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Note

Photochemical cleavage of the *N*-(benzyloxycarbonyl) group in amino sugar derivatives

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Since its discovery[1] and first application[2] in the chemistry of 2-amino-2-deoxy-D-glucose close to half a century ago, benzyl chloroformate has continued to be one of the most useful reagents for the protection of amino groups[3] It has found particular utility with amino acids, peptides, and the amino sugars[4], as it gives the corresponding *N*-(benzyloxycarbonyl) derivatives in high yield and, very often, in crystalline state The cleavage of this group, for regeneration of the amino function has been conducted under mild conditions, such as brief treatment with glacial acetic acid containing a hydrogen halide[1 5 6], or by hydrogenolysis[1] Cleavage can also be effected in sodium and liquid ammonia[7], and by the reductive action of triethylsilane[8]

In 1962, Barltrop and Schofield[9] reported the ready fission of the *N*-(benzyloxycarbonyl) group from *N*-(benzyloxycarbonyl)glycine by irradiation with u v light from a medium-pressure, mercury lamp The amino acid was detected chromatographically, and the mechanism of the photolytic cleavage was studied[9] More recently, the *N*-(3,5-dimethoxybenzyloxycarbonyl) group was investigated[10], following earlier observations[9] on the ease of cleavage of such groups containing electron-donating substituents, and it was found to be a useful, photosensitive, N-protecting group Finally, Patchornik and co-workers[11] utilized the *N*-(2-nitrobenzyloxycarbonyl) and *N*-(6-nitroveratryloxycarbonyl) groups as photolabile protecting groups in their studies on amino sugar derivatives

In connection with another synthetic problem, we were faced with the need to regenerate the amino group in an acid-sensitive (benzyloxycarbonyl)amino sugar derivative that also contained a halogen atom As acid-catalyzed cleavage and hydrogenolysis were excluded, we explored the possibility of a photolytic cleavage of the *N*-(benzyloxycarbonyl) group and have found the method to be suitable in this and other cases In initial studies, it was found that 2-(benzyloxycarbonylamino)-2-deoxy-D-glucose and methyl 2-(benzyloxycarbonylamino)-2-deoxy-α-D-glucopyranoside in aqueous methanol are readily converted by irradiation at 253 7 nm, during 4 h at 55°, into 2-amino-2-deoxy-D-glucose and methyl 2-amino-2-deoxy-α-D-glucopyranoside, respectively, isolated as their hydrochlorides in over 70% yield

Photolysis of methyl 2-(benzyloxycarbonylamino)-6-bromo-2 6-dideoxy-α-D-glucopyranoside[12] under the same conditions gave methyl 2-amino-6-bromo-2,6-dideoxy-α-D-glucopyranoside hydrochloride, which was characterized as the known *N*-acetyl-di-*O*-acetyl derivative[13]

Unfortunately, when applied to more-complex molecules containing three or more *N*-(benzyloxycarbonyl) groups, such as in the aminoglycoside series, the cleavage reaction was not complete, leading to mixtures The photolytic method of cleavage should nevertheless be useful in the case of mono(benzyloxycarbonylamino) sugar derivatives, which are frequently used in synthetic transformations

EXPERIMENTAL

General — Melting points are uncorrected Optical rotations were measured with a Perkin-Elmer automatic spectropolarimeter model 141 Thin-layer chromatograms on silica gel GF 254 plates were developed with 5 15 4 chloroform–methanol–ammonium hydroxide Photochemical reactions were performed in a Rayonet apparatus at 253 7 nm

Photolysis of 2-(benzyloxycarbonylamino)-2-deoxy-D-glucose — A solution of the title compound (249 mg) in 1 2 (v/v) water–methanol (60 ml) was irradiated for 4 h at 55–60° The solution was cooled, treated with M hydrochloric acid (1 5 ml), and concentrated to ~5–6 ml Treatment with charcoal filtration, and evaporation gave a pale-yellow syrup that crystallized from aqueous ethanol The crystals were filtered off, and dried for 12 h at 50 The mother liquor was evaporated to dryness, and the crystallization procedure was repeated, to give 2-amino-2-deoxy-D-glucose hydrochloride (total yield 124 mg 72 5%), m p 190–215° (dec) {lit [14] m p 190–210° (dec)}, $[\alpha]_D^{27}$ +100 9 → 50° (c 0 25, H_2O) {lit [14] $[\alpha]_D^{25}$ +100 → 72 5° (H_2O)}, R_F 0 40

Photolysis of methyl 2 (benzyloxycarbonylamino)-2-deoxy-α-D-glucopyranoside — A solution of the title compound[15] (215 mg) was irradiated as just described, to give 98 mg (71%) of methyl 2-amino-2-deoxy-α-D-glucopyranoside hydrochloride as a chromatographically homogeneous syrup which crystallized from ether–ethanol m p 115–120° (lit [16] m p 119°), $[\alpha]_D^{27}$ +129 (c 0 18, H_2O) {lit [16] $[\alpha]_D^{27}$ +127° (H_2O)}, R_F 0 73

Photolysis of methyl 2-(benzyloxycarbonylamino)-6-bromo-2 6-dideoxy-α-D-glucopyranoside — A solution of the title compound[12] (129 mg) {m p 154–154 5°, $[\alpha]_D^{23}$ +80 (c 0 15, MeOH)} in 3 1 methanol–water (60 ml) was irradiated as already described, to give a yellow, chromatographically homogeneous syrup Treatment with a mixture of 2-propanol–petroleum ether (b p 30–60°) gave methyl 2-amino-6-bromo-2,6-dideoxy-α-D-glucopyranoside hydrochloride (10 mg), m p 170–185° (dec), $[\alpha]_D^{27}$ +48 7° (c 0 10, H_2O), R_F 0 90 The filtrate was evaporated to dryness to give additional material (total yield 63%), this was not crystallized, but was acetylated in the usual way, to give crystalline methyl 2-acetamido-2,4-di-*O*-acetyl-6-bromo-2,6-dideoxy-α-D-glucopyranoside (62 mg), identical in all respects with an authentic sample, m p 163–165° (from ether) lit [13] m p 164–165°

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