characteristic of the hydrocarbon substituents and characteristic IR peaks at 1570, 1325, and 1040 cm^{-1}. Mass spectra all showed the M^+ peak and, except for the *N*-benzyl derivatives, a principal second peak representing loss of the *O*-alkyl group.

Acknowledgment. This work was supported in part by a grant from the Research Corporation, to whom we are grateful. We also appreciate the assistance of Robert Zimmermann with all NMR spectra run on the JEOL FX-90 Q and of Jim Spriggle with GC–mass spectra.

Registry No. 1 (R = R′ = CH_3), 90968-33-5; 1 (R = CH_3, R′ = C_2H_5), 90968-34-6; 1 (R = C_2H_5, R′ = CH_3), 90968-35-7; 1 (R = R′ = C_2H_5), 90968-36-8; 1 (R = $C_6H_5CH_2$, R′ = CH_3), 90968-37-9; 1 (R = $C_6H_5CH_2$, R′ = C_2H_5), 90968-38-0; 2 (R = R′ = CH_3), 90968-41-5; 2 (R = CH_3, R′ = C_2H_5), 90968-42-6; 2 (R = C_2H_5, R′ = CH_3), 90968-43-7; 2 (R = R′ = C_2H_5), 90968-44-8; 2 (R = $C_6H_5CH_2$, R′ = CH_3), 90968-45-9; 2 (R = $C_6H_5CH_2$, R′ = C_2H_5), 90968-46-0; Dibal, 1191-15-7; 1,5-dihydro-4-ethoxy-5-ethyl-1-methyl-2*H*-pyrrol-2-one, 90968-39-1; 1,5-dihydro-4-ethoxy-1,5-diethyl-2*H*-pyrrol-2-one, 90968-40-4; 3-ethoxy-2-ethyl-1-methylpyrrole, 90968-47-1; 3-ethoxy-1,2-diethylpyrrole, 90968-48-2; ethyl acetoacetate, 141-97-9; triethyl orthoformate, 122-51-0; ethyl 3-ethoxy-2-butenoate, 998-91-4; ethyl 4-bromo-3-ethoxy-2-butenoate, 1116-50-3.

Supplementary Material Available: ^1H NMR, ^{13}C NMR, IR, and mass spectral data of all 2 and of 1 (R = CH_3, R′ = C_2H_5) (5 pages). Ordering information is given on any current masthead page.

Stereochemistry of Ethyl 2,6-Dimethyl-4-oxocyclohex-2-enecarboxylate (6-Methyl Hagemann's Ester) and Its Products of Conjugate Addition by Vinylmagnesium Bromide/Copper(I) Iodide

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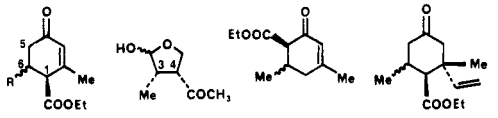
Received September 7, 1983

Given the ready availability and widespread use of 6-alkyl Hagemann's esters as building blocks for organic synthesis, it is remarkable (if not disconcerting) that no one has reported the fact that the 6-methyl derivative (ethyl 2,6-dimethyl-4-oxocyclohex-2-enecarboxylate, 1)

