Tetrahedron Vol. 37, No. 23, pp. 4041 to 4045, 1981
Printed in Great Britain.

0040-4020/81/234041-05$02.00/0
Pergamon Press Ltd.

SYNTHESIS APPLICATIONS OF AZA-COPE REARRANGEMENTS

A STEREOSELECTIVE SYNTHESIS OF 9a-ARYLHYDROLILOLIDINES [AND A NEW APPROACH TO THE SYNTHESIS OF *ASPIDOSPERMA*] ALKALOIDS

LARRY E. OVERMAN* and MICHAEL SWORIN
Department of Chemistry, University of California, Irvine, CA 92717, U.S.A.

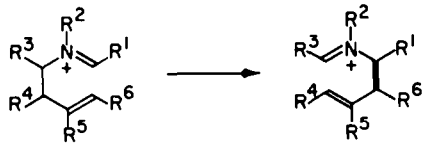
and

LAWRENCE S. BASS and JON CLARDY
Department of Chemistry, Cornell University, Ithaca, NY 14853, U.S.A.

(*Received in USA May* 5 1981)

Abstract—A "Mannich-directed" 2-azonia-[3,3]-sigmatropic rearrangement is the key step in a new, completely stereoselective, method for preparing 9a-arylhydrolilolidines. Specifically, *cis*-fused bicyclic aminoalcohols **24** upon treatment with formaldehyde and acid afford hydrolilolidines **25** in a single step and in excellent yield. The complete stereoselectivity of this "ring-enlarging pyrrolidine annulation" reaction follows stereorationally from the *trans*-relationship of vinyl and amine functions in the bicyclic precursor **24** (eqn 6).

The cationic aza-Cope rearrangement (2-azonia-[3,3]-sigmatropic rearrangement, eqn 1) was first described by Geissman[1,2] in 1950. This reversible C-C bond-forming reorganization occurs under remarkably mild conditions, typically at or near room temperature and, thus, 100–200° below that of the corresponding Cope rearrangements.[1,2] Since, in our view, the major impediment to general use of

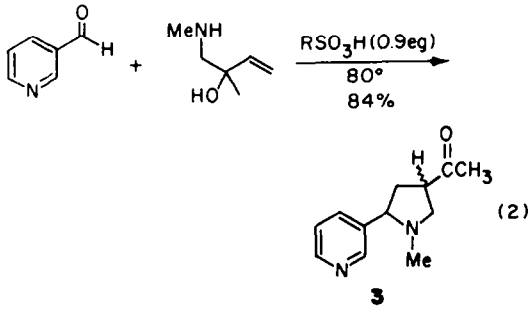


(1)

1 **2**

this reaction in synthesis was its reversibility, recent studies in our laboratory[3–7] have had as their objective the development of general methods for "directing" this rearrangement so that it would be irreversible (**1**→**2**) in the desired direction.

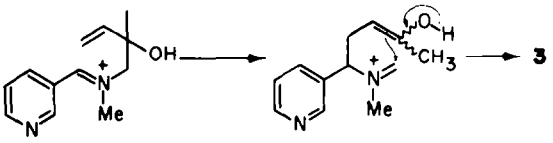
Our original report[3] described the reaction of salts of 2-alkoxy-3-butenamines with a variety of aldehydes to produce 3-acylpyrrolidines in a single step, and in excellent yield (eqn 2). This pyrrolidine synthesis exploited the stability of a properly placed O substituent



(2)

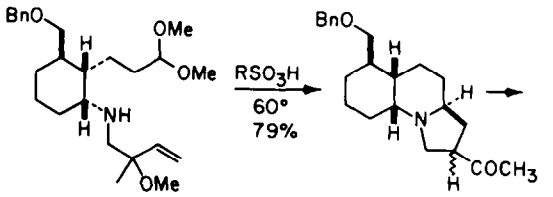
3

to direct the course of the aza-Cope rearrangement by capturing the rearranged sigmatropic isomer in an intramolecular Mannich fashion (eqn 3). When the starting

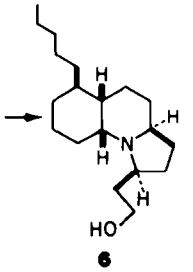


(3)

iminium ion was formed intramolecularly, this reaction was extended to achieve a one-step indolizidine annulation (**4**→**5**), which was the key step in our[5] recent total synthesis of *dl*-perhydrogephyrotoxin (**6**).[8]



