d, 3′-OH), 7.52 (1 H, d, H-6, $J_{1',6}$ = 1.2 Hz), 11.43 (1 H, s, NH).

Anal. Calcd for $C_{10}H_{13}BrN_2O_5 \cdot {}^1/_2C_2H_5OH$: C, 38.38; H, 4.67; Br, 23.32; N, 8.14. Found: C, 38.25; H, 4.50; Br, 23.22; N, 8.48. Contamination of $^1/_2$ molecule of C_2H_5OH was determined by ^1H NMR of this sample.

5-(β-D-Arabinofuranosyl)-1-methyluracil (10d, X = OH, R = H) was obtained in crystalline form by treatment of **9d** (X = OAc) (70 mg, 0.22 mmol) in water (25 mL) with Dowex-50 (H^+) (~5 mL) at 70 °C for 5 h, followed by filtration of the resin, condensation of the filtrate, and crystallization of the residue from EtOH: 35 mg (63%); mp 226–228 °C; ^1H NMR (Me_2SO-d_6) δ 3.25 (3 H, s, NMe), 3.40–3.53 (2 H, m, H-5′,5″), 3.62–3.67 (1 H, m, H-4′), 3.85 (2 H, s, H-2′,3′), 4.76 (1 H, d, H-1′), 7.39 (1 H, s, H-6), 11.24 (1 H, s, NH). This spectrum pattern is quite similar to that of 5-(β-D-arabinofuranosyl)uracil.[2]

Anal. Calcd for $C_{10}H_{14}N_2O_6 \cdot {}^1/_4H_2O$: C, 45.73; H, 5.52; N, 10.66. Found: C, 45.86; H, 5.73; N, 10.21.

Treatment of **9a** (X = N_3) (100 mg, 0.33 mmol) in aqueous solution with Dowex 50 (H^+) at room temperature for 24 h and regular workup yielded 50 mg (54%) of crystalline **5-(2′-azido-2′-deoxy-β-D-arabinofuranosyl)-1-methyluracil (10a, X = N_3, R = H)**, mp 186–188 °C, and 27 mg (25%) of the 3′-*O*-acetyl derivative **10a** (X = N_3, R = Ac) as a foam.

^1H NMR data for **10a** (X = N_3, R = Ac) in Me_2SO-d_6: δ 2.10 (3 H, s, Ac), 3.29 (3 H, s, NMe), 3.63 (2 H, m, H-5′,5″), 3.82–3.99 (1 H, m, H-4′), 4.35 (1 H, dd, H-2′, $J_{1',2'}$ = 4.5, $J_{2',3'}$ = 0.5 Hz), 4.82 (1 H, dd, H-1′, $J_{1',2'}$ = 4.5, $J_{1',6}$ = 0.5 Hz), 4.91 (1 H, t, 5′-OH), 5.00 (1 H, dd, H-3′, $J_{2',3'}$ = 0.5, $J_{3',4'}$ = 3.6 Hz), 7.59 (1 H, d, H-6, $J_{1',6}$ = 0.5 Hz).

Anal. Calcd for $C_{12}H_{15}N_5O_6 \cdot {}^1/_2H_2O$: C, 43.11; H, 4.82; N, 20.95. Found: C, 43.35; H, 4.88; N, 20.75.

^1H NMR (Me_2SO-d_6) for **10a** (X = N_3, R = H): δ 3.28 (3 H, s, NMe), 3.51–3.68 (3 H, m, H-4′,5′,5″), 3.99 (1 H, m, H-3′, became dd on addition of D_2O, $J_{2',3'}$ = 2.1, $J_{3',4'}$ = 4.6 Hz), 4.12 (1 H, dd, H-2′, $J_{1',2'}$ = 3.4, $J_{2',3'}$ = 2.1 Hz), 4.80 (1 H, t, 5′-OH), 4.88 (1 H, dd, H-1′, $J_{1',2'}$ = 3.4, $J_{1',6}$ = 1.2 Hz), 5.67 (1 H, d, 3′-OH), 7.56 (1 H, d, H-6, $J_{1',6}$ = 1.2 Hz), 11.44 (1 H, s, NH).

Anal. Calcd for $C_{10}H_{13}N_5O_5$: C, 42.40; H, 4.62; N, 24.73. Found: C, 42.93; H, 4.90; N, 24.96.

