1-(3-Furyl)-3-methyl-2-[1-(methylthio)-3-methylbutylidene]-1-cyclopentanol (53). *n*-Butyllithium (0.37 mL of a 2.00 M hexane solution) was added dropwise to a solution of 3-bromofuran (120 mg, 0.85 mmol) in 10 mL of ether at −78 °C under nitrogen. After 2 h, a solution of **52** in 5 mL of ether was added dropwise. The resulting solution was stirred at −78 °C for 0.5 h and then slowly warmed to 0 °C (over 2 h) whereupon the solution was diluted with 30 mL of saturated aqueous NH_4Cl. The aqueous phase was extracted with 4 25-mL portions of ether and the combined ether extracts were washed with H_2O, dried over $MgSO_4$, and concentrated in vacuo to afford 167.6 mg of crude **53**: IR (neat) 3480 (br, m), 1565 (m), 1520 (m), 1465 (m) cm^{-1}; NMR (60 MHz, CCl_4) δ 0.87 (d, J = 6.0 Hz, 6 H), 1.23 (d, J = 7.0 Hz, 3 H), 1.27–1.90 (m, 3 H), 1.90–2.50 (m, 4 H), 2.20 (s, 3 H), 3.13 (p, J = 6.5 Hz, 1 H), 3.53 (br s, 1 H), 6.37 (s, 1 H), 7.17 (s, 1 H), 7.35 (split s, 1 H).

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Registry No. 1, 90968-96-0; 2, 87711-77-1; 3, 90968-97-1; (±)-4, 89295-78-3; (±)-5, 89295-80-7; 8, 17649-89-7; 9, 84307-81-3; 10, 17649-90-0; 11, 79300-00-8; 12, 51507-08-5; 13, 87615-87-0; 14, 17649-86-4; 15a, 19429-40-4; 15b, 84307-82-4; 15c, 84307-83-5; 15d, 90968-98-2; 15e, 90968-99-3; 16a, 84333-35-7; 16b, 84307-84-6; 17a, 84307-85-7; 17b, 15081-74-0; 17c, 90969-00-9; 17d, 90969-01-0; 19a, 84307-87-9; 19b, 84307-86-8; 19c, 90969-02-1; 20b, 90969-03-2; 22a, 84307-90-4; 22b, 84307-91-5; 22c, 84307-93-7; 22d, 90969-04-3; 22e, 90969-05-4; 23b, 84307-92-6; 24, 90969-06-5; 25a, 84307-96-0; 25b, 84307-94-8; 26a, 84307-97-1; *cis*-26b, 90969-07-6; *trans*-26b, 90990-51-5; 27a, 84307-98-2; 27b, 5828-09-1; 27c, 90969-36-1; 28b, 90969-08-7; 29, 90969-09-8; 30a, 84308-01-0; 30b, 84308-02-1; (*E*)-31a, 90969-10-1; (*Z*)-31a, 90969-11-2; (*E*)-31b, 86467-33-6; 31c, 90969-12-3; (*E*)-33a, 90969-13-4; (*Z*)-33a, 90990-52-6; 33b, 90969-14-5; (*E*)-34a, 90969-15-6; (*Z*)-34a, 90969-16-7; 34b, 90969-17-8; 35a, 67209-77-2; 35b, 1560-11-8; 35c, 13148-94-2; 35d, 636-82-8; (*E*)-36, 90969-18-9; (*Z*)-36, 81911-91-3; 37, 16957-70-3; 40, 90969-19-0; 41, 90969-20-3; 42a, 1641-41-4; 42b, 529-35-1; 43a, 90969-21-4; 43b, 90969-22-5; 44a, 90969-23-6; 44b, 90969-24-7; 45, 90969-25-8; 46, 90969-26-9; 47a, 1123-73-5; 47b, 618-45-1; 48a, 90969-27-0; (*E*)-48b, 90969-28-1; (*Z*)-48b, 90969-29-2; 49a, 90969-30-5; 49b, 90969-31-6; (±)-50, 89295-81-8; 50 (α-hydroxy dithioacetal), 90969-34-9; (±)-51, 89362-67-4; (±)-52, 90969-32-7; 53, 90969-33-8; $CH_3CO(CH_2)_5CH_3$, 111-13-7; 5-hydroxy-8-(methylthio)-1,2,3,4-tetrahydronaphthalene, 54899-76-2; (±)-1-[(trimethylsilyl)oxy]-3-methylcyclopentene, 89295-85-2; 3-bromofuran, 22037-28-1; (±)-3-methyl-2-[(methylthio)methylene]cyclopentanone, 90969-35-0.

Ergoline Synthons: Synthesis of 3,4-Dihydro-6-methoxybenz[*cd*]indol-5(1*H*)-one (6-Methoxy-Uhle's Ketone) and 3,4-Dihydrobenz[*cd*]indol-5(1*H*)-one (Uhle's Ketone) via a Novel Decarboxylation of Indole-2-carboxylates

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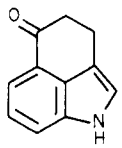
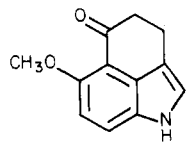
Received March 7, 1984

An efficient synthesis of a new substituted ergoline synthon, 3,4-dihydro-6-methoxybenz[*cd*]indol-5(1*H*)-one, is described. The general synthetic strategy has also been applied to the preparation of the known 3,4-dihydrobenz[*cd*]indol-5(1*H*)-one, Uhle's ketone. The key step, a formal decarboxylation of intermediate 2-carboxy-3,4-dihydrobenz[*cd*]indol-5(1*H*)-one, is accomplished by reduction of the carboxylate ethyl ester to the indole-2-carboxaldehyde followed by catalytic decarbonylation to the parent indole using in situ generated Rh(1,3-bis(diphenylphosphino)propane)$_2^+Cl^-$ catalyst. The catalytic decarbonylation reaction was extended to several other indole-2-carboxaldehydes and appears to be a general reaction of indole aldehydes.

