rotation but opposite in sign. The results of the present study extend these observations.

Experimental Section

Melting points were taken on a Fisher–Johns melting block and are corrected.

Preparation of the Methyl Pentofuranosides.—Methyl α- and β-L-arabinofuranoside were prepared by the method of Augestad and Berner[7] as syrups: $[\alpha]^{23}D$ −124° (*c* 2.0, water) and +97° (*c* 2.0, water), respectively; lit.[7] $[\alpha]D$ −128° and +118°, respectively. Methyl α-L-arabinofuranoside was also prepared as a syrup, $[\alpha]^{25}D$ −129° (*c* 1.3, methanol), by Zemplen[8] deacetylation of methyl 2,3,5-tri-*O*-benzoyl-α-L-arabinofuranoside.[9] Crystalline methyl α-D-xylofuranoside, mp 82–84°, $[\alpha]^{26}D$ +170° (*c* 2.35, water) (lit.[7] mp 84°, $[\alpha]D$ +182°), and syrupy methyl β-D-xylofuranoside, $[\alpha]^{30}D$ −80° (*c* 3.6, water) (lit.[7] $[\alpha]D$ −90°), were prepared by the method of Augestad and Berner.[7]

General Procedure for Periodate Oxidations, Borohydride Reductions, and *p*-Nitrobenzoylations.—Periodate oxidation of the four methyl pentafuranosides, borohydride reduction of the resulting dialdehydes, and esterification of the enantiomorphic triols were carried out using the methods described by Smith and Van Cleve.[4] The melting points and specific rotations of the tris-*p*-nitrobenzoates thus obtained are recorded in Table I. The mixture melting point of each of the derived tris-*p*-nitrobenzoates was undepressed upon admixture with the corresponding tris-*p*-nitrobenzoate derived from methyl α- or β-D-glucopyranoside.

(7) I. Augestad and E. Berner, *Acta. Chem. Scand.*, **8**, 251 (1954).
(8) G. Zemplen and E. Pacsu, *Ber.*, **62**, 1613 (1929).
(9) R. Barker and H. G. Fletcher, Jr., *J. Org. Chem.*, **26**, 4605 (1961).

Use of the 3,5-Dimethoxybenzyloxycarbonyl Group as a Photosensitive N-Protecting Group

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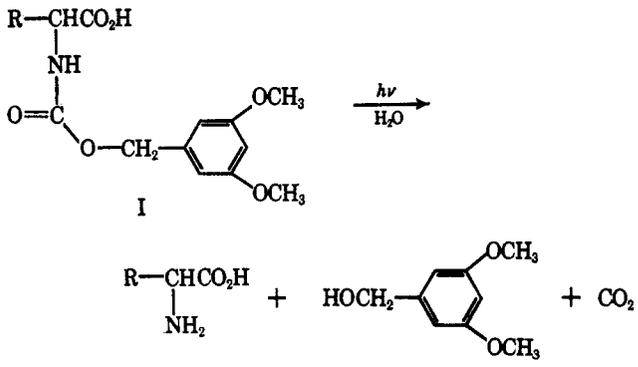
There are now a number of selectively removable groups which can be used for protection of the amino functions during peptide synthesis.[1] Removal of the protecting groups involves, in general, either treatment with acid or base, catalytic or chemical reduction, or a combination of these methods. More recently, Barltrop and Schofield[2] have reported on another method of potential usefulness in this field, *i.e.*, the removal of a protecting group by means of ultraviolet irradiation. Zimmerman and Sandel[3] studied the photochemical solvolysis of certain substituted benzyl acetates and found that *m*-methoxyl substitution enhanced reactivity. In this paper we wish to report on the photolytic cleavage of carbamates of general structure I.

To evaluate the use of this group in peptide synthesis, the 3,5-dimethoxybenzyloxycarbonyl derivatives of several amino acids and a dipeptide were prepared and irradiated in aqueous solution.