2′-Deoxy-1-methyl-ψ-uridine (10, X = R = H) from 10 (X = Cl, R = H). A mixture of **10** (X = Cl, R = H) (50 mg), *n*-Bu_3SnH (100 mg), and 2,2′-azobis(2-methylpropionitrile) (15 mg) in toluene (11 mL) was heated under reflux for 1 h. The mixture was concentrated in vacuo, and the residue was purified by chromatography on a silica gel column with $CHCl_3$–EtOH (9:1 v/v) as the eluent. The major nucleoside fraction was concentrated and the residue was directly examined by ^1H NMR spectroscopy. The spectrum of the product was identical with that of 2′-deoxy-1-methyl-ψ-uridine.[21]

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Registry No. 1, 13860-38-3; 2, 97416-14-3; 3, 97416-15-4; 4, 97416-16-5; 5, 97416-17-6; 6, 97416-18-7; 7, 97416-19-8; 7 (2′,3′-*O*-dibutylstannyl deriv), 97416-30-3; 8, 97430-85-8; 9a, 97416-20-1; 9b, 97416-21-2; 9c, 97416-22-3; 9d, 97416-23-4; 10 (X = R = H), 65358-15-8; 10a (X = N_3, R = H), 97416-24-5; 10a (X = N_3, R = Ac), 97416-25-6; 10b (X = Cl, R = H), 97416-26-7; 10b (X = Cl, R = Ac), 97416-27-8; 10c (X = Br, R = H), 97416-28-9; 10d (X = OH, R = H), 97416-29-0; 3′-*O*-acetyl-4,5′-anhydro-1-methyl-ψ-uridine, 97416-31-4; 2′-*O*-acetyl-4,5′-anhydro-1-methyl-ψ-uridine, 97416-32-5.

Bis(indole) Alkaloids. A Nonbiomimetic Approach to the Blue Pigment Trichotomine Dimethyl Ester

Giovanni Palmisano,* Bruno Danieli, Giordano Lesma, and Renata Riva

Dipartimento di Chimica Organica e Industriale della Facoltà di Scienze, Università degli Studi di Milano, Centro di Studio per le Sostanze Organiche Naturali del C.N.R., 20133 Milano, Italy

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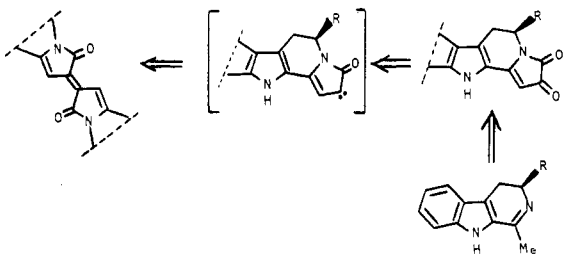
Two alternative routes have been developed for the synthesis of trichotomine dimethyl ester **2**. Both routes involve the synthesis of keto lactam **3** by reaction of the chiral imine **4** [obtained starting from (*S*)-(−)-tryptophan] with oxalyl chloride. The elaboration of **3** into **2** is achieved through the intermediacy of diazo lactam **5** and subsequent copper-assisted thermolysis furnishes **2**. A more efficient route involves a carbene-mediated olefination of keto lactam **3** to give trichotomine dimethyl ester **2** in good yield. The preparation of decarboxytrichotomine **6** is also described.

The bis(indole) alkaloid trichotomine **1**, is an unusual naturally occurring blue pigment, first isolated in 1974 by Iwadare et al.[1] from the fruits of *Clerodendron trichotomum* and *Premna microphylla*. In connection with the proof of structure and stereochemistry of **1**, its dimethyl ester **2** was synthesized through a five-step sequence of reactions in 5% overall yield.[2] A biomimetic variant of the first synthesis of **2** started from its presumptive natural precursors—tryptophan and α-ketoglutaric acid—and attempted to reproduce in vitro, albeit in poor yield (3%!), the regio- and stereoselectivity of the biogenetic process.[3]

Scheme I

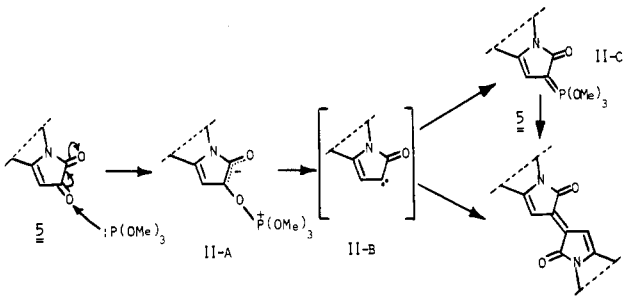


(1) Iwadare, S.; Shizuri, Y.; Sasaki, K.; Hirata, Y. Japanese Patent 7 641 415; *Chem. Abstr.* **1976**, *85*, 25376v.

