mg; 3.5 days, 326 mg; 4.5 days, 353 mg; 5.5 days, 331 mg; 6.5 days, 312 mg. The maximum at 4.5 days corresponded to a yield of 1.76 g/l.

3-D-Hydroxypalmitic Acid (1)

Crude acid (4.00 g, m.p. 70–80 °C) was crystallized from hexane (3.55 g, m.p. 78.8–79.8 °C). A small amount of yellow impurity (1%) was removed by charcoal. A second crystallization (200 mg) gave pure acid **1** (180 mg, m.p. 79.5–80.5 °C). $[\alpha]_D^{24}$ −13.6° (*c*, 1.3, $CHCl_3$); lit. (2), m.p. 78–79 °C, $[\alpha]_D^{25}$ −12.9° (*c*, 1.3, $CHCl_3$).

Anal. Calcd. for $C_{16}H_{32}O_3$: C, 70.54; H, 11.84. Found: C, 70.5; H, 11.9.

Methyl 3-D-Hydroxypalmitate (2)

Acid **1** (200 mg) was methylated with diazomethane. Crude ester (210 mg, m.p. 46.5–49 °C) was crystallized from hexane (160 mg, m.p. 49–49.8 °C) in fine needles. Infrared spectra of films deposited on KRS-5 plates showed hydroxyl absorption at 3390 cm^{-1} and 3300 cm^{-1} and carbonyl absorption at 1740 cm^{-1} and 1695 cm^{-1}.

Anal. Calcd. for $C_{17}H_{34}O_3$: C, 71.28; H, 11.96. Found: C, 70.9; H, 12.0.

p-Bromophenacyl 3-D-Hydroxypalmitate (3)

Acid **1** (100 mg) was converted to the *p*-bromophenacyl derivative in acetone (15 min at 70 °C) according to the DICE procedure (5). The crude product (167 mg, m.p. 108–109 °C) on crystallization from 95% ethanol gave 152 mg of *p*-bromophenacyl ester (111–111.5 °C).

Anal. Calcd. for $C_{24}H_{37}O_4Br$: C, 61.40; H, 7.94. Found: C, 61.5; H, 8.0.

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Imidazo(1,2-*a*)indole and *s*-triazolo(2,3-*a*)indole derivatives by intramolecular cyclization of 1-(*o*-acetylphenyl)azoles[1]

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9-Hydroxy-9-methyl derivatives of the ring systems named in the title are formed along with the expected 1-(*o*-acetylphenyl)azoles in the Ullmann condensations of *o*-bromoacetophenone with imidazole and with 1,2,4-triazole. The structures of these compounds follow from their characteristic proton magnetic resonance spectra.

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Common electrophilic substitution reactions with imidazole give 4(5)-substitution (1), although diazo coupling in alkaline media occurs at the 2-position (2). Reports of initial iodination at the 2-position are incorrect (3). These observations may be rationalized by assuming that 4(5)-substitution involves reaction of the conjugate acid, while 2-substitution involves the neutral molecule or the anion of imidazole (4). *N*-vinylimidazole undergoes 2-hydroxymethylation when heated with formaldehyde (5), and other *N*-substituted imidazoles undergo condensation with aldehydes to yield 2-(*N*-imidazolyl)-carbinols, while 4-alkylimidazoles give 4-alkyl-5-hydroxymethyl derivatives with formaldehyde (6).

In contrast, there is but one report classifiable as an electrophilic substitution in 1,2,4-triazoles; 4-phenyl-1,2,4-triazole is reported to undergo benzoylation in the 3-position by heating with benzoyl chloride (7). 1,2,3-Triazoles have been brominated (8) and nitrated (9) successfully.

This note reports some examples of intramolecular electrophilic substitution in imidazole and 1,2,4-triazole derivatives, leading to derivatives, of the imidazo(1,2-*a*)indole and *s*-triazolo-(2,3-*a*)indole ring systems.

