Photosensitive Protecting Groups of Amino Sugars and Their Use in Glycoside Synthesis. 2-Nitrobenzyloxycarbonylamino and 6-Nitroveratryloxycarbonylamino Derivatives[1]

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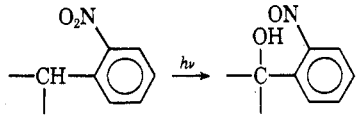
2-Nitrobenzyloxycarbonyl and 6-nitroveratryloxycarbonyl derivatives of 2-amino-2-deoxy-D-glucose and of 2-amino-2-deoxy-D-galactose were prepared and characterized. 2-Deoxy-2-(2-nitrobenzyloxycarbonyl)amino-1,3,4,6-tetra-*O*-acetyl-D-glucopyranose was prepared by acetylation in pyridine and was converted by hydrogen chloride in acetic acid to the 1-chloro derivative (under the same conditions a benzyloxycarbonyl group is removed). The latter compound was condensed with methanol, using mercuric cyanide, to yield methyl 2-deoxy-2-(2-nitrobenzyloxycarbonyl)amino-3,4,6-tri-*O*-acetyl-β-D-glucopyranoside. Irradiation of the 2-nitrobenzyloxycarbonyl and the 6-nitroveratryloxycarbonyl derivatives afforded the free amino derivatives in high yields. Polymer-bound aldehyde reagents were used in some of these photochemical reactions.

The use of photosensitive protecting groups is of potential importance to many areas of synthetic chemistry and especially in syntheses involving polyfunctional molecules such as peptides and saccharides. These groups should be stable to a variety of chemical treatments and cleaved readily by irradiation.

Nitro aromatic compounds containing benzylic hydrogens ortho to the nitro group are light sensitive.[3] The primary photochemical reaction that occurs in such compounds is the internal redox reaction shown in Scheme I.

Scheme I



This reaction was used in our laboratory for designing light-sensitive protecting groups for the amino, carboxyl, and sulfhydryl functions in amino acids and peptides.[4] Recently we have also prepared light-sensitive glycosides[5] and ethers.[1b,6] Such glycosides were even used for oligosaccharide synthesis on a solid support.[7]

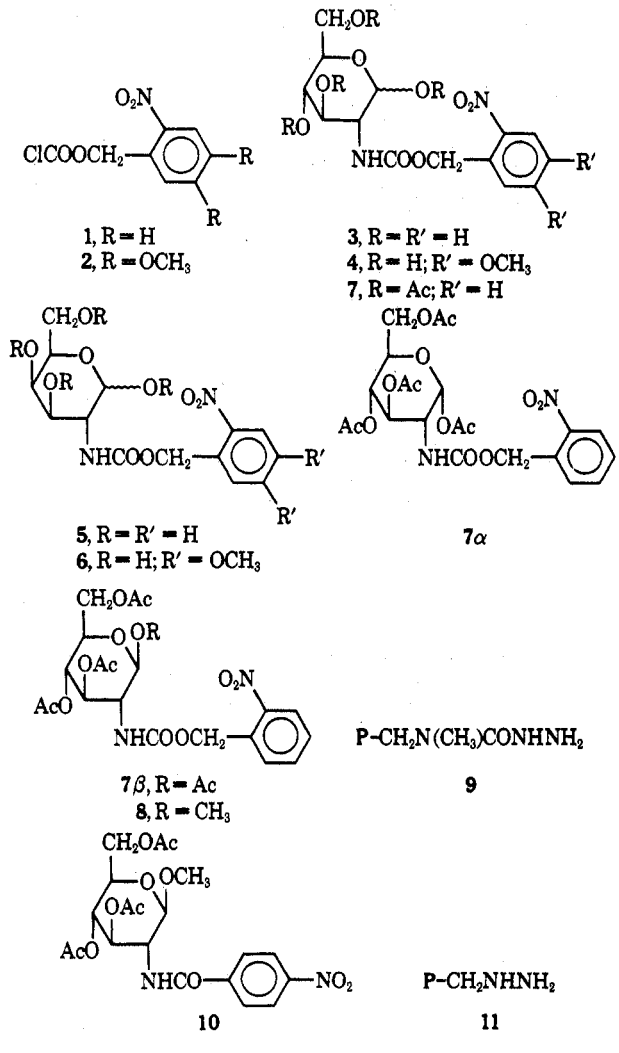
In the present work we describe the use of 2-nitrobenzyloxycarbonyl (NBOC) and 6-nitroveratryloxycarbonyl (NVOC) as protecting groups for the amino function in amino sugars.

Results and Discussion

2-Nitrobenzyloxycarbonyl chloride (NBOCCl, 1) and 6-nitroveratryloxycarbonyl chloride (NVOCCl, 2) were prepared by bubbling phosgene through dioxane solutions of 2-nitrobenzyl alcohol or 6-nitroveratryl alcohol (Scheme II).