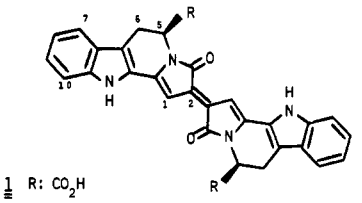
(2) Iwadare, S.; Shizuri, Y.; Yamada, K.; Hirata, Y. *Tetrahedron* **1978**, *34*, 1457 and references cited therein.

0022-3263/85/1950-3322$01.50/0

Scheme II



The key step in both sequences is the dimerization of the unsaturated lactam **3**. Aerial oxygen is sufficient to convert **3** to **2**.[4]



1 R: CO_2H
2 R: CO_2Me
8 R:H

Because of the symmetry inherent in trichotomine **1** and derivatives (C_2 axis perpendicular to the molecular plane), we reasoned that such compounds should also be accessible from the dimerization of appropriate α-keto carbene–carbenoid precursors.[5]

We now record the successful application of this methodology to the synthesis of **2** as outlined in Scheme I. In addition, this represents a novel exploitation of our recently described annulation of the C,N-ambident nucleophilic imine–enamines **4a,b**.[6] The chiral unit chosen as starting material for **2** was **4a**,[7] which was readily prepared by the Bischler-Napieralski cyclization (TFA, acetyl chloride, room temperature) of (*S*)-(−)-tryptophan, followed by $SOCl_2$–methanol treatment. Condensation of **4a** with oxalyl chloride in dimethoxyethane in the presence of triethylamine, proceeded regioselectively to give the indolizino[8,7-*b*]indole derivative **5a**. Several attempts[8] (Forster and Bamford–Stevens methods, dehydrogenation of hydrazones) to elaborate the carbonyl group present at C-2 in **5a** to a diazo function led either to the needed diazo lactam **6a** in unacceptable yields or to a diverse array of products. The most effective experimental conditions for obtaining the very sensitive **6a** (43% yield) included treatment of **5a** with hydroxylamine hydrochloride to give the (*Z*)-oxime **7a** followed by reaction with hydroxylamine *O*-sulfonic acid (HSA) in alkaline sulution[9] under carefully controlled conditions. Thermal decomposition of **6a** over copper bronze in refluxing benzene (1 h) afforded, after reversed-phase flash chromatography,[10] trichotomine dimethyl ester **2** in only 8% yield from **5a**. Compound **2** thus obtained gave spectra (UV, IR, and ^1H NMR) that were identical with those reported by Iwadare et al.[2] for the naturally occurring compound **2**.

3 X: H_2
5 X: O
6 X: N_2
7 X: NOH

4

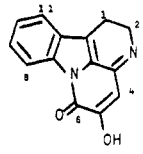
a R: CO_2Me **b** R: H

Unfortunately, the overall yield of **2** produced by the above sequence was unsatisfactory and we did not consider this approach to be competitive with those described earlier. The poor results seemed associated with the borderline stability of **6a** at room temperature and with undue byproduct formation during its copper-assisted thermolysis. Hence, we have investigated the deoxygenative dimerization of keto lactam **5a** as a means of directly transforming this stable compound to trichotomine dimethyl ester **2**. Tervalent phosphorus reagents would appear suited to the requirements of the proposed conversion. The value of this carbenoid-mediated olefination process has been recently emphasized by Farmitalia-Carlo Erba[11] and Sankyo[12] chemists in penem-forming reactions. Thus, keto lactam **5a** was smoothly and efficiently (63%) transformed into **2** when heated with trimethyl phosphite (2 equiv) in toluene solution at reflux for 1 h. From literature precedent[11] it seems likely that the initial reaction of **5a** with $(MeO)_3P$ would be expected to yield the resonance-stabilized betaine II-A by a two-electron transfer from phosphorus atom to the keto carbonyl oxygen. Under the thermal conditions, II-A generated the carbene II-B by extruding trimethyl phosphate. The electrophilic II-B is then trapped by a second molecule of $(MeO)_3P$ to yield the trimethoxyphosphorane II-C, precursor of a Wittig-like olefination (Scheme II).

