883. Organic Photochemistry. Part II.[1] Some Photosensitive Protecting Groups

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During a search for photosensitive protecting groups, it has been shown that benzyloxycarbonyl groups, particularly those substituted by electron-releasing groups, are readily fissioned by ultraviolet irradiation. The mechanism of these photolyses involves heterolysis to benzylic carbonium ions. This process has been used to detect benzyloxycarbonylamino-acids on paper chromatograms.

The removal of protecting groups introduced during the course of synthetic procedures is sometimes troublesome. The methods most commonly used for regeneration of the protected function, namely reductive fission and hydrolysis by acid or alkali, are limited, and it is not difficult to devise a molecule with a structure such that the use of any of these methods is precluded. The discovery that benzyloxycarbonylglycine (Cbzglycine) is readily converted into the free amino-acid by irradiating an aqueous solution with ultraviolet light from a medium pressure mercury arc led us to consider the possibility of designing protecting groups for which the regeneration of the protected function could be accomplished by photochemical means. Variations in the chromophores of such groups might lead to a range of photosensitive protecting groups, each capable of being removed in the presence of the others.

A number of such protecting groups have now been discovered, but this Paper is concerned only with the photolysis of Cbz-derivatives, which have been studied because of the importance of the Cbz protecting group in peptide synthesis and because the amino-acid products of photolysis can be separated, identified, and estimated with relative ease.

Solutions of Cbzglycine in aqueous sodium acetate or sodium hydroxide deposited, on irradiation with unfiltered light from a medium pressure mercury arc, small amounts of a yellowish polymer which contained small and variable amounts of nitrogen and had an empirical formula approximating to C_7H_8O. A solid having similar properties and composition was deposited on irradiating a saturated aqueous solution of benzyl alcohol containing glycine. The neutral, ether-soluble products of this photolysis were examined by gas–liquid chromatography (g.l.c.) and three components were detected; two of these had retention times identical with those of benzyl alcohol and bibenzyl. The major constituent of this mixture, benzyl alcohol, was identified as its 3,5-dinitrobenzoate. Irradiation of a solution of Cbzglycine in ethanol resulted in the formation of benzyl ethyl ether.

When an irradiated solution of Cbzglycine was stirred with a stream of nitrogen, carbon dioxide was detected in the effluent gases. The main water-soluble photolysis product, glycine, was isolated as hippuric acid by Schotten–Baumann acylation of the photolyte with benzoyl chloride. Paper chromatography of the aqueous photolyte revealed the presence of three ninhydrin-reacting substances other than glycine. Two of these products were identified as *N*-benzylglycine and phenethylamine by comparative paper chromatography and the amine was also isolated as its hydrochloride; the third product was not identified.

The quantum yields for the formation of these nitrogen-containing photolysis products (Table 1) were measured by separation and estimation of the components from an irradiated sample of [2-^{14}C]Cbzglycine. The irradiated solutions were also subjected to a direct colorimetric estimation for free amino-nitrogen (Table 2).

A comparison of Tables 1 and 2 reveals that direct colorimetric estimation of the irradiated Cbzglycine solution with ninhydrin is a satisfactory procedure for determining

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[1] Part I, R. Robson, P. W. Grubb, and J. A. Barltrop, *J.*, 1964, 2153.

TABLE 1

Quantum yields (ϕ) for formation of products from Cbzglycine

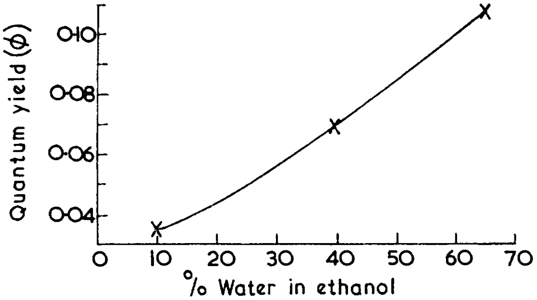
Product	Irradiation time (min.) 10	20	40	80
Glycine	0·16	0·16	0·16	0·12
Unknown *	0·017	0·005	0·008	0·009
N-Benzylglycine	0·025	0·016	0·015	0·015
Phenethylamine	—	0·024	0·028	0·027

* ϕ calculated on the assumption that the molecule contains a single glycine residue. The estimated accuracy of these measurements is ±10%.