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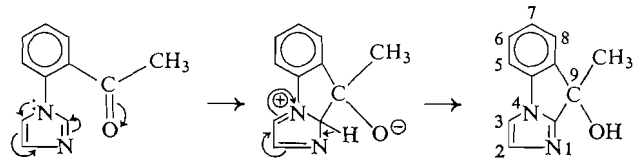

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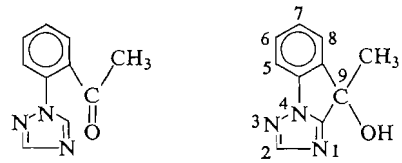

2 4

In connection with a program of synthesis of *N*-arylazoles (10), we prepared a series of 1-(*o*-acetylphenyl)diazoles and triazoles by the Ullmann condensation of the appropriate heteroaromatic compound with *o*-bromoacetophenone in pyridine solvent in the presence of copper(II) oxide and sodium carbonate. When using imidazole and 1,2,4-triazole, we isolated compounds isomeric with the expected products in addition to the azolylacetophenones **1** and **2**, and we have assigned structures **3** (9-hydroxy-9-methyl 9*H*-imidazo(1,2-*a*)indole(11)) and **4** (9-hydroxy-9-methyl-9*H*-*s*-triazolo(2,3-*a*)indole) to these compounds.

These products are formed by heating **1** and **2** under the conditions used for the Ullmann condensations, and the yield ratios **3**:**1** and **4**:**2** increase with increasing reaction times in the Ullmann reactions. The reactions almost certainly involve intramolecular electrophilic substitution, as shown for the conversion of **1** to **3**. The structures **3** and **4** are established by the following evidence: (*a*) the compounds are isomeric with the expected products **1** and **2**, yet lack any carbonyl stretching peak in the infrared spectrum, and show strong hydroxyl absorption between 3070–3160 cm^{-1}; (*b*) the proton magnetic resonance (p.m.r.) spectrum of the compound **3** in hexadeuteriodimethyl sulfoxide showed a 3-proton signal at δ 1.62 (*C*-methyl) (1-*o*-acetylphenylimidazole (**1**) showed the acetyl proton signal at δ 2.05), a broad 1-proton signal at δ 6.03 (the tertiary hydroxyl), and a 6-proton multiplet between 440 and 465 Hz (the 2-, 3-, 5-, 6-, 7-, and 8-protons). The low field signal characteristic of the 2-proton in an imidazole (cf. the 2-proton signal in 1-phenylimidazole, at δ 8.30) is absent; and (*c*) the p.m.r. spectrum of compound **4** in hexadeuteriodimethyl sulfoxide showed a 3-proton signal at δ 1.68 (C-methyl) (cf. 1-(*o*-acetylphenyl)1,2,4-triazole, acetyl protons at δ 2.20), a broad 1-proton signal at δ 6.33 (tertiary hydroxyl), a 4-proton multiplet between 435 and 462 Hz (protons 5, 6, 7, and 8 in **4**), and a 1-proton signal at δ 8.17 (proton 2 of **4**). Since the triazole ring proton signals in 1-(*o*-acetylphenyl)1,2,4-triazole fall at δ 8.20 (the 3-proton) and δ 9.00 (the 5-proton) (p.m.r. studies of various 1-aryldiazoles and -triazoles (12) confirm these assignments), it is evident that cyclization has occurred so as to occupy the position of the 5-proton of **2**.

Shirley and Alley (13) have obtained 4-oxoimidazo(1,2-*a*)indoline by dimetalation of 1-phenylimidazole followed by carbonation, so these cyclizations are not without precedent. However, these are the first examples of cyclization on to a carbon atom of a "π-electron-excessive" (14) heteroaromatic compound, and the first known examples of direct electrophilic substitution at the 5-position of 1,2,4-triazoles. Although we do not plan further work in this area, it seems likely that investigation of the thermal stability of 1-*o*-acetylphenylderivatives of other heteroaromatic compounds would be fruitful, and synthesis of fluorenol derivatives by cyclization of appropriately substituted 2-acetylbiphenyls seems promising.

Experimental

General

Analyses are by the Australian Microanalytical Service, Division of Organic Chemistry, Commonwealth Scientific and Industrial Research Organization and University of Melbourne, Parkville, Victoria, Australia.

Melting points were observed using a Gallenkamp apparatus and are uncorrected; boiling points are also uncorrected. Infrared (i.r.) spectra were recorded for the 600–3500 cm^{-1} region using a Perkin–Elmer 221 spectrophotometer. Solids were examined as mulls, and liquids as thin films. Proton magnetic resonance (p.m.r.) spectra were recorded using a Varian A-60A spectrometer fitted with a Varian V6058A Spin Decoupler, operating in the phase-lock mode. Signals are expressed in p.p.m. from tetramethylsilane, present as internal reference (for completely analyzed signals), or in Hertz (for multiplets which were not amenable to analysis). Hexadeuteriodimethyl sulfoxide was supplied by Merck, Sharp and Dohme of Canada.