To further explore the scope and the generality of this procedure, we prepared the nonnaturally occurring bis(indole) **8** by a sequence similar to that used for **2**. The lactam **5b**,[14] which proved readily accessible by appropriate imine **4b** in the predescribed manner (75%), was exposed to trimethyl phosphite in refluxing toluene (50 min) delivering **8**[15] rather cleanly (55% yield). For the sake of

(3) Kapadia, G. J.; Rao, R. E. *Tetrahedron Lett.* **1977**, 975.
(4) It is probable that oxidation of **3** to **2** is sluggish due to the steric congestion around the pivotal *E* double bond in **2** and this could allow degradative oxidations to become competitive.
(5) See: Kirmse, W. "Carbene Chemistry"; Blomquist, A. T., Ed; Academic Press: New York and London, 1964. Wulfman, D. S.; Linstrumelle, G.; Cooper, C. F. "The Chemistry of Diazonium and Diazo Groups"; Patai, S., Ed.; John Wiley and Sons: Chichester, 1978; Part 2, p 821.
(6) Danieli, B.; Lesma, G.; Palmisano, G. *J. Chem. Soc., Chem. Commun.* **1980**, 109; *Ibid*, **1980**, 800; *Tetrahedron Lett.* **1981**, 1827; *Gazz. Chim. Ital.* **1981**, *111*, 257. Calabi, L.; Danieli, B.; Lesma, G.; Palmisano, G. *Tetrahedron Lett.* **1982**, *23*, 2139. Danieli, B.; Lesma, G.; Palmisano, G.; Tollari, S. *J. Chem. Soc. Perkin Trans. 1* **1984**, 1237. Lesma, G.; Palmisano, G.; Tollari, S. *Ibid* **1984**, 1593. Danieli, B.; Lesma, G.; Palmisano, G.; Tollari, S. *Synthesis* **1984**, 353.
(7) Coletti-Previero, M.-A.; Axelrud-Cavadore, C.; Previero, A. *Biochem. Biophys. Res. Commun.* **1972**, *49*, 301.
(8) For an excellent review on the synthesis of diazo carbonyl compounds, see: Regitz, M. "The Chemistry of Diazonium and Diazo Groups", Patai, S., Ed.; John Wiley and Sons: Chichester, 1978; Part 2, p 751.
(9) Nassal, N. *Liebigs Ann. Chem.* **1983**, 1510.
(10) Kühler, T. C.; Lindsten, G. R. *J. Org. Chem.* **1983**, *48*, 358.
(11) Perrone, E.; Alpegiani, M.; Bedeschi, A.; Giudici, F.; Franceschi, G. *Tetrahedron Lett.* **1984**, *25*, 2399 and references cited therein.
(12) Yoshida, A.; Hayashi, T.; Takeda, N.; Oida, S.; Ohki, E. *Chem. Pharm. Bull.* **1983**, *31*, 768.
(13) Attempts at inducing olefination of **5a** to **2** by use of $(EtO)_3P$, $(PhO)_3P$, or tris(dimethylamino)phosphine under similar conditions gave poorer yields or failed at all.
(14) In addition to the expected product **5b**, the indolo[3,2,1-*de*]-[1,5]naphthrydine derivative **9**, arising from the cyclization on indole nitrogen, was obtained (19%).
(15) Like trichotomine dimethyl ester **2**, compound **8** is stable indefinitely in the solid phase and in solution and retains its deep-blue coloration over a long period of time but bleaches on exposure to light and air giving mainly the keto lactams **5a** and **5b**, respectively.

comparison, application of an alternative sequence including the thermolysis of diazo lactam **6b** (see Experimental Section), in our hands, gave **8** in only 31% yield (11% overall yield from **4b**), along with substantial amounts of intractable material.



9

Experimental Section

Melting points are uncorrected. Chemical shifts are expressed in part per million downfield from internal Me_4Si and coupling constants (J values) are given in hertz. Unless stated otherwise, thin-layer chromatography (TLC) was carried out on Merck precoated silica gel 60F-254 plates. Flash chromatography refers to the technique described by Still et al.[16]