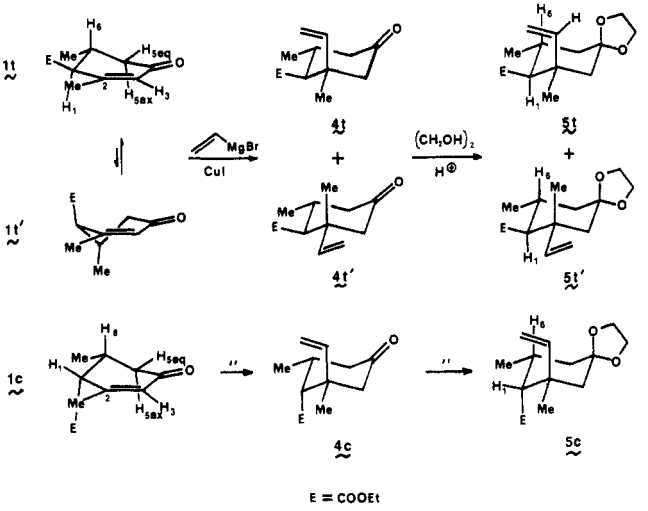


1 R=Me 2 3 4

exists as a readily interconverted pair of diastereomers. This is all the more true in the specific instance in which 1 was assumed to be of trans stereochemistry and then used as the starting material in a synthesis of botryodiplodin (2), thus "proving" the 3,4-cis relationship in the antibiotic.[1] In another study[2] it was recognized that the preparation of 1 gave a mixture of two isomers (which were characterized and separated as their 2,4-DNP derivatives), but these were assigned, incorrectly, as the regioisomers 1 and 3 and the stereochemical issue was again ignored. On the other hand, Kingsbury has demonstrated[3] that the 6-phenyl derivative 1, R = Ph (except as the methyl ester), has the trans configuration on the basis of the vicinal couplings: $J_{H(1),H(6)}$ = 9.1 Hz, $J_{H(5ax),H(6)}$ = 12.4 Hz, and $J_{H(5eq),H(6)}$ = 3.7 Hz. Having a need for the vinylated derivatives 4, we employed the Kametani method of copper(I)-mediated addition of vinylmagnesium bromide to 1 and describe the results here.

The McCurry procedure[5] for the piperidine-catalyzed condensation of ethyl acetoacetate (2 equiv) with acetaldehyde was reproduced, but the 80-MHz ^1H NMR spectrum of the distilled product indicated the presence of two isomers. Separation by HPLC provided a 3:2 ratio of the trans and cis isomers **1t** and **1c**. Either could be readily converted to the same 3:2 mixture by brief exposure to DBU in $CDCl_3$ at room temperature. Stereochemistry was assigned on the basis of high-field ^1H NMR data which suggested that (i) H(1) is pseudoaxial in the major isomer **1t** (since $J_{H(1),C(2)CH_3}$ = 1.2 Hz and $J_{H(1),H(3)}$ = 1.5 Hz) whereas it is pseudoequatorial in **1c** (since no nonvicinal coupling is observed), (ii) H(6) is axial in both **1t** and **1c** (since $J_{H(6),H(5ax)}$ = 11 Hz and 13 Hz and $J_{H(6),H(5eq)}$ = 4.4 Hz and 4.0 Hz, respectively), (iii) H(1) and H(6) are trans in **1t** (since $J_{H(1),H(6)}$ = 7.7 Hz) and cis in **1c** (since $J_{H(1),H(6)}$ = 5.0 Hz). It is interesting that a 0.7-Hz long-range coupling between H(3) and $H(5_{eq})$ is observed in **1c** but is nonexistent in **1t**. Model analysis suggests a distortion of the ring which reduces the allylic ($A_{1,2}$) strain[6] between the ethoxycarbonyl and C(2)-methyl groups in **1t** also precludes $H(5_{eq})$–CCC–H(3) planarity and results in a H(6)–CC–H(1) dihedral angle of ~150°.

The stereochemical assignments of **1c** and **1t** are supported by the reactions of the two isomers with vinyl cuprate. The cis isomer **1c** reacts to give a single product



assigned as **4c**, as does Hagemann's ester itself.[4] However, the trans isomer **1t** gives a 4:1 mixture of adducts **4t** and **4t′**, which we could not separate but whose stereochemistries were assigned after conversion to the ketals **5t** and **5t′**. If one assumes exclusive axial approach of the vinyl group in the conjugate addition, then the products **4t** and **4t′** arise from competitive addition to conformers **1t** and **1t′** via processes which involve a 1,2-interaction between the entering vinyl and the pseudoequatorial ethoxycarbonyl group vs. a (slightly less favorable) 1,3-diaxial

(1) McCurry, P. M., Jr.; Ahe, K. *J. Am. Chem. Soc.* **1973**, *95*, 5824.
(2) Binns, T. D.; Brettle, R. *J. Chem. Soc. C* **1966**, 336.
(3) Kingsbury, C. A.; Egan, R. S.; Perun, T. J. *J. Org. Chem.* **1970**, *35*, 2913.
(4) Kametani, T.; Tsubuki, M.; Nemoto, H. *J. Org. Chem.* **1980**, *45*, 4391.
(5) McCurry, P. M., Jr.; Singh, R. K. *Synth. Commun.* **1976**, *6*, 75.
(6) Johnson, F. *Chem. Rev.* **1968**, *68*, 375.