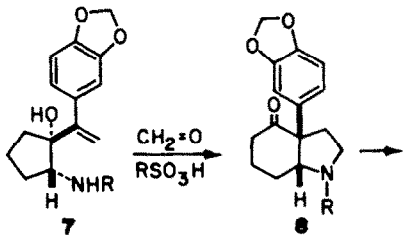
4 **5**



6

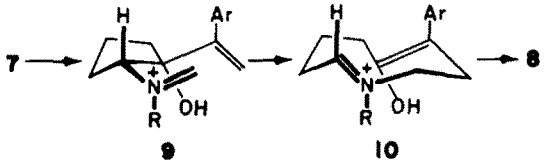
We have also described[7] a different and more unusual annulation sequence for the synthesis of *cis*-3a-aryloc-

tahydroindolones (7→8, R = $CHPh_2$). This reaction provides a stereoselective entry to the widely occurring[9]



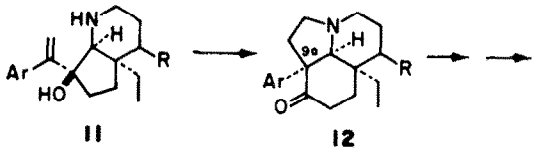
Crinine

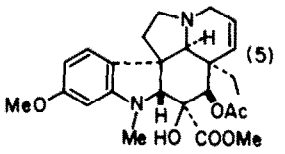
cis-3a-aryloctahydroindole ring system, and was first utilized by us[7] to achieve a formal total synthesis of the *Amaryllidaceae* alkaloid crinine. The formation of specifically the *cis* product from this "ring-enlarging pyrrolidine annulation" sequence follows *stereorationally* from the *trans* orientation of the amine and vinyl groups in precursor **7**. As a result of this *trans* relationship, the iminium ion **9** can undergo pericyclic rearrangement *via* only a single "chair-type" transition-state to generate the *trans,trans*-1,5-azacyclononadiene **10** would yield *cis*-presumed intermediate (eqn 4).[7] Intramolecular Mannich ring closure of azacyclononadiene **10** would yield *cis*-octahydroindolone **8** stereospecifically.



(4)

In this paper we describe a further extension of the "ring-enlarging pyrrolidine annulation" sequence. In particular, we report the use of this reaction for the completely stereoselective assembly of the tricyclic 9a-arylhydrolilolidine[10] ring system **12**. Hydrolilolidines, which incorporate the synthetically demanding quaternary aryl functionality, have not to our knowledge been prepared previously.[11] Hydrolilolidines of this type are key intermediates in a new approach to the *Aspidosperma* alkaloids which is currently under investigation in our laboratory (eqn 5). The results described here document the general feasibility of this synthesis plan, and provide a further illustration of the utility of "directed" cationic aza-Cope rearrangements for the stereoselective synthesis of complex heterocyclic systems.



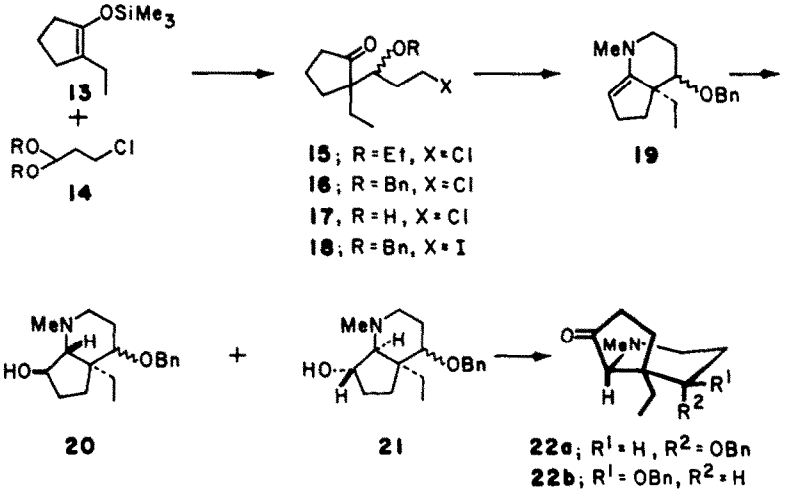


(5)

Aspidosperma Alkaloids
(Vindoline)