Reaction of Imines 4a and 4b with Oxalyl Chloride. A suspension of the hydrochloride of **4a** (1.23 g, 4.62 mmol) in absolute dimethoxyethane (60 mL) was stirred at −50 °C under nitrogen as triethylamine (2.0 mL, 14.32 mmol) was added dropwise. Stirring at −50 °C was continued for 5 min whereupon oxalyl chloride (410 μL, 4.70 mmol) was added and within a few seconds a brick-red solution resulted. After being stirred at −50 °C for 15 min, the mixture was allowed to warm at room temperature and then kept at 40 °C for 30 min. Since TLC (chloroform–methanol, 9:1) showed no starting material, the reaction mixture was evaporated to dryness in vacuo affording a red-brown residue. This was partitioned between ethyl acetate and water. The foam obtained on evaporation of the dried (Na_2SO_4) ethyl acetate extract was purified by flash chromatography (chloroform–ethyl acetate, 1:1) to afford 1.12 g (82%) of **5a** as a deep-red solid. An analytical sample of **5a** was crystallized from methanol: mp 243 °C dec; R_f 0.39 (ethyl acetate–chloroform, 1:1); UV (MeOH) λ_{max} (log ϵ) 213 (4.31), 250 (3.93), 354 (4.10), 407 (4.15), 430, (4.17); IR (KBr) ν_{max} 3300, 1750, 1730, 1695 cm^{-1}; ^1H NMR (DMSO-d_6) δ 3.48 (1 H, dd, $J_{6\alpha,6\beta}$ = 17.5, $J_{5,6\alpha}$ = 6.7 Hz, H-6α), 3.63 (3 H, s, CO_2Me), 3.79 (1 H, dd, $J_{6\alpha,6\beta}$ = 17.5, $J_{5,6\beta}$ = 2.3 Hz, H-6β), 5.29 (1 H, dd, $J_{5,6\alpha}$ = 6.7, $J_{5,6\beta}$ = 2.3 Hz, H-5), 5.93 (1 H, s, H-1), 7.16 (1 H, ddd, J = 7.8, 6.5, 1.7 Hz, H-8), 7.41 (1 H, ddd, J = 7.8, 6.5, 1.7 Hz, H-9), 7.54 (1 H, br d, J = 7.8 Hz, H-10), 7.79 (1 H, br d, J = 7.8 Hz, H-7), 12.20 (1 H, s, NH); m/z (200 °C) 296 ($M^{+\cdot}$, 27), 237 (28), 209 (100), 181 (57), 154 (22). Anal. Calcd for $C_{16}H_{12}N_2O_4$: C, 64.86; H, 4.08; N, 9.45. Found: C, 63.44; H, 4.13; N, 9.53.

Reaction of **4b** with oxalyl chloride with the same procedure gave **5b** (75%) and the indolo[3,2,1-*de*][1,5]naphthyridine derivative **9** (19%). **5a**: mp 223 °C dec as red needles from methanol; R_f 0.31 (ethyl acetate–chloroform, 1:1); IR (KBr) ν_{max} 3300, 1740, 1690 cm^{-1}; UV (MeOH) λ_{max} (log ϵ) 214 (4.31), 250 (3.92), 357 (4.23), 404 (4.11), 432 (4.17); ^1H NMR (200 MHz, DMSO-d_6) δ 3.23 (2 H, t, J = 6.4 Hz, H-6), 3.83 (2 H, t, J = 6.4 Hz, H-5), 5.77 (1 H, s, H-1), 7.19 (1 H, ddd, J = 7.8, 6.7, 1.2 Hz, H-9), 7.54 (1 H, br d, J = 7.8 Hz, H-10), 7.77 (1 H, br d, J = 7.8 Hz, H-7), 12.18 (1 H, br s, NH); m/z (200 °C) 238 ($M^{+\cdot}$, 44), 211 (98), 210 (94), 182 (22), 154 (100). Anal. Calcd for $C_{14}H_{10}N_2O_2$: C, 70.58; H, 4.23; N, 11.76. Found: C, 70.68; H, 4.21; N, 11.67.

9: mp 244 °C as lemon-yellow needles from methanol; R_f 0.21 (benzene–ethanol–ammonia, 98:10:1) as strong fluorescent spot; IR ($CHCl_3$) ν_{max} 1725, 1605 cm^{-1}; UV (MeOH) λ_{max} 210, 273, 332, 374 nm; ^1H NMR (DMSO-d_6) δ 3.02 (2 H, t, J = 7.2 Hz, H-1), 3.65 (2 H, t, J = 7.2 Hz, H-2), 5.50 (1 H, s, H-4), 7.37 (1 H, dt, J = 7.2, 1.8 Hz, H-10), 7.52 (1 H, dt, J = 7.2, 1.8 Hz, H-9), 7.77 (1 H, dd, J = 7.2, 1.8 Hz, H-11), 8.23 (1 H, dd, J = 7.2, 1.8 Hz, H-8), 8.30 (1 H, s, OH); m/z (150 °C) 238 ($M^{+\cdot}$, 74), 210 (100), 182 (28), 181 (26), 154 (75).

