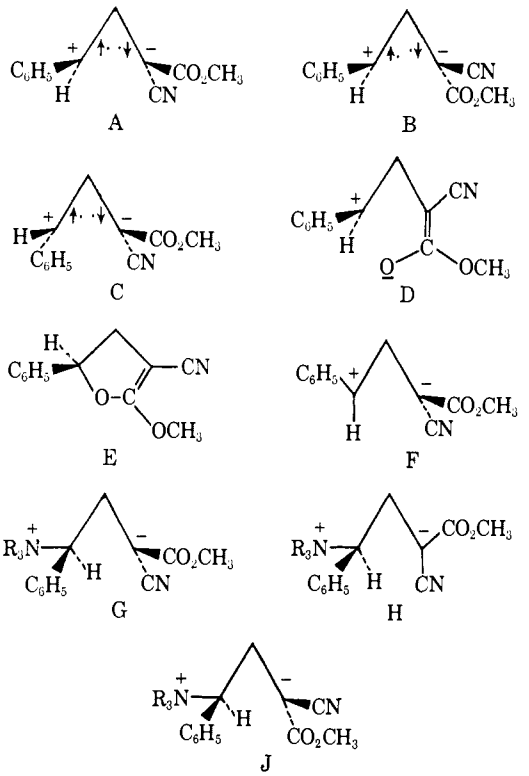
peratures and the more polar solvent favor larger spreads in rates of the three reactions. In DMF, in going from 100 to 126°, k_c/k_b decreased by 3.3 for a 26° temperature rise. Extrapolation to 175° gives only a factor of 2.7, not far from benzene at 175° (1.6). Possibly temperature differences are mainly responsible for changes in k_c/k_b, not solvent polarity or nucleophilicity.

Mechanisms of the three reactions might involve intermediates A–J. Of these only E is not an ion pair.[5] Mechanism (+)-(Z) → E → (+)-(E) is incompatible with the dramatic and similar response of k_c and k_b to solvent polarity. Epimerization at benzyl (k_b) cannot involve E as an intermediate. Mechanisms

$$(+)\text{-}(Z) \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \text{E} \xrightarrow{k_2} \text{D or G} \longrightarrow (+)\text{-}(E)$$

definitely are compatible with the solvent effects and nonaccumulation of E only if $k_{-1} \gg k_1 > k_2$. This scheme would make fortuitous the similar response of k_c and k_b to solvent polarity. An analogous mechanism for the I ⇄ E → D or G stages was found not to occur in methanol,[2a] although k_c and k (methanolysis) are not far from one another in value. These facts make such a scheme highly improbable. Mechanisms that involve G, H, and J are not possible in benzene, and yet epimerization occurs.



Mechanisms (+)-(Z) → A $\xrightarrow{D}$ B → (+)-(E), (+)-(Z) → A → D → B → (+)-(E), and (+)-(Z) → A → D ⇄ E → B → (+)-(E), with the first stage rate determining, are consistent with the solvent effect on k_c. Mechanisms

$$(+)\text{-}(Z) \longrightarrow \text{A} \xrightarrow{F} \text{C} \longrightarrow (-)\text{-}(E)$$

and (+)-(Z) → A → F → C → (−)-(E) are consistent with the solvent effect on k_b. Structure D either as a transition state or intermediate might provide less charge separation than F, and could be used to explain why $k_c > k_b$. A rapidly reversible D ⇄ E stage is equally attractive. In effect, inclusion of such stages in epimerization at cyanoacetate provides a path for a *conducted tour of C^+ of benzyl from C^- to O^-, to inverted C^-*, to product inverted at the cyanoacetate center, and resembles ionic conducted tour mechanisms suggested in other connections.[6] Intervention of intermediates G, H, and J in the epimerization at the cyanoacetate center in DMF also might explain $k_c > k_b$ in this medium. No such structures are available for epimerization at the benzyl center. Racemization rates appear equally sensitive to solvent character, and probably the same intermediates are involved as in the two epimerization reactions. For example, (+)-(Z) → A → B or C → enantiomer of A → (−)-(Z) are the simplest processes.