TABLE 2

Irradiation time (min.)	10	20	30	50
ϕ (±15%)	0·16	0·15	0·15	0·14

the quantum yield of glycine production (ϕ) in this photochemical fission and all subsequent quantum yield measurements were made in this way.



Quantum yield for glycine production from Cbzglycine ethyl ester in aqueous ethanol

The effect of solvent upon ϕ was investigated by irradiating solutions of Cbzglycine ethyl ester in ethanol–water. The Figure shows that the quantum yield of liberated glycine is a sensitive function of the water content of the solvent; a similar effect was noted with Cbzglycine sodium salt. These results suggested that ϕ might also be pH-dependent and this was confirmed by irradiating equimolar solutions of Cbzglycine in ethanol–water both as the free acid and as the sodium salt. The addition of one equivalent of sodium hydroxide to a solution of Cbzglycine in 50% ethanol–water caused the quantum yield to fall from 0·076 to 0·052.

In all the above quantum yield measurements the solution was flushed with nitrogen before irradiation in order to reduce the concentration of dissolved oxygen. When this procedure was omitted the observed quantum yield fell to approximately 50% of that for the de-gassed solutions, and the de-gassing procedure was therefore adopted for all such measurements.

The results of quantum yield measurements on various substituted Cbzglycines and on some closely related compounds are summarised in Table 3.

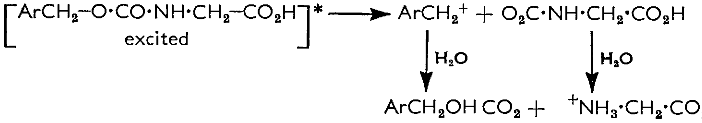
Irradiated solutions of glycine benzyl ester and Cbzpiperidine were examined qualitatively, and found to contain free glycine and piperidine, respectively. Phenoxycarbonylglycine appeared to be stable to irradiation.

TABLE 3

	Compound	ϕ
1	Cbzglycine	0·16 ± 0·02
2	*p*-Bromo-Cbzglycine	0·075 ± 0·03
3	*p*-Nitro- ,,	0·0055 ± 0·002
4	*p*-Methoxy- ,,	0·17 ± 0·03
5	*m*-Methoxy- ,,	0·28 ± 0·04
6	Cinnamyloxycarbonylglycine	0·13 ± 0·06
7	*p*-Phenylazo-Cbzglycine	$<2 \cdot 10^{-3}$
8	*p*-(4-Methoxyphenylazo)-Cbzglycine	$<2 \cdot 10^{-3}$
9	β-Phenylethyloxycarbonylglycine	$<2 \cdot 10^{-3}$
10	Ethyloxycarbonylglycine	$<10^{-2}$
11	Aceturic acid	$<10^{-2}$
12	Hippuric acid	$<1 \cdot 10^{-4}$
13	Thiohippuric acid	$<2 \cdot 10^{-3}$
14	Glycine dithiocarbamic acid ethyl ester	0·024 ± 0·01
15	Glycine dithiocarbamic acid benzyl ester	0·084 ± 0·04

DISCUSSION

These results indicate that, whatever may be the nature of the primary photochemical act, the final products of the photolysis are derived by heterolytic rather than homolytic fission of the benzyl–oxygen bond to entities identical with or closely related to benzylcarbonium ions:



$$\left[\mathrm{ArCH_2{-}O{\cdot}CO{\cdot}NH{\cdot}CH_2{-}CO_2H}\right]^*_{\text{excited}} \longrightarrow \mathrm{ArCH_2^+} + \mathrm{\bar{O}_2C{\cdot}NH{\cdot}CH_2{\cdot}CO_2H} \xrightarrow{\mathrm{H_2O}} \mathrm{ArCH_2OH\ CO_2} + \mathrm{{}^+NH_3{\cdot}CH_2{\cdot}CO_2^-}$$

