949. *Acyl Derivatives of 2-Oxobenzimidazoline.*

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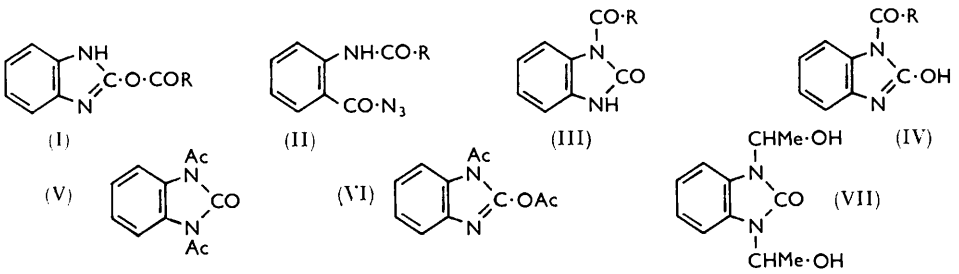
The structures of some mono- and di-acyl derivatives of 2-oxobenzimidazoline have been re-examined and some errors corrected. The ultraviolet and infrared spectra of these compounds are briefly considered.

MONOACETYL and monobenzoyl derivatives of 2-oxobenzimidazoline (2-hydroxybenzimidazole) were prepared by Heller *et al.*[1] by the reaction of the silver salt of 2-oxobenzimidazoline with the corresponding acid chloride, and formulated as (I; R = Me or Ph). We have prepared the same monoacetyl derivative by heating 2-oxobenzimidazoline with acetic anhydride and by thermal decomposition of the azide (II; R = Me) in xylene. The known benzoyl compound was similarly obtained from the benzoyl azide (II; R = Ph), and we conclude that these derivatives are 1-acyl-2-oxobenzimidazolines (III; R = Me or Ph) or the tautomeric 1-acyl-2-hydroxybenzimidazoles (IV). The acyl azides (II) were prepared by the action of the acid chloride in pyridine on *o*-aminobenzazide; the benzoyl azide was also prepared from methyl *o*-benzamidobenzoate *via* the hydrazide.



By the action of acetyl chloride in pyridine on 2-oxobenzimidazoline, and in other ways, Heller *et al.*[1] prepared 1,3-diacetyl-2-oxobenzimidazoline (V). The formation of an isomeric compound (VI) by boiling " benzimidazole oxide " with acetic anhydride is also recorded.[2] We have repeated both preparations and obtained identical products. The diacetyl derivative is conveniently prepared by boiling a solution of 2-oxobenzimidazoline in acetic anhydride for a longer time than used in the preparation of the monoacetyl compound. If Heller's formulation is correct, reduction of the diacetyl compound could yield either 1,3-bis-1'-hydroxyethyl-2-oxobenzimidazoline (VII) or 1,3-diethyl-2-oxobenzimidazoline. With lithium aluminium hydride in boiling ether or tetrahydrofuran, the reduction appeared to proceed satisfactorily, but the only isolable product was 2-oxobenzimidazoline. It is not clear whether the N–C bond is broken in the reduction or during the working up. Attempts to prepare the bishydroxyethyl compound (VII) from 2-oxobenzimidazoline and acetaldehyde failed. The corresponding bishydroxymethyl compound is easily prepared,[3] but is decomposed by dilute alkali. 1,3-Diethyl-2-oxobenzimidazoline, whose structure is deduced from a comparison of its ultraviolet and infrared spectra with those of the known 1,3-dimethyl compound, was obtained from 2-oxobenzimidazoline and diethyl sulphate in sodium hydroxide solution, but attempts to oxidise it to a 1,3-diacetyl compound were unsuccessful.

