creased to 38%, when the chloroaldehyde **2e** was used in place of **2d**. Furanones **6a** (31% yield from **2a** and 58% yield from **2f**) and **6b** (68% yield from **2b** and 44% yield from **2c**) were obtained in a similar manner. The furanone **6** is thought to be converted via the Michael addition of **3** to possible intermediate **5**. The hydrolysis of **6a** in 2 N aqueous NaOH gave the dicarboxylic acid **7**[6] in 76% yield (Scheme I).

The furanone **6c** was treated with an equivalent amount of $Br_2$ in $CCl_4$ to give the 4-bromofuranone **8b**[7] which was used without isolation for the next step. Heating **8b** in a mixture (1:3.5:10) of 48% HBr–$H_2O$–dioxane for 30 h under reflux gave the desired bislactone **9b** in 55% yield[8] from **6c**. The bislactone **9a** was obtained in 53% yield in a similar manner. Compound **9b** was successfully converted into *dl*-avenaciolide[9] by Johnson's procedure.[3a]

The present reaction provides an excellently simplified route for the construction of the bislactone skeleton of **9**.

**Registry No.** (±)**1**, 26057-70-5; (±)**2a**, 73368-19-1; (±)**2b**, 73368-20-4; (±)**2c**, 73368-21-5; (±)**2d**, 73368-22-6; (±)**2e**, 73368-23-7; (±)**2f**, 58031-09-7; **3**, 6148-64-7; (±)**6a**, 73368-24-8; (±)**6b**, 73368-25-9; (±)**6c**, 73368-26-0; (±)**7**, 73368-27-1; **8a**, 73368-28-2; **8b**, 73368-29-3; **8c**, 73368-30-6; (±)**9a**, 73368-31-7; (±)**9b**, 39949-88-7.

**Supplementary Material Available:** Experimental section describing the preparation details and spectral data (IR, $^1H$ NMR, and $^{13}C$ NMR) of **6a–c**, **7**, **9a**, and **9b** (4 pages). Ordering information is given on any current masthead page.

(5) IR 1787 and 1740 $cm^{-1}$; $^1H$ NMR ($CCl_4$) $\delta$ 0.89 (m, 3 H), 1.1–2.0 (m, 20 H), 2.35–3.14 (m, 3 H), 3.40 (d, 1 H, $J$ = 9 Hz), 4.08 (q, 2 H, $J$ = 7 Hz), 4.20 (q, 2 H, $J$ = 7 Hz), 3.90–4.40 (m, 1 H). The relative stereochemistry of the C-2 alkyl group and the C-3 acetic acid chain is confirmed to be trans by eventual transformation of **6c** to **1**. That of the acetic acid chain and the C-4 ester group is also assigned as trans on the basis of the reaction mechanism and $^1H$ NMR coupling constant of 4-H (9 Hz): A. Takeda, T. Sakai, S. Shinohara, and S. Tsuboi, *Bull. Chem. Soc. Jpn.*, **50**, 1133 (1977). All compounds exhibited acceptable elemental analyses. The yields are for isolated products.

(6) In the $^1H$ NMR spectrum of **7**, irradiation at $\delta$ 1.70 ($CH_2$ of ethyl group) converted the multiplet (2-H) at $\delta$ 4.17 into a sharp signal. This fact indicates that the ethyl group of **7** is bonded at the C-2 position.

(7) The formation of **8b** was confirmed by the $^1H$ NMR.

(8) The analogous cyclization of chlorofuranone **8c** (NaOCl) gave **9b** in 40% yield.

(9) The IR and $^1H$ NMR spectra of **1** were identical with those reported by Turner[1a] and Johnson.[3a] $^{13}C$ NMR (25 MHz, $CDCl_3$) $\delta$ 14.1 (q), 22.6 (t), 24.8 (t), 29.1 (t), 29.2 (t), 31.7 (t), 35.9 (t), 43.9 (d), 74.2 (d), 85.2 (d), 126.0 (t), 134.3 (s), 167.3 (s), 169.7 (s).

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## Triazoline Photochemistry. Pyrrole Formation by Retro-Diels-Alder Synthesis

*Summary:* Irradiation of triazoline **3**, prepared by intramolecular azide–olefin cycloaddition, in methanol solution gives pyrrole methyl ester **4**.