RESULTS

Since our primary interest in the *Aspidosperma* area are alkaloids with unsaturation in the D ring, e.g. vindoline, we sought a general approach for preparing the bicyclic intermediate **11** (eqn 5), which either incorporated unsaturation in the piperidine ring of this intermediate or a heteroatom function R. A direct method for assembling systems of this latter type is summarized in Scheme 1. Titanium tetrachloride promoted alkylation[12] of the thermodynamic trimethylsilyl enol ether **13**[13] of 2-ethylcyclopentanone with the diethyl[14] or dibenzyl[15] acetal of 3-chloropropionaldehyde **14** gave cyclopentanones **15** and **16** in 70% and 45% yields, respectively. The yield was somewhat lower with the benzyl acetal, since the debenzylated product **17** was also produced under these conditions. Treatment of **16** with NaI in

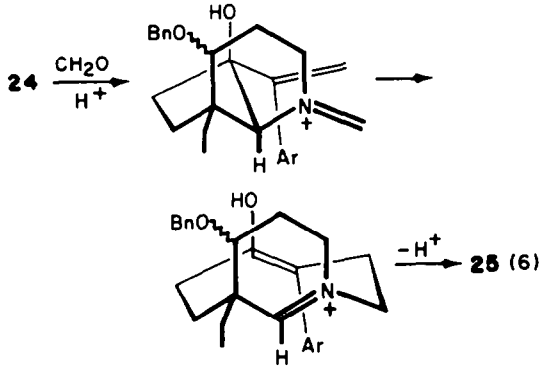


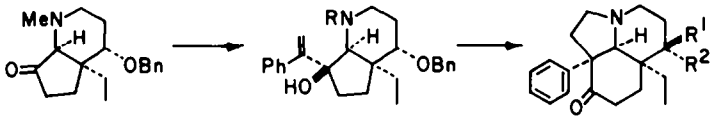
Scheme 1. Bn = CH_2Ph.

refluxing 2-butanone gave iodide **18**, which reacted smoothly with methyl amine in the presence of anhydrous magnesium sulfate to afford the bicyclic enamines **19**. Hydroboration of **19** by the procedure of Borowitz[16] gave a mixture of three of the four possible bicyclic alcohols in 75% yield from **16**. These alcohols were partially separated by chromatography on silica gel and tentatively characterized by their 250 MHz ^{1}H NMR spectra. However, they were more conveniently processed by DMSO-oxalyl chloride oxidation[17] and subsequent epimerization with sodium methoxide in refluxing methanol to give, after chromatographic separation, the two *cis*-bicyclic ketones **22a** (δ 3.36; dd, J = 4.1, 5.9 Hz) and **22b** (δ 3.51; dd, J = 4.4, 8.5 Hz) in yields of 31% and 29% from the alcohol mixture. An examination of molecular models leaves little doubt that the *cis*-fused isomer should be favored at equilibrium[18] for both benzyl diastereomers.

Since one of our objectives was to ascertain what functionality could be tolerated in the piperidine ring during the "ring-enlarging pyrrolidine annulation" reaction, ketones **22a** and **22b** were not merged, but rather independently converted to the hydrolilolidine ring-system. This three step sequence is summarized for the α-benzyloxy series in Scheme 2. Reaction of **22a** with 1-phenylvinyl lithium occurred to give a single alcohol **23a** in 52% yield based on converted ketone. A consideration of molecular models leaves little doubt that the stereoselective addition must have occurred from the less-hindered convex α-face of ketone **22a** (*cf.* the conformational drawing of **22a** in Scheme 1). Phenyl chloroformate demethylation of **23a** gave aminoalcohol **24a** in 55% yield. Pleasingly, when **24a** was heated [7] in refluxing benzene for 4 hr with 2.5 equiv of paraformaldehyde and 0.9 equiv of *d*-10-camphorsulfonic acid, hydrolilolidine **25a** was obtained in 83% *yield* after chromatographic purification. A crystalline sample of **25a**, m.p. 115.5–116.5°, was obtained from pentane and showed characteristic signals in the ^{1}H NMR spectrum for an equatorial benzyloxy methine hydrogen at δ 3.37 (apparent *t*, *J* = 2.6 Hz) and a triplet at δ 0.62 for the Me of the angular Et group. The strongly deshielded position of this Me signal is consistent only with a *cis*-1,3-diaxial orientation of the angular Et and Ph groups (Fig. 1), while the axial orientation of the benzyloxy group can arise only if both ring-fusions are *cis*.[19] The structural assignment for hydrolilolidine **25a** was confirmed by single crystal X-ray diffraction,[20] and a perspective drawing of the crystallographically determined structure is shown in Fig. 1. When an identical sequence of reactions was conducted with ketone **22b**, the β-benzyloxy hydrolilolidine **25b** was formed with similar efficiency.