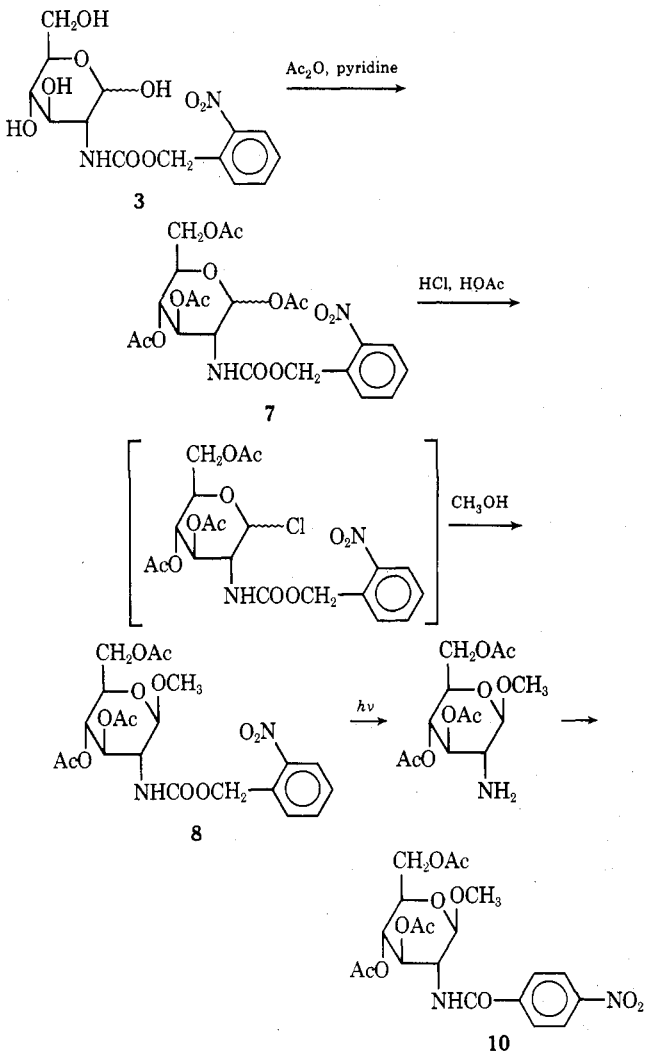
The two reagents that are quite stable in storage and react with 2-amino-2-deoxy-D-glucose under Schotten-Baumann conditions to give compounds 3 and 4, respectively. NBOCCl (1) and NVOCCl (2) reacted in the same fashion with 2-amino-2-deoxy-D-galactose, yielding compounds 5 and 6. Compound 3 was totally acetylated in pyridine, yielding the α,β mixture 7 that could be further separated on silica gel. The difference in specific rotation between the two is not particularly great (probably owing to the presence of the aromatic nitro chromophore). The nmr spectrum of compound 7α, however, has the expected $J_{1,2}$ value of 3.5 Hz while that of 7β has a $J_{1,2}$ value of 8.5 Hz. The ratio of compound 7α to compound 7β in the mixture 7 obtained by acetylation was found to be 2.1:1 by examination of the optical rotation and the uv absorbancy of the isomers after resolution on silica gel as described in the Experimental Section.

Scheme II



We have compared the stability of NBOC, NVOC, and benzyloxycarbonyl (Z) groups in 2-amino-2-deoxy-D-glucose and in alanine derivatives using hydrogen chloride in acetic acid or (when the solubility was low) hydrogen chloride in acetic acid–trifluoroacetic acid (Table I). As expected, under these conditions the order of increasing stability of these derivatives is Z < NVOC < NBOC, which may be explained by the effect of the aromatic

Scheme III



nitro or methoxy substituents on an intermediate benzylium ion. The NBOC grouping is, thus, an urethane type of protecting group, quite stable under strong acidic conditions, which permit the use of the NBOC group during the preparation of 1-chloro derivatives, necessary for Königs-Knorr condensations. Similar treatment of Z derivatives will remove the protecting group.

The mixture 7 was treated with hydrogen chloride in acetic acid, giving the chloro derivative that was not isolated but was treated immediately with methanol in the presence of mercuric cyanide, yielding methyl 2-deoxy-2-(2-nitrobenzyloxycarbonyl)amino-3,4,6-tri-*O*-acetyl-β-D-glucopyranoside (8) in 56% yield, based on the mixture 7 (Scheme III). It is pertinent to note that no formation of 2-nitrobenzyl chloride was observed in this preparation and no evidence for the formation of an α anomer was obtained. This selectivity may be a result of a neighboring-group participation by the NBOC function and of the less hindered equatorial approach.

In a previous study[4] on NBOC and NVOC derivatives of amino acids and peptides it turned out that, although the photoremoval of the protecting groups from amino functions was judged to be quantitative by the release of carbon dioxide, the newly formed amino function further reacted with components of this irradiation mixture (*e.g.*, 2-nitrosobenzaldehyde). In order to achieve quantitative yield of the amino derivative it was found necessary to add aldehyde reagents or sulfuric acid. As the result, it became subsequently difficult to isolate the desired product from the colored reaction mixture. In the present work, sulfuric acid was occasionally used during the photoremoval of NBOC or NVOC derivatives or, alternately, we have introduced polymeric carriers of aldehyde reagents. We have found that these polymeric reagents were the most suitable aldehyde reagents. They increase the yield of the free amino derivative, and will react with colored by-products in the reaction mixture. They could be filtered off following the photochemical reaction, thus affording the relatively pure amino product in solution.

