Reactivity of *N*-Phenacyloxycarbamates and Related Systems in the Presence of Bases: Study of a New [1,2] Anionic Rearrangement

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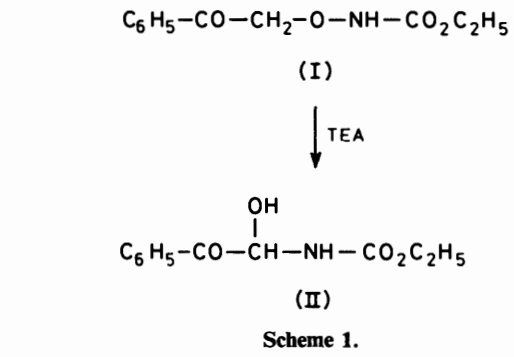
N-Phenacyloxycarbamates and other systems containing a CH_2–O–N= framework, in the presence of bases, undergo a CH_2–O–N= ⟶ CH(OH)–N= rearrangement. The mechanism of this reaction has been studied kinetically and through crossover and capture experiments. The bulk of the data favours an intermolecular ionic mechanism which occurs by removal of a proton from the methylene group in the rate-determining step, followed by interaction between a glyoxal molecule and a carbamate anion in the fast step of the reaction.

Base-catalysed rearrangements such as those of Stevens, Wittig, and Meisenheimer [1-3] have been extensively studied and the mechanistic interpretation of these reactions has been subjected to continuous refinement, mainly based on the findings of Ollis and his co-workers.[4] The most recent theories in this field, argue in favour of combined radical and ionic mechanisms.[5-8] The importance of the former mainly revealed by CIDNP n.m.r. spectroscopy [9,10] as the detection method for the determination of the existence of a radical pair process, is closely connected with the structure of the system as well as with the solvent employed; the inter- or intra-molecular character of these reactions gives rise to further problems often not easy of solution.

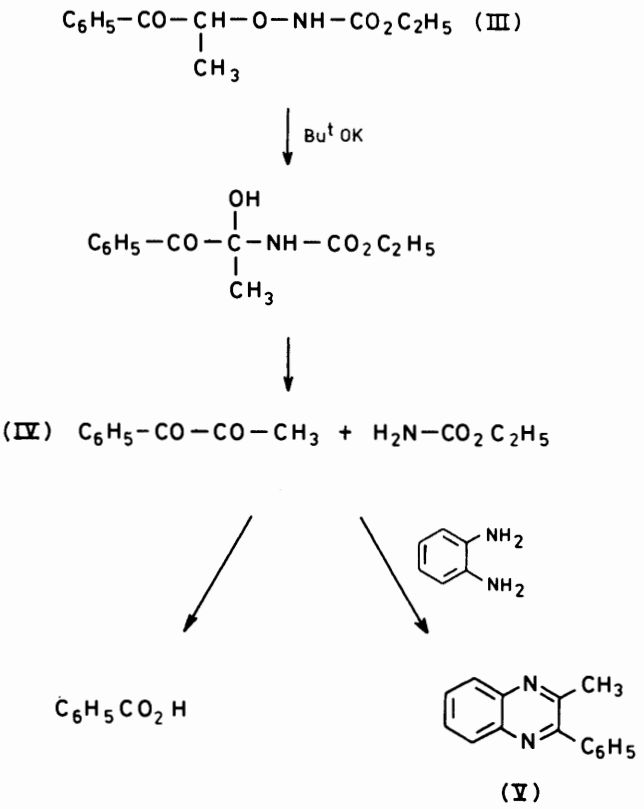
In this paper we report a mechanistic study of a new type of [1,2] anionic C–O–N ⟶ O–C–N rearrangement which is at least formally related to those previously mentioned and which takes place under very mild conditions and is catalysed by bases. To our knowledge the only report in which this reaction has been envisaged is a recent brief account of the reaction of phenacyl bromides with *NN*-dialkylhydroxylamines, leading to arylglyoxals and diethylamine.[11]

Results and Discussion

Ethyl phenacyloxycarbamate (I) under base catalysis in the presence of triethylamine (TEA), in apolar solvents, rearranges in quantitative yield (Scheme 1). This reaction moreover takes place, with different features, in several related systems with structural modifications in the phenacyl or carbamate frameworks. Thus replacement of one methylene hydrogen of (I) by a methyl group as in (III), does not lead to any rearrangement with catalytic amounts of TEA; however, in the presence of a stronger base such as Bu^{t}OK, the cleavage of (III) takes place (Scheme 2) giving rise to benzoic acid and ethyl carbamate as final products. If the reaction is performed in the presence of a stoicheiometric amount of *o*-phenylenediamine as trapping reagent, 2-phenyl-3-methylquinoxaline (V) is obtained; this indicates the presence in the reaction medium of the highly reactive 1-phenylpropane-1,2-dione (IV) originating from the rearranged structure. Similarly the TEA-catalysed reaction of (VI) leads to the isolation of benzil (VIII), arising from the rearranged product (VII) (Scheme 3). Modification of the carbamate framework as in 2-(2-phenyl-2-oxoethyl)-2,3-dihydro-1*H*-isoindolyl-1,3-dione (IX) where a tertiary nitrogen is present, does not



Scheme 1.



Scheme 2.