The evidence in support of this contention is: (1) The appearance of benzyl alcohol as the major aromatic fragment is difficult to account for unless an ionic intermediate is invoked. Homolysis of the benzyl–oxygen bond should lead to the formation of bibenzyl and only traces of this substance could be detected in the ether-soluble photolysis products. (2) The production of benzyl ether by photolysing Cbzglycine in ethanol is consistent with the mechanism outlined. It is inconsistent with both acyl–oxygen heterolysis and with homolysis of the benzyl–oxygen bond. The sensitivity of ϕ to the solvent system, more polar solvents being associated with higher values of ϕ and *vice versa,* is as expected for a heterolytic mechanism. (3) The variation of ϕ with the pH of the solvent is also in accord with a heterolytic mechanism. Repulsion between the negatively charged carboxyl group and the incipient charge on the oxygen of the benzyl–oxygen bond (I) could account for the observed decrease in ϕ on going from the free acid to the sodium salt. (4) Electron-attracting substituents (p-NO_2) as associated with lower, and electron-releasing substituents (p-MeO, m-MeO) with higher values of ϕ relative to the unsubstituted Cbzglycine molecule as would be expected for the mechanism proposed.

The mechanisms of many photochemical reactions in the gas phase [2] and in non-polar solvents [3] have been interpreted in terms of homolytic bond fissions to yield radicals. There is, however, no *a priori* reason for supposing that homolytic rather than heterolytic bond-fission is invariably favoured in such reactions.

The photochemical observations of Lifschitz [4] on the triphenylmethane dyes and of Havinga [5] and Zimmerman [6] on the nitrophenyl esters and ethers have been interpreted in terms of heterolytic mechanisms; the observation of concurrent homolysis and heterolysis has been made by Zimmerman *et al.*[6] and also by Horner and Stöhr [7] who studied the photolytic decomposition of diazonium compounds in aqueous alcohol. One of the earliest actinometers,[8] an aqueous solution of chloroacetic acid, undergoes photohydrolysis to glycollic acid and an analogous mechanism was suggested [9] for the photochemical deamination of amino-acids in aqueous solution. A common feature of all these examples is the use of a highly polar solvent and it seems likely that this is a necessary condition for photochemical heterolysis.

Comparison of the ultraviolet absorption spectra of some of the Cbzglycines with those of the corresponding toluenes reveals no discernible differences ascribable to the intervention of charge-transfer structures such as (II) in the excited state of the Cbzglycine. We therefore assume that the photochemically active transition is one which is confined to the π-orbitals of the benzene ring, and since all the photolyses of Cbz-derivatives described

[2] W. A. Noyes, G. B. Porter, and J. E. Jolley, *Chem. Rev.*, 1956, **56**, 49.

[3] D. H. R. Barton and W. C. Taylor, *J.*, 1958, 2500; J. J. Hurst and G. H. Whitham, *Proc. Chem. Soc.*, 1961, 116; M. A. Naylor and A. W. Anderson, *J. Org. Chem.*, 1953, **18**, 115; P. de Mayo, J. B. Stothers, and W. Templeton, *Canad. J. Chem.*, 1961, **39**, 488.

[4] J. Lifschitz, *Ber.*, 1925, **58**, 2434.

[5] E. Havinga and R. O. de Jongh, *Bull. Soc. chim. belges*, 1962, **71**, 803.

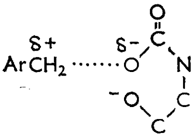
[6] (*a*) H. E. Zimmerman and V. R. Sandel, *J. Amer. Chem. Soc.*, 1963, **85**, 915; (*b*) H. E. Zimmerman and S. Somasekhara, *ibid.*, p. 922.

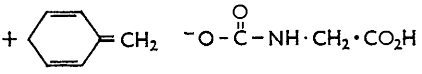
[7] L. Horner and H. Stöhr, *Chem. Ber.*, 1952, **85**, 993.

[8] L. Farkas and O. H. Wansborough-Jones, *Z. physik. Chem.*, 1932, **18***B*, 124.