Table I
Splitting of 2-Nitrobenzyloxycarbonyl (NBOC), 6-Nitroveratryloxycarbonyl (NVOC), and Benzyloxycarbonyl (Z) Groups by Hydrogen Chloride

Reactant	Product	Yield, %
NBOC-L-Ala[a]	Alanine	0.5
NVOC-L-Ala[a]	Alanine	8
Z-L-Ala[a,b]	Alanine	55
3[c]	2-Amino-2-deoxy-D-glucose	53
4[c]	2-Amino-2-deoxy-D-glucose	80
2-(Benzyloxycarbonyl)-amino-2-deoxy-D-glucose[c,d]	2-Amino-2-deoxy-D-glucose	98

[a] The reactant (30 mg/ml) dissolved in hydrogen chloride (1.4 *N*) in acetic acid was kept under seal at room temperature for 48 hr. [b] M. Hunt and V. du Vigneaud, *J. Biol. Chem.*, **124**, 699 (1938). [c] The reactant (30 mg/ml) dissolved in hydrogen chloride (1.4 *N*) in acetic acid–trifluoroacetic acid (1:3) was kept sealed at room temperature for 1 hr. [d] E. Chargaff and M. Bovarnick, *J. Biol. Chem.*, **118**, 421 (1937). Yields of products were determined by the amino acid analyzer (±3% error).

The NBOC was cleaved photochemically from compound 8 in the presence of sulfuric acid or P-$CH_2N(CH_3)CONHNH_2$ (9),[8] giving the free amino derivative, as suggested by its chromatographic behavior and staining properties and the preparation of its 2-(4-nitrobenzoyl) derivative (10).[9] Although the optical rotation of this compound is rather high for a β anomer (+34.7°), the nmr supports the proposed structure and in particular $J_{1,2}$ = 8.0 Hz corresponds to the axial-axial interaction present in the β anomer.

Furthermore, we have photochemically split the NVOC or NBOC groupings in compounds 4 and 3 to yield 2-amino-2-deoxy-D-glucose (Table II, Figure 1). The isolation of 2-amino-2-deoxy-D-glucose from the irradiated solution of compound 4 required, however, ion-exchange column fractionation[10] and afforded a low yield of product. The use of a hydrazine polymer (11) in the reaction mixture eliminated the need for column fractionation and increased the yield of 2-amino-2-deoxy-D-glucose isolated.

In conclusion, NBOC and NVOC derivatives of amino sugars are easily prepared. These protecting groups withstand a series of reactions during glycoside synthesis. They are photolyzed in high yield at wavelengths higher than 320 nm to give the free amino derivatives without affecting other functional groups in the molecule including acetates, glycoside, and hydroxy. The addition of polymeric aldehyde reagents to the reaction mixture did not affect the above functional groups and increased the yields of free amino derivatives. We have also demonstrated that using this approach one can obtain, very conveniently, a free amino function adjacent to the glycosidic bond, a situation present in many natural products.

Experimental Section

All melting points are corrected. Optical rotations were determined with a Bendix or a Perkin-Elmer Model 141 polarimeter. Nmr spectra were recorded on a Varian A-60 or a Bruker HFX-10

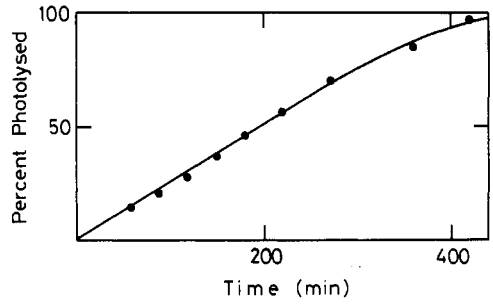


Figure 1. Photolysis of 4. 4 (59.2 mmol) in water (40 ml) was irradiated (see Experimental Section) under a stream of nitrogen. The evolved carbon dioxide was absorbed in benzylamine and titrated: A. Patchornik and Y. Shalitin, *Anal. Chem.*, **33**, 1887 (1961).

Table II
Splitting of 2-Nitrobenzyloxycarbonyl (NBOC) and 6-Nitroveratryloxycarbonyl (NVOC) Groups by Irradiation

Reactant[a]	Product	Yield, %	Yield in presence of sulfuric acid acid (5 equiv), %
3	2-Amino-2-deoxy-D-glucose	82	96
5	2-Amino-2-deoxy-D-galactose	80	97
4	2-Amino-2-deoxy-D-glucose	89	100
6	2-Amino-2-deoxy-D-galactose	91	98

[a] Reactants (10^{-3} *M* in water–ethanol, 2:1) were irradiated for 10 hr as described in the Experimental Section. Yields were determined by the amino acid analyzer (±3% error).