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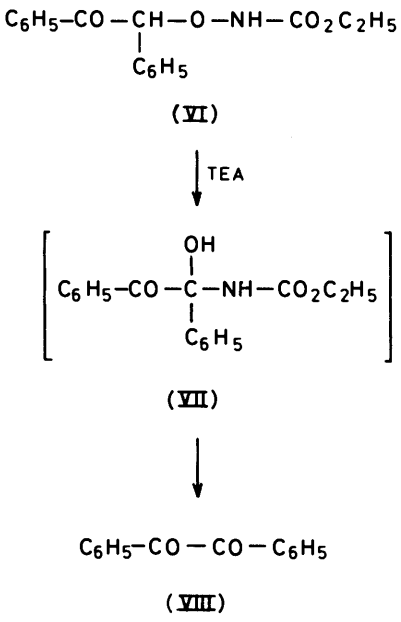
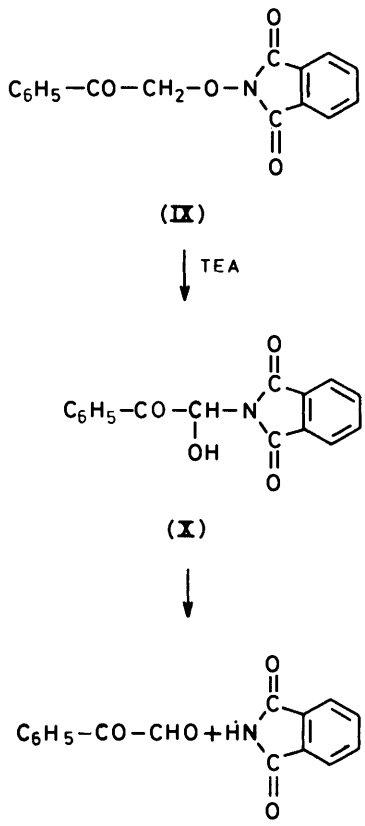
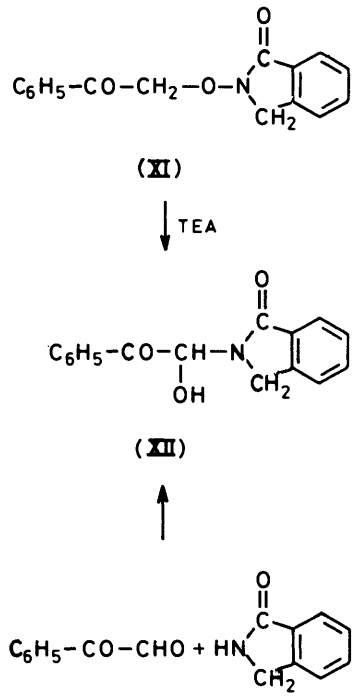


Scheme 3.

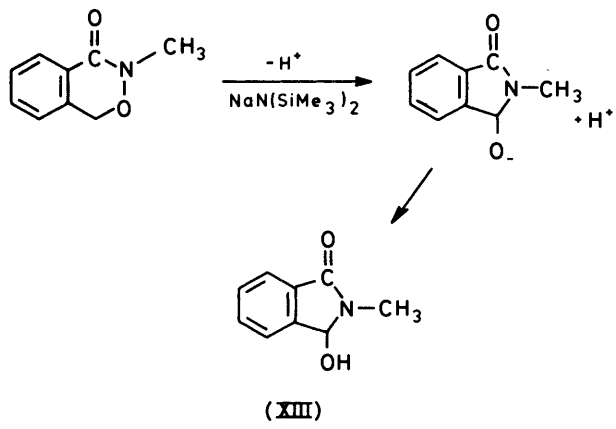


Scheme 4.

prevent the rearrangement. In the presence of catalytic amounts of TEA, (IX) affords in quantitative yield the rearrangement product (X) as shown by the disappearance in the ^{1}H n.m.r. spectrum of the signal at δ 5.42 ($CO-CH_2-O$) and the appearance of a new signal at δ 6.61 [$CO-C(-O)H-N$]; the new n.m.r. pattern is consistent with that shown by product (X) synthesized by an alternative route (see Experimental section); product (X), however, is quite unstable under the rearrangement conditions and is easily converted (Scheme 4) into phthalimide and glyoxal. On the other hand, as shown in Scheme 5, compound (XI) reacts in the presence of TEA to give a stable rearrangement product which can also be obtained from phenylglyoxal and phthalimidine.



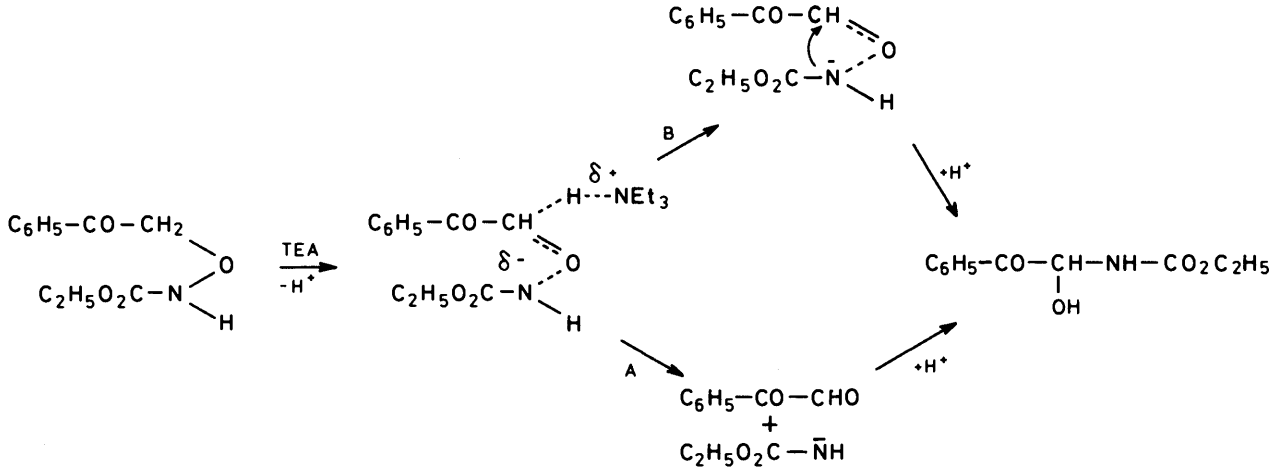
Scheme 5.