The ergot alkaloids interact with dopamine,[1] serotonin,[2] norepinephrine,[3] and histamine[4] receptors to produce a complex spectrum of pharmacological activities.[5] As part of an investigation of selective 5-hydroxytryptamine receptor agents,[6] we became interested in preparing synthetic ergot substructures which contain the serotonin molecule in its entirety. The successful elaboration of 3,4-dihydrobenz[*cd*]indol-5(1*H*)-one (Uhle's ketone), 1, to a host



1



2

of more complex compounds[7] suggested the 6-methoxy congener 2 as an intermediate for the preparation of ring oxygenated relatives. We report here a convenient, high yield synthesis of 2 and the parent ketone 1 via a novel decarboxylation of intermediate indole-2-carboxylates 12 and 13 under mild, neutral, nonoxidizing conditions. This

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(2) (a) Whitaker, P. M.; Seeman, P. *Psychopharmacology* **1978**, *59*, 1. (b) Whitaker, P. M.; Seeman, P. *Proc. Natl. Acad. Sci. USA* **1978**, *75*, 5783. (c) Fillion, G. M. B.; Rousselle, J. C.; Fillion, M. P.; Beaudoin, D. M.; Goiny, M. R.; Deniau, J. M.; Jacob, J. J. *Mol. Pharmacol.* **1978**, *14*, 50. (d) Peroutka, S. J.; Snyder, S. H. *Ibid.* **1979**, *16*, 687.

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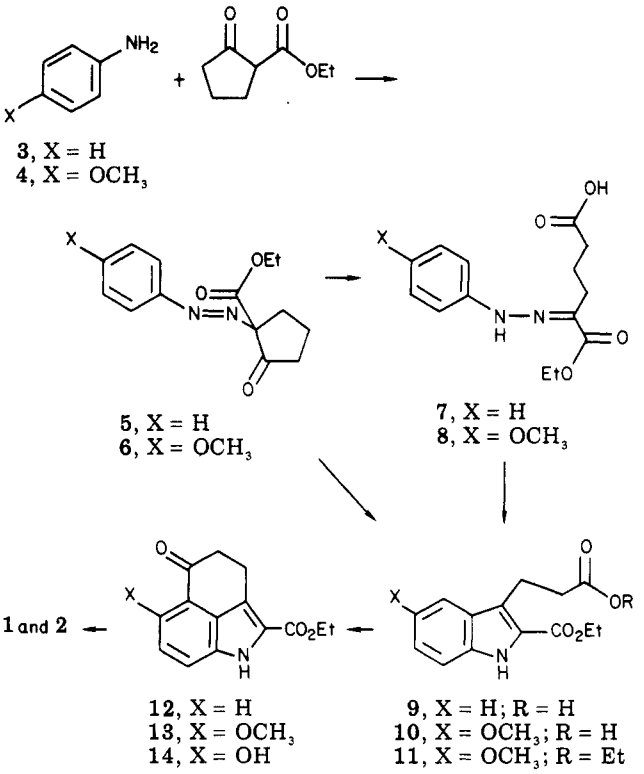
(5) Synthetic ergot derivatives have been prepared in an attempt to determine which structural features determine biological activity. See: (a) Stoll, A.; Petrzilka, T. *Helv. Chim. Acta* **1952**, *35*, 148. (b) Harris, L. S.; Uhle, F. C. *J. Pharmacol. Exp. Ther.* **1960**, *128*, 358. (c) Nichols, D. E.; Robinson, J. M.; Li, G. S.; Cassady, J. M.; Floss, H. G. *Org. Prep. Proced. Int.* **1977**, *9*, 277. (d) Bach, N. J.; Kornfeld, E. C.; Jones, N. D.; Chaney, M. O.; Dorman, D. E.; Paschal, J. W.; Clemens, J. A.; Smalstig, E. B. *J. Med. Chem.* **1980**, *23*, 481. (e) Bach, N. J.; Kornfeld, E. C.; Clemens, J. A.; Smalstig, E. B. *Ibid.* **1980**, *23*, 812. (f) Euvard, C.; Ferland, L.; Fortin, M.; Oberlander, C.; Labrie, F.; Boissier, J. R. *Drug Dev. Res.* **1981**, *1*, 151.

0022-3263/84/1949-3195$01.50/0

Scheme I

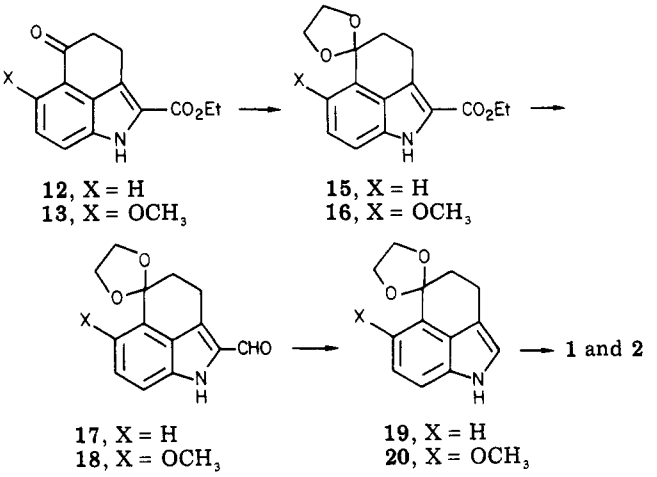


new procedure obviates the necessity of constructing the 3,4-carbocyclic bridge of **1** and **2** by a very sensitive "Dieckmann" cyclization[8] and more importantly, it appears general for the decarboxylation of sensitive indole-2-carboxylates.