(5) Intervention of ketene acetal in (+)-(Z)-I → (+)-(E)-I would nicely correlate this particular epimerization reaction with the well-known aldehydo or acylcyclopropane ⇄ dihydrofuran rearrangement [*e.g.*, see C. L. Wilson, *J. Amer. Chem. Soc.*, **69**, 3002 (1947); D. W. Boykin and R. E. Lutz, *ibid.*, **86**, 5046 (1964); E. Vogel, *Angew. Chem., Int. Ed. Engl.*, **2**, 1 (1963)].

(6) (a) D. J. Cram, "Fundamentals of Carbanion Chemistry," Academic Press, New York, N. Y., 1965, p 102; (b) T. D. Hoffman and D. J. Cram, *J. Amer. Chem. Soc.*, **91**, 1009 (1969).

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Photosensitive Protecting Groups

Sir:

The use of *o*-nitrobenzyl derivatives as photosensitive blocking reagents for amino and carboxyl functions in peptides has been described.[1-3] In this communication we describe some new photosensitive blocking groups, and conditions required for achieving photoremoval in quantitative yields.

Amino acid derivatives, in which the amino function was blocked with photosensitive protecting groups of two kinds, namely, 6-nitroveratryloxycarbonyl (NVOC) and 2-nitrobenzyloxycarbonyl (NBOC), were prepared and characterized (Table I). These blocking groups could be removed by irradiation with light of wavelength longer than 3200 Å. Under these conditions, even the most light-sensitive amino acid, tryptophan, was not affected when deblocked. Irradiations were done in an RPR-100 apparatus (Rayonet, the Southern Co., Middletown, Conn.) The amino acid and peptide derivatives were irradiated at concentrations of 10^{-2}–10^{-3} *M*. Irradiation times were 1–24 hr. Solvents used were dioxane, chloroform, tetrahydrofuran, dimethoxyethane, alcohols, and mixtures of alcohol–water, ether–water. Removal of the blocking groups was quantitative in all cases, as judged by the quantitative release of CO_2, which was determined titrimetrically.[4] The yield of the released amino function was

(1) J. A. Barltrop, P. J. Plant, and P. Schofield, *Chem. Commun.*, 822 (1966).

(2) A. Patchornik in "Pharmacology of Hormonal Polypeptides and Proteins," Plenum Publishing Co., New York, N. Y., 1968, p 11.

(3) A. Patchornik, B. Amit, and R. B. Woodward, presented at the Tenth European Peptide Symposium, Abano-Terme, Italy, Sept 1969.

(4) A. Patchornik and Y. Shalitin, *Anal. Chem.*, **33**, 1887 (1961).

Table I

NBOC, NVOC derivatives	Mp, °C[a]	Optical rotation, $[\alpha]^{25}D$, deg	% yield of free amine in presence of[b,c] Sulfuric acid (5 equiv)	Semicarbazide hydrochloride (10 equiv)
NVOC-L-Val[d]	148[e]	−7.4[f]	100 ± 3	100 ± 3
NVOC-L-Pro[g]	111–112[h]	−11.1[i]	100 ± 3	100 ± 3
NVOC-L-Met[j]	150–151[k]	−25.8[l]	100 ± 3	100 ± 3
NVOC-L-Trp[m]	194–195[n]	−22.6[o]		100 ± 3
NVOC-L-Phe-Gly[p]	167–168[q]	−11.9[r]	100 ± 3	100 ± 3
NBOC-Gly[s]	120–122[t]		100 ± 3	100 ± 3
NBOC-L-Ala[u,v]	132–134[w]	−10.6[x]	100 ± 3	100 ± 3