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interaction between the vinyl and C(6)-methyl groups, respectively. Moreover, the exclusive formation of **4c** arises from an unimpeded attack on the most stable conformer **1c** which lacks both of the steric interactions just mentioned. Consistent with this interpretation is the observation that a 60:40 mixture of **1t** and **1c**, when exposed to 0.4 equiv of the vinyl cuprate reagent, gave mostly **4c** with little formation of **4t** and **4t'**.

The stereochemistry of each of these intermediates was most readily ascertained after conversion to their ethylene ketals **5t**, **5t'**, and **5c**. The $J_{H(1),H(6)}$'s (11.6 Hz in **5t**, 11.5 Hz in **5t'**, and 5.0 Hz in **5c**) reconfirm the earlier trans/cis assignment, and **5t** is notably distinguished from **5t'** by the low-field (δ 6.58) resonance of the internal vinyl hydrogen which is oriented toward and has a 1,6-relationship to the axial ketal oxygen in **5t** as compared with a δ 5.77 for the analogous proton in **5t'** (cf. δ 5.88 for this proton in the material derived from Hagemann's ester[4] which is **5t'** lacking the C(6)-methyl group). Subsequent chemistry of these ketals, to be described elsewhere, is consistent with the stereochemistry assigned here.

Experimental Section[7]

(1α,6β)-(±)- and (1α,6α)-(±)-Ethyl 2,6-Dimethyl-4-oxocyclohex-2-enecarboxylate (1t and 1c). The distilled mixture[5] could be separated by HPLC (SiO_2, 6:1 hexanes:EtOAc) to give pure samples of **1c** and **1t** in a 2:3 ratio. **1t**: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.08 (d, J = 6.6), 1.31 (t, J = 7.1), 1.96 (dd, J = 1.2 and 1.2), 2.13 (H(5_{ax}), dd, J = 17.5 and 11.0), 2.57 (H(6), dddq, J = 11.0, 7.7, 4.4, and 6.6), 2.58 (H(5_{eq}), dd, J = 17.5 and 4.4), 3.02 (H(1), ddq, J = 7.7, 2, and 1), 4.24 (q, J = 7.1), 5.96 (dq, J = 1.5 and 1.5); ^{13}C NMR ($CDCl_3$, 75.6 MHz) δ 14.2, 19.7, 22.6, 32.8, 43.0, 54.4, 61.2, 127.9, 155.8, 171.8, 197.8; MS (EI), m/e (relative intensity) 154 (32), 126 (39), 123 (78), 109 (31), 98 (100), 95 (41), 79 (21), 67 (21), 55 (21), 53 (22), 41 (22), 39 (23); IR ($CDCl_3$) 3000, 2990, 1745, 1675, 1655 (sh), 1470, 1450, 1390, 1305, 1260, 1240, 1205, 1165, 1035, and 870 cm^{-1}; GC t_R 13.23 min. **1c**: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.09 (d, J = 6.6), 1.29 (t, J = 7.1), 1.97 (dd, J = 1.3, 0.6), 2.27 (H(5eq), dddd, J = 16.4, 4.1, 0.6, and 0.6), 2.44 (H(6), dddq, J = 13.4, 5.1, 4.1, and 6.6), 2.62 (H(5_{ax}), dd, J = 16.4 and 13.4), 3.17 (H1, br d, J = 5.1), 4.20 (q, J = 7.1), 5.97 (dq, J = 1.3 and 0.6); ^{13}C NMR ($CDCl_3$, 75.6 MHz) δ 14.3, 18.5, 23.3, 32.0, 40.7, 52.3, 61.2, 128.3, 156.5, 170.1, 199.2; MS (EI), m/e (relative intensity) 154 (39), 126 (42), 123 (42), 109 (26), 98 (100), 95 (33), 79 (19), 67 (18), 55 (18), 53 (19), 41 (20), 39 (21); IR ($CDCl_3$) 3000, 2980, 1745, 1680, 1655 (sh), 1455, 1395, 1310, 1265, 1245, 1205, 1170, 1155, 1040, and 870 cm^{-1}; GC t_R 13.39 min.