(1) (a) R. A. Boissonas, *Advan. Org. Chem.* **3**, 159 (1963); (b) J. Rudinger, *Pure Appl. Chem.*, **7**, 335 (1963).
(2) (a) J. A. Barltrop and P. Schofield, *Tetrahedron Letters*, 697 (1962); (b) *J. Chem. Soc.*, 4758 (1965).
(3) H. E. Zimmerman and V. R. Sandel, *J. Am. Chem. Soc.*, **85**, 915 (1963).



Preparation of the 3,5-dimethoxybenzyloxycarbonyl derivative was accomplished by treating the amino acid with 3,5-dimethoxybenzyl *p*-nitrophenylcarbonate in aqueous tetrahydrofuran in the presence of sodium hydroxide.[4] Properties of the derivatives are listed in Table I.

Irradiations were carried out in aqueous dioxane solution using a high-pressure mercury lamp (Hanovia 654A-36, Vycor glass filter). Initial experiments with 3,5-dimethoxybenzyloxycarbonyl-D-phenylglycine indicated that the maximum concentration of free amino acid was obtained after an irradiation time of approximately 1.5 hr (paper chromatographic assay). The results obtained in preparative experiments are summarized in Table II. Irradiation of benzyloxycarbonylglycine under these conditions resulted in a considerably lower yield (10%) of the free acid in comparison with that obtained from 3,5-dimethoxybenzyloxycarbonylglycine (85%). In the case of the L-lysine derivative (Table I), it was found possible to remove the 3,5-dimethoxybenzyloxycarbonyl group while leaving the ε-benzyloxycarbonyl group intact.

The dipeptide derivative, 3,5-dimethoxybenzyloxycarbonyl-D-phenylglycylglycine, was prepared in 72% yield by a mixed anhydride coupling procedure. Irradiation under the same conditions employed for the amino acid derivatives furnished D-phenylglycylglycine[5] in 65% yield.

No attempt was made to isolate other products of the irradiations except in the case of the glycine derivative where 3,5-dimethoxybenzyl alcohol was isolated in 38% yield.[6]

These results suggest that the 3,5-dimethoxybenzyloxycarbonyl group could be a practical protecting group for use in peptide synthesis and other areas of synthesis. Its removal does not involve the use of acid or base or reductive cleavage.

Experimental Section[7]

3,5-Dimethoxybenzyl *p*-Nitrophenylcarbonate.—Reduction of 3,5-dimethoxybenzoic acid (Aldrich Chemical Co.) with lithium aluminum hydride in tetrahydrofuran afforded 3,5-dimethoxy-

(4) The procedure was essentially that which has been described for the preparation of *t*-butyloxycarbonyl derivatives of amino acids: G. W. Anderson and A. C. McGregor, *ibid.*, **79**, 6180 (1957).
(5) The DL compound has been prepared previously: E. Fischer and J. Schmidlin, *Ann.*, **340**, 190 (1905).
(6) For a detailed analysis of the products from the photolysis of benzyloxycarbonylglycine and a discussion of the mechanism of this reaction, see ref 2b.
(7) Melting points were determined on a Fisher-Johns apparatus and are uncorrected. The ultraviolet spectra were obtained in ethanol solution on a Cary Model 14 recording spectropolarimeter. Optical rotations were obtained on a Rudolph Model 200 photoelectric polarimeter. Titrations were carried out in 2:1 dimethylformamide–water solution.