*Sir:* The photoconversion of triazolines to aziridines has been studied in some detail.[1] Stereochemical evidence suggests that nitrogen elimination proceeds in homolytic fashion to give a short-lived 1,3-diradical, from which ring closure occurs to give the aziridine. We wish to describe the new triazoline photoreaction **3** → **4**, for which a mechanism involving the ketene intermediate **7** is postulated.

Bromination of cyclohexenone **1a**[2] with *N*-bromosuccinimide–azobis(isobutyronitrile) in $CCl_4$ gives **1b**, which undergoes tetraethylammonium acetate promoted elimination of HBr to give azido dienone **2** in 80% overall isolated yield (Scheme I).[2] Triazoline **3** (mp 164–165 °C) is obtained from **2** in refluxing benzene solution by azide–olefin intramolecular cycloaddition.[3] The structure of **3** is formulated on the basis of elemental analysis (Anal. Calcd for $C_{19}H_{22}N_4O_3$: C, 64.39; H, 6.26; N, 15.81. Found: C, 64.40; H, 6.28; N, 15.76.)[4] and spectral data: $^1H$ NMR ($CDCl_3$) $\delta$ 3.73 (3 H, s, urethane methyl), 5.28 (1 H, s with weak allylic coupling, $H_a$), 6.40 (1 H, d with weak allylic coupling, $H_b$, $J_{bc}$ = 10 Hz), 3.17 (1 H, sharp d, $H_c$, $J_{bc}$ = 10 Hz); IR ($CHCl_3$) 1660, 1725 $cm^{-1}$; electron impact spectrum, $m/e$ 354. Stereochemical assignment in **3** is tentatively made by way of chemically based supposition (vide infra).

Brief Pyrex-filtered irradiation of **3** in methanol solution gives pyrrole carboxylic ester **4** in essentially quantitative yield (oil, isolated by silica gel chromatography in 75% yield): $^1H$ NMR ($CDCl_3$) $\delta$ 3.67 (3 H, s, methyl), 3.72 (3 H, s, methyl), 3.5–3.9 (1 H, m, $H_d$), 6.45 (1 H, m, $H_a$), 5.83 (1 H, m, $H_b$), 6.62 (1 H, m, $H_c$); chemical ionization spectrum, $m/e$ 359. On the other hand, irradiation of **3** in benzene solution gives the cyclobutane-1,3-dione dimer of ketene **7** of undetermined stereochemistry (Scheme II). This assignment is based primarily on chemical ionization mass spectral analysis ($m/e$ 653), on $^1H$ and $^{13}C$ NMR data, and on the presence of infrared absorption at 1810 $cm^{-1}$. Furthermore, the dimeric substance is converted to **4** on treatment with sodium methoxide in methanol at room temperature.

We believe a reasonable mechanism for these phototransformations involves homolytic extrusion of molecular nitrogen from **3** to give diradical **5**, from which recombination gives the bridged intermediate **6**. Tricycle **6** is formally an intramolecular pyrrole–ketene Diels–Alder adduct,[5] and retro-Diels–Alder reaction of **6** (thermal or photochemical?)[6] would lead to the pyrrole ketene **7**; reaction of **7** with methanol gives the methyl ester **4**, while in the nonnucleophilic solvent benzene, ketene dimerization results in formation of the cyclobutane-1,3-dione.

(1) P. Scheiner in "Selective Organic Transformations", Vol. 1, B. S. Thyagarajan, Ed., Wiley-Interscience, New York, 1970, pp 327–62.

(2) The preparation of **1a** begins with the enaminone of 1,3-cyclohexanedione and benzylaniline, which was sequentially alkylated with ethyl iodide (lithium diisopropylamide in THF/HMPA) and 1-bromo-3-chloropropane (LDA in THF/HMPA). Debenzylation ($H_2$, 5% Pd/c) was followed by treatment with *n*-butyllithium and methyl chloroformate to give **1a**. For recent developments in synthetic methodology of vinylogous amides, see F. J. Vinick and H. W. Gschwend, *Tetrahedron Lett.*, 315 (1978), and references cited therein. Spectral data for **2** include the following: $^1H$ NMR $\delta$ ($CDCl_3$) 7.55–7.08 (5 H, m), 6.78 (1 H, dd, $J$ = 10, 2 Hz), 6.21 (1 H, d, $J$ = 10 Hz), 5.69 (1 H, d, $J$ = 2 Hz), 3.76 (3 H, s), 3.35–3.02 (2 H, m), 2.30–1.05 (6 H, m), 0.72 (3 H, t, $J$ = 6.5 Hz); IR (neat) 2080, 1725, 1640 $cm^{-1}$.