[9] Ch. Weizmann, E. Bergmann, and Y. Hirshberg, *J. Amer. Chem. Soc.*, 1936, **58**, 1675.

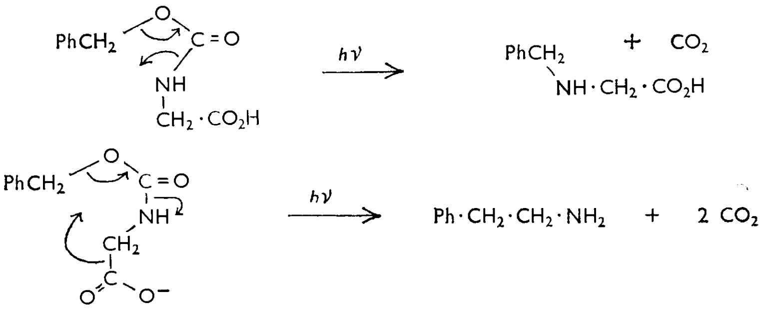
in this Paper are induced by 2537 Å radiation, it seems that this transition is that responsible for the 256 mμ band of benzene perturbed by the various substituents. Hence fission of the Cbzglycines must involve migration of some part of the excitation energy from the π-orbitals into the side-chain. Whether the subsequent fission occurs *via* vibrationally or electronically excited states of the molecules is a question which cannot be answered at present.


(I)


(II)

Examination of Table 3 reveals that the probability of decay of heterolytic mechanisms, as represented by ϕ, is crudely related to the stability of the corresponding carbonium ion. Compounds 9—13, which cannot give rise to resonance-stabilised carbonium ions are virtually unaffected by irradiation, whereas compounds 1—6, which can form benzylic carbonium ions, undergo photolysis. Furthermore, electron-attracting substituents inhibit photolysis whereas electron-releasing substituents accelerate the reaction. However, the relative values of ϕ for the *m*- and *p*-methoxyCbzglycines are contrary to expectations (but cf. ref. 6). It would be unwise to attempt a more detailed analysis of these data. It must be emphasised that the quantum yield represents the overall efficiency of an often complex sequence of changes. Attempts to correlate ϕ with structure must take account of all steps in the sequence and a direct comparison of ϕ with Hammett functions for the ground state would be naïve.

The formation of *N*-benzylglycine and phenethylamine in the irradiation of Cbzglycine can be rationalised in terms of intramolecular *N*- and *C*-alkylation mechanisms:



Alternatively, the *N*-benzylglycine could be formed by the interaction of benzylcarbonium ions and glycine, trapped in a solvent cage.

Dissociation on irradiation with ultraviolet light appears to be a general property of benzyl esters. With the exception of the *p*-phenylazo-compounds, where the modification to the chromophore is so extensive that entirely different electronic transitions may occur, all the substituted Cbzglycines examined showed this behaviour although with varying degrees of quantum efficiency; Cbzpiperidine and glycine benzyl ester behaved similarly as did the vinyl analogue of Cbzglycine derived from cinnamyl alcohol. The homologous esters phenethyloxycarbonylglycine and ethyloxycarbonylglycine were stable to photolytic fission.

N-Acyl amino-acids of the type $C_6H_5\cdot[CH_2]_n\cdot CO\cdot NHR$ are known to be subject to photolytic fission.[10] The quantum yields for this process are low (*ca.* 10^{-3}) and we were unable to detect any free glycine in irradiated solutions of aceturic and hippuric acids.

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[10] I. Mandl, B. Levy, and A. D. McLaren, *J. Amer. Chem. Soc.*, 1950, **72**, 1790.

The dithio-analogues of Cbzglycine and of ethoxycarbonylglycine were decomposed to glycine on irradiation although the quantum yields were low. The major chromophore in the latter case is the thiocarbonyl group.

From the practical viewpoint the improvement in the quantum yield of amino-acid from the substituted Cbzglycine (*e.g.*, by the use of the *m*-methoxyCbz derivative) is more than counterbalanced by the relative inaccessibility of the substituted benzyl alcohols.