Our synthetic approach to **1** and **2** relies upon known intermediates **12** and **13**, compounds which failed to provide **2** or useful amounts of **1** for lack of a practical method for removal of the 2-carboxylate functionality (Scheme I).[9] Modification of the published route[9] to **12** and **13** improved yields and reproducibility, and application of a novel catalytic decarbonylation procedure provided a simple and high yield route to ketones **1** and **2** (Scheme II).

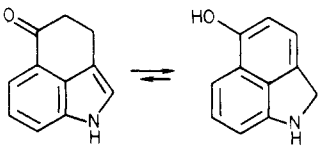
Although we found the original synthesis of **9** to be reproducible, low yields were consistently encountered in our attempts to prepare **10**. In addition, while subsequent cyclization of the acid chloride derived from **9** with $AlCl_3$ produced **12** as reported, cyclization of **10** under the original or a variety of other conditions produced only demethylated product **14**. In our initial attempts to overcome the troublesome problem of demethylation, we observed acid **10** cyclized cleanly in polyphosphoric acid (80 °C, 2 h) to give **13** contaminated with only traces of the demethylated product **14**. The low yields of monoacid precursor **10** which were obtained following the published Fischer

Scheme II



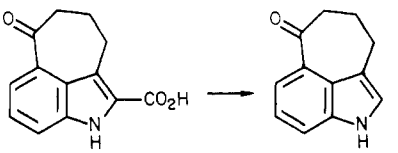
cyclization of **8**, and the subsequent problematical demethylation were simultaneously solved when we discovered the diester **11** would also undergo PPA cyclization to **13** under somewhat more vigorous conditions ("super" PPA,[10] 80 °C, 2.5 h). Unlike monoacid **10**, we were able to prepare the diester **11** in excellent yields by Fischer cyclization of the azo intermediate **6** in ethanolic HCl. With these modifications, the overall yield of **13** was 35–40% from *p*-anisidine.

Attempted decarboxylation by classical techniques (i.e., Cu bronze/quinoline, Cu(I)/DMAC, NaOH/Δ, etc.) of the free acids derived from **12** and **13** failed or resulted in extremely low yields (ca. 5%) of **1** and **2**. The low yields may result in part from the instability of the final ketones. Ketone **1** is known to equilibrate with the unstable naphthalene isomer **21**.[11] The importance of this isom-



1 **21**

erization as a cause for the low yields is evidenced by the observation that the homologue **23** which cannot undergo this type of isomerization, is formed in high yield via decarboxylation of the acid **22**.[9]



22 **23**

The unacceptably low yields encountered in direct decarboxylation procedures with **12** and **13** have been overcome by (1) blocking the ketone as an ethylene ketal, thus effectively preventing isomerization to the naphthalene nucleus, and (2) removing the 2-carboxylate by a rhodium-catalyzed decarbonylation of the corresponding aldehyde under mild, neutral, nonoxidizing conditions. Although there are numerous examples of stoichiometric decarbonylations under mild conditions, most using

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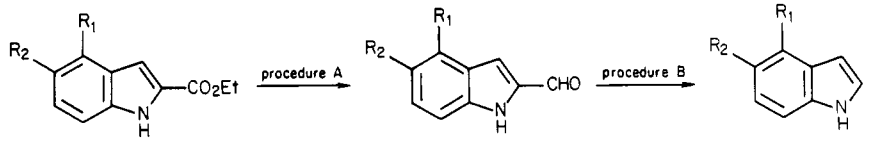
(11) Grob, C.; Payot, P. *Helv. Chim. Acta* **1953**, *36*, 839.

Table I. Effects of Reaction Conditions on Decarbonylation of Indole-2-carboxaldehydes



24a-c 25a-c 26a-c

					conditions[a] (B)			
entry	no.	R_1	R_2	% yield (A)	mol % Rh	time h	% yield (B)	% yield (Lit.)
A	**24a**	H	H	87	2	24	82	55[b]
B	**24b**	H	OCH_3	83	3	18	95	70[c]
C	**24c**	Br	OCH_3	77	4	18	95	34[d]
D	**24c**				1	24	93	
E	**24c**				0.5	48	82	
F	**24c**				5[e]	48	11	

[a] All reactions were run at 140 °C in xylene under nitrogen. [b] Elks, J.; Elliott, D. F.; Hems, B. A. *J. Chem. Soc.*, **1944**, 629. [c] Kralt, T.; Asma, W. J.; Haeck, H. N.; Moed, H. D. *Recl. Trav. Chim. Pay-Bas* **1961**, *80*, 313. [d] Meyer, M. D.; Kruse, L. I., unpublished results. Optimum yields were obtained by using the procedure of Casini and Goodman. (Casini, G.; Goodman, L. *Can. J. Chem.* **1964**, *42*, 1234.) [e] $(PPh_3)_2RhCOCl$ was used without the addition of bridging phosphine ligand.