(3) A. Padwa, *Angew. Chem., Int. Ed. Engl.*, **15**, 123 (1976).

(4) Microanalysis was carried out by Spang Microanalytical Laboratory, Eagle Harbor, MI.

(5) A. G. Schultz and M. Shen, *Tetrahedron Lett.*, 2969 (1979), and references cited therein.

(6) J. L. Ripoll, A. Rouessac, and F. Rouessac, *Tetrahedron*, **34**, 19 (1978).

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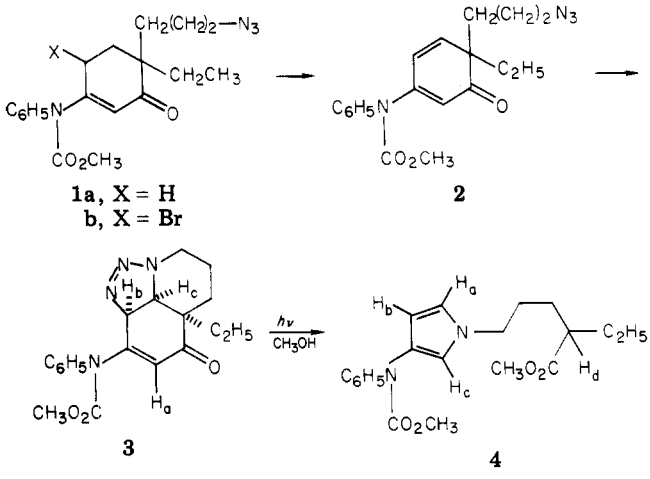
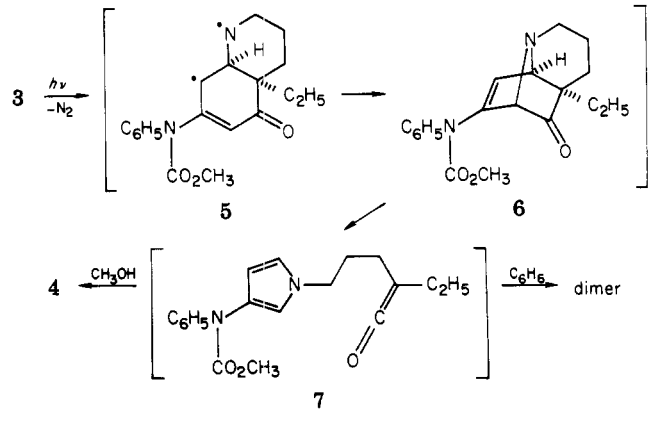
Scheme I



Scheme II



With regard to stereochemical assignment in triazoline **3**, we note that if the mechanism of the rearrangement of **3** → **4** has been correctly interpreted, then formation of **6** demands a *cis*-azaoctalone ring fusion in **3**. The remaining stereochemistry follows from the established cis mode of addition for azide–olefin cycloadditons.[7]

The high efficiency of the photorearrangement of **3** → **4** suggests that this reaction may have synthetic value, and for especially this reason, we are exploring means of intercepting tricyclic intermediates such as **6**. We also are involved in a detailed study of intramolecular azide–olefin cycloadditions and resulting triazoline photochemistry.

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**Registry No. 1a**, 73367-82-5; **1b**, 73367-83-6; **2**, 73367-84-7; **3**, 73367-85-8; **4**, 73367-86-9; **6**, 73367-87-0; **7**, 73367-47-2; **7** dimer, 73367-48-3.

(7) P. Scheiner, J. H. Schomaker, S. Deming, W. J. Libbey, and G. P. Nowack, *J. Am. Chem. Soc.*, **87**, 306 (1965); R. Huisgen, L. Mobius, G. Mueller, H. Stangl, G. Szeimies, and J. M. Vernon, *Chem. Ber.*, **98**, 3992 (1965); R. Huisgen and G. Szeimies, *ibid.*, **98**, 1153 (1965); P. Scheiner, *J. Am. Chem. Soc.*, **88**, 4759 (1966).