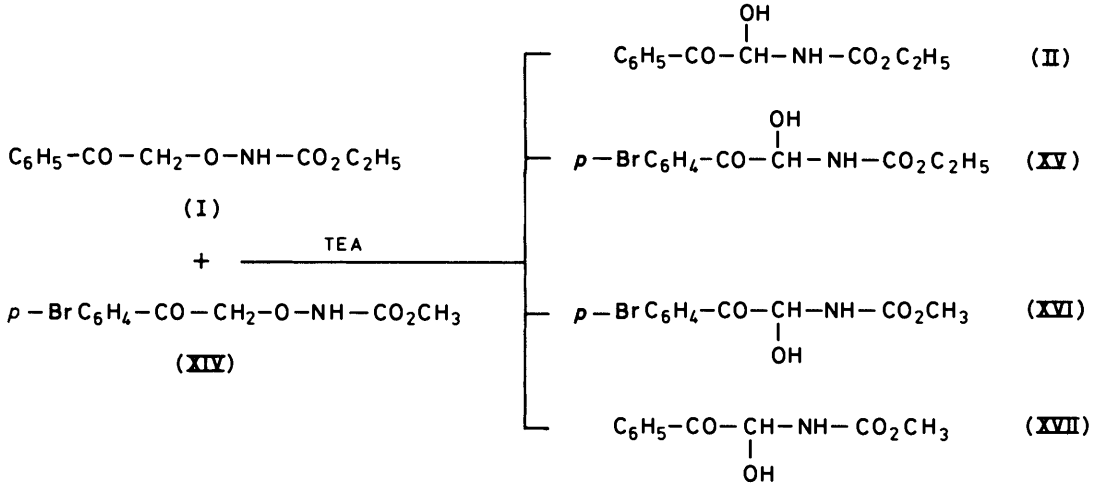
Scheme 6.

Finally the same type of rearrangement, coupled with ring contraction, applies to cyclic systems, as shown in Scheme 6. Thus 3-methyl-1*H*-2,3-benzoxazin-4(3*H*)-one is transformed in the presence of a stoicheiometric amount of the sodium salt of hexamethyldisilazane, into 2-methyl-3-hydroxy-2,3-dihydro-1*H*-isoindol-1-one (XIII).

The significant features of the reactions so far described are as follows. (i) Radical inhibitors such as bis-(3-t-butyl-4-hydroxy-5-methylphenyl) sulphide do not slow down the rate of the rearrangement. (ii) When the reactions are carried out in the n.m.r. probe, no emission signals are observed, in line with the absence of any CIDNP phenomenon. Features (i) and (ii), coupled with the observation that rearrangement in the



Scheme 7.



Scheme 8.

presence of trityl radicals [12] does not lead to any capture product, and the absence of escape products such as C_6H_5-C(OH)O-CH(OH)-CH-CO-C_6H_5 or C_2H_5-CO_2-NH-NH-$CO_2C_2H_5$ allows us to rule out an even partial radical pair process for this reaction.

The rates of the rearrangement were measured by ^{1}H n.m.r., following the disappearance of the methylene signal and the appearance of the signal for the methine hydrogen. Whereas substrates (IX) and (XI) obey a simple kinetic law, the reaction being first order in the product with a catalytic coefficient of *ca.* 1, the kinetic law is more complicated for the parent derivative (I), approaching first order in the product only at low catalyst concentrations. The instantaneous shift of the -NH- singlet in the ^{1}H n.m.r. spectrum of (I) in the presence of an excess of TEA suggests that interaction of the proton at the nitrogen with the catalyst might be responsible for the abnormal kinetic behaviour of this derivative. Replacement of $-CH_2-$ with $-CD_2-$ in (I) and (IX) gives rise to a sizeable primary kinetic isotope effect (k_H/k_D 2.98), thus indicating that removal of a proton from the $-CH_2-$ by the catalyst occurs in the slow step of the reaction. The first-order rate coefficients are listed in the Table.

On the grounds of the above considerations, two ionic mechanistic pathways can be envisaged for these rearrangement reactions (Scheme 7). In order to choose between the intermolecular (A), and the intramolecular (B) mechanisms, several capture and crossover experiments have been performed. Noteworthy features of these experiments are the following. (a) If the rearrangement reaction is performed with equimolar amounts of the phenacyloxycarbamates (I) and (XIV), the four possible crossover products are obtained (Scheme 8). (b) From a mixture of (II) and (XVI), or (XV) and (XVII), in the presence of TEA, the starting compounds are recovered unchanged. (c) When (I) is treated under TEA catalysis with an equimolar amount of *p*-BrC_6H_4-CO-CHO, a

First-order rate constants for the TEA-catalysed rearrangement of *N*-phenacyloxycarbamates in C_6D_6 at 30°

Compound	[Substrate]/M	[TEA]/M	$10^4k_{obs}/s^{-1}$	$10^4k_{cat}/s^{-1}$
(I)	0.15	0.075	3.17	42.21
[$^2H_2$]-(I)	0.15	0.075	1.16	14.18
(IX)	0.50	0.50	23.58	47.17
	0.39	0.13	5.97	45.97
	0.39	0.065	3.07	47.23
	0.195	0.13	5.89	45.38
	0.78	0.13	5.93	45.61
[$^2H_2$]-(IX)	0.78	0.13	1.98	15.21
(XI)	0.39	0.065	3.57	54.87
	0.39	0.130	6.82	52.46

$$C_6H_5-CO-CH_2-O-NH-CO_2C_2H_5$$

(I)