Preparation of Diazo Lactams 6a and 6b. Hydroxylamine hydrochloride (500 mg, 7.24 mmol) was added at room temperature to a solution of lactam **5a** (1.07 g, 3.62 mmol) in methanol (75 mL) and the mixture was gently refluxed under nitrogen for 2 h, during which time a yellow product began to separate from solution. The cooled reaction mixture was concentrated in vacuo and filtered and the separated product was then crystallized from methanol affording the (*Z*)-oxime **7a** (878 mg, 78%) as yellow needles: mp 213 °C dec; R_f 0.22 (chloroform–ethyl acetate, 1;1); IR (KBr) 3450, 3220, 1730, 1705, 1640 cm^{-1}; ^1H NMR (DMSO-d_6) δ 3.34 (1 H, dd, $J_{6\alpha,6\beta}$ = 17.2, $J_{5,6\alpha}$ = 6.4 Hz, H-6α), 3.61 (3 H, s, CO_2Me), 3.65 (1 H, dd, $J_{6\alpha,6\beta}$ = 17.2, $J_{5,6\beta}$ = 2.2 Hz, H-6β), 5.19 (1 H, dd, $J_{5,6\alpha}$ = 6.4, $J_{5,6\beta}$ = 2.2 Hz, H-5), 6.26 (1 H, s, H-1), 11.79 (1 H, br s, NH), 12.60 (1 H, br s, OH). Anal. Calcd for $C_{16}H_{13}N_3O_4$: C, 61.73; H, 4.21; N, 13.50. Found: C, 62.08; H, 4.26; N, 13.40. The (*Z*)-oxime **7a** (310 mg, 0.99 mmol) was dissolved in methanol–water (7:3)(10 mL) and hydroxylamine *O*-sulfonic acid (226 mg, 2.0 mmol) in 1 N NaOH solution (4 mL) was added the reaction flask being covered with aluminum foil to avoiding exposing the reaction mixture to light. The reaction mixture was stirred under nitrogen at 0 °C for 3 h and then concentrated at room temperature in vacuo. The gummy residue was taken up in water and extracted with diethyl ether and then the dried solvent removed in vacuo. The dark residue was rapidly subjected to flash chromatography (ethyl acetate–chloroform, 1;1). The eluate was kept cold during collection and the solvent was removed at room temperature or below to give the pure diazo lactam **6a** (138 mg, 43%) as a brown foam: R_f 0.32 (ethyl acetate–chloroform, 1:1); UV (MeOH) λ_{max} (log ϵ) 220 (4.21), 298 (3.70), 310 (3.82), 370 (3.93); IR ($CHCl_3$) ν_{max} 3460, 2083, 1735, 1670 cm^{-1}; ^1H NMR ($CDCl_3$) 3.26 (1 H, dd, $J_{5,6\alpha}$ = 6.5, $J_{6\alpha,6\beta}$ = 17.0 Hz, H-6α), 3.67 (1 H, dd, $J_{5,6\beta}$ = 2.2, $J_{6\alpha,6\beta}$ = 17.0 Hz, H-6β), 3.69 (3 H, s, CO_2Me), 5.23 (1 H, dd, $J_{5,6\alpha}$ = 6.5, $J_{5,6\beta}$ = 2.2 Hz, H-5), 5.88 (1 H, s, H-1), 8.90 (1 H, br s, NH).

Oximation of **5b** followed by reaction with HSA with the same procedure gave **6b** as amorphous brown solid in 47% overall yield: R_f 0.29 (ethyl acetate–chloroform, 1:1); IR ($CHCl_3$) ν_{max} 3430, 2080, 1665 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.10 (2 H, t, J = 6.4 Hz, H-6), 3.95 (2 H, t, J = 6.4 Hz, H-5), 5.96 (1 H, br s, H-1), 7.55 (1 H, br d, J = 7.7 Hz, H-7), 8.25 (1 H, br s, NH).