It is important to stress that the stereoselectivity of this hydrolilolidine synthesis follows directly from the *trans* relationship of the vinyl and amine groups on the cyclopentane ring of precursor **24**. This feature of the rearrangement is illustrated in eq 6.





22a **23a**; R = Me **25a**; R^1 = H, R^2 = OBn
24a; R = H **25b** R^1 = OBn, R^2 = H

Scheme 2. Bn = CH_2Ph.

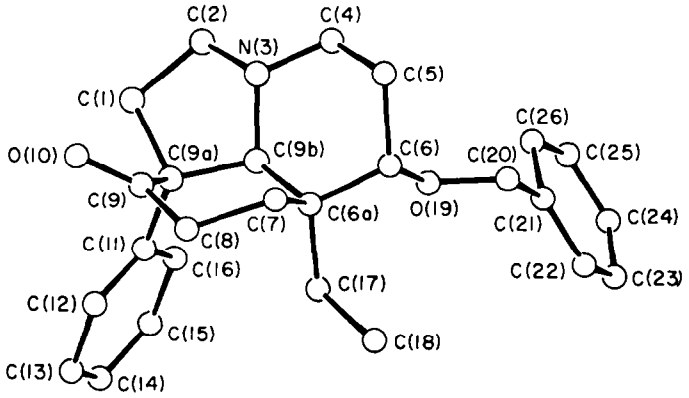


Fig. 1. A computer-generated perspective drawing of the X-ray model of hydrolilolidine **25a**.

CONCLUSION

The synthesis of 9a-arylhydrolilolidines described in this report provides a further illustration of the considerable utility of "directed" cationic aza-Cope rearrangements in organic synthesis. Of particular importance is the demonstration that the rearrangement step occurs under mild conditions *with complete stereoselectivity and in excellent yield.* The preparative sequence described in Schemes 1 and 2 provides a quick entry to 9a-arylhydrolilolidines. The application of this chemistry to total synthesis objectives in the *Aspidosperma* alkaloid area, as well as further synthesis applications of "directed" aza-Cope rearrangements, will be described in future publications from this laboratory.

EXPERIMENTAL[23]

2 - *Ethyl* - 2 - (1 - *benzyloxy* - 3 - *chloropropyl*) *cyclopentanone* (**16**). Titanium tetrachloride (19.1 g, 0.10 mol) was slowly added at −78° to a soln of 29.1 g (0.10 mol) of **14** (R = CH_2Ph; prepared by the general procedure of Reeves[15]) and 500 mL CH_2Cl_2. A soln of 19.3 g (0.105 mol) of **13** (bp 82–83°, 20 mm; prepared from 2-ethylcyclopentanone by the general procedure of Fleming[13]) and 200 mL CH_2Cl_2 was added dropwise at −78° over 1.5 hr, and the reaction was stirred for an additional 3 hr at −78°. The reaction was quenched with 500 mL sat $NaHCO_3$ aq and the aqueous layer was extracted with $CHCl_3$ (3 × 250 mL). The combined organic extracts were washed with sat $NaHCO_3$ aq (500 mL), brine (500 mL), dried ($CaSO_4$), and concentrated. The resulting oil was fractionally distilled to give a low boiling fraction (11.14 g) which was mainly benzyl alcohol. A second fraction (7.40 g) contained **16** plus the debenzylated product **17**: b.p. 94–98° (0.085–0.095 mm). A third fraction (9.28 g) contained pure **16**: b.p. 147–148° (0.06–0.08 mm). The pot residue was distilled (Kugelrohr) to give an additional 2.88 g of **16** and the second fraction was redistilled to give 1.22 g of **16** for a total yield of 13.38 g (45%) of **16** as a viscous yellow oil. Separation of a comparable sample of diastereomers was accomplished by flash chromatography (silica gel, 3:1 hexane–$CHCl_3$) and distillation (Kugelrohr; 145–150°, 0.075 mm) to give the faster moving isomer: ^{1}H NMR δ 7.36–7.23 (m, Ph), 4.50 (AB q, J = 11.0 Hz, Δν = 9.2 Hz, CH_2Ph), 4.02 (dd, J = 9.3, 3.4 Hz, OCH), 3.69–3.63 (m, CH_2Cl), 1.45 (q, J = 7.3 Hz, CH_2CH_3), 0.88 (t, J = 7.4 Hz, CH_3); IR (neat) 1732, 1087, 1068, 747, 732, 693, 655 cm^{-1}; MS (CI) m/e 295 (5), 203 (7), 189 (9), 187 (32), 91 (100); and the slower moving isomer: ^{1}H NMR δ 7.35–7.28 (m, Ph), 4.68 (s, CH_2Ph), 3.80 (dd, J = 9.5, 2.5 Hz, OCH), 3.70–3.55 (m, CH_2Cl), 1.60 (dq, J = 7.3, 1.5 Hz, CH_2CH_3), 0.88 (t, J = 7.4 Hz, CH_3); IR (neat) 1731, 1082, 1067, 732, 692, 649 cm^{-1}; MS (CI) *m/e* 295 (5), 203 (13), 189 (6), 187 (20), 91 (100).