(1α,2β,6α)-(±)-, (1α,2α,6β)-(±)-, and (1α,2β,6β)-(±)-Ethyl 2-Ethenyl-2,6-dimethyl-4-oxocyclohexanecarboxylate (4c, 4t, and 4t'). Vinyl bromide (10 mL, 141 mmol) in 50 mL of dry THF was added under N_2 to magnesium turnings (2.6 g, 0.11 mol) in 25 mL of THF. This mixture was refluxed for 10 min until all Mg was consumed and refluxed for 0.4 h under a stream of N_2 to remove excess CH_2=CHBr. The volume was adjusted to 150 mL with additional THF, the solution was cooled to −78 °C, and CuI (9.9 g, 52 mmol) was added in one portion. This slurry was warmed with efficient stirring over 5 min to −6 °C (internal temperature) in an ice–salt bath. The color of the slurry then changed from tan to grey-green to very dark grey over 13 min and was then recooled to −78 °C. The enones **1c** and **1t** (9.2 g, 47 mmol) were added dropwise in 20 mL of THF. After 0.5 h at −78 °C the mixture was warmed to −40 °C for 1 h and quenched with 10% aqueous HCl.[8] Extraction with hexanes/ethyl acetate, washing with saturated $NaHCO_3$ and brine, drying with Na_2SO_4, concentration, and chromatography on SiO_2 provided the ketones **4c**, **4t**, and **4t'** (6.3 g, 60%). The cis isomer was obtained pure by MPLC on SiO_2 (9:1 hexanes:EtOAc; R_f's ~0.1). **4c**: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.98 (d, J = 6.6), 1.07 (s), 1.31 (t, J = 7.2), 2.17 (H(5_{eq}), m), 2.24 (H(6), dddq, J = 2.3, 4.5, 13.0, and 6.8), 2.38 (H(3_{eq}), ddd, J = 1.7, 1.7, and 14.9), 2.49 (H(1), d, J = 4.6), 2.62 (H(5_{ax}), dd, J = 12.7 and 14.3), 2.92 (H(3_{ax}), d, J = 14.9), 4.21 (q, J = 7.1), 5.03 (d, J = 17.5), 5.06 (d, J = 10.9), 5.61 (ddd, J = 0.7, 10.8, and 17.4); ^{13}C NMR ($CDCl_3$, 75.6 MHz) δ 14.3, 19.2, 26.9, 30.4, 42.4, 44.3, 45.9, 54.0, 60.0, 114.7, 144.6, 172.7, 210.4; MS (EI), m/e (relative intensity) 224 (12), 209 (7), 195 (5), 179 (20), 178 (16), 151 (38), 149 (29), 128 50), 123 (32), 115 (36), 109 (63), 95 (68), 81 (50), 69 (89), 67 (50), 55 (65), 41 (100); IR (neat) 1715, 1705, 1625 cm^{-1}; GC t_R 14.47 min. Anal. Calcd for $C_{13}H_{20}O_3$: C, 69.61; H, 8.99. Found: C, 69.44; H, 8.99. The trans isomers coeluted as a 4:1 mixture of **4t:4t'**. **4t**: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.97 (d, J = 6.2), 1.16 (s), 1.30 (t, J = 7.1), 1.94 (H(5_{ax}), dd, J = 12.1 and 15.0), 2.24 (H(3_{ax}), d, J = 14.6), ~2.3 (H(6), m), 2.40 (H1, d, J = 14), 2.44 (H(5_{eq}), ddd, J = 2.1, 4.5, and 14.9), 2.58 (H(3_{eq}), dd, J = 2.1 and 14.6), 4.21 (q, J = 7.2), 4.99 (d, J = 17.6), 5.11 (d, J = 11.1), 6.06 (dd, J = 10.9 and 17.6); ^{13}C NMR ($CDCl_3$, 75.6 MHz) 14.2, 19.9, 27.7, 31.1, 42.1, 47.9, 51.5, 59.3, 60.1, 115.0, 140.4, 172.3, 208.2; MS (EI), m/e (relative intensity) 224 (21), 209 (5), 195 (2), 179 (25), 155 (26), 128 (55), 110 (31), 109 (30), 95 (35), 81 (35), 69 (93), 67 (41), 55 (57), 41 (85); IR (neat, mixture of **4t** and **4t'**) 1720, 1705, 1630 cm^{-1}; GC t_R 14.48 min. **4t'**: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.01 (d, J = 5.8), 1.11 (s), 1.25 (t, J = 7.1), 2.03 (H(3_{ax}), J = 13.5 and 14.3), 2.12 (H(3_{eq}), dd, J = 13.6 and 2.0), 2.30–2.49 (3 H, m), 4.14 (q, J = 7.1), 5.00 (d, J = 17.4), 5.02 (d, J = 10.6), 5.83 (dd, J = 17.3 and 10.9); ^{13}C NMR ($CDCl_3$, 75.6 MHz) δ 14.3, 18.1, 20.6, 31.5, 42.8, 48.1, 53.1, 58.1, 60.2, 112.4, 144.6, 172.5, 208.4; MS (EI), m/e (relative intensity) 224 (6), 209 (8), 195 (6), 179 (31), 155 (23), 151 (22), 139 (28), 128 (71), 115 (34), 113 (67), 110 (62), 109 (45), 107 (23), 99 (35), 95 (47), 86 (55), 81 (43), 69 (100), 67 (41), 55 (61), 41 (75); GC t_R 14.48 min.