+

$$p\text{-}BrC_6H_4-CO-CHO \xrightarrow{TEA} (II) + (XV)$$

Scheme 9.

$$C_6H_5-CO-\underset{\displaystyle OH}{\underset{|}{CH}}-NH-CO_2C_2H_5$$

+

$$p\text{-}BrC_6H_4-CO-CHO \xrightarrow{TEA} (II) + (XV)$$

Scheme 10.

mixture of ethyl (2-phenyl-1-hydroxy-2-oxoethyl)carbamate (II) and ethyl 2-(4-bromophenyl)-1-hydroxy-2-oxoethylcarbamate (XV) is obtained (Scheme 9). (d) No trapping of the carbamate framework occurs when (I) is added in the presence of catalytic amounts of TEA, to $CH_3O-CO-NH_2$. (e) On treatment of the rearranged product (II) with *p*-$BrC_6H_4-CO-CHO$, under TEA catalysis, a mixture of (II) and (XV) is obtained, according to Scheme 10.

The above features suggest that an intermolecular mechanistic pathway, such as A in Scheme 7, should be preferred for the mechanism of this rearrangement reaction. In fact since the rearranged products are stable under the reaction conditions, all the trapping and crossover reactions must occur between reactive intermediate species such as $C_6H_5-CO-CHO$ and $RO-CO-NH^-$ proposed to take place in mechanism A. Features (d) and (e), however, might appear to contradict the intermolecular interpretation but this discrepancy is only apparent: the failure to trap $CH_3O-CO-NH_2$ in the rearrangement of (I) can be reasonably explained by the much lower reactivity of $RO-CO-NH_2$ with respect to $RO-CO-NH^-$ (the reaction between $C_6H_5-CO-CHO$ and $C_2H_5O-CO-NH_2$ requires several hours at reflux). On the other hand, trapping of the substituted glyoxal by (II) to give a mixture of (II) and (XV) as in Scheme 10, which even though at first sight might appear to restrict the significance of the crossover experiment (a), still indirectly supports the intermolecular interpretation of this rearrangement since Scheme 10 implies the presence of free glyoxal which can only be formed during an intermolecular process.

In the light of these results, the rearrangement of (I) and related systems is more easily rationalized by the intermolecular mechanism A (Scheme 7), occurring through abstraction of a methylene proton in the rate-determining step. The overall second-order kinetics (Table), the size of the primary kinetic isotope effect (k_H/k_D 2.98), smaller than that expected for a fully concerted elimination, and also the presence of a stabilizing group β to the carbanionic centre, support the proposal of an *E*1cB-like (irreversible) mechanism, where the degree of C–H bond breaking in the rate-limiting step is intermediate between those for *E*2 and *E*1 eliminations. Furthermore the negligible differences in the reaction rates of (I), (IX), and (XII) (Table), supports interaction of $C_2H_5-O-CO-NH^-$, $C_6H_4-(COCH_2)N^-$, and $C_6H_4(CO)_2N^-$ with $C_6H_5-CO-CHO$ in a fast subsequent step of the reaction to give the rearrangement products. Due to the properties of the solvent employed (C_6D_6), however, it is difficult to stress the formal separation of species such as $C_6H_5-CO-CHO$ and $RO-CO-NH^-$ before the fast step, but solvent cage and electrostatic interactions between the partners do not appear crucial in preventing their capture by external electrophiles ($XC_6H_4-CO-CHO$) or by nucleophilic species ($RO-CO-NH^-$).

Experimental

Instruments used were a Perkin-Elmer 170 spectrophotometer for i.r. spectra, a Hitachi–Perkin-Elmer RMU 6L spectrometer for mass spectra, and a Perkin-Elmer R 32 or a Bruker WH 270 spectrometer for ^1H n.m.r. spectra. M.p.s were determined on a capillary apparatus and are uncorrected. Ethyl *N*-hydroxycarbamate was synthesized by the method described by Fuller and King.[13] The crude product was used without further purification. Methyl *N*-hydroxycarbamate was prepared following the procedure of Boyland and Nery [14] and purified by distillation, b.p. 95° at 0.25 mmHg.

Potassium Salt of Ethyl N-*Hydroxycarbamate*.—Ethyl *N*-hydroxycarbamate (7.4 g, 0.06 mol; 85% pure) was added dropwise at room temperature to a solution of potassium hydroxide (5.6 g, 0.1 mol) in absolute ethanol (70 ml). After 20 min, the remaining part of ethyl *N*-hydroxycarbamate (3.7 g, 0.03 mmol) was added and the mixture was vigorously stirred for 30 min. After cooling to 0°, a crystalline solid separated; it was filtered off, washed with a small amount of ice-cold ethanol and then with dry ether. After drying under vacuum, the yield of product, evaluated by means of titration with $HClO_4$ (indicator Crystal Violet), was 61%.

Potassium Salt of Methyl N-*Hydroxycarbamate*.—This salt was prepared from potassium hydroxide and methyl *N*-hydroxycarbamate in methanol, following the previously outlined procedure.

