Amino-oxy-derivatives. Part VII.[1] Some 5,6-Dihydro-5-oxo-3-phenyl-1,4-dioxazines

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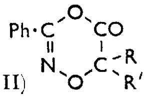
Cyclisation of α-benzamido-oxy-acids with acetic anhydride gives 5,6-dihydro-5-oxo-3-phenyl-1,4-dioxazines.

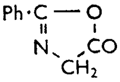
DERIVATIVES of a novel heterocyclic ring system have been obtained from α-benzamido-oxy-acids (I) by a method[2] used for the cyclisation of hippuric acid to 2-phenyl-5-oxazolone (II). Thus, treatment of the appropriate α-benzamido-oxy-acid with acetic anhydride gave 5,6-dihydro-5-oxo-3-phenyl-1,4-dioxazines (III; R = H or Me; R′ = H or alkyl).

$Ph{\cdot}CO{\cdot}NH{\cdot}O{\cdot}CRR'{\cdot}CO_2H$

(I)



(III)



(II)

The oxodioxazines are, like the oxazolones,[2] susceptible to hydrolysis and alcoholysis, and on standing they revert to the parent α-benzamido-oxy-acid. The ring is also readily cleaved by treatment with aniline to yield α-benzamido-oxy-anilides. The latter behaviour suggested that, since the benzoyl group of a benzamido-oxy-compound is generally easily cleaved by alcoholic hydrogen chloride,[3] the oxodioxazines might serve as useful intermediates for the preparation of amino-oxy-peptides. Attempts to prepare amino-oxyacetylglycine by this method have so far been unsuccessful.

The methylene group of 5,6-dihydro-5-oxo-3-phenyl-1,4-dioxazines (III; R = R′ = H), unlike that of 2-phenyl-5-oxazolone,[2] failed to undergo a condensation reaction with benzaldehyde.

EXPERIMENTAL

5,6-Dihydro-5-oxo-3-phenyl-1,4-dioxazines.—The α-benzamido-oxy-acid[4] (2 g.) and acetic anhydride (20 ml.) were

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[1] Part VI, P. Mamalis, M. J. Rix, and A. A. Sarsfield, *J. Chem. Soc.*, 1965, 6278.

[2] J. W. Cornforth in " The Chemistry of Penicillin," ed. H. T. Clarke, J. R. Johnson, and Sir R. Robinson, Princeton University Press, Princeton, 1949.

[3] Part II, P. Mamalis, J. Green, and D. McHale, *J. Chem. Soc.*, 1960, 229.

[4] Part I, D. McHale, J. Green, and P. Mamalis, *J. Chem. Soc.*, 1960, 225.

TABLE 1

5,6-Dihydro-5-oxo-3-phenyl-1,4-dioxazines (III)

(III)					Found (%)			Reqd. (%)		
R	R′	B. p.	M. p.	Formula	C	H	N	C	H	N
H	H[a]	100°/0·08 mm.	36—38°	$C_9H_7NO_3$	61·0	4·0	7·7	61·0	4·0	7·9
H	Me	80—110/0·04	65	$C_{10}H_9NO_3$	62·9	4·9	7·2	62·8	4·7	7·3
H	Et	120/0·2		$C_{11}H_{11}NO_3$	63·9	5·5	7·1	64·4	5·4	6·8
H	Pr	98—110/0·03		$C_{12}H_{13}NO_3$	65·3	6·1	6·4	65·7	6·0	6·4
H	Pr^i	120—130/0·1		$C_{12}H_{13}NO_3$	65·4	6·1	6·1	65·7	6·0	6·4
H	Decyl	140/0·05	47—48	$C_{19}H_{27}NO_3$	72·3	8·8	4·4	71·9	8·6	4·4
H	Tetradecyl	140/0·05	53	$C_{23}H_{35}NO_3$	73·7	9·5	4·2	73·9	9·4	3·8
Me	Me	110/0·1		$C_{11}H_{11}NO_3$	64·0	5·2	6·5	64·4	5·4	6·8

[a] Recrystallised from light petroleum (b. p. 40—60°).

heated on a steam-bath for 3 hr. After removal of acetic acid and acetic anhydride under vacuum, distillation of the resulting oil gave the oxodioxazine. Compounds prepared in this way are given in Table 1.

Anilides.—The oxodioxazine (0·25 g.) was treated with aniline (1 ml.) and warmed to dissolve and left overnight. The solution was poured into 2N-hydrochloric acid (5 ml.) and the solid collected. Recrystallisation gave the anilides listed in Table 2.

Methyl Benzamido-oxyacetate.—5,6-Dihydro-5-oxo-3-phenyl-1,4-dioxazine (9 g.) and methanol (50 ml.) were heated to reflux on a steam-bath for 1 hr. On cooling, solid (3·7 g.), m. p. 104—106° separated. Partial evaporation of the solvent gave a second crop of solid (4·1 g.), m. p. 103—104°. Crystallisation of the combined crops from ethyl acetate gave the *ester* (7·3 g.), m. p. 105—106° (Found: C, 57·4; H, 5·3; N, 6·7. $C_{10}H_{11}NO_4$ requires C, 57·8; H, 5·7; N, 5·0%).

TABLE 2

α-Benzamido-oxy-anilides, BzNH·O·X·CO·NHPh

Parent acid HXCO$_2$H	M. p.	Formula	Found (%) C	H	N	Reqd. (%) C	H	N
Acetic[a]	138—139°	$C_{15}H_{14}N_2O_3$	66·7	5·4	10·4	66·7	5·2	10·4
Butyric[a]	135	$C_{17}H_{18}N_2O_3$	68·3	6·0	8·9	68·5	6·1	9·4
Isobutyric[a] ...	144	$C_{17}H_{18}N_2O_3$	68·9	6·1	8·9	68·5	6·1	9·4
Valeric[b]	122	$C_{18}H_{20}N_2O_3$	68·8	6·4	9·4	69·2	6·4	8·9
Isovaleric[a] ...	145—146	$C_{18}H_{20}N_2O_3$	69·2	6·4	8·8	69·2	6·4	8·9
Dodecanoic[c]...	75—76	$C_{25}H_{34}N_2O_3$	73·5	8·8	6·7	73·1	8·3	6·8
Hexadecanoic[c]	90	$C_{29}H_{42}N_2O_3$	74·4	9·2	6·0	74·6	9·1	6·0

Recrystallised from [a] ethyl acetate—light petroleum, [b] aqueous ethanol, [c] light petroleum (b. p. 80—100°).

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