[a] All melting points are uncorrected. [b] Yields were determined by the amino acid analyzer. [c] Yields of free amines without addition of auxiliary reagents are as follows: NVOC-L-Val, 42%; NVOC-L-Pro, 42%; NVOC-L-Met, 41%; NVOC-L-Trp, 40%; NVOC-L-Phe-Gly, 40%; NBOC-Gly, 17%; NBOC-L-Ala, 35%. [d] *Anal.* Calcd for $C_{15}H_{20}N_2O_8$: C, 50.56; H, 5.66; N, 7.86. Found: C, 50.61; H, 5.64; N, 7.81. [e] Crystallized from benzene. [f] *c* 2, dimethylformamide (DMF). [g] *Anal.* Calcd for $C_{15}H_{18}N_2O_8$: C, 50.85; H, 5.12; N, 7.91. Found: C, 51.00; H, 5.14; N, 7.65. [h] Crystallized from benzene. [i] *c* 2, DMF. [j] *Anal.* Calcd for $C_{15}H_{20}N_2O_8S$: C, 46.39; H, 5.19; N, 7.21; S, 8.24. Found: C, 46.45; H, 5.14; N, 7.11; S, 8.39. [k] Crystallized from methanol–water. [l] *c* 2, DMF. [m] *Anal.* Calcd for $C_{21}H_{21}N_3O_8$: C, 56.88; H, 4.77; N, 9.48. Found: C, 57.00; H, 4.90; N, 9.25. [n] Crystallized from methanol–water. [o] *c* 2, DMF. [p] *Anal.* Calcd for $C_{21}H_{23}N_3O_9$: C, 54.66; H, 5.02; N, 9.11. Found: C, 54.58; H, 5.22; N, 9.18. [q] Crystallized from methanol. [r] *c* 2.7, DMF. [s] *Anal.* Calcd for $C_{10}H_{10}N_2O_6$: C, 47.26; H, 3.97; N, 11.02. Found: C, 47.13; H, 3.83; N, 11.00. [t] Crystallized from ethyl acetate–petroleum ether. [u] Absence of racemization on irradiation was proved by the Moore and Manning method (J. M. Manning and S. Moore, *J. Biol. Chem.*, **243**, 5591 (1968)). [v] *Anal.* Calcd for $C_{11}H_{12}N_2O_6$: C, 49.25; H, 4.51; N, 10.45. Found: C, 49.38; H, 4.52; N, 10.32. [w] Crystallized from ethyl acetate–petroleum ether. [x] *c* 3.3, DMF.

Table II

Amino acid derivatives	Mp, °C[a]	Optical rotation, $[\alpha]^{25}D$, deg	% yield of free amine[b,c]
NBOC-L-Ala[d]	132–134[e]	−10.6[f]	35 ± 3
NVOC-L-Ala[g]	180[h]	−11.8[i]	80 ± 3
DNBOC-L-Ala[j]	172–179[k]	−38.6[l]	95 ± 3
NBOC-L-Phe[m]	112–114[k]	−37.3[n]	17 ± 3
NVOC-L-Phe[o]	167[p]	−27.7[q]	35 ± 3
DNBOC-L-Phe[r]	196–200[k]	−21.35[s]	70 ± 3

