Anal. Calcd. for $C_{48}H_{50}N_8SiO_2$: C, 72.14; H, 6.31; Si, 3.52. Found: C, 72.38; H, 6.59; Si, 3.79.

Bis(1-octyloxy)phthalocyaninosilicon, $PcSi(OC_8H_{17})_2$, was put on a melting point block (Fisher-Johns) at 200° and then heated slowly. At 260° a green liquid phase appeared but upon continued heating the liquid turned violet and became solid. Infrared spectra indicated that this product contained $(PcSiO)_x$ and $PcSi(OC_{18}H_{37})_2$.

Bis(1-octadecyloxy)phthalocyaninosilicon, $PcSi(OC_{18}H_{37})_2$.—A mixture of 0.40 g. of $PcSi(OH)_2$, 5.6 g. of 1-octadecanol, and 40 ml. of tetrahydronaphthalene was refluxed for 1 hr., filtered, cooled to −20° for 1 hr., allowed to stand at room temperature for 0.5 hr., and diluted with 20 ml. of ether and 10 ml. of ethanol. This gave 0.57 g. of product. A 9.0-ml. portion of benzene was used to recrystallize 0.28 g. yielding almost no residue and 0.25 g.

Anal. Calcd. for $C_{68}H_{90}N_8SiO_2$: C, 75.65; H, 8.40; Si, 2.60. Found: C, 75.66; H, 8.84; Si, 2.80.

It melted at 152–153° in a sealed tube without decomposition.

Properties.—The dialkoxides were treated with hot hydrochloric acid to determine their acid stability. All but the trichlorethanol derivative were subjected to concentrated hydrochloric acid on a steam bath while it was refluxed with 6 *N* hydrochloric acid. In each case $PcSi(OH)_2$ was obtained as the product. The stability of the dialkoxides to the action of base was measured by refluxing them with 2 *M* sodium hydroxide. Only $PcSi(OC_2H_5)_2$ was hydrolyzed and it was hydrolyzed only to a small extent. $PcSi(OCH_2C_6H_5)_2$ and $PcSi(OCH_2CCl_3)_2$ also were not hydrolyzed by refluxing alcoholic sodium hydroxide. The fact that neither $PcSi(OC_2H_5)_2$ nor $PcSi(OCH_2C_6H_5)_2$ could be satisfactorily vacuum sublimed because of decomposition shows the relatively low thermal stability of these dialkoxides.

Spectra.—The maxima in the visible range obtained from benzene solutions containing 2 to 4 × 10^{-6} g./ml. were $PcSi(OCH_2CCl_3)_2$, 612, 650, 679; $PcSi(OC_5H_{11})_2$, 606, 643, 673; $PcSi(OC_8H_{17})_2$, 606, 645, 674; $PcSi(OC_{18}H_{37})_2$, 606, 644, 674 mμ. In all cases the 680-mμ band was strongest.[8]

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A Re-examination of the Reaction of Certain α-Acyloxy Ketones with Ammonium Acetate, Their Conversion to the Oxazoles, and Imidazoles, and the Identification of Intermediate Products

P. P. E. STRZYBNY, T. VAN ES, AND O. G. BACKEBERG

Department of Chemistry, University of the Witwatersrand, Johannesburg, South Africa

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The reaction of four α-acyloxy ketones with ammonium acetate has been reinvestigated, the resulting oxazoles and imidazoles characterized, and the identity of an intermediate product established in two cases.

The formation and reactions of substituted oxazoles from α-acyloxy ketones have been studied by several authors.[1-3] The mechanism of their formation, together with the corresponding imidazoles by the interaction of such esters with ammonium acetate, was formulated as follows by Davidson, Weiss, and Jelling,[1] the proportion of IV and V formed varying from case to case.

Although compounds of the type II have not been isolated in such reactions, Theilig[4] suggested that they might be intermediates in the formation of oxazoles from enediol esters by reaction with ammonium acetate. It also has been shown that amides of the type III are converted to the imidazole IV by the action of ammonium acetate,[5] and to the oxazole V by phosphorus pentachloride,[6] sulfuric acid,[7] thionyl chloride,[8] and polyphosphoric acid.

Aldous, *et al.*,[2] prepared ethyl 2,4-diphenylimidazole-5-carboxylate (IVa) from ethyl α-benzoyloxybenzoylacetate (Ia) and claimed to have converted it into 2,4-diphenyloxazole-5-carboxylic acid (Vb) by refluxing with potassium hydroxide. Whereas oxazoles may be converted into imidazoles, for example by the action of formamide,[4] the reverse conversion involved in the procedure referred to has not been reported. As the oxazole referred to was required for another investigation, the procedure mentioned was repeated. Although Aldous, *et al.*, reported the formation of only imidazole IVa by the action of ammonium acetate on Ia, we obtained in addition the oxazole ethyl 2,4-diphenyloxazole-5-carboxylate (Va). Hydrolysis of the compounds IVa and Va gave the corresponding carboxylic acids IVb and Vb, respectively. Hence the reaction with potassium hydroxide merely hydrolyzed the ester group without further change to the heterocyclic structure.