(7α,8β,9β)-(±)-, (7α,8α,9β)-(±)-, and (7α,8β,9α)-(±)-Ethyl 7-Ethenyl-7,9-dimethyl-1,4-dioxaspiro[4.5]decane-8-carboxylate (5c, 5t, and 5t'). A standard ketalization ($HOCH_2CH_2OH$, *p*-TsOH, PhH, reflux) of **4c** gave **5c** (71%, after MPLC on SiO_2, 9:1 hexanes:EtOAc; R_f 0.2): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.93 (d, J = 6.9), 1.01 (s), 1.27 (t, J = 7.1), 1.48 (H(5_{eq}), dddd, $J \approx$ 13, 3, 2 and 2), 1.55 (H(3_{eq}), ddd, J = 13.6, 2, and 2), 2.01 (H(5_{ax}), dd, $J \approx$ 13.1 and 13.1), 2.08 (H(3_{ax}), d, J = 13.6), 2.21 (H(6), m), 2.54 (H(1), ddd, $J \approx$ 5, 2, and 2), 3.90–3.95 (m, 4 H), 4.14 (q, J = 7.1), 4.98 (d, J = 11), 4.99 (d, J = 18), 6.20 (dd, J = 18 and 11); ^{13}C NMR ($CDCl_3$, 75.6 MHz) δ 14.4, 19.4, 27.0, 27.9, 37.4, 39.3, 41.6, 53.6, 59.6, 63.6, 64.3, 109.2, 110.3, 146.4, 172.9; MS (EI), m/e (relative intensity) 268 (3), 253 (2), 223 (4), 200 (6), 195 (9), 154 (23), 139 (48), 113 (97), 99 (17), 86 (100); IR (neat) 1730, 1630 cm^{-1}; GC t_R 19.19. Anal. Calcd for $C_{15}H_{24}O_4$: C, 67.14; H, 9.01. Found: C, 67.02; H, 8.78. A similar ketalization of **4t** and **4t'** gave the faster eluting (SiO_2, 19:1 hexanes:EtOAc; R_f 0.1) **5t'** (12%) followed by **5t** (56%). **5t**: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.91 (d, J = 6.5), 1.23 (t, J = 7.0), 1.23 (s), 1.29 (H(5_{ax}), dd, $J \approx$ 13 and 13), 1.54 (H(3_{ax}), d, J = 13.6), 1.71 (H(3_{eq}), dd, J = 13.6 and 2.5), 1.82 (H(5_{eq}), ddd, J = 13.4, 3.5, and 2.5), 1.95 (H(1), d, J = 11.6), 2.30 (H(6), m), 3.85–3.97 (m, 4 H), 4.10 (q, J = 7.0), 4.89 (dd, J = 17.5 and 2.5), 4.97 (dd, J = 11.0 and 2.5), 6.58 (dd, J = 17.5 and 11.0); ^{13}C NMR ($CDCl_3$, 75.6 MHz) δ 14.3, 20.2, 26.9, 28.5, 40.1, 42.8, 47.7, 59.8, 60.8, 63.7, 64.5, 108.0, 111.0, 142.7, 173.0, MS (EI), m/e (relative intensity) 268 (3), 253 (2), 223 (5), 200 (2), 199 (3), 195 (2), 154 (16), 139 (53), 113 (100), 99 (14), 89 (79); IR (neat) 1720, 1630 cm^{-1}; GC t_R 19.83. Anal. Found: C, 67.24; H, 8.80. **5t'**: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.91 (d, J = 6.4), 1.22 (t, J = 7.2), 1.22 (s), 1.26 (H(5_{ax}), dd, $J \approx$ 13 and 13), 1.52 (H(3_{eq}), dd, J = 12.5 and 2.1), 1.62 (H(3_{ax}), d, J = 12.5), 1.81 (H(5_{eq}), ddd, J = 13.5, 3.7, and 2.1), 1.98 (H(1), d, J = 11.5), 2.22 (H(6), m), 3.85–4.00 (m, 4 H), 4.10 (q, J = 7.2), 4.94 (d, J = 10.7), 4.96 (d, J = 17.4), 5.77 (dd, J = 17.4 and 10.7); ^{13}C NMR ($CDCl_3$, 75.6