4 - *Benzyloxy* - 4*a* - *ethyl* - 1 - *methyloctahydro* - 1*H* - 1 - *pyrindin* - 7 - *ols* (**20**) *and* (**21**). A soln of **16** (4.42 g, 15 mmol) NaI (3.38 g; 22.5 mmol) and 2-butanone (150 ml) was heated at reflux for 21 hr. After cooling to room temp, the mixture was diluted with 600 mL H_2O and extracted with $CHCl_3$ (3 × 250 mL). The combined organic extracts were washed with 250 mL 5% $Na_2S_2O_3$ aq, dried ($CaSO_4$), and concentrated to give crude **18**: IR (neat) 1729, 1082, 1067, 731, 692 cm^{-1}. A glass Fischer–Porter pressure bottle was charged with this sample of **18**, 8.0 g (67 mmol) of anhyd $MgSO_4$, 20 mL (14 g, 450 mmol) of anhyd methylamine, and 100 mL toluene. The sealed mixture was stirred at room temp for 60 hr, and the excess amine was removed under a stream of Ar. Filtration through Celite in a funnel blanketed with Ar gave crude **19**: IR ($CHCl_3$) 1634, 1082, 1072 cm^{-1}. Hydroboration of this enamine sample was accomplished by a modification of the procedure of Borowitz.[16] A 1 M soln of borane–tetrahydrofuran (35 mL, Aldrich) was added dropwise over 30 min at room temp to a soln of **19** and 20 mL of dry THF. This soln was kept at room temp for 24 hr, and concentrated to give a syrup. The syrup was dissolved in 60 mL 95% EtOH and 1.92 g (48 mmol) NaOH was added, followed by the *cautious* dropwise addition of 5.44 g (1.63 g H_2O_2, 48 mmol) of 30% H_2O_2. The resulting mixture was heated at reflux for 3 hr, diluted with 250 mL brine, extracted with ether (3 × 200 mL), and the combined ether extracts were extracted with 1 N HCL (3 × 100 mL). The combined acidic soln was basified with solid NaOH, extracted with ether (3 × 200 mL), dried ($CaSO_4$), and concentrated to give 3.25 g (75%) of the crude mixture of three alcohols. The three alcohols showed characteristic signals in the 250 MHz ^{1}H NMR spectrum for their benzyloxy methine hydrogens at: δ 3.52 (apparent *t*, *J* = 2.6 Hz); δ 3.40 (dd, J = 4.1 and 7.4 Hz), δ 3.19 (dd, J = 5.2 and 10.2 Hz).

