbonyl (1768 cm^{-1}) and C=C groups (1653 cm^{-1}), while the UV spectrum displayed a shift in these bands to the long-wave region as compared with the spectrum of β-quinindane methiodide. When excess alkanoyl chloride is present the reaction probably does not stop at the monoketone stage (III) but forms V as a water-insoluble, quaternary salt.

*See [1] for communication III.

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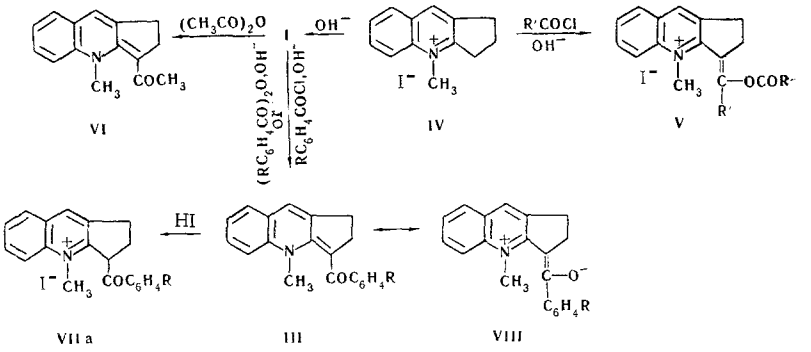
TABLE 1. 3-Aroyl Derivatives of 4-Methyl-1,2-dihydro-4H-β-quinindine (IIIa-e)

Compound	mp (dec.) (crystallization solvent)	R_s	Empirical formula	Found, %			Calculated, %			Yield, %
				C	H	N	C	H	N	
III a	193—194 (Alcohol)	0,94	$C_{20}H_{17}NO$	83,5	5,9	—	83,6	5,9	—	81
III b	199—200 (Alcohol)	1,02	$C_{20}H_{16}ClNO$	74,7	4,7	—	74,8	5,0	—	74
III c	188—189 (Dioxane)	0,92	$C_{20}H_{16}N_2O_3$	72,7	5,0	8,7	72,3	4,7	8,4	Quantitative
III d	178—179 (Alcohol)	0,89	$C_{21}H_{19}NO$	83,9	5,8	4,7	83,7	6,3	4,7	65
III e	197—197,5 (Alcohol)	0,78	$C_{21}H_{19}NO_2$	79,4	6,0	4,2	79,5	6,0	4,4	79



R'=$CH_3(CH_2)_9$; a R=H; b R=*m*-Cl; c R=p-NO_2; d R=p-CH_3; e R=p-OCH_3

Compound I can also be acylated in an anhydrous medium. Heating of methiodide IV with benzoyl chloride in acetone in the presence of triethylamine leads to a 70% yield of IIIa. Similarly, 3-acetyl-4-methyl-1,2-dihydro-4H-β-quinindine (VI) is formed by the action of acetyl chloride in the cold, but acylation proceeded more slowly by heating methiodide IV with acetic anhydride in the presence of triethylamine.

Ketones IIIa-e and VI are converted to quaternary salts by acids; this is accompanied by decoloration of the solutions. Thus a colorless methiodide of 3-benzoyl-β-quinindane (VIIa) was obtained by treatment of IIIa with potassium iodide in acetic acid; its UV spectrum was similar to the UV spectrum of 3-benzoyl-β-quinindane [2] in acid.

A number of systematically observed bands can be noted in the IR spectra of ketones III in mineral oil: 1400-1600 cm^{-1}, 1420-1425 cm^{-1} (medium-strong), 1500-1520 (very strong), and 1590-1600 cm^{-1} (medium) (Table 2). These bands can be assigned to the β-acylenamine grouping since bands $\left(\rangle N-\underset{|}{C}=\underset{|}{C}-COR\right)$, were observed at 1530-1570 and 1640-1680 cm^{-1} for β-amino-substituted α,β-unsaturated ketones containing a similar grouping. As compared with these aminoketones, the absorption bands for ketones III are shifted by an average of 40-60 cm^{-1} to the long-wave region. This can be explained by the greater (in the case of III) contribution of dipolar structure VIII. As would be expected, one observes a shift in the absorption bands to higher frequencies (by ~10-20 cm^{-1}) for acetyl derivative VI. The band at 1500-1520 cm^{-1} can be assigned to vibrations of the carbonyl group, since it is the most intense and more subject to structural effects than the others (Table 2). The usual carbonyl band at 1689 cm^{-1} is observed in the IR spectrum of methiodide VIIa. The UV spectra of ketones III and VI contain a characteristic, very intense absorption in the visible region (455-480 nm), while this maximum for p-nitrobenzoyl derivative IIIc is shifted to longer wavelengths, and a hypsochromic shift is observed for acetyl derivative VI.