Ethyl Phenacyloxycarbamate (I).—The potassium salt of ethyl *N*-hydroxycarbamate (24.7 g, 0.105 mol; 61% pure), was added over 30 min with vigorous stirring to a solution, cooled at 5°, of ω-bromoacetophenone (19.9 g, 0.1 mol) in dry DMF (100 ml). After the addition, the mixture was stirred for 30 min at room temperature, then poured into water (900 ml) and extracted with ether. The extracts were washed with water, dried (Na_2SO_4), and the solvent evaporated. Addition to the residual oil, cooled at 0°, of a small amount of di-isopropyl ether afforded a solid (8.3 g, 37.2%), m.p. 77—79°; recrystallization from methylene dichloride–di-isopropyl ether (1 : 1 v/v) afforded a crystalline *product*, m.p. 81—82°; $\nu_{max.}$ (Nujol) 3 300 (NH), 1 740 (O–C=O), and 1 690 cm^{-1} (C=O); δ (C_6D_6) 1.1 (3 H, t), 3.95 (2 H, q), 4.95 (2 H, s), 7.05—7.6 (5 H, m), and 8.5 (1 H, s) (Found: C, 59.4; H, 5.9; N, 6.4. $C_{11}H_{13}NO_4$ requires C, 59.2; H, 5.9; N, 6.3%).

Ethyl [ω-$^2H_2$]*Phenacyloxycarbamate*.—This was synthesized from [ω-$^2H_2$]-ω-bromoacetophenone [15] and the potassium salt of ethyl *N*-hydroxycarbamate, employing the procedure previously reported for (I); m.p. 80—81° (Found: C, 58.9; H, 5.9; N, 6.2. $C_{11}H_{11}D_2NO_4$ requires C, 59.2; H, 5.9; N, 6.3%).

Ethyl (2-*Phenyl*-1-*hydroxy*-2-*oxoethyl*)*carbamate* (II).—Triethylamine (1.65 ml, 0.012 mol) was added dropwise at room temperature to a solution of (I) (7.87 g, 0.04 mol) in dry benzene (200 ml). After 90 min solid (II) (5.8 g, 66.8%) was filtered off and a *sample* crystallized from ethanol, m.p. 112—113°; $\nu_{max.}$ ($CDCl_3$) 3 420 (OH), 3 390 (NH), 1 715 (O–

C=O), and 1 680 cm^{-1} (C=O); δ (C_6D_6) 0.95 (3 H, t), 3.95 (2 H, q), 5.3br (1 H, s), 6.3br (1 H, s), and 7.05—7.6 (6 H, m) (Found: C, 59.2; H, 5.9; N, 6.2. $C_{11}H_{13}NO_4$ requires C, 59.2; H. 5.9; N, 6.3%).

Ethyl (2-Phenyl-1-methyl-2-oxoethoxy)carbamate (III).—To a solution of α-bromopropiophenone (8.5 g, 0.04 mol) in dry dimethylformamide (DMF) (40 ml), the potassium salt of ethyl *N*-hydroxycarbamate (9.4 g, 0.041 mol) was added over 15 min at 5°. After stirring for 30 min at room temperature, the mixture was poured into water (400 ml) and extracted with ether (3 × 60 ml). The organic layer was washed with water (5 × 30 ml), dried (Na_2SO_4), and the solvent evaporated. The residual was crystallized twice from di-isopropyl ether to give the expected product (4.45 g, 47%), m.p. 70—71°; $\nu_{max.}$ (Nujol) 3 250 (NH), 1 735 (O-C=O), and 1 680 cm^{-1} (C=O); δ ($CDCl_3$) 1.28 (3 H, t), 1.56 (3 H, d), 4.24 (2 H, q), 5.49 (1 H, q), and 7.5—8.2 (6 H, m) (Found: C, 60.8; H, 6.3; N, 5.9. $C_{12}H_{15}NO_4$ requires C, 60.7; H, 6.4; N, 5.9%).

Ethyl (1,2-Diphenyl-2-oxoethoxy)carbamate (VI).—A suspension of the potassium salt of ethyl *N*-hydroxycarbamate (6 g, 0.0262 mol; 63% pure), in dry DMF (30 ml) was added during 30 min to a solution of desyl chloride [5] (6.04 g, 0.025 mol) in dry DMF (25 ml), cooled to 0°. The mixture was stirred for 1 h at room temperature, poured into water (300 ml), and extracted with ether (4 × 50 ml). The organic layer was washed with water (5 × 30 ml) and dried. Evaporation of the solvent afforded a waxy solid (5.9 g) formed by (VI) and benzil. After several recrystallizations from di-isopropyl ether, (VI) (0.44 g, 5.9%) was obtained, m.p. 114—115°; $\nu_{max.}$ (Nujol) 3 300 (NH), 1 740 (O-C=O), and 1 685 cm^{-1} (C=O); δ ($CDCl_3$) 1.28 (3 H, t), 4.27 (2 H, q), 6.43 (1 H, s), 7.2—8.2 (10 H, m), and 8.12 (1 H, s) (Found: C, 68.5; H, 5.7; N, 4.6. $C_{12}H_{17}NO_4$ requires C, 68.2; H, 5.7; N, 4.7%).

Rearrangement of (III) *with* Bu^{t}OK.—To a solution of Bu^{t}OK (from *ca.* 20 mg of potassium and 25 ml Bu^{t}OH) was added a solution of (III) (237 mg, 1 mmol) in Bu^{t}OH (7 ml) and the resulting mixture was stirred overnight. The dark brown reaction mixture was poured into water (40 ml) and extracted several times with CH_2Cl_2. The organic extracts were washed with a saturated solution of sodium chloride and dried; evaporation of the solvent afforded a red oil (98 mg) which was sublimed (70° and 150 mmHg) to give ethyl carbamate identical to an authentic sample; from the aqueous layer after treatment with 10% hydrochloric acid and extraction with CH_2Cl_2, was obtained a dark oil (70 mg) containing benzoic acid. This was identified by methylation with diazomethane and comparison (i.r. and g.l.c.) of the methyl ester with an authentic sample.