The photolytic method of removal of the Cbz group is useful in another context. The methods currently available for the detection of Cbz-amino-acids on paper chromatograms are not entirely satisfactory, but it has been found that by exposing such chromatograms to the unfiltered light of a mercury arc, the Cbz-amino-acids are converted into the free amino-acids which can then be detected by the usual ninhydrin spray technique.

EXPERIMENTAL

Ultraviolet irradiations on a preparative scale (250 ml.) were carried out in a quartz, water-cooled photochemical reaction vessel with a Hanovia 500 w medium pressure mercury arc source.

Isolation of the Products of the Irradiation of Cbzglycine.—(*A*) A solution of Cbzglycine (1·98 g.) in sodium hydroxide (95 ml., 0·1N) was made up to 250 ml. with water and irradiated for *ca.* 12 hr. The photolyte was then centrifuged and the solid material was collected, washed with ether, dilute hydrochloric acid, and water, then dried *in vacuo* (Found: C, 76·4, 76·2, 77·4, 77·6; H, 7·95, 7·9, 7·7, 7·6; N, 2·8, 2·7, 1·4, 1·6. $(C_7H_8O)_n$ requires C, 77·8; H, 7·4%). A similar product was obtained by irradiating for 22 hr. a solution of benzyl alcohol (520 mg.), and glycine (360 mg.) in sodium hydroxide (48 ml. of 0·1N) and water (200 ml.).

The aqueous photolyte remaining after centrifuging was concentrated to small volume *in vacuo* and analysed by filter-paper chromatography in a variety of solvents. Spraying with ninhydrin showed that glycine was the major component (see later), and revealed the presence of three minor ninhydrin-positive spots,designated *A*, *B*, and *C*, in order of increasing R_F value. By comparison with chromatograms of authentic specimens, spots *B* and *C* were shown to be *N*-benzylglycine and phenethylamine, respectively. This identification was confirmed by electrophoresis on filter paper in 1N-acetic acid. Spot *B* and *N*-benzylglycine moved the same distance (towards the cathode, 5 cm.) as did spot *C* and phenethylamine (13 cm.).

Spot *A*, which gave a grey coloration with ninhydrin was found to be ultraviolet-absorbing ($\lambda_{max.}$ 280 mμ). It was not identical with *N*-*o*-tolylglycine and has not yet been identified.

(*B*) A solution of Cbzglycine (8·3 g.) and sodium acetate (*ca.* 50 g.) in water (2·5 l.) was irradiated in 250 ml. portions for 4 hr. Extraction with ether gave a brown oil (1·06 g.) which when distilled yielded benzyl alcohol; 3,5-dinitrobenzoate, m. p. and mixed m. p. 113°.

(*C*) A solution of Cbzglycine (500 mg.) in sodium hydroxide (24 ml., 0·1N) was made up to 250 ml. with water and irradiated for 3 hr. The photolyte was made strongly alkaline and extracted with ether. The ethereal layer was washed with dilute hydrochloric acid and water, and dried (solution *a*).

A solution of Cbzglycine (500 mg.) in ethanol (100 ml.) was irradiated for 3 hr., then evaporated *in vacuo*. The residue was dissolved in ether and the ethereal solution was washed with alkali, acid, and water, and finally dried (solution *b*). Solutions *a* and *b* were examined by vapour-phase chromatography on the following two columns: (1) a 200 cm. column of diethylene glycol adipate polyester (25% w/w of support) plus phosphoric acid (3%) on Embacel operated at 165° at a nitrogen (carrier gas) pressure of 60 cm. Hg; (2) a 120 cm. column of Apiezon " L " (29%) and sodium hexanoate (3·7%) on Embacel operated at 136° at an argon pressure of 10 lb./sq. in. Solution *a* contained mainly benzyl alcohol and small amounts of bibenzyl and other substances; in solution *b*, the benzyl alcohol was replaced by benzyl ethyl ether.