(7) Elemental analyses were performed by M-H-W Laboratories, Phoenix, AZ. Infrared spectra were recorded on a Perkin-Elmer Model 297 spectrophotometer. ^{1}H NMR spectra were taken on a Varian Model HFT-80 or Nicolet Model NT-300 WB instrument. MPLC refers to chromatography done at 10–50 psi through EM Lobar columns packed with LiChroprep Si60 (40–63 μm) and monitored by refractive index and/or ultraviolet (254/280 nm) detection. Gas chromatography retention times were determined on a 25 m × 0.25 mm OV-101 capillary column at an initial temperature of 50 °C for 4 min with a ramp rate of 30 °C/min to a final hold temperature of 175 °C.

(8) This method of cuprate generation minimized the lower yields and more complex product mixtures which we observed when the cuprate was prepared at −5 °C and then cooled to −78 °C (ref 9) and which we presumed to arise from decomposition of the divinyl cuprate at ~0 °C.

(9) Funk, R. L.; Vollhardt, K. P. C. *J. Am. Chem. Soc.* **1980**, *102*, 5253.

MHz) δ 14.4, 18.6, 20.2, 28.4, 40.5, 43.0, 45.5, 58.8, 59.7, 63.6, 64.7, 108.1, 111.2, 147.5, 173.2; MS (EI), m/e (relative intensity) 268 (4), 253 (2), 241 (1), 223 (6), 200 (3), 195 (6), 154 (15), 139 (48), 113 (100), 99 (16), 86 (66); IR (neat) 1725 and 1645 cm^{-1}; GC t_R 20.17. Anal. Found: C, 67.14; H, 9.01.