4 - *Benzyloxy* - 4*a* - *ethyl* - 1 - *methyloctahydro* - 7*H* - 1 - *pyrindin* - 7 - *ones* (**22a**) *and* (**22b**). A 2.19 g (7.60 mmol) sample of the crude mixture of **20** and **21** was oxidized according to the procedure of Swern.[17] The resulting crude product was dissolved in 50 mL MeOH, a catalytic amount of NaOMe (~25 mg) was added, the soln was degassed, and heated at reflux for 30 min. The reaction was then diluted with 50 mL brine, extracted with $CHCl_3$ (3 × 50 mL), and the organic extracts were washed with brine and dried ($CaSO_4$). Distillation (Kugelrohr; 150–155°, 0.8 mm) gave 1.70 g (78%) of an ≈1:1 mixture of **22a** and **22b**. Separation by flash chromatography (silica gel, 100:1 $CHCl_3$–MeOH) followed by distillation (Kugelrohr; 145–150°, 0.06 mm) gave 665 mg (31%) of **22a** and 630 mg (29%) of **22b**. Compound **22a**: ^{1}H NMR δ 7.37–7.25 (m, Ph), 4.49 (AB q, J = 11.8 Hz, Δν = 78.5 Hz, CH_2Ph), 3.36 (dd, J = 5.9, 4.1 Hz, OCH), 2.68–2.51 (m, NCH_2), 2.47 (s, NCH), 2.44 (s, NCH_3), 0.87 (t, J = 7.3 Hz, CH_2CH_3); ^{13}C NMR δ 217.0 (s), 138.8 (s), 128.4 (d), 127.5 (d), 74.5 (d), 73.2 (d), 70.7 (t), 48.6 (t), 45.9 (s), 43.0 (q), 32.7 (t), 24.3 (t), 23.6 (t), 23.5 (t), 7.6 (q); IR (neat) 1742, 1093, 733, 693 cm^{-1}; MS (CI) *m/e* 289 (19), 288 (MH^+, 100), 231 (16), 180 (23); high resolution MS (EI) *m/e* 287.189 (287.189 calcd for $C_{18}H_{25}NO_2$). Compound **22b**: ^{1}H NMR δ 7.38–7.24 (m, Ph), 4.52 (AB q, J = 11.8 Hz, Δν = 68.9 Hz, CH_2Ph), 3.51 (dd, J = 8.5, 4.4 Hz, OCH), 2.94 (ddd, J = 11.4, 5.9, 3.7 Hz, C_7-Heq), 2.40 (s, NCH_3), 2.25 (s, NCH), 0.80 (t, J = 7.3 Hz, CH_2CH_3); ^{13}C NMR δ 216.0 (s), 138.8 (s), 128.4 (d), 127.4 (d), 76.3 (d), 73.0 (d), 70.5 (t), 50.9 (t), 45.7 (s), 43.1 (q), 33.6 (t), 28.4 (t), 26.0 (t), 25.5 (t), 8.2 (q); IR (neat) 1744, 1094, 1071, 734, 692 cm^{-1}; MS (CI) *m/e* 289 (19), 288 (MH^+, 100), 231 (14), 180 (10); high resolution MS (EI *m/e* 287.189 (287.189 calcd for $C_{18}H_{25}NO_2$).

4α - *Benzyloxy* - 4a - *ethyl* - 1 - *methyl* - 7 - (1-*phenylethenyl*) *octahydro* - 1H - 1 - *pyrindin* - 7 - *ol* (**23a**). A pentane soln of 1.85 M t-BuLi (6.4 mL, 11.8 mmol, Aldrich) was added dropwise at −78° to a soln of 2.12 g (11.6 mmol) of α-bromostyrene[22] and 50 mL dry THF. The red-violet soln was stirred for 20 min at −78° and then a soln of **22a** (665 mg; 2.31 mmol) and 25 mL THF was added over 45 min. The mixture was stirred at −78° for 1 hr, warmed to 0° for 30 min, and quenched with 15 mL of 1:2 H_2O-THF. The mixture was diluted with brine (250 mL), extracted with ether (3 × 100 mL), and the ether extracted with 1 N HCl (3 × 10 mL). The combined acidic soln was basified with solid NaOH, extracted with $CHCl_3$ (3 × 100 mL), the organic extracts were washed with brine and dried ($CaSO_4$). Concentration and purification of the residue by flash chromatography (silica gel, $CHCl_3$ then 10:1 $CHCl_3$ – MeOH) followed by distillation (Kugelrohr) gave 179 mg (27%) of recovered **22a** and 341 mg (38%) of **23a**: bp 190–200°, 0.015 mm: ^{1}H NMR δ 7.36–7.22 (m, 2PH), 5.63 (d, J = 2.2 Hz, =CHH), 5.00 (d, J = 2.2 Hz, =CHH), 4.47 (AB q, J = 11.4 Hz, Δν = 52.9 Hz, CH_2Ph), 3.64 (dd, J = 8.1, 5.8 Hz, OCH), 2.82–2.67 (m, NCH_2), 2.63 (s, NCH), 2.32 (s, NCH_3), 0.67 (t, J = 7.3 Hz, CH_2CH_3); IR ($CHCl_3$) 3368, 1073, 1026, 918, 689 cm^{-1}; MS (CI) *m/e* 393 (23), 392 (MH^+, 100), 391 (25), 284 (52), 91 (12).