(*D*) A solution of Cbzglycine (12 g.) in sodium hydroxide (60 ml., 1N) was made up to 2 l. with water and irradiated in 250 ml. portions for 3 hr. The photolyte was filtered, concentrated *in vacuo* to a volume of *ca.* 50 ml., made strongly alkaline with sodium hydroxide, and extracted continuously with ether for 12 hr. The aqueous layer was then acidified with hydrochloric acid, washed with two portions (2 × 50 ml.) of ethyl acetate, and concentrated to dryness *in vacuo*. The residue was dissolved in water (20 ml.). The solution was filtered and the filtrate was then treated with benzoyl chloride (9·4 g.) under Schotten–Baumann conditions.

The product recrystallised from water to give hippuric acid, m. p. and mixed m. p. 187—189°, ν 2·4, 5·7, 8·5 μ.

The ethereal extract was concentrated and extracted with dilute hydrochloric acid. The aqueous phase, when basified, gave an oil which was distilled and converted into its hydrochloride. Recrystallisation from ethanol–light petroleum gave phenethylamine hydrochloride, m. p. 208—212° (lit.,[11] m. p. 216—217°) (Found: N, 8·8. Calc. for $C_8H_{11}N,HCl$, N, 8·9%).

Measurement of Quantum Yields.—The lamp was a low-pressure mercury arc in the form of a flat spiral, external diameter 8·5 cm. (Hanovia 758/62). The output was stabilised to $\pm 7\%$ by sealing it into a Perspex tank which was filled with distilled water maintained at 29·2° ± 0·1° by a contact thermometer operating a heater through a valve relay. The lamp power unit was also connected to the mains through a constant voltage transformer (Advance Components Ltd., MT/104A). This system is effectively monochromatic. At least 95% of the emission of the lamp is at 2537 Å, the remaining energy being at *ca.* 1800 Å (absorbed by the 3 cm. of water separating the lamp from the absorption cells) and at $\lambda > 3000$ Å (not absorbed by the material being photolysed).

Cells were constructed by cementing 5 cm. diameter quartz discs (Thermal Syndicate, " Spectrosil " quality) on a section of 5 cm. external diameter glass tubing which was fitted with a lead-in tube and a ground glass stopper. The volume to fill the cells was 23·5 ml.

For quantum yield measurements on [2-^{14}C]Cbzglycine where the optical density was relatively low, allowance was made for incomplete absorption of the incident light by the chromophore. In all other cases, the optical density of the solution was arranged to be >2 and actinometry showed complete absorption of the 2537 Å radiation.

Glycine was estimated by the colorimetric method of Yemm and Cocking.[12] The lamp output was measured with a ferrioxalate actinometer solution.[13] Standards were included in every analytical run and " blank " readings were also recorded.

(*A*) A solution of Cbzglycine (1·002 g.) in sodium hydroxide (48 ml., 0·1N) was made up to 250 ml. with water. Portions of this Cbzglycine solution were irradiated for various times and the lamp output was measured both before the first and after the last irradiations. The average value of the output ($6·42 \times 10^{-8}$ einsteins/sec.) was used in computing the quantum yield. The amino-nitrogen content of the irradiated solutions was measured colorimetrically on 1 ml. portions of these solutions, appropriately diluted. The quantum yields are given in Table 2.

(*B*) [2-^{14}C]Glycine (350 mg.) containing 100 μc of ^{14}C was converted into Cbzglycine by the usual Schotten–Baumann reaction with benzyl chloroformate. The crude product (807 mg.) was recrystallised from water to give [2-^{14}C]Cbzglycine (715 mg., 73%) as needles, m. p. 119—120° (lit.,[14] m. p. 120°).