The 1,3-diacyl formulation was finally deduced by the following indirect method. A monopropionyl derivative was prepared from 2-oxobenzimidazoline and assigned a 1-acyl structure on account of the close similarity of its ultraviolet spectrum to that of

[1] Heller, Buchwaldt, Fuchs, Kleinicke, and Kloss, *J. prakt. Chem.*, 1925, **111**, 1.
[2] Montanari and Risaliti, *Gazzetta*, 1953, **83**, 278.
[3] Monti and Venturi, *Gazzetta*, 1946, **76**, 364.

the 1-acetyl compound. On boiling this 1-propionyl derivative with acetic anhydride the acetyl-propionyl compound obtained was identical with that obtained by boiling 1-acetyl-2-oxobenzimidazoline with propionic anhydride. Since under these conditions migration of acyl groups may have occurred, the second acyl group was also introduced by using acetyl or propionyl chloride in cold pyridine, but the result was the same. Hence the acetyl-propionyl compound must have the 1,3-diacyl structure. Since the ultraviolet spectra of the diacetyl, dipropionyl, and acetyl-propionyl compounds are almost identical, it is concluded that these three compounds have similar structures. Experiments of this type were also carried out with acetyl-benzoyl compounds.

The ultraviolet spectra of simple benzimidazoles are characterised in the region 260—290 mμ by a group of three maxima, the first sometimes only appearing as an inflection, but the other two being very sharply marked. Substituents in the 1- and the 2-position leave the basic pattern unchanged.[4,5] The details of the spectra of a number of 1,3-disubstituted 2-oxobenzimidazolines are included in the Table; they show a single broad

Ultraviolet absorption spectra of 2-oxobenzimidazolines in ethanol

1-Subst.	3-Subst.	$\lambda_{max.}$ (mμ) (log ε in parentheses)
H	H	225·5 (3·86); 280 (3·88)
Me	Me	232 (3·82); 283 (3·88); 287 (3·83) *
Et	Et	233 (3·82); 284 (3·88); 288 (3·82) *
CH_2Cl	CH_2Cl	226 (3·88); 279 (3·80); 284 (3·76) *
CH_2·OH	CH_2·OH	227 (3·88); 280 (3·85); 285 (3·80) *
CH_2·N$<$$[CH_2]_5$	CH_2·N$<$$[CH_2]_5$	226 (3·87) *; 281·5 (3·84)
H	Ac	220 (4·40); 253 (3·74); 277·5 (3·48)
H	CO·Et	220 (4·40); 251·5 (3·78); 278 (3·56)
H	Bz	244·5 (4·31); 275 (3·78); 283 (3·73) *
Ac	Ac	237 (4·12); 272 (3·36); 280 (3·30)
CO·Et	CO·Et	237 (4·13); 273 (3·41); 281 (3·34)
Ac	CO·Et	236 (4·14); 272·5 (3·38); 280·5 (3·30)
Ac	Bz	247 (4·30)

* Inflection.

maximum near 280 mμ. With diacetyl-2-oxobenzimidazoline, conjugative interaction of the acetyl groups with the ring system complicates the situation, and the spectrum has two broad maxima at 272 and 282 mμ (ε approximately one-third of its value for the reference compounds). Nevertheless, the difference from the benzimidazole-type spectrum supports the 1,3-diacetyl structure.

The infrared spectra of the mono- and the di-acyl-2-oxobenzimidazolines were determined originally to assist in the determination of their structure, but interpretation proved to be difficult. The amide I band in 2-oxobenzimidazoline itself [6] is at an abnormally high frequency compared with that of the 1,3-dimethyl and 1,3-diethyl compounds, and with certain substituted 2-oxoimidazolines.[7] In the spectra of 1-acetyl-2-oxo- and 2-oxo-1-propionyl-benzimidazoline there are two strong bands in the 1700—1750 $cm.^{-1}$ region, but these are probably better regarded as associated with the –CO·N·CO·NH– system as a whole than as separate carbonyl stretching frequencies. A strong band near 3180 $cm.^{-1}$ in these compounds can be assigned to N–H stretching (hydrogen-bonded), but the origin of other bands in this region is less certain since C–H frequencies are possible near 3000 $cm.^{-1}$. The presence of the N–H band is, however, strong evidence against structures such as (IV). The spectra of the 1,3-diacyl compounds contained two or three strong bands between 1700 and 1770 $cm.^{-1}$ but again assignment to specific carbonyl groups is of doubtful validity.