These authors also prepared a number of 4-phenyl-5-methyl-2-substituted oxazoles from the corresponding esters. In three cases they reported the formation in addition of a substituted amide in the preparation of these oxazoles in which the substituent in the 2-position was phenyl, 6-quinolyl, and 2,6-dipyridyl. To these by-products they assigned the structure VI in which R″ was one of the three radicals mentioned. This is, therefore, the first case of the isolation of an intermediate compound in the preparation of oxazoles from α-acyloxy ketones. Aldous, *et al.*, did not report the formation of an imidazole during the preparation of these oxazoles, whereas we have isolated these compounds in the examples studied.

As the amides VIa and VIb are different from, but isomeric with, the postulated intermediates IIIa and IIIb it was decided to re-examine the compounds VIa and VIb. Both VIa[9] and IIIa[10,11] are known compounds and were consequently synthesized when it was found that the intermediate isolated and described by

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(2) D. L. Aldous, J. L. Reibsomer, and R. N. Castle, *ibid.*, **25**, 1151 (1960).
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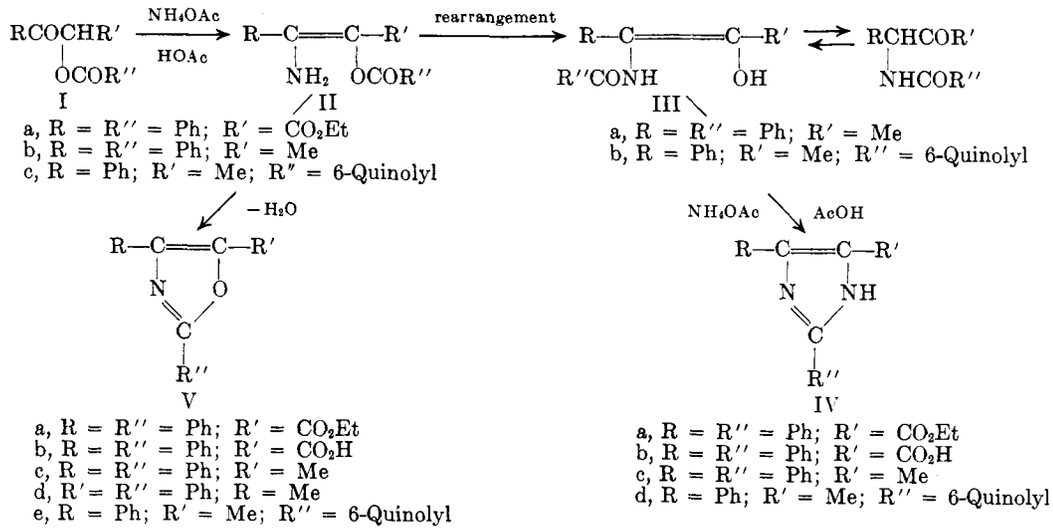

Aldous, *et al.*, as VIa proved in fact to be IIIa. Similarly, the 6-quinolyl derivative described as VIb proved to be IIIb. In the case of the corresponding 2,6-dipyridyl derivative, we were not able to isolate this product, but we suggest that, if it were formed, it would also have a structure corresponding to III. It should be noted that both III and VI would lead to the same imidazole but this is not the case in their conversion into an oxazole; III would form a 2-substituted 4-phenyl-5-methyloxazole, whereas VI would yield the isomeric 2-substituted 5-phenyl-4-methyl compound.

$C_6H_5COCHCH_3$ (NHCOR'')
a, R'' = Ph
b, R'' = 6-Quinolyl
c, R'' = 2,6-Dipyridyl
VI

Experimental[12]

Ethyl-2,4-diphenyloxazole-5-carboxylate (Va).—Ethyl-α-benzoyloxybenzoylacetate[2] (4.8 g.), ammonium acetate (9.0 g.), and acetic acid (75 ml.) were refluxed for 1 hr., after which all the solvent was removed under diminished pressure. The residue was extracted with sufficient boiling alcohol to dissolve the organic material; on cooling, Va (1.8 g., 41%) crystallized, m.p. 93–94°.

Anal. Calcd. for $C_{18}H_{15}NO_3$: N, 4.78. Found: N, 4.77.

2,4-Diphenyloxazole-5-carboxylic Acid (Vb).—This acid was obtained quantitatively by the hydrolysis of the previous ester, using the procedure described by Aldous, *et al.*[13] It crystallized from dilute alcohol, m.p. 222–223°; Aldous, *et al.*, reported m.p. 222–223°.