A solution of this compound (100·4 mg.) in sodium hydroxide (5 ml., 0·01N) was made up to 250 ml. with water. The optical density of this solution at 254 mμ was 0·290. The lamp output was $6·30 \times 10^{-8}$ einsteins/sec. Portions of the Cbzglycine solution (23·5 ml.) were irradiated for periods of 10, 20, 40, and 80 min., respectively. Each portion was concentrated to *ca.* 4 ml. in a rotatory evaporation apparatus and the products in each portion were separated by paper chromatography [solvent, ethyl methyl ketone–propionic acid–water (15 : 5 : 6)]. When dry, the chromatograms were divided into a series of numbered horizontal strips 1 cm. wide and each strip was monitored for radioactivity with an end-window Geiger counter fitted with a metal mask in which was cut a rectangular aperture 3 × 1 cm. In this way the radioactivity contained in each of the numbered 1 cm. strips was estimated and these measurements were used to locate the radioactive areas. The chromatograms were cut into sections corresponding to each of the four components of the photolysis mixture. These sections were eluted with water into counter tubes, the tubes were evaporated to dryness *in vacuo* over calcium chloride, and water (0·1 ml.) was then added to each tube to dissolve the contents followed by scintillator solution[15] (10 ml.). The tubes were shaken and counted. Each tube was washed carefully, filled with scintillator solution (10 ml.), and again counted to give the blank reading and finally a sample (0·1 ml.) of the concentrated photolyte mixture was added to the tube and another count was taken. By this method the ratio of ^{14}C in each of the products to the total

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[11] K. Kindler, *Arch. Pharm.*, 1927, 397.

[12] E. W. Yemm and E. C. Cocking, *Analyst*, 1955, **80**, 209.

[13] C. G. Hatchard and C. A. Parker, *Proc. Roy. Soc.*, 1956, *A*, **235**, 518.

[14] M. Bergmann and J. S. Fruton, *J. Biol. Chem.*, 1937, **118**, 405.

[15] W. H. Langham, W. J. Eversole, F. N. Hayes, and T. Trujillo, *J. Lab. Clin. Med.*, 1956, **47**, 819.

^{14}C can be measured and the molar concentration of the products can be evaluated. The original unirradiated [2-^{14}C]Cbzglycine solution was chromatographed and the glycine: Cbzglycine ratio was determined in the same way. These results appear in Table 1.

(*C*) Quantum yield measurements on the other compounds described in this Paper were made in a manner similar to that described in (*A*), the free amino-acid being estimated colorimetrically. For *p*-methoxyCbzglycine, which is not stable to the conditions of the colorimetric estimation, the liberated glycine was determined as its copper complex by polarography.[16]

Irradiation of Cbzglycine Ethyl Ester in Ethanol–Water.—Cbzglycine ethyl ester, prepared from glycine ethyl ester and benzyl chloroformate, was obtained as needles, m. p. 33—36° (lit.,[17] m. p. 35·5—36·5°). Solutions of this compound (10^{-2}M) in aqueous ethanol (65, 40, and 10% water, respectively) were prepared. Solutions of Cbzglycine (10^{-2}M) sodium salt and free acid in ethanol–water (50 : 50) were also prepared. Portions of each of these solutions (23·5 ml.) were irradiated for 4 min. After irradiation of the *ester* solutions 1 ml. portions of each solution were allowed to stand overnight with 0·01N-sodium hydroxide (1 ml.) before the amino-nitrogen content of the solution was measured colorimetrically. The lamp output was $5·78 \times 10^{-8}$ einsteins/sec. The results of these irradiations are in Table 4.

Synthesis of Substituted Cbzglycine and of Related Compounds.—Esters of glycine-*N*-carbamic acid were prepared by reaction of the appropriate chloroformates (from the alcohol and phosgene) with glycine under Schotten–Baumann conditions.

(a) m-*MethoxyCbzglycine.* *m*-Methoxybenzyl alcohol (5·2 g.) was converted into the chloroformate which reacted with glycine (2·8 g.) to give m-*methoxybenzyloxycarbonylglycine* as plates (from benzene), m. p. 60—61·5° (5·8 g., 65%) (Found: C, 55·2; H, 5·7; N, 5·8. $C_{11}H_{13}NO_5$ requires C, 55·3; H, 5·4; N, 5·9%).