[4] Efros and Eltsov, *Zhur. obschei Khim.*, 1957, **27**, 684.
[5] Leandri, Mangini, Montanari, and Passerini, *Gazzetta*, 1955, **85**, 769.
[6] Harrison and Smith, *J.*, 1959, 3157.
[7] Gompper and Herlinger, *Chem. Ber.*, 1956, **89**, 2825.

Experimental

Infrared spectra were determined in potassium bromide discs, and only strong bands in the regions 1650—1800 cm.$^{-1}$ and 3000—3500 cm.$^{-1}$ are recorded.

o-*Acetamidobenzazide*.—Acetyl chloride (0·4 ml.) was added to a stirred solution of *o*-aminobenzazide [8] (0·65 g.) in pyridine (1·5 ml.). After 15 min., addition of water (10 ml.) precipitated a solid which was collected, washed with water, and dried *in vacuo* (0·63 g., 77%). Recrystallisation from ethanol (N.B. overheating must be avoided) gave o-*acetamidobenzazide* as colourless needles, m. p. 84—85° (Found: C, 53·0; H, 3·9; N, 27·8. $C_9H_8N_4O_2$ requires C, 52·9; H, 3·95; N, 27·4%).

o-*Benzamidobenzhydrazide*.—A mixture of methyl *o*-benzamidobenzoate (12·7 g.), ethanol (75 ml.), and 98% hydrazine hydrate (15 ml.) was boiled under reflux for 30 min. On cooling, the hydrazide separated as a white solid (10·3 g., 81%); after recrystallisation from ethanol it had m. p. 183—185° (lit.,[9] 176°) (Found: C, 65·8; H, 5·4; N, 16·9. Calc. for $C_{14}H_{13}N_3O_2$: C, 65·9; H, 5·1; N, 16·5%). As the m. p. of the cyclized product 3-amino-3,4-dihydro-4-oxo-2-phenylquinazoline is given as 184—186° [9] and as 178—179°,[10] a mixed m. p. determination was necessary to show that cyclization had not occurred; a depression of 10° was observed.

o-*Benzamidobenzazide*.—(*a*) To a solution of *o*-benzamidobenzhydrazide (5·1 g.) in 1·5N-hydrochloric acid (175 ml.), 10% aqueous sodium nitrite (16 ml.) was added. The gummy precipitate was collected after 30 min., washed with water (4 × 20 ml.), dried, and recrystallised cautiously from ethanol to give o-*benzamidobenzazide* (2·6 g., 48%) as yellow needles, m. p. 108—110° (decomp.) (Found: C, 62·8; H, 4·1; N, 21·3. $C_{14}H_{10}N_4O_2$ requires C, 63·1; H, 3·7; N, 21·0%).

(*b*) By a method similar to that used for *o*-acetamidobenzazide, *o*-aminobenzazide was benzoylated, giving a product, m. p. 108—110° (decomp.) not depressed on admixture with a sample prepared by method (*a*).

1-*Acetyl*-2-*oxobenzimidazoline*.—(a) *From* 2-*oxobenzimidazoline*. 2-Oxobenzimidazoline (1 g.) was boiled under reflux for 30 min. with acetic anhydride (6 ml.). After addition of water (20 ml.), further boiling (10 min.), and cooling, the crude product was collected, washed with water (3 × 5 ml.), and dried. Recrystallisation from benzene gave the 1-acetyl derivative (0·74 g., 56%), m. p. 205—207° (lit.,[1] 205°), $\nu_{max.}$ 3180, 3100, 3050, 1740, 1709 cm.$^{-1}$.