[a] All melting points are uncorrected. [b] Yields were determined by amino acid analyzer. [c] Yields were quantitative in all cases when 5 equiv of sulfuric acid or 10 equiv of semicarbazide hydrochloride was added before irradiation. [d] *Anal.* Calcd for $C_{11}H_{12}N_2O_6$: C, 49.25; H, 4.51; N, 10.45. Found: C, 49.38; H, 4.52; N, 10.32. [e] Crystallized from ethyl acetate–petroleum ether. [f] *c* 3.3, dimethylformamide (DMF). [g] *Anal.* Calcd for $C_{13}H_{16}N_2O_8$: C, 47.56; H, 4.91; N, 8.53. Found: C, 47.80; H, 4.74; N, 8.40. [h] Crystallized from benzene–dioxane. [i] *c* 2, DMF. [j] *Anal.* Calcd for $C_{17}H_{15}N_3O_8$: C, 52.44; H, 3.88; N, 10.70. Found: C, 52.69; H, 4.05; N, 10.50. [k] Crystallized from ethyl acetate–petroleum ether. [l] *Anal.* Calcd for $C_{17}H_{16}N_2O_6$: C, 59.30; H, 4.68; N, 8.14. Found: C, 59.34; H, 4.50; N, 8.02. [m] *c* 1.9, DMF. [n] *Anal.* Calcd for $C_{19}H_{20}N_2O_8$: C, 56.43; H, 4.99; N, 6.93. Found: C, 56.61; H, 4.91; N, 6.80. [o] Crystallized from methanol–water. [p] *Anal.* Calcd for $C_{23}H_{19}N_3O_8$: C, 59.35; H, 4.12; N, 9.03. Found: C, 59.41; H, 4.18; N, 8.91. [q] *c* 3, DMF.

Scheme I

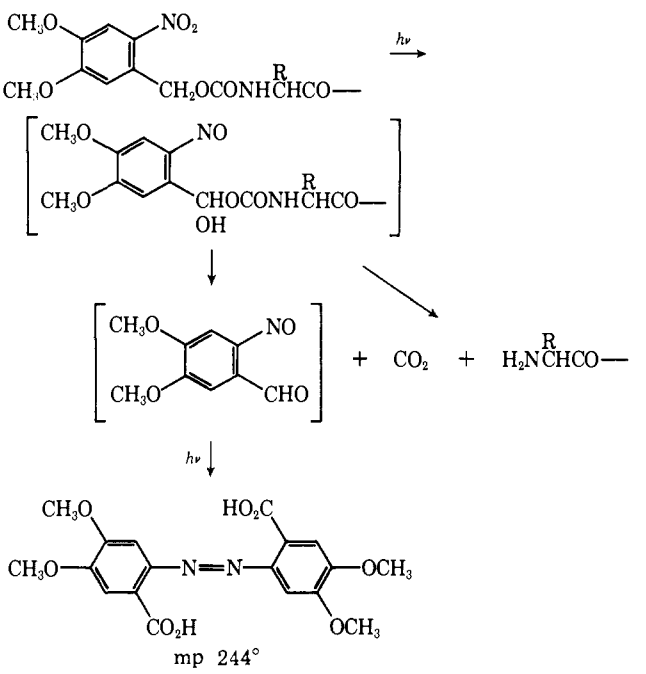


Table III

2,2′-Dinitrodiphenylmethyl ester of	Mp, °C[a]	Optical rotation, $[\alpha]^{25}D$, deg	% yield of free acid
Benzoic acid[d]	163–164[e]		100 ± 5[b]
Phenylacetic acid[f]	108–110[e]		100 ± 5[b]
α-Naphthylacetic acid[g]	145–147[h]		100 ± 5[b]
tert-Butyloxycarbonyl-L-alanine[i]	129–130[h]	−18.86[j]	100 ± 3[c]
tert-Butyloxycarbonyl-L-phenylalanine[k]	124–126[e]	−38.48[l]	100 ± 3[c]