Copper-Assisted Decomposition of Diazo Lactams 6a and 6b. A solution of **6a** (102 mg, 0.33 mmol) in dry benzene (10 mL) was added to a refluxing stirred suspension of copper bronze (60 mg) in benzene (15 mL) under nitrogen and the heating continued for 1 h, a color change from brown to deep-blue occurring over this period. The cooled mixture was filtered through Celite and the filtrate evaporated in vacuo. The residue was purified by preparative reversed-phase (RP-18) thin-layer chromatography (methanol) to yield trichotomine dimethyl ester **2** (46 mg, 25%): mp 283–284 °C (lit.[2] mp 285–287 °C) as deep-blue needles from methanol; R_f 0.48 (ethyl acetate–chloroform, 1:1); UV ($CHCl_3$) λ_{max} (log ϵ) 240 (4.50), 337 (4.46), 342 (4.54), 602 (4.76), 655 (4.85); IR (KBr) ν_{max} 1740, 1670, 1600 cm^{-1}; ^1H NMR (200 MHz, DMSO-d_6) δ 3.48 (1 H, dd, $J_{6\alpha,6\beta}$ = 17.0, $J_{5,6\alpha}$ = 7.0 Hz, H-6α), 3.63 (3 H, s, CO_2Me), 3.68 (1 H, dd, $J_{5,6\beta}$ = 2.1, $J_{6\alpha,6\beta}$ = 17.0 Hz, H-6β), 5.26 (1 H, dd, $J_{5,6\alpha}$ = 7.0, $J_{5,6\beta}$ = 2.1 Hz, H-5), 7.12 (1 H, ddd, J = 7.8, 6.8, 1.3 Hz, H-8), 7.29 (1 H, ddd, J = 7.8, 6.8, 1.3 Hz, H-9), 7.32 (1 H, s, H-1), 7.45 (1 H, br dd, J = 7.8, 1.3 Hz, H-10), 7.65 (1 H, br d, J = 7.8 Hz, H-7), 11.80 (1 H, s, NH); ^{13}C NMR (DMSO-d_6) δ 96.7 (C-1), 125.4[a] (C-2), 168.3 (C-3), 49.5 (C-5), 23.4 (C-6), 112.9 (C-6a), 127.1[a] (C-6b), 119.3[b] (C-7), 125.4 (C-8), 119.7[b] (C-9), 111.5 (C-10), 138.8 (C-10a), 136.4 (C-11a), 124.6[a] (C-11b), 52.4 (CO_2Me), 170.4 (CO_2Me) ([a,b] indicates assignments may be interchanged). Anal. Calcd for $C_{32}H_{24}N_4O_6$: C, 68.56; H, 4.32; N, 10.10. Found: C, 68.49; H, 4.17; N, 9.58.

The diazo lactam **6b** under the same conditions gave **8** in 31% yield: mp 274 °C dec as blue needles from methanol; UV ($CHCl_3$) λ_{max} (log ϵ) 241 (4.50), 339 (4.45), 349 (4.51), 608 (4.73), 655 (4.85); IR (KBr) ν_{max} 1700, 1670, 1600 cm^{-1}; ^1H NMR (DMSO-d_6) δ 3.14 (2 H, t, J = 6.5 Hz, H-6), 3.86 (2 H, t, J = 6.5 Hz, H-5), 7.21 (1 H, s, H-1), 7.06 (1 H, ddd, J = 7.2, 6.5, 1.6 Hz, H-8), 7.24 (1 H, ddd, J = 7.2, 6.5, 1.6 Hz, H-9), 7.43 (1 H, br dd, J = 7.2, 1.6 Hz, H-10), 7.62 (1 H, br d, J = 7.2 Hz, H-7), 11.90 (1 H, br s, NH). Anal. Calcd. for $C_{28}H_{20}N_4O_2$: C, 75.66; H, 4.54; N, 12.60. Found: C, 75.81; H, 4.72; N, 12.53.

$(MeO)_3P$-Induced Deoxygenative Dimerization of Keto Lactams 5a and 5b. The keto lactam **5a** (300 mg, 1.01 mmol) was suspensed in dry toluene (10 mL) in a round-bottomed flask

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fitted with a Teflon stirbar and nitrogen inlet and outlet. After the mixture was brought to reflux, trimethyl phosphite (360 μL, 3.04 mmol) was added. The reaction was followed by reversed-phase (RP-18) TLC (methanol). The red suspensin turned blue upon addition of $(MeO)_3P$ and this color deepened over the course of 10–20 min. After the consumption of **5a** (1 h) was complete, the solvent was removed under reduced pressure (0.05 torr). The blue-green residue was quickly purified by reversed-phase flash chromatography on octadecyldimethylsilyl-modified silica gel[10] (MeOH as eluant) to yield pure **2** (356 mg, 63%).

Reaction of **5b** with $(MeO)_3P$ in refluxing toluene gave **8** in 55% yield.