The instability of 1-phenylpropane-1,2-dione (IV) in the basic medium was proved as follows. A mixture of Bu^{t}OK and (IV) (1.48 g, 0.01 mol) was stirred overnight at room temperature. The mixture was then poured into water (70 ml) and extracted with CH_2Cl_2. The aqueous layer was then decolourized with carbon powder, acidified with hydrochloric acid, and extracted with CH_2Cl_2 (4 × 30 ml). Evaporation of the solvent gave crude benzoic acid (0.83 g).

Rearrangement of (III) *with* Bu^{t}OK *in the Presence of o-Phenylenediamine.*—To a solution of Bu^{t}OK [from potassium (78 mg, 2 mmol) and Bu^{t}OH (10 ml)] was added *o*-phenylenediamine (216 mg, 2 mmol) and, after 30 min, a solution of (III) (474 mg, 2 mmol) in Bu^{t}OH (6 ml). The mixture was stirred overnight at room temperature, then poured into water (50 ml), and extracted with ether (3 × 30 ml). The combined organic extracts were washed with water and dried to give, after evaporation of the solvent, a dark oil (350 mg). Sublimation of this crude product afforded a mixture of *o*-phenylenediamine and ethyl carbamate. The residue from the sublimation was purified by preparative t.l.c. on silica gel (Merck F 254) eluting with cyclohexane–ethyl acetate (7 : 3 v/v), affording 2-phenyl-3-methylquinoxaline (V) (150 mg), identical with an authentic sample.

Rearrangement of (VI) *with TEA.*—To a solution of (VI) (300 mg) in CH_2Cl_2 (15 ml) was added a drop of TEA and the mixture was warmed for 24 h. The organic layer was then washed with water, dried, and the solvent distilled under vacuum. The residue was extracted several times with hot di-isopropyl ether, from which, by cooling, benzil (150 mg, 71%), m.p. 91—94° (lit.,[16] 94—95°), was recovered.

Potassium Salt of N-Hydroxyphthalimide.—A solution of 1N-potassium hydroxide (61 ml, 0.061 mol) was added dropwise at 5° to a solution of *N*-hydroxyphthalimide (10 g, 0.61 mol) in 1,2-dimethoxyethane. After 90 min at 5—10°, the mixture was filtered and the solid was washed with ether giving the expected salt (9.8 g, 79.3%; 96.1% pure) (estimated by titration with $HClO_4$ in acetic acid).

2-(2-Phenyl-2-oxoethoxy)-2,3-dihydro-1H-isoindole-1,3-dione (IX).—The potassium salt of *N*-hydroxyphthalimide (96.1% pure; 9.36 g, 0.046 mol) was added at 5—10° with vigorous stirring to a solution of ω-bromoacetophenone (9 g, 0.045 mol) in dry DMF. After the addition, the mixture was stirred at room temperature for 30 min, poured into water (500 ml), and extracted with ethyl acetate. The extracts were washed with water, dried, and evaporated. The residue was crystallized from ethyl acetate to give (IX) (10 g, 77.4%) as a crystalline *solid*, m.p. 135°; $\nu_{max.}$ (Nujol) 1 800, 1 725 (CO-N-CO), and 1 700 cm^{-1} (C=O); δ ($CDCl_3$) 5.42 (2 H, s) and 7.4—8.2 (9 H, m) (Found: C, 68.5; H, 3.8; N, 5.0. $C_{16}H_{11}NO_4$ requires C, 68.3; H, 3.9; N, 5.0%).

2-(2-Phenyl-2-oxo[1-$^2H_2$]ethoxy)-2,3-dihydro-1H-isoindole-1,3-dione.—This was synthesized in 70% yield from the potassium salt of *N*-hydroxyphthalimide and [ω-$^2H_2$]bromoacetophenone according to the previously outlined procedure.

2-(2-Phenyl-1-hydroxy-2-oxoethyl)-1H-isoindole-1,3-dione (X).—Phenylglyoxal (15.7 g, 0.11 mol) and phthalimide (15.63 g, 0.11 mol) were added to dry DMF (5 ml), and stirred at room temperature for 2 h. The crystalline product obtained was filtered and washed with dry ether to give (X) (12.52 g, 44.7%), m.p. 134°; $\nu_{max.}$ (Nujol) 3 450 (OH), 1 780, 1 725 (CO-N-CO), and 1 700 cm^{-1} (C=O); δ ($CDCl_3$) 5.29 (1 H, s), 6.70 (1 H, d), and 7.2—8.2 (9 H, m) (Found: C, 68.3; H, 3.9; N, 5.2. $C_{16}H_{11}NO_4$ requires C, 68.3; H, 3.9; N, 5.0%).

Rearrangement of (IX) *with TEA.*—By treatment of (IX) dissolved in CH_2Cl_2 or DMF with a catalytic amount of TEA, phthalimide was obtained by spontaneous crystallization from the mixture. Further support for the instability of (X) under the rearrangement conditions was achieved by treatment of (X) (0.3 g, 0.001 mmol) dissolved in CH_2Cl_2 with a few drops of TEA; after 24 h, at room temperature, phthalimide, m.p. 234°, spontaneously crystallized from the reaction mixture.