instrument with tetramethylsilane as an internal standard. The uv spectra were taken on a Cary Model 14 spectrophotometer. Thin layer chromatography was carried out on fluorescent silica gel plates SIF or on aluminum oxide plates AlF (Reidel-de-Haën, Hannover), and the spots were observed under a uv lamp. Thick layer chromatography was carried out on plc plates silica gel F_{254} supplied by Merck. Plates were viewed after development under a uv lamp. The band of the desired material was extracted with ethyl acetate or methylene chloride, filtered, and evaporated. 2-Nitrobenzyl alcohol was purchased from Fluka, Switzerland. NBOC and NVOC derivatives were kept in the dark. Irradiations were carried out in an RPR-100 apparatus (Rayonet the Southern Co., Middletown, Conn.) using 3500-Å lamps and Pyrex equipment.

2-Nitrobenzyloxycarbonyl Chloride (NBOCCl, 1). 2-Nitrobenzyl alcohol (50 g) was dissolved in 1,4-dioxane (400 ml), and phosgene (200 g) was bubbled through the solution at such a rate that the temperature of the reaction mixture was kept below 40°. The reaction mixture was left at room temperature overnight, the excess of phosgene was then removed by bubbling nitrogen through, and the solution was evaporated *in vacuo* at a bath temperature under 40°. The residual oil (70 g, quantitative yield) constituted the pure product 1. Compound 1 was clean by tlc (silica gel, developed with dichloromethane), d^{25} 1.32. The neutralization equivalent of this compound was determined[11] to be 217 (theoretical 215.5) by dissolving a sample of compound 1 (*ca.* 30 mg) in hot ethanol (5 ml) and titrating the released hydrochloric acid with 0.1 *N* sodium methoxide in methanol–benzene (3:7) using Thymol Blue as an indicator (color change from red to yellow). Little decomposition was observed when the solution was kept at 0° for 1 month.

6-Nitroveratryloxycarbonyl Chloride (NVOCCl, 2). 6-Nitroveratryl alcohol (50 g) was dissolved in dioxane (700 ml) with gentle heating. The solution was treated as described for compound 1, yielding 64 g (quantitative yield) of yellow solid 2 that was kept for long periods at 0°. The neutralization equivalent, 283 (theoretical 275.5) was determined as described for compound 1. A sample was recrystallized from benzene, mp 125–127° dec.

Anal. Calcd for $C_{14}H_{18}N_2O_9 \cdot \frac{1}{2}H_2O$: C, 45.78; H, 5.21; N, 7.63. 5.08. Found: C, 43.38; H, 3.59; Cl, 13.03; N, 5.01.

2-Deoxy-2-(2-nitrobenzyloxycarbonyl)amino-D-glucose (NBOC Glucosamine, 3). 2-Amino-2-deoxy-D-glucose hydrochloride (7.0 g, 32.5 mmol) and sodium bicarbonate (7.0 g, 83 mmol) were dissolved in water (140 ml). The reaction mixture was mechanically stirred and a solution of compound 1 (7.0 g, 32.5 mmol) in dioxane (200 ml) was added. The stirring was stopped after 6 hr, 1 *N* hydrochloric acid (18 ml) was added, and the solution was concentrated to one-third of its original volume. The precipitate was collected by suction and crystallized from ethanol–water (7:3): yield 10 g (83%); mp 202–204°; $[\alpha]^{24}D$ +59.6° (3 min) → +64.6° (20 hr, final, *c* 2.5, pyridine).

Anal. Calcd for $C_{14}H_{18}N_2O_9 \cdot \frac{1}{2}H_2O$: C, 45.78; H, 5.21; N, 7.63. Found: C, 46.00; H, 5.18; N, 7.46.

A sample was heated to 110° for 5 hr under high vacuum.

Anal. Calcd for $C_{14}H_{18}N_2O_9$: C, 46.93; H, 5.06; N, 7.82. Found: C, 46.72; H, 4.94; N, 7.70.

2-Deoxy-2-(6-nitroveratryloxycarbonyl)amino-D-glucose (NVOC Glucosamine, 4). 2-Amino-2-deoxy-D-glucose hydrochloride (431 mg, 2 mmol) and sodium bicarbonate (420 mg, 5 mmol) were dissolved in water (50 ml). The reaction mixture was mechanically stirred and a solution of compound 2 (1.1 g, 4 mmol) in dioxane (70 ml) was added. The stirring was stopped after 6 hr, water (200 ml) was added, and the reaction mixture was washed with ethyl acetate (5 × 50 ml). The aqueous layer was concentrated to one-fourth of its original volume. The resulting precipitate was collected by suction and crystallized from ethanol–water (7:3): yield 575 mg (70%); mp 199–201°; $[\alpha]^{24}D$ +64.5° (4 min final, *c* 1.2, pyridine).

Anal. Calcd for $C_{16}H_{22}N_2O_{11} \cdot \frac{1}{2}H_2O$: C, 44.96; H, 5.42; N, 6.56. Found: C, 45.07; H, 5.69; N, 6.74.

A sample was heated to 135° for 5 hr under high vacuum.