Registry No. **2**, 53869-87-7; **4a**, 51372-96-4; **4b**, 525-41-7; **5a**, 96165-60-5; **5b**, 96165-61-6; **6a**, 96165-62-7; **6b**, 96165-63-8; **7a**, 96165-64-9; **8**, 96165-65-0; **9**, 96165-66-1; oxalyl chloride, 79-37-8.

Novel One-Pot Synthesis of a New Class of Compounds Involving Coupling of Sugars and Amino Acids via Triflates[1]

W. Kowollik, A. Malik,[†] N. Afza,[‡] and W. Voelter*

Abteilung für Physikalische Biochemie, Physiologisch-chemisches Institut der Universität Tübingen, D-7400 Tübingen, West Germany

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A new class of pharmacologically interesting compounds has been synthesized by way of a novel C–N coupling reaction between partially blocked sugars and a variety of suitably protected naturally occurring amino acids. The free amino functions of the latter were utilized as effective nucleophiles to cause smooth S_N2 displacement of the triflyl group in benzyl 2,3-anhydro-4-triflyl-α-D-ribopyranoside and its β-L-isomer, respectively (Scheme I). The formation of a new type of aziridino sugars was also observed to a minor extent in a majority of reactions and their origin could be rationalized by a novel isomerization of an α-imino oxirane into an α-hydroxy epimine, analogus to epoxide migration (Scheme II). The reaction pathway also provided an efficient route to benzyl 2,3-anhydro-α-D- and -β-L-lyxopyranosides. The structures and conformations of all the compounds were fully supported by field desorption mass and ^1H and ^{13}C NMR spectroscopies.

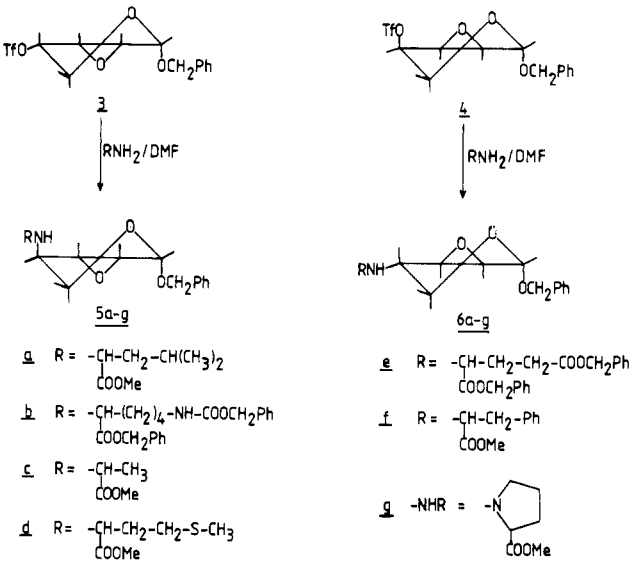
Perfluoralkanesulfonic esters are important intermediates in modern synthetic as well as mechanistic organic chemistry. Particularly the trifluoromethanesulfonates, commonly referred to as triflates, have shown excellent leaving group properties and serve in numerous synthetic transformations.[2] Triflate derivatives have also been used in sugar chemistry. They are well suited for displacement reactions leading to deoxy sugars,[3,4] deoxy azido sugars,[5] deoxy halo sugars,[6] and several disaccharides.[7]

Recently we have described[8] a new and efficient approach to deoxy amino sugars. In the reaction sequence, direct displacement of the triflyl group was affected by passing gaseous ammonia into acetonic solutions of sugar triflates at low temperature. From the high selectivity observed during these reactions, it appeared that the substitution of triflyl group in partially blocked sugar triflates by the free amino functions of suitably protected naturally occurring amino acids should perform the desired C–N coupling between two important groups of natural products, resulting in novel synthesis of a new class of pharmacologically interesting compounds. We now present a full account of these studies which appear to provide an entry to the preparations of these compounds.

Results and Discussion

Benzyl 2,3-anhydro-α-D-ribopyranoside (**1**) and benzyl 2,3-anhydro-β-L-ribopyranoside (**2**) were used partially blocked sugars in the present investigations. The benzyl ether and the oxirane ring were selected as protecting groups in view of their stability in mild conditions and ease of cleavage. Both **1** and **2** were easily prepared by previously published method[9,10] from D- and L-arabinose, respectively. The dichloromethane solution of each partially

Scheme I



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[†] Ministerium für Wissenschaft und Kunst Baden-Württemberg, West Germany, postdoctoral fellow.

[‡] Kernforschungszentrum Karlsruhe, West Germany, postdoctoral fellow.

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