Anal. Calcd. for $C_{16}H_{11}NO_3$: N, 5.27. Found: N, 5.24.

2,4-Diphenylimidazole-5-carboxylic Acid (IVb).—The alcoholic mother liquor from Va was evaporated to dryness, giving crude ethyl 2,4-diphenylimidazole-5-carboxylate (1.8 g., 41%), which crystallized from dilute alcohol, m.p. 163–164°; Aldous, *et al.*, reported m.p. 166–167.5°. This ester was hydrolyzed quantitatively as previously,[13] giving the acid IVb which crystallized from dilute alcohol, m.p. 209–210° dec.

Anal. Calcd. for $C_{16}H_{12}N_2O_2$: N, 10.61. Found: N, 10.59.

Reaction of 2-Benzoyloxy-1-phenyl-1-propanone (Ib) with Ammonium Acetate.—The procedure described by Aldous, *et al.*, yielded the oxazole Vc and the by-product described, but in addition, on making the aqueous layer from the ether extraction alkaline, 2,4-diphenyl-5-methylimidazole (IVc) separated (0.6 g., 5%), which crystallized from dilute alcohol, m.p. 213–214°.[14]

Examination of the By-product.—Aldous, *et al.*, described this compound as 2-benzoylamido-1-phenyl-1-propanone (VIa), but the synthesis of this known compound[9] gave a product, m.p. 104–105°, the mixture melting point with the by-product, 80–85°. Infrared spectra of the two compounds were similar, but not identical. The known isomeric 1-phenyl-1-benzoylamidoacetone (IIIa) was then synthesized[10,11] and proved to be identical with the by-product by mixture melting point and by infrared spectra. Both the compounds, IIIa and VIa, formed the same imidazole IVc when refluxed with ammonium acetate in acetic acid solution. However, they formed known isomeric oxazoles when they were each (1 g.) heated with polyphosphoric acid (5 g.) at 160° for 10 min. (or allowed to stand overnight with 5 ml. of concentrated sulfuric acid, poured into water, and crystallized from alcohol). The compound IIIa yielded 2,4-diphenyl-5-methyloxazole (Vc) mentioned previously, m.p. 72–72.5°, whereas VIa formed 2,5-diphenyl-4-methyloxazole (Vd),[7] m.p. 83–84°.

When the ester 1-phenyl-1-benzoyloxyacetone, PhCH(OCOPh)$COCH_3$,[15] which is isomeric with Ib, was refluxed with ammonium acetate in acetic acid solution, the only product which could be isolated from the reaction was the oxazole Vd.

Reaction of 2-(6-Quinolyloxy)-1-phenyl-1-propanone (Ic) with Ammonium Acetate.—Repetition of the procedure described previously using the ester Ic (5.08 g.) yielded the oxazole Ve (2.1 g., 44%), m.p. 150–151°, together with the by-product (1.8 g., 35.6%), m.p. 195–197°, as described by Aldous, *et al.* In addition, the aqueous layer from the ether extraction was made alkaline and yielded 2-(6-quinolyl)-4-phenyl-5-methylimidazole (IVd), 0.7 g., 11.8%, which crystallized from dilute alcohol as a hydrate, m.p. 98°; crystallization from ethyl acetate–petroleum ether, gave the anhydrous compound, m.p. 254–255°.

Anal. Calcd. for $C_{19}H_{15}N_3$: N, 14.73. Found: N, 14.70.

Examination of the By-product.—With polyphosphoric acid or concentrated sulfuric acid, as described, the by-product formed the oxazole Ve, which would indicate that it was 1-phenyl-1-(6-quinolyl)amidoacetone (Ic), and this was confirmed by the following synthesis: 1-Amino-1-phenylacetone hydrochloride[16] (0.372 g., 0.002 mole) was dissolved in water (5 ml.) together with sodium acetate (2.0 g.) and 6-quinolyl chloride (0.456 g., 0.002 mole), prepared from the acid and thionyl chloride, was added. The mixture was shaken vigorously for 15 min., made alkaline with sodium hydroxide, shaken a further 5 min., and filtered. The product (0.22 g., 45%) crystallized from dilute alcohol was identical with IIIb (mixture melting point and infrared spectra). It was converted into the imidazole IVd described previously by first refluxing it (1 g.) with ammonium acetate (8 g.) and acetic acid (20 ml.) for 1 hr. The mixture was then poured into water and was made alkaline (0.9 g., 77%). The product was crystallized from ethyl acetate–petroleum ether, m.p. 254–255°.

(12) All melting points are uncorrected and were determined in an electrically heated copper block. The compounds described were all obtained as colorless microcrystals and, unless otherwise stated, yields were almost quantitative.