Anal. Calcd for $C_{16}H_{22}N_2O_{11}$: C, 45.93; H, 5.30; N, 6.70. Found: C, 45.75; H, 5.58; N, 6.78.

2-Deoxy-2-(2-nitrobenzyloxycarbonyl)amino-D-galactose (NBOC Galactosamine, 5). This compound was prepared as described for compound 4 but using 2-amino-2-deoxy-D-galactose hydrochloride (300 mg, 1.39 mmol) and compound 1 (430 mg, 2 mmol): yield 350 mg (70%); mp 165–166°; $[\alpha]^{24}D$ +103° (7 min) → 74.2° (24 hr, final *c* 0.9, pyridine).

Anal. Calcd for $C_{14}H_{18}N_2O_9$: C, 46.93; H, 5.06; N, 7.82. Found: C, 46.79; H, 4.97; N, 7.71.

2-Deoxy-2-(6-nitroveratryloxycarbonyl)amino-D-glactose (NVOC Galactosamine, 6). This compound was prepared as described for compound 4 but using 2-amino-2-deoxy-D-galactose hydrochloride (430 mg, 2 mmol): yield 580 mg (70%); mp 193–195°; $[\alpha]^{24}D$ +114° (10 min) → +98.5° (24 hr, final *c* 1.2, pyridine).

Anal. Calcd for $C_{16}H_{22}N_2O_{11} \cdot \frac{1}{2}H_2O$: C, 44.96; H, 5.42; N, 6.56. Found: C, 44.98; H, 5.59; N, 6.36.

A sample was heated to 135° for 5 hr under high vacuum.

Anal. Calcd for $C_{16}H_{22}N_2O_{11}$: C, 45.93; H, 5.30; N, 6.70. Found: C, 46.10; H, 5.55; N, 6.80.

2-Deoxy-2-(2-nitrobenzyloxycarbonyl)amino-1,3,4,6-tetra-*O*-acetyl-α- and -β-D-glucopyranose (7). Compound 3 (7.34 g) was dissolved in pyridine (70 ml) and acetic anhydride (15 ml) was added. The reaction mixture was left at room temperature overnight. Water (10 ml) was then added and the mixture was evaporated *in vacuo* after an additional 30 min. The oily residue was dissolved in chloroform (100 ml) and washed sequentially with 0.1 *N* hydrochloric acid, water, 5% sodium bicarbonate, and water. The solution was then dried over sodium sulfate and evaporated to yield 10 g (95%) of oil that solidified after being kept under petroleum ether (bp 30–60°) at −20° for 72 hr, $[\alpha]^{20}D$ +50.9° (*c* 3.3, chloroform). Mixture 7 (80 mg) was resolved by preparative tlc using ether–methylene chloride (1:9) for development. The uv-absorbing bands were extracted with methylene chloride, evaporated to dryness, and dissolved in ethanol. The proportion of 7α and 7β was determined to be 2.1:1 by the absorbance at 260 nm of the extraction solutions and by the optical rotation of mixture 7. Compound 7α (52 mg) was crystallized from ether–ethyl acetate: mp 107°; $[\alpha]^{20}D$ +69.0° (*c* 1.5, chloroform); λ_{max} (ethanol) 262 nm (ε 6200); nmr (90 MHz, $CDCl_3$) τ 1.89–2.73 (m, 4, aromatic), 3.84 (d, 1, H-1, $J_{1,2}$ = 3.5 Hz), 4.36–5.08 (m, 5, including benzylic CH_2 at τ 4.58, d, *J* = 3.0 Hz), 5.63–6.20 (m, 4), 7.80 (s, 3, $OCOCH_3$), 7.93 (s, 3, $OCOCH_3$), 7.97 (s, 3, $OCOCH_3$), 7.99 (s, 3, $OCOCH_3$).

Irradiation at τ 4.82 causes the collapse of the H-1 signal into a singlet.

Anal. Calcd for $C_{22}H_{26}N_2O_{13}$: C, 50.19; H, 4.98; N, 5.32. Found: C, 50.07; H, 5.27; N, 5.45.

Compound 7β (25 mg) was crystallized from 2-propanol: mp 151–152°; $[\alpha]^{20}D$ +13.0° (*c* 2.2, chloroform); λ_{max} (ethanol) 262 nm (ϵ 6120); nmr (90 MHz, $CDCl_3$) τ 1.93–2.70 (m, 4, aromatic), 4.33 (d, 1, H-1, $J_{1,2}$ = 8.5 Hz), 4.48–5.20 (m, 5, including benzylic CH_2 at τ 4.59, s, 2, and at τ 4.91, t, 1, J = 8.5 Hz), 7.95 (s, 6, two $OCOCH_3$), 8.00 (s, 3, $OCOCH_3$), 8.02 (s, 3, $OCOCH_3$).

Anal. Calcd for $C_{22}H_{26}N_2O_{13}$: C, 50.19; H, 4.98; N, 5.32. Found: C, 50.18; H, 5.24; N, 5.40.