$(PPh_3)_3RhCl$,[12] there are very few examples of catalytic decarbonylations which do not require high temperatures (>250 °C) and long reaction times. One exception is a procedure recently reported by Doughty and Pignolet.[13] Although these workers have shown that a number of simple aliphatic and aromatic aldehydes[14] can be cleanly decarbonylated at 110–170 °C using catalytic quantities of $Rh(dppp)_2^+Cl^-$,[15] this procedure has, surprisingly, not been applied in a synthetic sequence. In an extension of their work, we have found that this catalyst can be generated in situ, and a nearly quantiative yield of **19** and **20** can be obtained from the aldehydes **17** and **18**, respectively. The reaction proceeds readily in xylene at 140 °C using 1–5 mole % of the rhodium catalyst, and is generally complete in 8–16 h. The synthesis of **1** and **2** is completed by hydrolysis of the ketals **19** and **20** in aqueous acetic acid (25° C, 5 min).

We have extended the decarbonylation reaction to several other simple indole-2-carboxaldehydes (Table I) and found it to be effective for all examples studied. In each case, the overall yield from the ethyl indole-2-carboxylate to the parent indole was comparable to or significantly better than the yield obtained via direct decarboxylation. This was particularly apparent with bromoindole **24c**, which showed low reactivity and extreme instability toward copper-catalyzed decarboxylation. Product isolation on a large scale also favors the decarbonylation procedure over direct decarboxylation; products from our decarbonylation reactions are isolated simply by vacuum filtration of the cooled reaction mixture through a short pad of silica gel to remove catalyst followed by evaporation of solvent. The isolated product, which is generally of greater than 95% purity, may be recrystallized or distilled if so desired. This simple procedure contrasts the troublesome product isolations frequently encountered in copper-catalyzed decarboxylation reactions.

Experimental Section

General Methods. Melting points were determined in open capillary tubes on a Thomas Hoover apparatus and are uncorrected. Infrared (IR) spectra were determined on a Perkin Elmer 783 spectrophotometer. Nuclear magnetic resonance (NMR) spectra were recorded at 90 MHz (Varian EM 390); chemical shifts are reported in parts per million (δ) relative to tetramethylsilane (δ 0.0) as an internal standard. Mass spectra were recorded on a Finnigan Model 3600 GC/MS equipped with chemical-ionization capability. Elemental analyses were performed by the Analytical, Structural, and Physical Chemistry Department of Smith Kline & French Laboratories. All solvents and chemicals were reagent grade. Tetrahydrofuran was dried by distillation from sodium benzophenone ketyl prior to use. Thin-layer chromatography (TLC) was performed on Analtech (Uniplate) glass plates precoated with silica GF (250 μM). Ultraviolet (UV) light or iodine was used to visualize spots.

General Procedure A: Preparation of Indole-2-carboxaldehydes. The following procedure for the synthesis of 4-bromo-5-methoxyindole-2-carboxaldehyde (**25c**) is representative. A solution of ethyl 4-bromo-5-methoxyindole-2-carboxylate[16] (**24c**) (17.0 g, 0.057 mol) in anhydrous THF (200 mL) was stirred at 0 °C under nitrogen during the portionwise addition (15 min) of $LiAlH_4$ (2.50 g, 0.0675 mol). The mixture was stirred an additional 45 min at 0 °C and then quenched by the sequential addition of water (2.5 mL), 15% aqueous NaOH (2.5 mL), and water (7.5 mL). The mixture was vacuum filtered through a Celite pad and the filter pad was washed with THF (2 × 75 mL). The filtrate was dried (Na_2SO_4) and concentrated under reduced pressure to yield 13.7 g of off-white crystals. The crude intermediate alcohol was dissolved in dichloromethane (400 mL), and activated manganese dioxide (60 g) was added. The mixture was stirred rapidly at 25 °C for 1 h and then filtered. The filter cake was washed with hot acetone[17] (4 × 100 mL), and the combined filtrates were concentrated under reduced pressure to yield 12.05 g (83%) of **25c** as yellow crystals: mp 203–206 °C. An analytical sample was recrystallized from chloroform: yellow needles; mp 206–207 °C; IR (KBr) 3310, 1670 cm^{-1}; NMR ($CDCl_3$) δ 3.9 (s, 3 H), 7.15 (d, 1 H, J = 9 Hz), 7.2 (s, 1 H), 7.45 (d, 1 H, J = 9 Hz), 9.8 (br s, 1 H); mass spectrum (methane CI), m/e 254, 256.

Anal. Calcd for $C_{10}H_8BrNO_2$: C, 47.27; H, 3.17; N, 5.51. Found: C, 47.05; H, 3.27; N, 5.47.