(b) *From* o-*acetamidobenzazide*. A solution of the azide (0·07 g.) in xylene (1 ml.) was kept at 100° for 30 min., then cooled, and the solid was collected, washed with ether, and dried, to give 1-acetyl-2-oxobenzimidazoline (0·04 g.), m. p. 204—207°, not depressed by samples prepared either by method (a) above or from the silver salt of 2-oxobenzimidazoline.[1]

2-*Oxo*-1-*propionylbenzimidazoline*.—Modification of the method used for the 1-acetyl compound was necessary in order to avoid extensive dipropionylation. The following procedure gave only moderate yields. 2-Oxobenzimidazoline (5·42 g.), water (4 ml.), and propionic anhydride (33 ml.) were mixed and heated for 15 min. under reflux at 140—150°. More propionic anhydride (5 ml.) was then added and the bath temperature raised to 170—180° for 15 min. Cooling and pouring the mixture into water (300 ml.) afforded a solid of indefinite m. p. This was boiled with benzene (100 ml.), insoluble matter was filtered off, and the filtrate concentrated to give the required *propionyl derivative* (1·37 g., 18%), m. p. 173—175°, raised by recrystallisation from benzene to 181—183°, $\nu_{max.}$ 3180, 3100, 1737, 1716 cm.$^{-1}$ (Found: C, 63·0; H, 5·5; N, 15·0. $C_{10}H_{10}N_2O_2$ requires C, 63·1; H, 5·3; N, 14·7%).

1-*Benzoyl*-2-*oxobenzimidazoline*.—A solution of *o*-benzamidobenzazide (1·25 g.) in xylene (20 ml.) was boiled under reflux for 30 min. The solid which separated on cooling was washed with ether and recrystallised from benzene, to give 1-benzoyl-2-oxobenzimidazoline (0·84 g., 75%), m. p. 198—200° (lit.,[1] 205°), $\nu_{max.}$ 3190, 3115, 1730, 1692 cm.$^{-1}$. The m. p. was not depressed on admixture with a sample prepared from the silver salt of 2-oxobenzimidazoline.[1]

1,3-*Diacetyl*-2-*oxobenzimidazoline*.—2-Oxobenzimidazoline (1 g.) was boiled under reflux for 4 hr. with acetic anhydride (6 ml.). On cooling, the diacetyl derivative separated (1·15 g., 71%), forming needles (from ethanol), m. p. 149—151°, $\nu_{max.}$ 1770, 1724 cm.$^{-1}$. Samples were also prepared (*a*) from 2-oxobenzimidazoline and acetyl chloride in pyridine [1] (lit., m. p. 149°)

[8] Heller and Siller, *J. prakt. Chem.*, 1926, **116**, 9.
[9] Hirwe and Kulkarni, *Proc. Indian Acad. Sci.*, 1942, **16**, *A*, 294.
[10] Heller, *Ber.*, 1915, **48**, 1191.

and (*b*) by boiling benzimidazole *N*-oxide [11] with acetic anhydride [2] (lit., m. p. 154—155°). By determinations of mixed m. p. and ultraviolet spectra the samples were shown to be identical.

2-Oxo-1,3-dipropionylbenzimidazoline.—2-Oxobenzimidazoline (1 g.) was heated for 30 min. with propionic anhydride (6 ml.) in a bath at 140—160°. The solid which separated on cooling (1·55 g., 84%) afforded *2-oxo-1,3-dipropionylbenzimidazoline* (needles from ethanol), m. p. 167—169°, $\nu_{max.}$ 1758, 1731, 1718sh cm.$^{-1}$ (Found: C, 63·4; H, 5·8; N, 10·5. $C_{13}H_{14}N_2O_3$ requires C, 63·4; H, 5·7; N, 11·3%).