Methyl 2-Deoxy-2-(2-nitrobenzyloxycarbonyl)amino-3,4,6-tri-*O*-acetyl-β-D-glucopyranoside (8). A solution of mixture 7 (3.5 g) in 70 ml of 1.5 *N* hydrogen chloride in acetic acid was stored in a stoppered flask at room temperature for 48 hr. Chloroform (600 ml) was then added and the solution was rapidly washed with cold 5% sodium bicarbonate solution and cold water to neutrality. The chloroform layer was dried over sodium sulfate and concentrated *in vacuo* at room temperature to 30 ml. Mercuric cyanide (2 g), crushed calcium sulfate (2 g), and methanol (2 ml) were added and the reaction mixture was left under reflux overnight and then filtered. The filtrate was examined by tlc (silica gel, chloroform) and found to contain one major product. It was then evaporated to dryness and the residual oil solidified upon trituration with 2-propanol. The crude product was recrystallized from 2-propanol to give 1.9 g (57%) of chromatographically pure product: mp 163°; $[\alpha]^{24}D$ −4.3° (*c* 0.7, methanol); λ_{max} (chloroform) 262 nm (ϵ 6280); nmr (60 MHz, $CDCl_3$) τ 1.80–2.65 (m, 4, aromatic), 4.3–6.4 (unresolved m, 10), 6.48 (s, 3, OCH_3), 7.93 (s, 3, $OCOCH_3$), 7.99 (s, 6, two $OCOCH_3$).

Anal. Calcd for $C_{21}H_{26}N_2O_{12}$: C, 50.60; H, 5.26; N, 5.62. Found: C, 50.70; H, 5.56; N, 5.92.

P-$CH_2N(CH_3)CONHNH_2$ (9). This compound was prepared according to Rubinstein, *et al.*,[12] in the following way. Chloromethylated 2% cross-linked styrene–divinylbenzene copolymer (P-CH_2Cl, 10 g) containing 3 mmol/g of chlorine was swelled for 5 hr in dioxane (100 ml). The mixture was cooled to 0° and methylamine was bubbled through to saturate the solution, and the solution was subsequently left with stirring at room temperature overnight. The polymer was collected by filtration, washed with a solution of triethylamine in dioxane, water, and methanol, and dried at high vacuum.

Anal. Found: N, 3.90.

The polymer from the last stage was swelled once again in dioxane (100 ml), and phosgene (15 g) was bubbled into the stirred mixture. The stirring was continued overnight. The excess of phosgene was removed by a stream of nitrogen, and the polymer was collected by filtration and washed with anhydrous ether and petroleum ether. The resulting polymer was suspended overnight in hydrazine hydrate (50 ml). The polymer **9** was filtered, washed with water and methanol, and dried *in vacuo*.

Anal. Found: N, 7,85.

The increase in nitrogen content corresponds to 1.41 mmol/g of hydrazide groups.

Methyl 2-Deoxy-2-(4-nitrobenzoyl)amino-3,4,6-tri-*O*-acetyl-β-D-glucopyranoside (10).[9] **A.** Compound 8 (122 mg) was dissolved in anhydrous dioxane (30 ml), and a solution of 1 *N* sulfuric acid in dioxane (1.25 ml) was added. The mixture was irradiated for 6 hr at room temperature. The resulting dark red solution that contained a major ninhydrin-positive spot when checked by tlc (silica gel, chloroform–ethanol, 19:1) was treated with charcoal, filtered, and evaporated under high vacuum at room temperature. The resulting red oil was dissolved in pyridine (5 ml), 4-nitrobenzoyl chloride (226 mg) was added, and the mixture was left with stirring overnight. Water (2 ml) was then added and the stirring was continued for an additional 30 min. The solution was diluted with chloroform (50 ml) and the chloroform solution was washed with 0.1 *N* hydrochloric acid, water, 5% sodium bicarbonate solution, and water. It was then dried over sodium sulfate and evaporated. The residual solid was purified by preparative tlc (chloroform–ethanol, 19:1). The product was eluted with ethyl acetate, the extract was evaporated, and the residue was recrystallized from 2-propanol: yield 57 mg (50%); mp 227°: $[\alpha]^{20}D$ +34.7° (*c* 0.3, chloroform) [lit.[9] mp 227–228°, $[\alpha]^{19}D$ +35.1° (*c* 0.77, chloroform)].

Anal. Calcd for $C_{20}H_{24}N_2O_{11}$: C, 51.28; H, 5.16; N, 5.98. Found: C, 51.25; H, 5.10; N, 6.00.