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## Chemistry of Naturally Occurring Polyamines. 1. Total Synthesis of Celacinnine, Celabenzine, and Maytenine

*Summary:* New methods for the selective functionalization of spermidine and other naturally occurring polyamines have been employed in highly convergent total syntheses of the title compounds.

*Sir:* Among nature's simplest macrocycles are the plant alkaloids derived from spermine (**1**) and spermidine (**2**),[1,2] two polyamines which are important constituents of every living cell.[3] In 1974 a new family of spermidine alkaloids typified by celacinnine (**3**) and celabenzine (**4**) was isolated from *Maytenus serrata* by Kupchan and co-workers.[4] These structures, which have never been synthesized, have in common a 13-membered lactam ring apparently originating in nature from the combination of spermidine with one β-phenylpropionate unit as depicted in Scheme I.

In this communication we report a biomimetic route to celacinnine and celabenzine directly from spermidine, which relies on a simple and effective new method for differentiating the basic nitrogens of **2**.

Retrosynthetic analysis suggested diamino lactam **5** as a preparatively useful intermediate for the entire family of alkaloids since selective monoacylation of **5** ought to be favored at the nonbenzylic secondary nitrogen. The planned precursor of **5**, triamino acid salt **6**,[5] is difficult to synthesize from free spermidine because the two primary amino groups in **2** have similar basicity[6] and reactivity.[7] This feature is characteristic of the general problem which for over a century has confronted synthetic biochemists working on metabolically important polyamines.[8] However, the 1,3-disposition of $N^1$ and $N^2$ in spermidine led us to believe that a number of strain-free, cyclic, six-center derivatives might form reversibly in preference to seven-membered structures and thus serve as compact, temporary blocking agents. For example, we discovered that urea **8** (Scheme II) arose in 95% yield from spermidine by exhaustive acylation ($ClCO_2CH_3$) and then hydrolysis [$Ba(OH)_2$]. As an illustration of its utility, straightforward chemistry on **8** (acrylonitrile, reduction, hydrolysis) resulted in the first rational synthesis of spermine (**1**) from spermidine (three steps, >50%). An even simpler derivative of **2** is hexahydropyrimidine **9** which was produced (87%) merely by mixing equivalent amounts of spermidine and formalin solution in water.

A well-defined order of amine reactivity exists in **9** which, as with many related substances we have prepared, can be exploited in a number of highly regioselective acylations and alkylations. For instance, treatment of **9** with 2 equiv of cinnamoyl chloride followed by deprotec-

(1) Hesse, M.; Schmid, H. "International Review of Science"; Hey, D. H., Wiesner, K., Eds.; 1976; pp 265–307, Series II, Vol. 9.
(2) Badawi, M. M.; Bernauer, K.; Van den Broek, P.; Groger, D.; Guggisberg, A.; Johne, S.; Kompis, I.; Schneider, F.; Veith, H.-J.; Hesse, M.; Schmid, H. *Pure Appl. Chem.* **1973**, *33*, 81.
(3) Bachrach, U. "Function of Naturally Occurring Polyamines"; Academic Press: New York, 1973.
(4) (a) Kupchan, S. M.; Hintz, H. P. J.; Smith, R. M.; Karim, A.; Cass, M. W.; Court, W. A.; Yatgai, M. *J. Chem. Soc., Chem. Commun.* **1974**, 329. (b) *J. Org. Chem.* **1977**, *42*, 3660.
(5) Collum, D. B.; Chen, S.-C.; Ganem, B. *J. Org. Chem.* **1978**, *43*, 4393.
(6) Palmer, B. N.; Powell, H. K. J. *J. Chem. Soc., Dalton Trans.* **1974**, 2089.
(7) See, for example, the following syntheses of $N^1,N^3$-dicinnamoylspermidine (maytenine): (a) Husson, H.-P.; Poupat, C.; Potier, P. *C. R. Hebd. Seances Acad. Sci.* **1973**, *276*, 1039; (b) Schlittler, E.; Spitaler, M.; Weber, N. *Helv. Chim. Acta* **1973**, *56*, 1097.
(8) For other examples of a "protected" spermidine, see: (a) Wachli-Schaer, E.; Eugster, C. H. *Helv. Chim. Acta* **1978**, *61*, 928; (b) Humora, M.; Quick, J. *J. Org. Chem.* **1979**, *44*, 1166.

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