General Procedure B: Decarbonylation of Indole-2-carboxaldehydes. The following procedure for the decarbonylation of **25c** to 4-bromo-5-methoxyindole (**26c**) is representative. $(PPh_3)_2RhCOCl$[18] (0.100 g, 0.145 mmol) was added to xylene (100 mL) under nitrogen, and the mixture was warmed to 80 °C with stirring until the rhodium complex dissolved. 1,3-Bis(diphenylphosphino)propane (0.130 g, 0.315 mmol) was added and the solution was stirred at 80 °C for ca. 15 min until a fine yellow precipitate formed.[19] The aldehyde **25c** (3.67 g, 14.5 mmol) was

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(13) Doughty, D. H.; Pignolet, L. H. *J. Am. Chem. Soc.* **1978**, *100*, 7083.
(14) Doughty, D. H.; McGuiggan, M. F.; Wang, H.; Pignolet, L. H. *Fundam. Res. Homogeneous Catal.* **1979**, *3*, 909.
(15) Here and subsequently, dppp means 1,3-bis(diphenylphosphino)propane, $Ph_2P(CH_2)_3PPh_2$.
(16) Julia, M.; Lallemand, J.-Y. *Bull. Soc. Chem. Fr.* **1973**, 2046.
(17) For the isolation of **17** and **18**, the acetone wash was replaced with a dichloromethane wash.
(18) Tsuji, J.; Ohno, K. *Tetrahedron Lett.* **1965**, 3969.

then added, and the mixture was heated at reflux under nitrogen for 24 h, then cooled, and concentrated under reduced pressure. The product was dissolved in 1:1 ethyl acetate–hexane (100 mL) and filtered through a 6-cm pad of silica gel (230–400 mesh). The silica was washed with ethyl acetate–hexane (2 × 100 mL) and the combined filtrates were evaporated to dryness. The product was recrystallized from chloroform–hexane to yield 3.03 g (92.5%) of **26c**: mp 111–112 °C; IR (KBr) 3370, 1245, 1088 cm^{-1}; NMR ($CDCl_3$) δ 3.9 (s, 3 H), 6.6 (m, 1 H), 6.9 (d, 1 H, J = 9 Hz), 7.2 (m, 1 H), 7.3 (d, 1 H, J = 9 Hz), 8.2 (br s, 1 H); mass spectrum (methane CI), m/e 226, 228.

Anal. Calcd for C_9H_8BrNO: C, 47.82; H, 3.57; N, 6.20. Found: C, 48.02; H, 3.69; N, 6.19.

Ethyl 3-(2-(Ethoxycarbonyl)-5-methoxyindol-3-yl)-propionate (11). *p*-Anisidine (12.3 g, 0.100 mol) was added to a mixture of concentrated hydrochloric acid (19 mL) and water (52 mL), and the resulting solution was stirred and cooled at 0 °C during the addition (15 min) of a saturated aqueous solution of sodium nitrite (7.6 g, 0.110 mol). Ethyl 2-oxocyclopentanecarboxylate (15.6 g, 0.100 mol) was added to an ice cold solution of NaOEt (0.100 mol) in ethanol prepared from Na (2.3 g, 0.1 mol) and absolute ethanol (100 mL). The above two solutions were added simultaneously (10 min) to a rapidly stirred solution of sodium acetate trihydrate (20 g, 0.15 mol) in water (52 mL) at 0 °C. After the addition was complete, the mixture was allowed to warm to 25 °C, stirred for an additional 2 h, and extracted with diethyl ether (2 × 150 mL). The combined ether extracts were washed with water, dried (Na_2SO_4), and evaporated under reduced pressure to yield 28.0 g (96%) of **6** as a dark red oil:[20] IR (NaCl film) 1760, 1740, 1610, 1590 cm^{-1}; NMR ($CDCl_3$) δ 1.3 (t, 3 H, J = 7 Hz), 1.8–2.8 (m, 6 H), 3.8 (s, 3 H), 4.3 (q, 2 H, J = 7 Hz), 6.9 (d, 2 H, J = 9 Hz), 7.8 (d, 2 H, J = 9 Hz). A solution of the crude azo compound **6** (28 g) in absolute ethanol (100 mL) was added to a 10% solution of anhydrous HCl in ethanol (200 mL) at 0 °C. The solution was then heated at reflux for 30 min, cooled to 25 °C, and poured slowly into 10% aqueous Na_2CO_3 solution (1 L). After 30 min, the mixture was filtered, and the crude product was washed twice with water and dried under vacuum to yield 26.1 g (82%) of **11**: mp 104–106 °C. Recrystallization from methanol yielded 19.7 g (62%): mp 109–111 °C (lit.[21] mp 110 °C); IR (KBr) 3320, 1740, 1695 cm^{-1}; NMR ($CDCl_3$) δ 1.3 (t, 3 H, J = 7 Hz), 1.5 (t, 3 H, J = 7 Hz), 2.8 (t, 2 H, J = 8 Hz), 3.4 (t, 2 H, J = 8 Hz), 3.9 (s, 3 H), 4.2 (q, 2 H, J = 7 Hz), 4.5 (q, 2 H, J = 7 Hz), 7.2 (m, 3 H), 9.2 (br s, 1 H).

2-(Ethoxycarbonyl)-3,4-dihydrobenz[*cd*]indol-5(1*H*)-one (12). A mixture of acid **9**[9] (62 g, 0.238 mol), thionyl chloride (50 mL, 0.68 mol), *N,N*-dimethylformamide (1 mL), and chloroform (1 L) was heated on a steam bath for 1 h, and filtered to remove a little tar. The filtrate was concentrated under reduced pressure and concentrated from two 500-mL portions of carbon tetrachloride to remove excess thionyl chloride. The crude solid acid chloride was dissolved in 1,2-dichloroethane (1.5 L) and stirred under argon at ambient temperature during the addition (10 min) of anhydrous aluminum chloride (133 g, 1 mol). The resulting green solution was stirred at ambient temperature for 3.5 h and then poured onto concentrated hydrochloric acid (250 mL) and ice (2 kg). The biphasic mixture was filtered through a layer of Celite to remove a little tar, the organic layer of the filtrate was separated, and the aqueous layer of the filtrate was extracted twice with chloroform. The combined organic layers were washed twice with water, dried (brine, Na_2SO_4), and concentrated. The residue was purified by flash chromatography[22] with 3:1 chloroform–ethyl acetate as eluent to yield 18 g (31%) of **12** as yellow needles: mp 186–188 °C (lit.[9] mp 189–191 °C); IR (nujol mull) 3250, 1705, 1660, 1460 cm^{-1}; NMR (Me_2SO-d_6/$CDCl_3$) δ 1.45 (t, J = 8 Hz, 3 H), 2.9 (t, J = 7 Hz, 2 H), 3.4 (t, J = 7 Hz, 2 H), 4.3 (q, J = 8 Hz, 2 H), 7.2–7.8 (m, 3 H total).