EXPERIMENTAL

3-Aroyl-4-methyl-1,2-dihydro-4H-β-quinindines (IIIa-e). 1) Ether (5 ml) and 2.5 ml of 10% sodium hydroxide were added to a suspension of 2 mmole of β-quinindane methiodide (IV) [5] in 5 ml of water. The

TABLE 2. IR and UV Spectra of 3-Acyl Derivatives of 4-Methyl-1,2-dihydro-4H-β-quinindines

Compound	λ_{max}, nm (log ε), in alcohol	Band frequencies (1400-1650), cm^{-1} (mineral oil)
III a	230 (4,42); 265 (4,08); 320 (pl) (3,65); 455 (4,40)	1420 m, 1434 m, 1450 s, 1500 v.s, 1560 m, 1595 m, 1640 w
III b	230 (4,41); 270 (3,97); 325 (3,61); 457 (4,42)	1420 s, 1440 m, 1460 w, 1510 s, 1560 m, 1595 m, 1647 w
III c	222 (4,45); 252 (4,10); 270 (4,19); 320 (3,87); 480 (4,33)	1420 s, 1460 w, 1490 s, 1520 v.s, 1558 s, 1590 m, 1638 w,
III d	230 (4,44); 268 (4,14); 330 (pl) (3,65); 455 (4,42)	1423 m, 1440 w, 1454 w, 1518 s, 1567 m, 1598 m, 1644 w,
III e	231 (4,51); 274 (4,12); 295 (4,07); 335 (3,80); 455 (4,45)	1425 w, 1460 w, 1515 v.s, 1567 m, 1583 m, 1600 m, 1650 w,
VI	226 (4,55); 270 (3,73); 317 (3,84); 437 (4,30)	1430 s, 1440 m, 1460 m, 1525 v.s, 1577 w, 1613 s, 1655 w

mixture was stirred under argon for 10 min, and 4 mmole of the substituted benzoyl chloride was added. IIIa-e precipitated after 10 min. The ketones were chromatographed in a thin layer of aluminum oxide in a dichloroethane-acetone system (4:1) (Table 1). The reference spot was β-quinindane with R_f 0.8.

2) A mixture of 0.62 g (2 mmole) of IV, 3 ml of acetone, 3 ml of triethylamine, and 0.46 ml (4 mmole) of benzoyl chloride was stirred under argon at 40° for 40 min. The resulting precipitate was filtered to give 0.4 g (70%) of IIIa with mp 193-193.5°.

3) Ether (5 ml), 10 ml of water, and 3.5 ml of 10% sodium hydroxide were added under argon to a suspension of 0.93 g (3 mmole) of IV. After 10 min, a solution of 1.36 g (6 mmole) of benzoic anhydride in 5 ml of ether was added. The resulting mixture was stirred for 1 h, and the precipitate was filtered to give 0.6 g (70%) of IIIa.

3-(α-Undecanoyloxyundecalidene)-β-quinindane methiodide (V). Chloroform (15 ml) and a solution of 0.84 g (21 mmole) of sodium hydroxide in 15 ml of water were added under argon to a suspension of 1.86 g (6 mmole) of IV in 15 ml of water. After 10 min, 2.45 g (12 mmole) of undecanoyl chloride was added. After 1 h, the chloroform layer was separated, and the oil after removal of the solvent was triturated with ether to give 1.18 g of V with mp 136-138° (dec., from alcohol). Found %: C 65.4; H 8.4; I 19.1; N 2.4. $C_{35}H_{54}INO_2$. Calc. %: C 65.2; H 8.3; I 19.6; N 2.2. UV spectrum (alcohol), λ_{max}, nm (log ε): 215 (4.58), 247 (4.32), 273 (3.91), 296 (3.22), 373 (4.35).

3-Acetyl-4-methyl-1,2-dihydro-4H-γ-quinindine (VI). Acetic anhydride (5 ml) was added under argon to a suspension of 1.24 g (4 mmole) of β-quinindane methiodide (IV) in 6 ml of triethylamine. The mixture was heated at 60° for 40 min. The solution was acidified with 10% hydrochloric acid to pH 1 and extracted with chloroform. Alkalization of the aqueous layer and extraction with ether yielded (after drying and distillation of the solvent) 0.35 g of VI with mp 101-103° (from ether).

The chemical shifts (in the δ scale) in the PMR spectrum of VI (in $CDCl_3$, relative to tetramethylsilane) were as follows: $C_{(9)}$ 6.83 ppm (singlet); N-CH_3 3.52 ppm (singlet); CH_3CO 2.21 ppm (singlet); a symmetrical multiplet centered at 2.91 ppm from the four methylene protons attached to $C_{(1)}$ and $C_{(2)}$, and a multiplet from the aromatic protons attached to $C_{(5)}$, $C_{(6)}$, $C_{(7)}$, and $C_{(8)}$ at 6.9-7.3 ppm. Found %: C 79.6; H 6.5; N 6.2. $C_{15}H_{15}NO$. Calc. %: C 80.0; H 6.7; N 6.2.

3-Benzoyl-β-quinindane Methiodide (VIIa). A solution of 0.16 g of potassium iodide in 1 ml of 80% acetic acid was added to a solution of 0.29 g of IIIa in 1.5 ml of 80% acetic acid. The resulting precipitate was filtered to give 0.34 g (83%) of methiodide VIIa with mp 215-216° (dec., from alcohol). Found %: C 57.5; H 4.3; I 30.7; N 3.7. $C_{21}H_{20}INO$. Calc. %: C 57.8; H 4.3; I 30.6; N 3.4. UV spectrum in alcohol with added HCl, λ_{max}, nm (log ε): 330 (4.26), 238 (4.72).

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