1-Acetyl-2-oxo-3-propionylbenzimidazoline.—A stirred solution of 1-acetyl-2-oxobenzimidazoline (0·2 g.) in pyridine (3 ml.) was cooled in an ice-bath and treated with propionyl chloride (0·3 ml.). After 10 min., water (15 ml.) was added and the solid collected. Recrystallisation from ethanol gave *1-acetyl-2-oxo-3-propionylbenzimidazoline* (0·14 g., 40%) as colourless needles, m. p. 151—152°, $\nu_{max.}$ 1757, 1733, 1716sh cm.$^{-1}$ (Found: C, 62·3; H, 5·4; N, 11·7. $C_{12}H_{12}N_2O_3$ requires C, 62·1; H, 5·2; N, 12·1%). Samples were also prepared from 2-oxo-1-propionylbenzimidazoline (*a*) by reaction with acetyl chloride in pyridine, and (*b*) by heating it with acetic anhydride at 130—140° for 1 hr. The three samples were shown to be identical in the usual way.

1-Acetyl-3-benzoyl-2-oxobenzimidazoline.—The method used for the 1-acetyl-3-propionyl compound, but with benzoyl chloride in place of propionyl chloride, afforded *1-acetyl-3-benzoyl-2-oxobenzimidazoline* (needles from ethanol), m. p. 167—169°, $\nu_{max.}$ 1759, 1720, 1707 cm.$^{-1}$ (Found: C, 68·6; H, 4·3; N, 9·9. $C_{16}H_{12}N_2O_3$ requires C, 68·6; H, 4·3; N, 10·0%). An identical product was obtained from 1-benzoyl-2-oxobenzimidazoline and acetyl chloride in pyridine.

1,3-Diethyl-2-oxobenzimidazoline.—A mixture of 2-oxobenzimidazoline (5 g.), 10% aqueous sodium hydroxide (40 ml.), and diethyl sulphate (12 ml.) was boiled under reflux for 3 hr. More sodium hydroxide (10 g.) was then added and heating continued for a further 30 min. Addition of water (75 ml.) and extraction with benzene (3 × 50 ml.) furnished an oil (4·43 g., 62·4%). This was distilled, and the fraction of b. p. 92—100°/0·3 mm. crystallised. Recrystallisation from light petroleum (b. p. 60—80°) gave *1,3-diethyl-2-oxobenzimidazoline*, m. p. 67—71°, $\nu_{max.}$ 1693 cm.$^{-1}$ (Found: C, 69·4; H, 7·4; N, 14·5. $C_{11}H_{14}N_2O$ requires C, 69·5; H, 7·4; N, 14·7%).

Other Compounds.—The following were prepared by recorded methods:

1,3-Dimethyl-2-oxobenzimidazoline, m. p. 107—109° (lit.,[12,13] 107·5° and 106·5—107°), $\nu_{max.}$ 1690 cm.$^{-1}$.

1,3-Bishydroxymethyl-2-oxobenzimidazoline, m. p. 156—159° (lit.,[3,12] 164—165° and 165°). The unexpected solubility of this compound in dilute aqueous sodium hydroxide, noted by Monti and Venturi,[3] was confirmed. It is probably due to reversible decomposition into formaldehyde and 2-oxobenzimidazoline, since the ultraviolet spectrum of the hydroxymethyl compound in 0·1N-sodium hydroxide was identical with that of 2-oxobenzimidazoline in the same solvent.

1,3-Bischloromethyl-2-oxobenzimidazoline, m. p. 168—171° [lit.,[12] 167° (decomp.)].

2-Oxo-1,3-bispiperidinomethylbenzimidazoline, m. p. 125—127° (lit.,[12] 125°).

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[11] Niementowski, *Ber.*, 1910, **43**, 3012.
[12] Zinner and Spangenburg, *Chem. Ber.*, 1958, **91**, 1433.
[13] Efros, Poras-Koshits, and Farbenstein, *Zhur. obschei Khim.*, 1953, **23**, 169.