2-(Ethoxycarbonyl)-6-methoxy-3,4-dihydrobenz[*cd*]indol-5(1*H*)-one (13) from 10. Polyphosphoric acid (500 g) was heated to 80 °C and stirred during the addition (5 min) of **10**[9] (12.5 g, 0.043 mol). After 1 h at 80 °C, the reaction mixture was poured onto ice (1.5 kg) and then extracted with ethyl acetate (3 × 300 mL). The combined extracts were washed with 10% aqueous Na_2SO_4 solution, 5% aqueous $NaHCO_3$ solution, dried (Na_2SO_4), and concentrated under reduced pressure. The crude product was recrystallized from ethyl acetate–hexane to yield 9.8 g (83%) of **13** as red crystals: mp 195–198 °C (lit.[9] mp 197–200 °C); IR (KBr) 3260, 1710, 1650 cm^{-1}; NMR ($CDCl_3$) δ 1.4 (t, 3 H, J = 7 Hz), 2.9 (t, 2 H, J = 8 Hz), 3.4 (t, 2 H, J = 8 Hz), 4.0 (s, 3 H), 4.4 (q, 2 H, J = 7 Hz), 7.1 (d, 1 H, J = 9 Hz), 7.6 (d, 1 H, J = 9 Hz), 9.2 (br s, 1 H).

2-(Ethoxycarbonyl)-6-methoxy-3,4-dihydrobenz[*cd*]indol-5(1*H*)-one (13) from 11. Polyphosphoric acid (125 g) and P_2O_5 (25 g) were heated with mechanical stirring to 170–180 °C for 1 h and then cooled to 80 °C. The diester **11** (1.59 g, 5.00 mmol) was added and the mixture was stirred at 80–85 °C for 2.5 h and then poured onto ice (500 g). The mixture was extracted with ethyl acetate (3 × 200 mL), and the combined extracts were washed with 10% aqueous Na_2SO_4 and 5% aqueous $NaHCO_3$ solutions, dried (Na_2SO_4), and concentrated under reduced pressure to yield 0.96 g of a yellow solid. The crude product was purified by flash chromatography[22] with chloroform as eluent to yield 0.89 g (65%) of **13** as yellow crystals: mp 196–198 °C (lit.[9] mp 197–200 °C). Spectral data were identical to the sample prepared from **10**.

Ethyl 5,5-(1,2-Ethylenedioxy)-1,3,4,5-tetrahydrobenz[*cd*]indole-2-carboxylate (15). The ketone **12** (1.215 g, 5.00 mmol) was combined with benzene (75 mL), ethylene glycol (5 mL), and pyridinium *p*-toluenesulfonate (0.200 g, 0.80 mmol). The mixture was heated at reflux with a Dean–Stark water separator for 3 h, poured into 5% aqueous $NaHCO_3$ solution (150 mL), and extracted with ethyl acetate (2 × 100 mL). The combined extracts were washed with water (3 × 100 mL) and 10% aqueous Na_2SO_4 solution, dried (Na_2SO_4), and evaporated to dryness under reduced pressure to yield 1.41 g (98%) of the ketal **15**: mp 139–143 °C; IR (KBr) 3330, 1690 cm^{-1}; NMR ($CDCl_3$) δ 1.4 (t, 3 H, J = 7 Hz), 2.3 (t, 2 H, J = 8 Hz), 3.3 (t, 2 H, J = 8 Hz), 4.2 (m, 4 H), 4.4 (q, 2 H, J = 7 Hz), 7.2 (m, 3 H), 9.0 (br s, 1 H); mass spectrum (methane CI), m/e 288.

Anal. Calcd for $C_{16}H_{17}NO_4$: C, 66.89 H, 5.96; N, 4.88. Found: C, 66.86; H, 5.88; N, 5.07.

Ethyl 5,5-(1,2-Ethylenedioxy)-6-methoxy-1,3,4,5-tetrahydrobenz[*cd*]indole-2-carboxylate (16). The ketal **16** was prepared from the ketone **13** in 85% yield by using the procedure described for the preparation of **15**: mp 122–124 °C; IR (KBr) 3320, 1685 cm^{-1}; NMR ($CDCl_3$) δ 1.4 (t, 3 H, J = 7 Hz), 2.3 (t, 2 H, J = 7 Hz), 3.2 (t, 2 H, J = 7 Hz), 3.9 (s, 3 H), 4.2 (m, 4 H), 4.4 (q, 2 H, J = 7 Hz), 7.0 (d, 1 H, J = 9 Hz), 7.2 (d, 1 H, J = 9 Hz), 8.9 (br s, 1 H); mass spectrum (methane CI), m/e 318.

Anal. Calcd for $C_{17}H_{19}NO_5$: C, 64.34; H, 6.03; N, 4.41. Found: C, 64.37; H, 6.01; N, 4.41.