TABLE I

3,5-Dimethoxybenzyloxycarbonyl derivative of	% yield[a]	Mp, °C	$[\alpha]^{25}D$, deg (c, $CHCl_3$)	Formula	Carbon, % Calcd	Carbon, % Found	Hydrogen, % Calcd	Hydrogen, % Found	Nitrogen, % Calcd	Nitrogen, % Found
Glycine[b]	71	97–98	...	$C_{12}H_{15}NO_6$	53.53	53.43	5.62	5.51	5.20	5.03
DL-Methionine[b]	68	86–88	...	$C_{15}H_{21}NO_6S$[c]	52.46	52.68	6.11	6.18	4.08	3.99
D-Phenylglycine[b]	76	132.5–133.5	−100 (1.05)	$C_{18}N_{19}NO_6$	62.60	62.89	5.54	5.57	4.06	4.04
L-Serine[d]	55	44–56	+15.0 (1.02)	$C_{13}H_{17}NO_7$	52.17	51.91	5.73	5.97	4.68	4.61
ε-Benzyloxycarbonyl-L-lysine[b]	75	120.5–121.5	+11.7 (1.02)	$C_{24}H_{30}N_2O_8$	60.75	60.98	6.37	6.51	5.91	5.95

[a] The yields are for recrystallized products. [b] Recrystallized from methanol–water. [c] *Anal.* Calcd: S, 9.34. Found: S, 9.04. [d] Recrystallized from ethyl acetate–Skellysolve B.

TABLE II

Irradiation product	% yield	$[\alpha]^{24}D$, deg
Glycine	85	...
DL-Methionine	60	...
D-Phenylglycine	66	−168 (*c* 1.00, 5 *N* HCl)[a]
L-Serine	72[b]	+13.5 (*c* 2.00, 1 *N* HCl)[c]
ε-Benzyloxycarbonyl-L-lysine	42[b]	+17.0 (*c* 1.00, 1 *N* HCl)[d]

[a] Starting D-phenylglycine (Ott Chemical Co.) had $[\alpha]^{24}D$ −167° (*c* 1.00, 5 *N* HCl). D. Rudman, A. Meister, and J. P. Greenstein [*J. Am. Chem. Soc.*, **74**, 551 (1952)] reported $[\alpha]^{26}D$ −169.0° (*c* 1,5 *N* HCl). [b] Recrystallized from acetone–water. [c] Starting L-serine (Nutritional Biochemicals Corp.) had $[\alpha]^{24}D$ +13.5° (*c* 2.00, 1 *N* HCl). J. P. Greenstein and M. Winitz ("Chemistry of the Amino Acids," Vol. 3, John Wiley and Sons, Inc., New York, N. Y., 1961, p 2202) reported $[\alpha]^{25}D$ +15.1° (*c* 2, 1 *N* HCl). [d] Starting ε-benzyloxycarbonyl-L-lysine (Nutritional Biochemicals Corp.) had $[\alpha]^{24}D$ +17.0° (*c* 1.00, 1 *N* HCl). A. Neuberger and F. Sanger [*Biochem. J.*, **37**, 515 (1943)] reported $[\alpha]D$ +14.4° (*c* 1.6, 2 equiv of HCl).

benzyl alcohol in 74% yield: mp 48–50° (lit.[8] mp 47–48°); λ_{max} 220 mμ (ε 7410), 280 mμ (ε 1760).

To an ice-cold solution of 28.0 g (0.167 mole) of 3,5-dimethoxybenzyl alcohol and 5.90 g (0.150 mole) of pyridine in 100 ml of acetone was added with stirring 30.4 g (0.150 mole) of *p*-nitrophenyl chloroformate (prepared as described in ref 4). Immediately after the last portion had been added, the product began to precipitate. The mixture was added to 700 ml of water; the product was collected by filtration, washed several times with water, and recrystallized from methanol (2500 ml). There was obtained 30.7 g (61%) of 3,5-dimethoxybenzyl *p*-nitrophenylcarbonate, mp 114–115°.

Anal. Calcd for $C_{16}H_{15}NO_7$: C, 57.65; H, 4.54; N, 4.20. Found: C, 57.91; H, 4.77; N, 3.95.