B. Polymer **9** (2 g) was suspended in a solution of compound 8 (100 mg) in chloroform (200 ml) and the mixed suspension was irradiated for 50 hr at ambient temperature (mixing the two in the dark did not affect compound 8). The polymer was filtered off and the colorless filtrate was evaporated to dryness, giving a crude yellowish residue of methyl 2-amino-2-deoxy-3,4,6-tri-*O*-acetyl-β-D-glucopyranoside (63 mg) possessing a major ninhydrin-positive spot in tlc (silica gel, chloroform–ethanol, 19:1). No aromatic and benzylic protons were detected in the nmr (60 MHz, $CDCl_3$); the compound had an OCH_3 resonance at τ 6.43 and acetate resonances at τ 7.92 (6 protons) and 7.97 (3 protons). The crude amino derivative was acylated and processed as described in part A: yield 75 mg (80%); mp 227°; $[\alpha]^{20}D$ +30.5° (*c* 0.7, chloroform); nmr (90 MHz, $CDCl_3$) τ 1.71 (d, 2, aromatic, J = 9.0 Hz), 2.06 (d, 2, aromatic, J = 9.0 Hz), 3.33 (d, 1, NH, J = 9.0 Hz), 4.57 (t, 1, H-3, $J_{2,3} = J_{3,4}$ = 10 Hz), 4.84 (t, 1, H-4, $J_{4,5}$ = 9.5 Hz), 5.31 (d, 1, H-1, $J_{1,2}$ = 8.0 Hz), 5.60–5.94 (unresolved m, 3, H-2 and CH_2), 6.19 (m, 1, H-5), 6.46 (s, 3, OCH_3), 7.87 (s, 3, $OCOCH_3$), 7.92 (s, 3, $OCOCH_3$), 7.98 (s, $OCOCH_3$). Irradiation at τ 1.71 caused the collapse of the doublet at τ 2.06 into a singlet. Irradiation at τ 4.84 affected H-3 and narrowed H-5. Irradiation at τ 5.89 caused the collapse of the NH signals into singlets, H-3 into a doublet (J = 10 Hz), and H-5 into a doublet (J = 9.5 Hz). Irradiation at τ 6.19 changed the H-4 triplet to a doublet (J = 10 Hz). An Indor effect, affecting the multiplet τ 5.60–5.94, was observed when irradiating any of the NH or the H-1 lines. The NH signal disappeared after prolonged mixing with D_2O.

Anal. Calcd for $C_{20}H_{24}N_2O_{11}$: C, 51.28; H, 5.16; N, 5.98. Found: C, 51.34; H, 5.06; N, 6.02.

Photolysis of Compound 4 and the Isolation of 2-Amino-2-deoxy-D-glucose. Compound 4 (312 mg) was dissolved in water (800 ml) and the solution was irradiated for 12 hr at ambient temperature. The dark reaction mixture was concentrated to 10 ml and applied to a Dowex 50 × 8 (H^+ form) column (2.5 × 30 cm). The elution was carried out according to Gardell[10] with 0.3 *N* hydrochloric acid. The initial volume of 320 ml was discarded and the next 240 ml was collected, treated with active charcoal, and evaporated almost to dryness. White crystals formed on the addition of acetone. The material was recrystallized by dissolving it in water–methanol and acetone was added till turbidity, yield 109 mg (70%), mp 190–195° dec, $[\alpha]^{23}D$ +77.5° (30 min) → 72.5° (7 hr, *c* 2.4, water). The product was indistinguishable from 2-amino-2-deoxy-D-glucose hydrochloride when examined by descending paper chromatography on Whatman No. 1 paper using 1-butanol–acetic acid–water (25:6:25, upper phase) or ethyl acetate–pyridine–water (2:1:2, upper phase) as the solvent and a ninhydrin on a silver nitrate stain.

P-CH_2NHNH_2 (11). Chloromethylated 2% cross-linked styrene–divinylbenzene copolymer (P-CH_2Cl, 10 g) containing 3 mmol/g of chlorine was suspended in ethanol (100 ml) containing hydrazine hydrate (16 g) and the mixture was kept under reflux for 6 hr. The product **11** was filtered off, washed with water, methanol, and ether, and dried *in vacuo*.

Anal. Found: N, 8.00.

The nitrogen analysis corresponds to 2.85 mmol/g of bound hydrazine.

Photolysis of Compound 3 and the Isolation of 2-Amino-2-deoxy-D-glucose. Polymer **11** (4 g) was suspended in a solution of compound **3** (157 mg) in water–ethanol (3:2, 250 ml) and the mixed suspension was irradiated at ambient temperature for 16 hr. The polymer was filtered off and the filtrate was treated with active charcoal, filtered again, evaporated almost to dryness, and treated with acetone. The solid residue was pure by paper chromatography (1-butanol–acetic acid–water, 25:6:25, upper phase) and was recrystallized by dissolving it in dilute hydrochloric acid–methanol and adding acetone till turbidity, yield 88 mg (95%), mp 190° dec, $[\alpha]^{24}D$ +80.0° (10 min) → +73.8° (7 hr, final, *c* 1.6, water).

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Registry No. 1, 42854-99-9; **2**, 42855-00-5; **3**, 42855-01-6; **4**, 42855-02-7; **5**, 42855-03-8; **6**, 42855-04-9; 7α isomer, 42855-05-0; 7β isomer, 42855-06-1; **8**, 42855-07-2; **10**, 42854-51-3; **10** amine, 42854-52-4; 2-nitrobenzyl alcohol, 612-25-9; 6-nitroveratryl alcohol, 1016-58-6; 2-amino-2-deoxy-D-galactose hydrochloride, 1772-03-8; 2-amino-2-deoxy-D-glucose, 3416-24-8; 2-amino-2-deoxy-D-glucose hydrochloride, 66-84-2.