Potassium Salt of 2-Hydroxy-2,3-dihydro-1H-isoindol-1-one.—A solution of 2-hydroxy-2,3-dihydro-1*H*-isoindol-1-one [17] (1.49 g, 0.01 mol) and potassium hydroxide (0.56 g, 0.01 mol) in methanol (50 ml) was stirred at room temperature for 30

* α-Chloro-α-phenylacetophenone.

min. The solvent was evaporated and the solid recovered (1.65 g, 88% yield) was dried under vacuum and used without further purification.

2-(2-Phenyl-2-oxoethoxy)-2,3-dihydro-1H-isoindol-1-one (XI).—The potassium salt of 2-hydroxy-2,3-dihydro-1*H*-isoindol-1-one (1.65 g, 0.0076 mol) was slowly added with vigorous stirring to a solution of ω-bromoacetophenone (1.78 g, 0.09 mol) in dry DMF (10 ml). After 15 min at room temperature, the solution was poured onto crushed ice and extracted with ether. The extracts were washed with water, dried, and evaporated. The residue was crystallized from n-hexane–acetone to give (XI) (1.05 g, 51.3%), m.p. 110—112°; $\nu_{max.}$ (Nujol) 1 700 (C=O) and 1 680 cm^{-1} (N–C=O); δ ($CDCl_3$) 4.80 (2 H, s), 5.53 (2 H, s), and 7.3—8.2 (9 H, m) (Found: C, 71.8; H, 4.8; N, 5.3. $C_{16}H_{13}NO_3$ requires C, 71.9; H, 4.9; N, 5.2%).

2-(2-Phenyl-1-hydroxy-2-oxoethyl)-2,3-dihydro-1H-isoindol-1-one (XII).—(i) *From rearrangement of* (XI) *with TEA.* TEA (4 ml) was added to a solution of (XI) (100 mg, 3.7×10^{-4} mol) in dry benzene (5 ml). After 6 h at room temperature, the mixture was washed with a small amount of water, dried, and evaporated. The residue was crystallized from ethyl acetate–n-hexane to give (XII) (80 mg, 80%), m.p. 130—131°; $\nu_{max.}$ (Nujol) 3 300 (OH), 1 700 (C=O), and 1 650 cm^{-1} (N–C=O); δ ($CDCl_3$) 4.14—4.33 (2 H, dd), 4.93 (1 H, d), 7.05 (1 H, d), and 7.2—8.3 (9 H, m) (Found: C, 71.6; H, 4.8; N, 5.4. $C_{16}H_{13}NO_3$ requires C, 71.9; H, 4.9; N, 5.2%).

(ii) *From reaction of 2,3-dihydro-1H-isoindol-1-one and phenylglyoxal.* A solution of phenylglyoxal (1.34 g, 0.01 mol), 2,3-dihydro-1*H*-isoindol-1-one (1.33 g, 0.01 mol) and TEA (0.36 ml, 0.0025 mol) in CH_2Cl_2 (15 ml) was stirred at room temperature for 5 h. The solvent was evaporated and the residue crystallized from n-hexane–ethyl acetate to give (XII) (1.9 g, 75.5%), m.p. 129—130°.

2-Methyl-3-hydroxy-2,3-dihydro-1H-isoindol-1-one (XIII).—Metallic sodium (1.17 g, 0.052 mol) was added under nitrogen to a solution of naphthalene (5.28 g, 0.040 mol) and hexamethyldisilazane (12 ml, 0.058 mol) in dry tetrahydrofuran (THF) (80 ml); the mixture was stirred at room temperature until the dark green colour disappeared, cooled to −60° and a solution of 3-methyl-1*H*-2,3-benzoxazin-4(3*H*)-one [18] (8.5 g, 0.052 mol) in dry THF (30 ml) was added. After 90 min at −60°, the temperature was slowly raised to 20°, and after stirring for 1 h, the mixture was poured into water (500 ml), extracted with CH_2Cl_2 (3 × 200 ml), and then with ethyl acetate (4 × 100 ml). These last extracts were dried (Na_2SO_4) and the solvent evaporated. Crystallization of the residue with di-isopropyl ether afforded (XIII) (3.3 g), m.p. 132°. The CH_2Cl_2 extracts were also dried, the solvent evaporated, and the residual oil, after treatment with n-hexane (50 ml), was chromatographed on silica gel [eluant toluene–ethyl acetate (6 : 4 v/v)], affording a solid which after crystallization with di-isopropyl ether gave (XIII) (1.5 g), m.p. 132° (lit.,[19] 130°). The overall yield of (XIII) was 56.6%; $\nu_{max.}$ (Nujol) 3 300 (OH) and 1 680 cm^{-1} (C=O); δ ($CDCl_3$) 2.96 (3 H, s), 3.83 (1 H, d), 5.68 (1 H, d), and 7.5—8.0 (4 H, m).

Methyl 2-(4-Bromophenyl)-2-oxoethoxycarbamate (XIV).—This compound was prepared by the method outlined for (I), starting from the potassium salt of methyl *N*-hydroxycarbamate (4.05 g, 0.025 mol) and 2′,4′-dibromoacetophenone (6.8 g, 0.024 mol) in DMF (25 ml) as solvent. Two crystallizations from cyclohexane afforded (XIV) (2.14 g, 31.4%), m.p. 102—103°; $\nu_{max.}$ (Nujol) 3 380 (NH), 1 750 (O–C=O), and 1 700 cm^{-1} (C=O); δ ($CDCl_3$) 3.87 (3 H, s), 5.14 (2 H, s), 7.7—7.8 (4 H, m), and 8.22 (1 H, s) (Found: C, 42.0; H, 3.7; N, 5.0. $C_{10}H_{10}BrNO_4$ requires C, 41.7; H, 3.5; N, 4.9%).