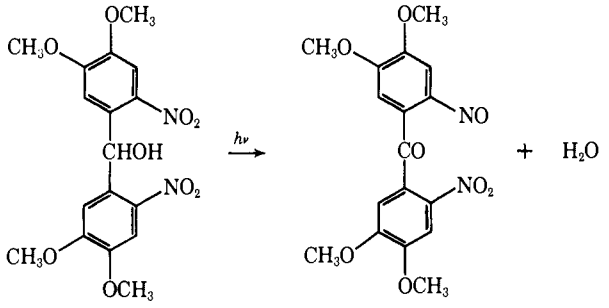
[a] All melting points are uncorrected. [b] Determined by gas chromatography of the methyl esters. [c] Determined by amino acid analyzer. [d] *Anal.* Calcd for $C_{20}H_{14}O_6N_2$: C, 63.41; H, 3.73; N, 7.41. Found: C, 63.43; H, 3.92; N, 7.27. [e] Crystallized from methanol. [f] *Anal.* Calcd for $C_{21}H_{16}N_2O_6$: C, 64.28; H, 4.11; N, 7.19. Found: C, 64.34; H, 3.97; N, 7.21. [g] *Anal.* Calcd for $C_{25}H_{18}N_2O_6$: C, 67.87; H, 4.10; N, 6.33. Found: C, 67.73; H, 4.29; N, 6.15. [h] Crystallized from ethyl acetate–petroleum ether. [i] *Anal.* Calcd for $C_{21}H_{23}N_3O_8$: C, 56.62; H, 5.20; N, 9.43. Found: C, 56.40; H, 5.10; N, 9.30. [j] *c* 2.3, dimethylformamide (DMF). [k] *Anal.* Calcd for $C_{27}H_{27}N_3O_8$: C, 62.18; H, 5.22; N, 8.06. Found: C, 62.30; H, 5.10; N, 8.24. [l] *c* 1.6, DMF.

not quantitative, as it probably reacts with the aldehyde intermediate formed during irradiation (see Scheme I). Quantitative yields of amino acids and peptides were, however, obtained by addition to the photoreaction

mixture of acids or of aldehyde reagents such as hydrazine, hydroxylamine hydrochloride, or semicarbazide hydrochloride (see Table I).

In an attempt to avoid the side reaction with the aldehyde intermediate formed during irradiation, we used α-substituted *o*-nitrobenzyl alcohol derivatives as starting materials for a second kind of blocking group. Symmetrical carbinols were chosen in order to avoid formation of diastereoisomers during the blocking step. We have shown that on irradiation of such alcohols, a ketonic product is formed, which is less reactive toward the amino function than the aldehydic intermediate mentioned above. Such a ketone was isolated and characterized as shown in Scheme II.

Scheme II



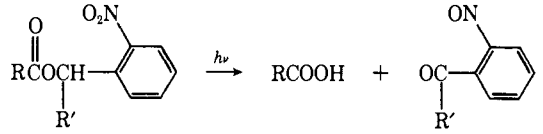
2, mp 202–203° **3**, mp 190–192°

A comparison of yields of photoremoval of 2,2′-dinitrodiphenylmethyloxycarbonyl (DNBOC) amino acid derivatives and (NBOC) and (NVOC) amino acid derivatives is given in Table II. It can be seen that in the case of DNBOC derivatives, the highest yields of deblocking were obtained.

We have also used 2,2′-dinitrodiphenylmethanol as a blocking group for the carboxylic function. Conditions for photoremoval of this blocking group were similar to those required for deblocking of the amino function. In this case, however, no auxiliary reagents were needed. Some examples are given in Table III.

The photoremoval of *o*-nitrobenzyl derivatives from the carboxylic function can be illustrated generally as in Scheme III.

Scheme III



In accordance with this scheme, it is likely that such groups could also be used for the protection of hydroxyl and phosphate functions. Work is now in progress to elucidate the applicability of this approach for carbohydrate and nucleotide synthesis.

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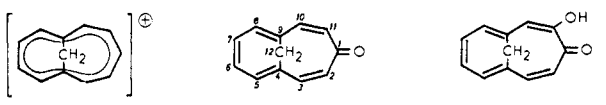
4,9-Methano[11]annulenone.[1a,b] A Ten-π-Electron Analog of Tropone

Sir:

In the course of our studies on aromatic bridged [10]annulenes[2] we recently synthesized the bicyclo[5.4.1]dodecapentaenylium ion (**1**) (as its BF_4^- and ClO_4^- salts),[3] a carbonium ion that can be looked upon as a 10π-electron analog of the tropylium ion.[4] The ion **1** has a pK_{R^+} value of 6.2 ± 0.1,[5] as compared with pK_{R^+} = 4.7 of the tropylium ion[6] and pK_{R^+} = −7.4 of the cyclopropenylium ion,[7] and thus represents the most stable unsubstituted (disregarding the CH_2 bridge) Hückel-type carbonium ion known. Although X-ray data for **1** are not yet available[8] the resonance stabilization of the ion strongly implies that its peripheral 11-membered ring is approximately planar. The