Ullmann Condensations between Imidazole and o-Bromoacetophenone

(*a*) A mixture of imidazole (1.7 g), *o*-bromoacetophenone (5 g), copper(II) oxide (0.25 g), and anhydrous potassium carbonate (5 g) in pyridine (10 ml) was heated under reflux for 48 h. The reaction mixture was cooled and filtered and the residue was extracted with chloroform. Solvents were removed from the combined filtrate and extract, and the residue thus obtained was dissolved in ethanol, treated twice with charcoal, and the ethanol was removed. Crystallization of the residue from aqueous ethanol yielded 9-hydroxy-9-methyl 9*H*-imidazo(1,2-*a*)indole, 3.2 g, (65%) m.p. 182–183°.

Anal. Calcd. for $C_{11}H_{10}N_2O$: C, 71.0; H, 5.4; N, 15.1; O, 8.6. Found: C, 70.4; H, 5.5; N, 14.8; O, 9.0.

(*b*) Reaction (*a*) was repeated using a heating time of 7 h. The residue from the chloroform extract of the reaction mixture was chromatographed over alumina (Type H, Light & Co.) with benzene as eluting solvent. A small quantity of unreacted *o*-bromoacetophenone was recovered, and the eluting liquid was changed to 1:1 chloroform–benzene (v/v). Removal of solvent from the various fractions yielded 1.6 g (33%) of 1-(*o*-acetylphenyl)-imidazole as a syrupy liquid, showing ν_{CO} 1690 cm^{-1}. Found: C, 70.5; H, 5.8; N, 13.7. 1-(*o*-Acetylphenyl)imidazole formed a picrate, m.p. 185–186° (from ethanol).

Anal. Calcd. for $C_{17}H_{13}N_5O_8$: C, 49.2; H, 3.1; N, 16.9. Found: C, 49.1; H, 3.3; N, 16.6.

Further development of the chromatography column with chloroform and evaporation of the eluate yielded 2.2 g (47%), of 9-hydroxy-9-methyl 9*H*-imidazo(1,2-*a*)indole, m.p. 182–183°, identical in all respects with the product obtained in (*a*).

Thermal Cyclization of 1-(o-Acetylphenyl)imidazole

1-(*o*-Acetylphenyl)imidazole was heated for 24 h in the presence of anhydrous potassium carbonate and copper-(II) oxide in pyridine as in procedure (*a*). On working up the reaction mixture as in (*b*) above, a virtually quantitative yield of 9-hydroxy-9-methyl-9*H*-imidazo(1,2-*a*)indole, m.p. 182–183°, was obtained, identical with the product obtained in (*a*).

Ullmann Condensation Between 1,2,4-Triazole and o-Bromoacetophenone

Condensation between 1,2,4-triazole (1.73 g) and *o*-bromoacetophenone (5 g) was carried out by heating under reflux for 48 h using the general conditions described for imidazole and *o*-bromoacetophenone. The reaction mixture was cooled and filtered, and the residue was extracted with chloroform. Solvents were removed from the combined extract and filtrate and the residue thus obtained was chromatographed on alumina. Elution with benzene afforded a trace of unreacted *o*-bromoacetophenone, and elution with 1:4 chloroform–benzene (v/v), yielded 1-(*o*-acetylphenyl)1,2,4-triazole, 1.69 g (37%) m.p. 84–86°, ν_{CO} 1690 cm^{-1}. An analytical sample, m.p. 87–88°, was obtained by crystallization from chloroform–petroleum (b.p. 40–60°).

Anal. Calcd. for $C_{10}H_9N_3O$: C, 64.2; H, 4.8; N, 22.5. Found: C, 64.4; H, 4.8; N, 22.5. 1-(*o*-Acetylphenyl)1,2,4-triazole formed a picrate, m.p. 121–122° (from ethanol).

Anal. Calcd. for $C_{16}H_{12}N_6O_8$: C, 46.2; H, 2.9; N, 20.2. Found: C, 46.5; H, 3.2; N, 19.9.

Further elution with 1:1 chloroform–benzene yielded a solid, m.p. 148–151°, after removal of the eluting liquids. This material was crystallized from chloroform–petroleum (b.p. 40–60°), giving 9-hydroxy-9-methyl-9*H*-*s*-triazolo(2,3-*a*)indole, 1.07 g, (23%) m.p. 158–159°. Found: C, 63.8; H, 4.9; N, 22.7.

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