3,5-Dimethoxybenzyloxycarbonyl-D-phenylglycine. General Procedure for the Preparation of 3,5-Dimethoxybenzyloxycarbonylamino Acids.—A mixture of 3.66 g (0.024 mole) of D-phenylglycine (Ott Chemical Co.), 10.0 g (0.030 mole) of 3,5-dimethoxybenzyl *p*-nitrophenylcarbonate, 24.0 ml of 2 *N* sodium hydroxide solution, and 48 ml of tetrahydrofuran was stirred at room temperature for 21 hr.[4] The tetrahydrofuran was evaporated under reduced pressure. The precipitated solid was collected by filtration and extracted several times with 1 *M* sodium bicarbonate solution. The pH of the combined filtrates was adjusted to 5.8 with 1 *N* hydrochloric acid, and the resulting mixture was extracted three times with ether to remove *p*-nitrophenol and any unreacted 3,5-dimethoxybenzyl *p*-nitrophenylcarbonate. The aqueous phase was then over-layered with ether and the pH was adjusted to 2.0. The ether layer was separated and the aqueous layer was extracted twice more with ether. The ether extracts were combined, washed twice with water and once with saturated sodium chloride solution, and dried with sodium sulfate. Evaporation of the solvent and crystallization of the residue from methanol–water afforded 6.40 g (77%) of 3,5-dimethoxybenzyloxycarbonyl-D-phenylglycine, mp 130–132.5°. The analytical sample melted at 132.5–133.5°.

The properties of the 3,5-dimethoxybenzyloxycarbonylamino acids are summarized in Table I.

3,5-Dimethoxybenzyloxycarbonyl-D-phenylglycylglycine.—A solution of 1.38 g (0.004 mole) of 3,5-dimethoxybenzyloxycarbonyl-D-phenylglycine in 20 ml of tetrahydrofuran was cooled in a salt–ice bath, and 0.56 ml of triethylamine was added, followed by 0.52 ml of isobutyl chloroformate. The mixture was stirred for 15 min. A cold solution of 0.300 g (0.004 mole) of glycine (Eastman Kodak Co.) and 0.56 ml of triethylamine in 20 ml of 1:1 water–tetrahydrofuran was then added dropwise. After stirring for 1 hr in the cold and 1 hr at room temperature, the tetrahydrofuran was removed under reduced pressure; the residue was diluted with 20 ml of water and extracted once with 20 ml of ethyl acetate. The aqueous phase was separated, diluted with 40 ml of water, and over-layered with 40 ml of ethyl acetate, and the pH was adjusted to 2.5 with 10% hydrochloric acid. The aqueous phase was extracted once more with 40 ml of ethyl acetate. The combined extracts were washed once with water and dried with anhydrous sodium sulfate. The solid residue obtained upon evaporation of the solvent was slurried with ether and filtered to give 1.16 g (72%) of 3,5-dimethoxybenzyloxycarbonyl-D-phenylglycylglycine, mp 156–157°. The anayltical sample was obtained by recrystallization from methanol–water: mp 156.5–157.5°, $[\alpha]^{25}D$ −60.3° (*c* 0.823, ethanol).

Anal. Calcd for $C_{20}H_{22}N_2O_7$: C, 59.69; H, 5.51; N, 6.96. Found: C, 59.42; H, 5.68; N, 6.69.

General Procedure and Apparatus for Irradiation.—The irradiations were carried out with a Hanovia 654A-36 high-pressure mercury lamp housed in a water-cooled quartz immersion well and fitted with a Vycor glass (Corning No. 7910) filter sleeve. The compound to be irradiated (0.0035–0.005 mole) was dissolved in 1 l. of 1:1 dioxane–water. Nitrogen was passed through the solution during the course of the reaction. An irradiation time of 1.5 hr was employed for the preparative experiments. The progress of the reactions was followed by paper chromatography (Whatman No. 1 paper, 3:1:1 *n*-butyl alcohol–acetic acid–water, authentic samples of the amino acids as reference standards). In all cases studied, no free amino acid was detected by this method in aliquot samples maintained in the dark during the irradiation period. The dipeptide and the amino acids were isolated by evaporating the solution to dryness, treating the residue with a minimum volume of acetone, and collecting the product by filtration.