Rate Measurements.—The reaction rates were measured with a Perkin-Elmer R 32 n.m.r. spectrometer operating at 90 MHz in C_6D_6 as solvent and at 30°. Tetramethylsilane was used as internal standard. The progress of the reaction for compounds (I), (IX), and (XI) was followed by observing the decrease of the singlet at δ 4.82 ($CO-CH_2-O-N$) for (I), at δ 5.42 for (IX), and at δ 5.53 for (XI), with respect to the multiplets centred at δ 7.5, 7.4, and 7.3. In the case of deuteriated (I) and (IX) the progress of the reaction was followed by measuring the increase of the multiplet centred at δ 8.05.

Crossover Experiments.—Rearrangement of (I) *with TEA in the presence of an equimolar amount of* (XIV). To a solution of (I) (0.056 g, 0.25 mmol) and (XIV) (0.073 g, 0.025 mmol) in dry CH_2Cl_2 (10 ml), a drop of TEA was added at room temperature with stirring. After 3 h, the solvent was evaporated under vacuum to give product (0.13 g). H.p.l.c. analysis showed that this comprised an equimolar mixture of the four possible rearrangement products (II), (XV), (XVI), and (XVII).

Reaction between (II) *and* (XVI), *and* (XV) *and* (XVII) *in the presence of TEA.* Solutions of (II) (0.056 g, 0.25 mmol) and (XVI) (0.073 g, 0.025 mmol), or of (XV) (0.25 g, 0.86 mmol) and (XVII) (0.18 g, 0.83 mmol) in dry CH_2Cl_2 treated with TEA as previously described and submitted to h.p.l.c. analysis showed only the presence of unchanged starting materials.

H.p.l.c. analysis was performed on dilute methanolic solutions (0.1%, w/w) of the reaction products, employing a Du Pont model 830 instrument with a u.v. detector, and a 250 × 0.2 cm Zorbax 0.05 column, with 35% acetonitrile in water as eluant at 1 200 lb in^{-2} and 20°. Products (II), (XV), (XVI), and (XVII) were identified by comparison with authentic samples obtained by condensation of substituted phenylglyoxals with carbamates. The appropriate carbamate was added to a stirred solution of the phenylglyoxal (0.02 mol) in dry benzene (30 ml). The mixture was then refluxed for 9 h, concentrated to *ca.* 15 ml, and cooled to give the expected product. Compound (II), m.p. 111—112°, was identified by comparison with the product obtained by the above procedure. *Ethyl 2-p-bromophenyl-1-hydroxy-2-oxoethylcarbamate* (XV) had m.p. 146—147°, $\nu_{max.}$ (Nujol) 3 350 (OH), 3 260 (NH), and 1 680 cm^{-1} (C=O); δ ([$^2H_6$]DMSO) 1.25 (3 H, t), 4.10 (2 H, q), 6.15 (1 H, dd), 6.55 (1 H, d), and 7.6—8.2 (6 H, m) (Found: C, 43.7; H, 4.0; N, 4.6. $C_{11}H_{12}BrNO_4$ requires C, 43.6; H, 3.9; N, 4.5%). *Methyl 2-p-bromophenyl-1-hydroxy-2-oxoethylcarbamate* (XVI) had m.p. 162—163°; $\nu_{max.}$ (Nujol) 3 360 (OH), 3 260 (NH), and 1 680 cm^{-1} (C=O); δ ([$^2H_6$]DMSO) 3.63 (3 H, s), 6.13 (1 H, dd), 6.57 (1 H, d), and 7.6—8.2 (6 H, m) (Found: C, 41.9; H, 3.7; N, 4.8. $C_{10}H_{10}BrNO_4$ requires C, 41.7; H, 3.5; N, 4.9%). *Methyl 2-phenyl-1-hydroxy-2-oxoethylcarbamate* (XVII) had m.p. 140—141°; $\nu_{max.}$ (Nujol) 3 360 (NH, OH) and 1 680 cm^{-1} (C=O); δ ($CDCl_3$) 3.61 (3 H, s), 6.04 (1 H, dd), 6.17 (1 H, d), and 7.4—8.2 (6 H, m) (Found: C, 57.4; H, 5.3; N, 6.7. $C_{10}H_{11}NO_4$ requires C, 57.5; H, 5.2; N, 6.7%).

Trapping Experiments.—Reaction between carbamate (I) *and p-bromophenylglyoxal. p*-Bromophenylglyoxal (1.12 g, 0.005 mol) and (I) (1.07 g, 0.005 mol) were dissolved in dry benzene (25 ml) and TEA (0.15 ml) was added. After two days at room temperature, a solid precipitated which was filtered off and washed with n-hexane to give (XV) (0.35 g). Evaporation of the benzene to a small volume (5 ml) afforded a mixture (0.15 g) of (II) and (XV).

Reaction between carbamate (II) *and* p-*bromophenylglyoxal.* To a solution of (II) (0.67 g, 0.003 mol) and *p*-bromophenylglyoxal (0.64 g, 0.003 mol) in CH_2Cl_2 (10 ml) was added TEA (10 ml). After 2 h at room temperature, the solvent was evaporated and the residue, after treatment with benzene (4 ml), gave a mixture (0.27 g) of (II) and (XV).

Reaction between carbamate (I) *and methyl carbamate.* A catalytic amount of TEA was added to a solution of (I) (0.2 g, 0.9 mmol) and methyl carbamate (0.3 g, 3.6 mmol) in CH_2Cl_2 (5 ml). After 3 h at 20°, the mixture was diluted with CH_2Cl_2 (20 ml) and washed with water; after drying, the solvent was evaporated to give (II) (0.17 g).

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