Acknowledgment. This investigation was supported by Grant 24056 from the National Cancer Institute, DHHS. Purchase of the high-field NMR instrument was made possible by NSF Grant CHE 79-26027.

Condensation of 2,4-Diamino-6(1*H*)-pyrimidinone with 2-(Aminomethylene)cyclopentanone[1]

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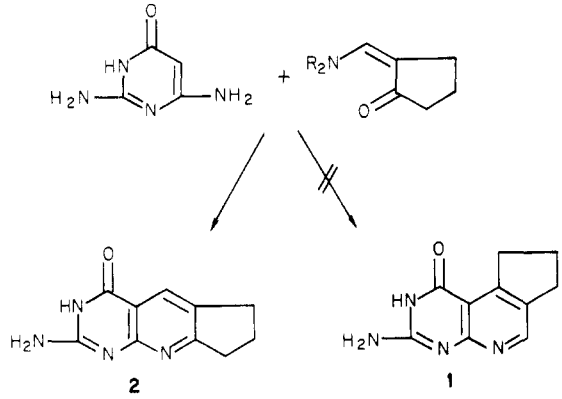
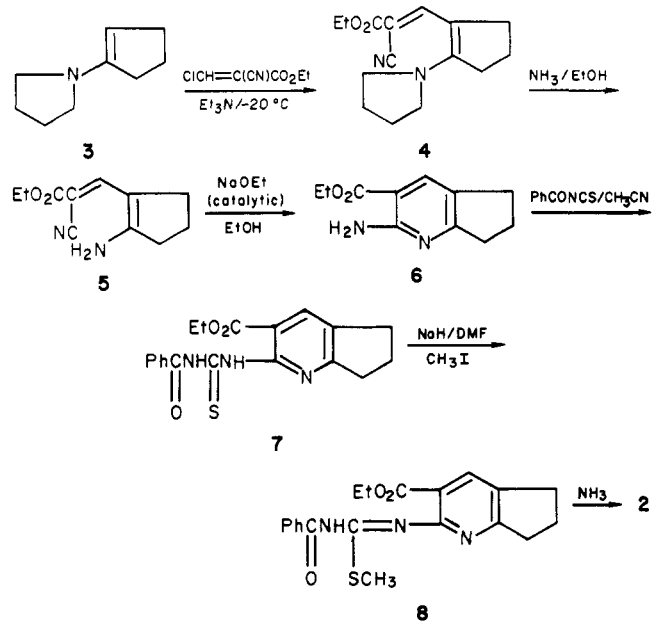
Received January 5, 1984

Interest in annulated 5-deazapteridines (pyrido[2,3-*d*]-pyrimidines) as potential inhibitors of dihydrofolate reductase and thymidylate synthetase prompted us to reinvestigate the structure of the product arising from the condensation of 2,4-diamino-6(1*H*)-pyrimidinone with 2-(aminomethylene)cyclopentanone, a reaction described in 1973 by Stark and Breitmaier.[2] At that time it could not be determined by these authors whether the product possessed the 5,6-annulated structure **1** or the 6,7-annulated isomeric structure **2**. Following the conditions described by Stark and Breitmaier, we obtained a compound whose physical characteristics corresponded precisely with those previously described. The same compound could be obtained by using 2-[(dimethylamino)methylene]cyclopentanone instead of the aminomethylene derivative. By an independent and unequivocal synthesis, we have been able to show that this compound does not possess structure **1** but is instead the 6,7-annulated isomer **2**.