TABLE 4

Compound	Solvent– % water	Amino-nitrogen measured (μg. N/ml.)	ϕ
Cbzglycine ethyl ester	65	0·905	0·11
,, ,, ...	40	0·584	0·069
,, ,, ...	10	0·282	0·034
Cbzglycine Na salt	50	0·440	0·053
Cbzglycine	50	0·631	0·076

(b) *Cinnamyloxycarbonylglycine.* Cinnamyl alcohol (10 g.) was converted into the corresponding chloroformate which was coupled with glycine (5·7 g.) to give *cinnamyloxycarbonylglycine* (15·7 g., 88%) as plates (from water), m. p. 131—132°, ν 3·1, 6·0 μ; $\lambda_{max.}$ 250, 282, 291 mμ (Found: C, 61·6; H, 5·5; N, 6·1. $C_{12}H_{13}NO_4$ requires C, 61·3; H, 5·5; N, 6·0%).

(c) *Phenethyloxycarbonylglycine.* β-Phenylethyl alcohol (3 g.) was converted into the corresponding chloroformate which was coupled with glycine (1·9 g.) to give *phenethyloxycarbonylglycine* (4·88 g., 89%) as a syrup which crystallised on repeated trituration with light petroleum. It had m. p. 40—44° (Found: C, 59·4; H, 5·9; N, 6·2. $C_{11}H_{13}NO_4$ requires C, 59·2; H, 5·8; N, 6·3%).

Irradiation of Glycine Benzyl Ester.—A solution of glycine benzyl ester hydrochloride (700 mg.) in water (250 ml.) was irradiated for 3 hr. The solution was concentrated *in vacuo* to *ca.* 10 ml. and a sample was applied to a paper chromatogram together with a glycine control spot. After development of the chromatogram in ethyl methyl ketone–propionic acid–water (15 : 5 : 6), drying, and spraying with ninhydrin, the photolyte gave a single spot R_F 0·17 identical with that of the glycine control. No ester spot was detected on the chromatogram.

Irradiation of Benzyloxycarbonylpiperidine.—Benzyl chloroformate (17·3 g.) in ether (50 ml.) was added dropwise with stirring and ice-cooling to a solution of piperidine (25 ml.) in ether (50 ml.). After 30 min., the ethereal solution was filtered from piperidine hydrochloride, washed with acid and water, then dried and distilled to give N-*benzyloxycarbonylpiperidine* (18·2 g., 82%) as a liquid, b. p. 129—131°/0·5 mm.; ν 5·9 μ, n_D^{25} = 1·5272 (Found: C, 71·4; H, 7·8; N, 6·5. $C_{13}H_{17}NO_2$ requires C, 71·3; H, 7·8; N, 6·4%).

A solution of this compound (374·8 mg.) in ethanol–water was irradiated with a low pressure mercury arc for 676 min. and the photolyte (1 drop) was tested for free piperidine with copper

[16] A. J. P. Martin and R. Mittelmann, *Biochem. J.*, 1948, **43**, 353.

[17] A. E. Barkdoll and W. F. Ross, *J. Amer. Chem. Soc.*, 1944, **66**, 951.

sulphate–carbon disulphide.[18] A positive test was obtained: a comparison test on the unirradiated solution was negative. The quantum yield of piperidine, as determined by titration of the liberated base with 0·01N-acid, was estimated to be of the order of 0·08.

Irradiation of Phenoxycarbonylglycine Ethyl Ester.—Phenylchloroformate (11·2 g.), prepared from phenol and carbonyl chloride, was coupled with glycine ethyl ester to give an oil which was eluted from a short column of deactivated alumina with benzene–light petroleum. A portion of this product was distilled in a bulb tube at 0·2 mm. to give *phenoxycarbonylglycine ethyl ester* as a glassy liquid; ν 2·9, 5·75, 8·3 μ (Found: C, 59·4; H, 6·0; N, 6·4. $C_{11}H_{13}NO_4$ requires C, 59·2; H, 5·8; N, 6·3%).

A solution of this ester (126 mg.) in ethanol–water was irradiated with a low pressure mercury arc for 16 hr. After removal of the solvent *in vacuo* a colourless oil was obtained, ν 2·9, 5·75, 8·3 μ, which appeared to be unchanged starting material.

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[18] Feigl, " Spot Tests in Organic Analysis," 5th edn., Elsevier, London, 1956, p. 262.