5,5-(1,2-Ethylenedioxy)-1,3,4,5-tetrahydrobenz[*cd*]indole-2-carboxaldehyde (17). The aldehyde **17** was prepared from **15** in 89% yield following the general procedure A. White needles (from chloroform): mp 170–172 °C; IR (KBr) 3300, 1645, 1620 cm^{-1}; NMR ($CDCl_3$) δ 2.3 (t, 2 H, J = 7 Hz), 3.3 (t, 2 H, J = 7 Hz), 4.2 (m, 4 H), 7.2 (m, 3 H), 9.2 (br s, 1 H), 9.9 (s, 1 H); mass spectrum (methane CI), m/e 244.

Anal. Calcd for $C_{14}H_{13}NO_3 \cdot {}^1/_2\,H_2O$: C, 66.66; H, 5.59; N, 5.55. Found: C, 66.92, H, 5.57, N, 5.46.

5,5-(1,2-Ethylenedioxy)-6-methoxy-1,3,4,5-tetrahydrobenz[*cd*]indole-2-carboxaldehyde (18). The aldehyde **18** was prepared from **16** in 88% yield by following general procedure A. Yellow needles (from chloroform): mp 161–163 °C; IR (KBr) 3320, 2850, 1660 cm^{-1}; NMR ($CDCl_3$) δ 2.3 (t, 2 H, J = 7 Hz), 3.3 (t, 2 H, J = 7 Hz), 3.9 (s, 3 H), 4.2 (m, 4 H), 7.1 (d, 1 H, J = 10 Hz), 7.3 (d, 1 H, J = 10 Hz), 9.2 (br s, 1 H), 9.9 (s, 1 H); mass spectrum (methane CI), m/e 274.

Anal. Calcd for $C_{15}H_{15}NO_4$: C, 65.93; H, 5.53; N, 5.13. Found: C, 65.95; H, 5.65; N, 4.77.

(19) The procedure is similar to that described by Chatt and Shaw (Chatt, J.; Shaw, B. L. *J. Chem. Soc. A* **1966**, 1437) for the synthesis of $Rh(dppp)_2{}^+Cl^-$, except the rhodium species is not isolated.

(20) It has been reported that conditions nearly identical with those described here yield the hydrazone rather than the azo intermediate: Feofilaktov, V. V. *J. Gen. Chem. USSR (Engl. Transl.)* **1947**, *17*, 993; *Chem. Abstr.* **1948**, *42*, 4537h. However, we have observed that the isolable azo intermediate requires strongly basic conditions to be converted to the hydrazone.

(21) Renson, M. *Bull. Soc. Chim. Belg.* **1959**, *68*, 258.

(22) "Flash chromatography" refers to the technique developed by Still: Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.

5,5-(1,2-Ethylenedioxy)-6-methoxy-1,3,4,5-tetrahydrobenz[*cd*]indole (20). The ketal **20** was prepared from the aldehyde **18** by following general procedure B in 96% yield. White prisms (from ethyl acetate–hexane): mp 141–143 °C; IR (KBr) 3330 cm^{-1}; NMR ($CDCl_3$) δ 2.2 (t, 2 H, J = 6 Hz), 3.0 (t, 2 H, J = 6 Hz) 3.9 (s, 3 H), 4.2 (m, 4 H), 6.8 (s, 1 H), 6.9 (d, 1 H, J = 9 Hz), 7.2 (d, 1 H, J = 9 Hz), 7.9 (br s, 1 H); mass spectrum (methane CI), m/e 246.

Anal. Calcd for $C_{14}H_{15}NO_3$: C, 68.56; H, 6.16; N, 5.71. Found: C, 68.49; H, 6.29; N, 5.47.

3,4-Dihydrobenz[*cd*]indol-5(1*H*)-one (1). The aldehyde **17** (4.86 g, 20.0 mmol) was treated as described in general procedure B by using 3 mol % rhodium catalyst. The ketal **19** was isolated as a colorless oil:[7a] IR (NaCl film) 3420 cm^{-1}; NMR ($CDCl_3$) δ 2.2 (t, 2 H, J = 7 Hz), 3.0 (t, 2 H, J = 7 Hz), 4.2 (m, 4 H), 6.8 (s, 1 H), 7.2 (m, 3 H), 7.9 (br s, 1 H); mass spectrum (methane CI), m/e 216. The ketal **19** was dissolved in acetic acid (9 mL) and water (1 mL). After 10 min at 25 °C, water (10 mL) was added and the mixture was cooled to 0 °C for 30 min. The product was collected by filtration, washed twice with water, and dried under vacuum for 48 h at 25 °C to yield 3.04 g (89%) of the ketone **1** as red crystals: mp 161–163 °C (lit.[8] mp 162–164 °C); IR (KBr) 3260, 1655, 1620, 1605, 1495 cm^{-1}; NMR ($CDCl_3$) δ 2.9 (t, 2 H, J = 7 Hz), 3.3 (t, 2 H, J = 7 Hz), 7.1 (s, 1 H), 7.3 (t, 1 H, J = 7 Hz), 7.5 (d, 1 H, J = 7 Hz), 7.6 (d, 1 H, J = 7 Hz), 8.5 (br s, 1 H); mass spectrum (methane CI), m/e 172.