2 **1**

Thus, treatment of 1-pyrrolidinocyclopentene with ethyl (chloromethylene)cyanoacetate[3] in the presence of 1 equiv of triethylamine at −20 °C in methylene chloride gave the alkylated enamine **4**, which was converted in high yield to the primary enamine **5** with ethanolic ammonia. Ring closure to **6** was then effected by treatment with a catalytic amount of sodium ethoxide in ethanol under reflux for 12 h. Although the usual conditions for pyrimidine annulation of *o*-amino esters with guanidine failed with **6**, we were able to convert **6** to **2** by reaction with benzoyl isothiocyanate to give **7**, which was then S-methylated with methyl iodide/sodium hydride/DMF to **8**. Aminolysis of **8** then gave **2**,[4] which was identical in every respect with the compound prepared by the procedure of Stark and Breitmaier.[2]



3 **4** **5** **6** **7** **8**

Since we have also shown by an unequivocal and independent synthesis that condensation of 2,4-diamino-6-(1*H*)-pyrimidinone with 1-[4-*tert*-butoxycarbonyl)-phenyl]-3-(aminomethylene)-4-piperidinone gives a linear pyrido[2,3-*d*]pyrimidine analogous to **2**,[5] it seems probable that all of the cycloalkeno-5-deazapteridines described by Stark and Breitmaier[2] possess 6,7-annulated structures.[6]

Experimental Section

1-(Pyrrolidino)-2-(2-carbethoxy-2-cyanoethylene)cyclopentene (4). Ethyl (chloromethylene)cyanoacetate[3] (4.65 g, 0.0365 mol) in 10 mL of methylene chloride was added dropwise to a solution of 5 g (0.0365 mol) of 1-pyrrolidinocyclopentene and 5 mL (0.0365 mol) of triethylamine in 100 mL of methylene chloride cooled to −20 °C. After addition was complete (10 min), the reaction mixture was stirred for 1 h and warmed to room temperature, and 10 mL of water was added. The organic phase was separated, dried ($MgSO_4$), and evaporated to give a red solid which was triturated with ethanol. Filtration then gave 4.6 g (48%) of **4** as yellow crystals, mp 153–154 °C.

Anal. Calcd for $C_{15}H_{20}N_2O_2$: C, 69.23; H, 7.69; N, 10.77. Found: C, 69.14; H, 7.57; N, 10.51.

2-Amino-3-carbethoxy-5,6-trimethylenepyridine (6). A suspension of 2.0 g of **4** in 25 mL of saturated ethanolic ammonia was stirred at room temperature for 96 h, and the resulting precipitate of **5** was collected by filtration and recrystallized from acetic acid: yield 1.35 g (88%), mp 323–324 °C. Ring closure was then effected by heating 0.6 g of **5** for 18 h in 20 mL of ethanol

(1) We are indebted to the National Cancer Institute, National Institutes of Health (Grant No. R01 CA 28351) for support of this work.
(2) Stark, E.; Breitmaier, E. *Tetrahedron* **1973**, *29*, 2209.
(3) Josey, A. D.; Dickinson, C. L.; Dewhirst, K. C.; McKusick, B. C. *J. Org. Chem.* **1967**, *32*, 1940.
(4) For another application of this procedure for the conversion of an *o*-amino ester to a fused 2-amino-4(3*H*)-pyrimidinone, see: Lewis, A. F.; Townsend, L. B. *J. Am. Chem. Soc.* **1982**, *104*, 1073.
(5) Taylor, E. C.; Skotnicki, J. S.; Fletcher, S. R. *J. Org. Chem.*, submitted for publication.
(6) In footnote *a* to Table III (see ref 2), Stark and Breitmaier wrote that "Aufgrund neuerer Messungen der ^{13}C-^1H Kopplungskonstanten an den Cycloalkeno-5-desazapteridinen und analogen Verbindungen ist nicht auszuschliessen, dass die Zuordnung der ^{13}C-Signale von C-5 und C-7 in Abb. 2 und den Tab. 4-6 umzukehren ist. Dementsprechend wäre der Cycloalkenring in den Verbindungen 12–14 und 17–21 linear, d.h. in 6,7-Stellung des 5-Desazapteridins ankondensiert". A linear structure was later confirmed for the condensation product of 4-aminouracil with 2-(hydroxymethylene)-5α-dihydrotestosterone (Bouchon, G.; Stark, E.; Pech, H.; Breitmaier, E. *Chem. Ztg.* **1973**, *97*, 509). We thank Prof. Breitmaier for drawing our attention to this latter paper.

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