1 **2** **3**

similarities between **1** and the tropylium ion suggested the interesting possibility that the keto and ketohydroxy derivatives of **1**, such as **2** and **3**, would have chemical properties analogous to those of tropone and tropolone.[9] These expectations have now been borne out by the syntheses of **2** and some of its isomers.[2c,10] In this communication we elaborate on the preparation and properties of **2**.

Our approach to 4,9-methano[11]annulenone (**2**) started out from 4,5-benzocycloheptenone and followed the pattern, previously developed in this laboratory, for the synthesis of 1,6-bridged cycloheptatrienes.[11] Treatment of 4,5-benzocycloheptenone with ethylene glycol and a catalytic amount of *p*-toluenesulfonic acid in benzene afforded the ketal **4**, mp 110°, in 94% yield. This ketal was submitted to the Birch reduction

(1) (a) In the terminology proposed by Pilling and Sondheimer[1b] 4,9-methano[11]annulenone is a [4*n* + 3]annulenone with *n* = 2. (b) G. M. Pilling and F. Sondheimer, *J. Amer. Chem. Soc.*, 90, 5610 (1968).

(2) For reviews see: (a) E. Vogel, *Chem. Soc. Spec. Publ.*, **No. 21**, 113 (1967); (b) E. Vogel, *Chimia*, **22**, 21 (1968); (c) E. Vogel, *Proc. Robert A. Welch Found. Conf. Chem. Res.*, **12**, 215 (1968).

(3) (a) W. Grimme, H. Hoffmann, and E. Vogel, *Angew. Chem.*, 77, 348 (1965); (b) E. Vogel, R. Feldmann, and H. Düwel, *Tetrahedron Lett.*, 1941 (1970).

(4) W. Grimme, E. Heilbronner, G. Hohlneicher, E. Vogel, and J.-P. Weber, *Helv. Chim. Acta*, **51**, 225 (1968).

(5) As determined by potentiometric titration in water as solvent.

(6) W. v. E. Doering and L. H. Knox, *J. Amer. Chem. Soc.*, **76**, 3203 (1954).

(7) R. Breslow and J. T. Groves, *ibid.*, **92**, 984 (1970).

(8) An X-ray structure determination of the ion 1 is being carried out by Professor M. Simonetta, University of Milan, Italy.

(9) Macrocyclic [4*n* + 1]annulenones, specifically derivatives of [13]- and [17]annulenone, have recently been synthesized by G. M. Pilling and F. Sondheimer (see ref 1b) and by G. W. Brown and F. Sondheimer, *J. Amer. Chem. Soc.*, **91**, 760 (1969), respectively.

(10) Methano-bridged [11]annulenones with the bicyclo[5.4.1]dodecane carbon skeleton were first obtained by H. Hoffmann in this laboratory (Dissertation, University of Cologne, 1967) by the SeO_2 oxidation of bicyclo[5.4.1]dodeca-2,4,7,9,11-pentaene[3] following the procedure of P. Radlick (*J. Org. Chem.*, **29**, 960 (1964)), for the conversion of tropilidene into tropone. This method leads to a mixture of at least four methano[11]annulenones from which apart from **2**, 2,7-methano[11]-annulenone and 3,8-methano[11]annulenone could be isolated by laborious chromatography on alumina.[2c] Rational syntheses of 2,7-methano- and 3,8-methano[11]annulenone are currently in progress and will be reported later.

(11) (a) E. Vogel, W. Wiedemann, H. Kiefer, and W. F. Harrison, *Tetrahedron Lett.*, 673 (1963); (b) E. Vogel, *Pure Appl. Chem.*, 20, 237 (1969).