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Oxidation of Steroidal Ketones. III. Selenium Dioxide-Catalyzed Hydrogen Peroxide Oxidation of 4-En-3-ones[1]

E. CASPI[2] AND S. N. BALASUBRAHMANYAM

Worcester Foundation for Experimental Biology, Shrewsbury, Massachusetts

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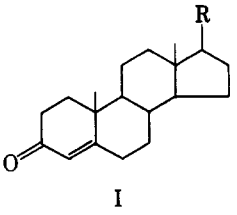
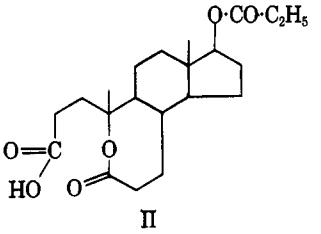
Oxidation of steroidal 4-en-3-ones with hydrogen peroxides in the presence of catalytic amounts of selenium dioxide yields products of structure II. The ϵ-lactones II can be easily rearranged to the more stable γ-lactones III. The resistence of 17β-acetyl moieties to the oxidation was confirmed.[1,3] The method is a facile and efficient route for the oxidative elimination of an α-carbon of an α,β-conjugated ketone and the formation of norseco acid lactones, II. Isolated Δ^5-bonds are converted to 5α,6β-diols.

The oxidation of cyclic stereoidal ketones to lactones with hydrogen peroxide in the presence of catalytic amounts of selenium dioxide was described in previous papers.[3-5] The acetyl moiety at C-17 resisted oxidation.[3,5] In further exploration of the reaction, the oxidations of 4-en-3-ones and of an isolated double bond at C-5 were investigated.

Oxidation of testosterone propionate (Ia) gave a syrupy residue from which the ϵ-lactone II was isolated. The lactone, m.p. 154–155°, had the formula $C_{21}H_{32}O_6$ and did not absorb ultraviolet light. Its infrared spectrum showed, among others, bands at 1750, 1730, and 1195 cm.$^{-1}$. On saponification the unstable lactone V was formed and, when recrystallized, gave the γ-lactone IIIa. Treatment of IIIa with propionic anhydride–pyridine yielded IIIb which was distinctly different from II. When IIIa was first treated with ethereal diazomethane, IIIc was obtained and on propionation gave IIId. Alternatively, IIId was prepared by esterification of IIIb with ethereal diazomethane. Attempts to prepare lactone II from V or the methyl ester analog of V failed and instead IIIb and IIIc were formed, respectively. Saponification of the syrupy mother liquor of II gave IIIa directly.



I

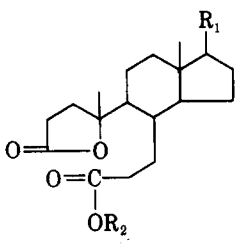


II

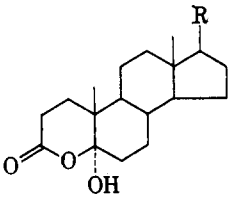
a, R = O·CO·C_2H_5

b, R = AcO—(CH$_3$)—H

c, R = CH_3·CO



III

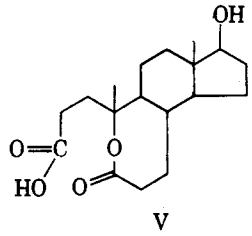


IV

a, R_1 = OH; R_2 = H
b, R_1 = O·CO·C_2H_5; R_2 = H
c, R_1 = OH; R_2 = CH_3
d, R_1 = O·CO·C_2H_5; R_2 = CH_3
e, R_1 = HO—(CH$_3$)—H; R_2 = H
f, R_1 = HO—(CH$_3$)—H; R_2 = CH_3
g, R_1 = AcO—(CH$_3$)—H; R_2 = CH_3
h, R_1 = CH_3·CO; R_2 = CH_3
i, R_1 = CH_3·CO; R_2 = H

a, R = O·CO·C_2H_5

b, R = AcO—(CH$_3$)—H



V

The structure of the seven-membered lactone II was proved by an independent synthesis. Lactol IVa was prepared by ozonolysis of testosterone propionate and then treated with acetic acid–hydrogen peroxide to yield II. Assignment of the structure rests on the documented observation that oxidation with peracids of saturated steroidal ketones in an acid medium proceeds *via* scission of the more substituted bond.[6,7] The carbonyl band[8] at 1750 cm.$^{-1}$ and the downfield shift of the C-10 methyl[9] to τ 8.64, are consistent for a seven-membered lactone and for the presence of an oxygen atom on the carbon bearing the methyl. Absence of a band in the n.m.r. ascribable to a methylene group bearing an oxygen atom supports structure II. Appearance of a carbonyl at 1770 cm.$^{-1}$

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(2) Recipient of a Public Health Career Program Award CA-K3-16614 from National Cancer Institute.

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