Irradiation of 3,5-Dimethoxybenzyloxycarbonylglycine.—A solution of 1.345 g (0.005 mole) of 3,5-dimethoxybenzyloxycarbonylglycine in 1 l. of 1:1 dioxane–water was irradiated, and the amino acid was isolated as described above. The crystalline glycine amounted to 0.318 g (85%).

The acetone filtrate was evaporated to dryness. The residue was taken up in ethyl acetate and passed through a column of Woelm neutral alumina (activity III, 25 g). Elution with ethyl acetate provided 0.734 g of yellowish oil that crystallized on standing: mp 34–43°. The infrared spectrum of this material was identical with that of 3,5-dimethoxybenzyl alcohol. Recrystallization from Skellysolve B afforded 0.235 g of the alcohol, mp 43–46° (lit.[8] mp 47–48°), and a second crop of 0.088 g, mp 40–45°. The total yield of recrystallized material amounted to 38%.

Table II summarizes the results of the irradiations of the 3,5-dimethoxybenzyloxycarbonylamino acids.

Irradiation of Benzyloxycarbonylglycine.—Following exactly the same procedure as described above, irradiation of a solution of 1.045 g (0.005 mole) of benzyloxycarbonylglycine (Aldrich Chemical Co.) yielded 0.037 g (10%) of glycine.

Irradiation of 3,5-Dimethoxybenzyloxycarbonyl-D-phenylglycylglycine.—A solution of 1.00 g (0.00249 mole) of 3,5-dimethoxybenzyloxycarbonyl-D-phenylglycylglycine in 1 l. of 1:1 dioxane–water was irradiated for 1.5 hr. Following the isolation procedure described above, there was obtained 0.335 g (65%) of D-phenylglycylglycine:[5] mp 226–228°, $[\alpha]^{25}D$ −112° (*c* 0.484, 0.1 *N* HCl), $pK_a' = 5.35, 7.55$.

Anal. Calcd for $C_{10}H_{12}N_2O_3$: neut equiv, 208. Found: neut equiv, 216.

(8) F. Mauthner, *J. Prakt. Chem.*, **100**, 176 (1920).

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The Preparation of Diarylcyclopropenones by the Reaction of Phenyl(bromodichloromethyl)mercury with Diarylacetylenes[1]

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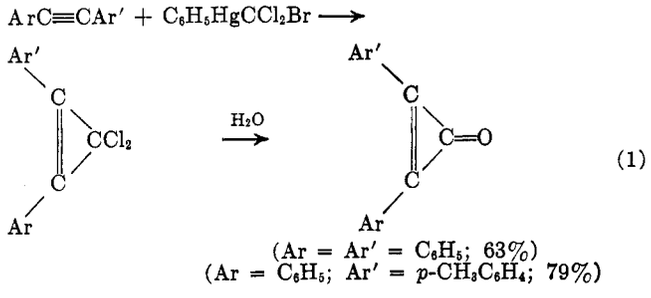
Diarylcyclopropenones have been of interest in recent years, and considerable effort has been expended on the development of useful procedures for their preparation. The best route to symmetrically substituted diarylcyclopropenones is Breslow's elimination of HBr from α,α'-dibromobenzyl ketones.[4] Vol'pin, *et al.*,[5] have reported that reaction of diphenylacetylene with bromoform and potassium *t*-butoxide produces diphenylcyclopropenone in 20–30% yield. All other routes reported to date appear to be considerably less practical.[6]

In an extension of our study of the reactions of olefins with phenyl(trihalomethyl)mercury compounds,[7] we have found that diarylacetylenes react with phenyl(bromodichloromethyl)mercury to give, after hydrolysis of the reaction mixture, high yields of diarylcyclopropenones (eq 1). This procedure should find especially useful application in the preparation of unsymmetrical diarylcyclopropenones and of diarylcyclopropenones containing base-sensitive functional groups. Analogous reactions could not be realized with dialkylacetylenes.