4α - *Benzyloxy* - 4a - *ethyl* - 7 - (1 - *phenylethenyl*) *octahydro* - 1H - 1 - *pyrindin* - 7 - *ol* (**24a**). A soln of **23a** (327 mg; 0.835 mmol) phenyl chloroformate (1.57 g; 10 mmol) powdered $KHCO_3$, (2 g; 20 mmol) and 100 mL $CHCl_3$ was heated at reflux for 38 hr and filtered. After removing excess phenyl chloroformate by distillation (Kugelrohr; 100°, 0.03 mm), the residue was heated at reflux for 42 hr with KOH (30 g; 0.54 mol), 100 mL MeOH, and 5 mL H_2O. The basic product was isolated (following a procedure similar to that described for **23a**) to give 174 mg (55%) of crude **24a**. An analytical sample was prepared by flash chromatography (silica gel, 5:1 $CHCl_3$–MeOH) and distillation (Kugelrohr; 170–175° 0.01 mm): ^{1}H NMR δ 7.36–7.18 (m, 2Ph),

5.48 (d, J = 1.8 Hz, =CHH), 5.01 (d, J = 1.9 Hz, =CHH), 4.51 (AB q, J = 11.4 Hz, $\Delta\nu$ = 41.6 Hz, CH_2Ph), 3.76 (dd, J = 9.9, 7.0 Hz, OCH), 3.05 (s, NCH), 0.66 (t, J = 7.7 Hz, CH_2CH_3); ^{13}C NMR δ 154.3, 141.6, 139.2, 128.9, 128.7, 128.5, 128.1, 127.6, 127.3, 115.1, 83.6, 71.7, 64.9, 47.1, 40.4, 36.1, 32.1, 29.9, 25.8, 23.9, 8.1; IR ($CHCl_3$) 3331, 1093, 1026, 907, 691 cm^{-1}; MS (CI) *m/e* 379 (19), 378 (MH^+, 100), 377 (16), 360 (13), 270 (70), 91 (16); high resolution MS (EI) *m/e* 377.235 (377.235 calcd for $C_{25}H_{31}NO_2$).

(9bα) - 6α - *Benzyloxy* - 6aα - *ethyldecahydro* - 9aα - *phenyl* - 9H - *pyrrolo* [3,2,1 - *ij*] *quinolin* - 9 - *one* (**25a**). A mixture of crude **24a** (151 mg, 0.399 mmol), paraformaldehyde (30 mg; 1.0 mmol) d-10-camphorsulfonic acid (81 mg; 0.35 mmol) and 25 mL benzene was heated at reflux for 4 hr. The mixture was quenched with 5 mL 1 N NaOH and extracted with $CHCl_3$ (2 × 25 mL). The combined organic extracts were washed with brine (25 mL), dried ($CaSO_4$), and concentrated. The residue was purified by flash chromatography (silica gel, $CHCl_3$) to give after distillation (Kugelrohr; 185–190°, 0.04 mm) 129 mg (83%) of **25a** as a chromatographically homogeneous heavy oil. Precipitation of this sample from pentane followed by recrystallization from pentane gave 56.2 mg clear crystals. A second recrystallization from pentane led to smaller cubes which were used for the X-ray analysis; while concentration of the mother liquid (from this crop) gave the analytical sample: m.p. 115.5–116.5°; ^1H NMR δ 7.37–7.12 (m, 2Ph), 4.49 (AB q, J = 11.8 Hz, $\Delta\nu$ = 80.3 Hz, CH_2Ph), 3.37 (t, J = 2.5 Hz, OCH), 3.16 s, NCH), 0.62 (t, J = 7.3 Hz, CH_2CH_3) ^{13}C NMR δ 212.1 (s), 143.4 (s), 139.2 (s), 128.7 (d), 128.5 (d), 127.7 (d), 127.6 (d), 126.7 (d), 126.5 (d), 75.7 (d), 73.2 (d), 71.0 (t), 62.9 (s), 52.0 (t), 47.9 (t), 42.0 (s), 36.9 (t), 35.8 (t), 27.2 (t) 23.7 (t), 23.6 (t), 7.0 (q); IR (KBr) 1700, 1160, 1087, 1070, 1055, 753, 741, 691 cm^{-1}; MS (CI) *m/e* 391 (25), 390 (MH^+, 100), 298 (19), 283 (9). Calc. for $C_{26}H_{31}NO_2$: C, 80.17; H, 8.02; N, 3.60%. (Found: C, 80.40; H, 8.12; N, 3.57).