References and Notes

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Solution and Solid-State Photodimerization of Some Styrylthiophenes

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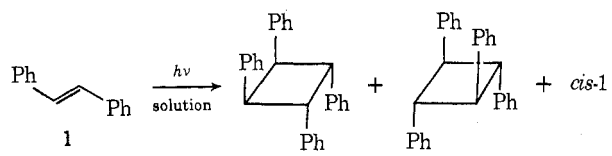
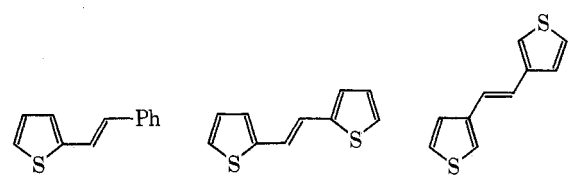
The Pyrex-filtered uv irradiation of *trans*-1-phenyl-2-(2-thienyl)ethene (4), *trans*-1-(2,4-dichlorophenyl)-2-(2-thienyl)ethene (7), and *trans*-1-(3,4-dichlorophenyl)-2-(2-thienyl)ethene (8) has been performed in the crystalline state and in benzene solution. The solid-state behavior is crystal lattice controlled: 4 and the two crystal modifications of 8 are light stable; 7 yields the topochemically expected mirror-symmetric dimer **9**. Contrary to a previous report, 4 undergoes photodimerization in solution and one of the photoproducts has been assigned the centrosymmetric structure **23**. The two dichloro derivatives also afforded solution photodimers and there is a striking substituent effect on their solution photobehaviors. The 2,4-dichloro isomer, 7, yields only the two dimers 9 and **11**, both of cis,anti,cis stereochemistry. By contrast, the 3,4-dichloro isomer, 8, yields all four cyclobutane isomers possible from the union of trans monomers: two all-trans isomers, **16** and **17**, and two cis,anti,cis isomers, **14** and **15**. The photodimerization rates in benzene solution of 7, 4, 8, and *trans*-stilbene were in the ratio 1.0:2.1:2.4:15. Attention is drawn to a correlation between the monomer crystal structures and their solution photodimerization.

In the solid state *trans*-stilbene (**1**) is unreactive when irradiated[1] but in solution it yields the two photodimers, **2** and **3**.[2] The absence of reaction in the solid can be ascribed to the lack of short intermolecular C=C double bond contacts in the crystal,[3] since substituted stilbenes whose crystal structures have such short spacings (parallel double bonds separated by 3.7–4.2 Å) do undergo solid-state photodimerization, affording the dimers predicted on the basis of the monomer lattices.[4] Irradiation of substituted stilbenes in solution generally yields mixtures of photodimers, although the stereochemistries of the products have been unambiguously established in only a few cases.[5]



1 2 3

In contrast to the above, it has been reported that irradiation of saturated benzene solutions of the thiophene analogs of **1**, namely **4**, **5**, and **6**, does not yield photodimers, although these molecules, like stilbene, photoisomerize to the cis isomers which, in turn, undergo photocyclization to unstable dihydrophenanthrene-like intermediates.[6] In the course of our investigation of the packing characteristics and photobehavior of dichloro-substituted molecules[7] we prepared 1-(2,4-dichlorophenyl)-2-thienyl-*trans*-ethene (**7**) and 1-(3,4-dichlorophenyl)-2-thienyl-*trans*-ethene (**8**). The solid-state photobehavior of 7 and 8, reported herein, conformed to topochemical expectations and we therefore investigated their solution photobehavior, as well as that of the previously investigated unsubstituted styrylthiophene, **4**.



4 5 6

In addition, this research sought to inquire into the possible correlation of solid-state photobehavior with solution photobehavior. There may well be such correlation in a photodimerization reaction in which the approach of two molecules in solution may be governed by intermolecular forces similar to those operative in the crystal. If preformed aggregates are important in the solution reaction we might also anticipate such a correlation. Evidence supporting a nonbonded *attractive* interaction between halogen atoms in organic molecules[7] made the dichloro derivatives 7 and 8 especially suitable subjects for this study.

Results and Discussion

Solid State. The crystallographic constants of the three stylthiophenes investigated are presented in Table I. The 2,4-dichloro derivative, **7**, crystallizes in needles having a 4-Å axis and it was therefore expected to yield, on irradiation, the mirror-symmetric photodimer, **9**; indeed, exposure (Westinghouse sun lamps, Pyrex filter) of solid 7 afforded 9 in high yield. The structure of 9 was suggested by spectral data and confirmed by oxidative degradation to the known tetrachloro-β-truxinic acid, **10a**,[8] whose dimethyl ester, **10b**, was identical with an authentic sample.

In addition to 9 the centrosymmetric dimer **11** was formed in small quantities on irradiation of crystalline 7, even at −20°. The presence of this nontopochemical product may be due to "local melting" and disruption of lat-