(1)

Experimental Section

General Comments.—All reactions were carried out under an atmosphere of prepurified nitrogen. Diphenylacetylene was purchase from Orgmet; phenyl-*p*-tolylacetylene was prepared by the method of Stephens and Castro[8] in 83% yield: mp 72.5–74°. The preparation of phenyl(bromodichloromethyl)mercury has been described in a previous paper of this series.[9]

Diphenylcyclopropenone.—A solution of 3.56 g (20 mmoles) of diphenylacetylene and 8.82 g (20 mmoles) of phenyl(bromodichloromethyl)mercury in 50 ml of dry benzene was heated at reflux with stirring under a nitrogen atmosphere for 1 hr. The reaction mixture was cooled and filtered to remove phenylmercuric bromide (6.3 g, 88%). The filtrate was hydrolyzed by heating it at reflux with 25 ml of 95% ethanol for 5 min.[10] The solvents were removed at reduced pressure to leave a hard, yellow solid. The latter was dried at 0.05 mm for 18 hr to give 4.65 g of light yellow crystals. These were sublimed at 82° (0.03 mm), giving 4 g (97%) of slightly yellow crystals which melted over a range of 100–140°. This crude product was recrystallized from dry cyclohexane, being separated from some yellow, cyclohexane-insoluble solid in the process. Slow crystallization from cyclohexane solution at room temperature gave 2.60 g (63.3%) of pure diphenylcyclopropenone, mp 120–122° (cor), lit.[4] mp 119–121°. The infrared spectrum of the product (CCl_4 and CS_2) was identical with that of an authentic sample prepared by Breslow's method,[4] as was the ultraviolet spectrum in ethanol solution.

Phenyl-*p*-tolycyclopropenone.—Essentially the same procedure was used in the reaction of 20 mmoles each of phenyl-*p*-tolylacetylene and phenyl(bromodichloromethyl)mercury. The yield of crude product (light yellow crystals, mp ~116°) was 3.50 g (79.6%). Recrystallization of 1.0 g of this material from benzene gave 0.55 g of solid with mp 128.5–129°. An analytical sample melted at 129.5–131.5°.

Anal. Calcd for $C_{16}H_{12}O$: C, 87.24; H, 5.49. Found: C, 87.14; H, 5.27.

The infrared spectrum (CCl_4–CS_2 composite, Perkin-Elmer 337) showed bands at 3075 (w), 3060 (w), 3025 (w), 2975 (w), 2915 (w), 1850 (s), 1630(s), 1510 (m), 1485 (m), 1450 (m), 1340 (m), and 788 (s) cm^{-1}. The nmr spectrum ($CDCl_3$ solution, Varian A-60) showed a singlet (3 H) at 2.44 ppm and a 9 H multiplet at 7.26–8.04 ppm downfield from tetramethylsilane. The ultraviolet spectrum (in ethanol) showed the following bands, $m\mu$ (log ϵ): 223 (4.25), 228 (sh) (4.22), 234 (sh) (4.16), 293 (sh) (4.40), 302 (4.47), and 317 (sh) (4.29).

Acknowledgments.—The authors are grateful to the U. S. Air Force Office of Scientific Research for generous support of this work. This investigation was supported in part by Public Health Service Fellowship 5-F1-GM-24,781-02 (to R. D.).

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(10) Hydrolysis procedure of S. W. Tobey, Ph.D. Thesis, University of Wisconsin, 1965. We are indebted to Dr. Tobey for bringing this procedure to our attention.

Determination of the Hammett σ Constants for the Picryl Group

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In a recent communication from this laboratory[1] the values for the σ constants for *m*- and *p*-picrylbenzoic acids were reported. These values were determined by measuring the rates of reaction of these acids with diphenyldiazomethane (DDM) and are 0.430 and 0.412 for the *meta* and *para* compounds, respectively.

(1) H. E. Ruskie and L. A. Kaplan, *J. Org. Chem.*, **30**, 319 (1965).