6-Methoxy-3,4-dihydrobenz[*cd*]indol-5(1*H*)-one (2). The ketal **20** (4.50 g, 18.4 mmol) was dissolved with warming in acetic acid (9 mL) and water (1 mL). After 5 min at 50 °C, the solution was diluted with water (8 mL) and cooled at 0 °C for 30 min. The product was collected by filtration, washed twice with water, and dried under vacuum for 48 h at 25 °C to yield 3.12 g (84.5%) of **2** as a light yellow powder: mp 165–166 °C, IR (KBr) 3310, 1660, 1618, 1601 cm^{-1}; NMR ($CDCl_3$) δ 2.8 (t, 2 H, J = 6 Hz), 3.1 (t, 2 H, J = 6 Hz), 3.9 (s, 3 H), 6.8 (d, 1 H, J = 9 Hz), 7.0 (s, 1 H), 7.5 (d, 1 H, J = 9 Hz), 8.9 (br s, 1 H); mass spectrum (methane CI), m/e 202.

Anal. Calcd for $C_{12}H_{11}NO_2$: C, 71.63; H, 5.51; N, 6.96. Found: C, 71.42; H, 5.51; N, 7.03.

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Registry No. **1**, 3744-82-9; **2**, 90858-79-0; **11**, 90858-80-3; **12**, 65602-68-8; **13**, 65602-69-9; **15**, 90858-81-4; **16**, 90858-82-5; **17**, 90858-83-6; **18**, 90858-84-7; **19**, 89331-00-0; **20**, 90858-85-8; **24a**, 3770-50-1; **24b**, 4792-58-9; **24c**, 30933-69-8; **25a**, 19005-93-7; **25b**, 21778-81-4; **25c**, 90858-87-0; **26a**, 120-72-9; **26b**, 1006-94-6; **26c**, 90858-86-9; $Rh(dppp)_2Cl$, 53450-82-1; $(PPh_3)_2RhCOCl$, 13938-94-8; 1,3-bis(diphenylphosphino)propane, 6737-42-4.

Synthesis and Structural Study of Azidonaphtho-*as*-triazines: "Annelation Effect" in Azide–Tetrazole Equlibria[1]

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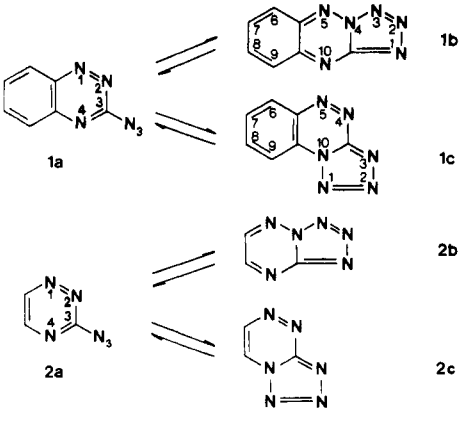
Azide derivatives of the three possible (two angular and one linear) naphtho-as-triazines **7a**, **10a**, and **15a** were prepared and the equilibria leading to fused tetrazoles were investigated by NMR spectroscopy and X-ray analysis. Comparison of the differently annelated systems (topological isomers) revealed an essential "annelation effect": while 3-azidonaphtho[2,1-*c*]-*as*-triazine (**7a**) and 3-azidonaphtho[1,2-*c*]-*as*-triazine (**10a**) formed "*b*-fused" tetrazoles **7b** and **10b**, the linear 3-azidonaphtho[2,3-*e*]-*as*-triazine (**15a**) resulted in the "*c*-fused" tetrazole compound **15c**. For the differences between behavior of the angular and the linear azidonaphthotriazines, a possible interpretation is presented by extension of Clar's principle to heteroaromatic systems.

Earlier we have shown[2,3] that isomerization of 3-azidobenzo-*as*-triazine (**1a**) affords predominantly tetrazolo[5,1-*a*]benzo-*as*-triazine (**1c**), whereas the other possible tetrazole isomer **1b** can only be detected in dipolar aprotic solvents (e.g., in dimethyl sulfoxide) in small amounts.[4] Ring closure of the monocyclic azido-*as*-triazine **2a** as reported later by Paudler et al.[5] proceeds, however, in an essentially different way: tetrazolo[1,5-*b*]-*as*-triazine (**2b**) was found exclusively as product and no trace of [5,1-*c*]-fused isomer **2c** was detected.

As the presence of the additional fused benzene ring in **1** (compared to **2**) caused a dramatic change in direction of the ring closure (i.e., cyclization occurred at N-4 rather than at N-2), the problem of whether "*b*- or "*c*-fused" types predominate in tetrazole systems having one more annelated benzene ring was of interest.

Scheme I



Only one of the three possible azidonaphtho-*as*-triazines (two angular and one linear ring systems) is described in the literature. Vilarrasa et al. reported in their first

(1) Presented in part at the Fifth IUPAC Conference on Physical Organic Chemistry, Santa Cruz, CA, 1980; Abstr pp 115.
(2) Messmer, A., Hajós, Gy., Benkő, P.; Pallos, L. *J. Heterocycl. Chem.* **1973**, *10*, 575.
(3) Messmer, A.; Hajós, Gy.; Tamás, J.; Neszmélyi, A. *J. Org. Chem.* **1979**, *44*, 1823.
(4) Increased participation of **1b** in equilibria for substituted cases was found recently by Castillon, S.; Meléndez, E.; Pascual, C.; Vilarrasa, J. *J. Org. Chem.* **1982**, *47*, 3883.
(5) Goodman, M. M.; Atwood, J. L.; Carlin, R.; Hunter, W.; Paudler, W. W. *J. Org. Chem.* **1976**, *41*, 2860.

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