(9bα) - 6β - *Benzyloxy* - 6aα - *ethyldecahydro* - 9aα - *phenyl* - 9H - *pyrrolo* - [3,2,1 - *ij*] *quinolin* - 9 - *one* (**25b**). Using the procedure described for the preparation of **25a**, an 86% yield of **25b** was obtained: m.p. 99.5–100.5° ^1H NMR δ 7.39–7.13 (m, 2Ph), 4.51 (AB q, J = 11.8 Hz, $\Delta\nu$ = 65.4 Hz, CH_2Ph), 3.46 (dd, J = 11.0, 4.7 Hz, OCH), 2.81 (s, NCH), 0.61 (t, J = 7.3 Hz, CH_2CH_3); ^{13}C NMR δ 212.6 (s), 143.4 (s), 139.1 (s), 128.7 (d), 128.4 (d), 127.5 (d), 127.4 (d), 126.6 (d), 78.8 (d) 74.2 (d), 70.8 (t), 63.3 (s), 52.3 (t), 50.9 (t), 40.8 (s), 37.0 (t), 36.9 (t), 28.4 (t), 25.4 (t), 25.1 (t) 7.9 (q); IR (KBr) 1705, 1180, 1093, 1073, 755, 732, 691 cm^{-1}; MS (CI) *m/e* 391 (26), 390 (MH^+, 100), 283 (18), 282 (17). Calc. for $C_{26}H_{31}NO_2$: C, 80.17; H, 8.02; N, 3.60%. (Found: C, 80.24; H, 8.06; N, 3.55).

Acknowledgement—Support from the National Institutes of Health (NS-12389) and the Cammille and Henry Dreyfus Foundation (teacher-scholar award to L.E.O.) is gratefully acknowledged. NMR and mass spectra were determined with spectrometers purchased with the assistance of NSF instrumentation grants.

REFERENCES

[1]R. M. Horowitz and T. A. Geissman, *J. Am. Chem. Soc.* **72**, 1518 (1950).

[2]For a recent review see: H. Heimgartner, H. -J. Hansen,; H. Schmid, *Iminium Salts in Organic Chemistry* (Edited by Böhme, H.,; Viehe, H. G.,) Part 2: 655–732. Wiley New York (1979).

[3]L. E. Overman and M. Kakimoto, *J. Am. Chem. Soc.* **101**, 1310 (1979).

[4]L. E. Overman, M. Kakimoto and M. Okawara, *Tetrahedron Letters* 4041 (1979).

[5]L. E. Overman and C. Fukaya, *J. Am. Chem. Soc.* **102**, 1454 (1980).

[6]L. E. Overman and T. Yokomatsu, *J. Org. Chem.* **45**, 5229 (1980).

[7]L. O. Overman and L. T. Mendelson, *J. Am. Chem. Soc.* in press.

[8]For a total synthesis of dl-gephyrotoxin see: R. Fujimoto, Y. Kishi and J. F. Blount, *Ibid.* **102**, 7154 (1980).

[9]*Cf* D. R. Dalton, *The Alkaloids. The Fundamental Chemistry* Marcel Dekker, New York (1979).

[10]This ring system is often called (incorrectly) hydrolulolidine in the literature.[11] Hydrolilolidine **12** (R = H) would be correctly named 9a α - *aryl* - 6a α - ethyl - 1,2,4,5,6,6a,7,8,9a,9b α - decahydro - 9H - pyrrolo [3,2,1 - ij] quinolin - 9 - one.

[11]Hydrolilolidines with 9a-hydrogen substituents were intermediates in the original Stork and Ban syntheses of the *Aspidosperma skeleton*: see K. Nakanishi, T. Goto, S. Ito, S. Natori, and S. Nozoe, *Natural Products Chemistry* Vol 2 pp 400–405. Academic Press, New York (1975); Other syntheses of hydrolilolidines with 9a-hydrogen substituents include: M. E. Kuehne and C. Bayha, *Tetrahedron Letter* 1311 (1966); R. V. Stevens, J. M. Fitzpatrick, M. Kaplan,; R. L. Zimmerman, *J. Chem. Soc.* Chem. Commun. 857 (1971) S. F. Martin, S. R. Desai, G. W. Philips, A. C. Miller, *J. Am. Chem. Soc.* **102**, 3294 (1980).

[12]Cf. T. Muhaiyama, H. Ishihara, K. Inomata, *Chem. Lett.* 527 (1975).

[13]Cf. I. Fleming and I. Paterson, *Synthesis* 736 (1979).

[14]*Commercially available from Aldrich.*

[15]Prepared from acrolein and benzylalcohol by the general procedure of Reeves: H. G. Reeves, *J. Chem. Soc.* 2477 (1927).

[16]I. J. Borowitz and G. J. Williams, *J. Org. Chem.* **32**, 4157 (1967).

[17]A. J. Mancuso, S. -L. Huang, and D. Swern, *Ibid.* **43**, 2480 (1978).

[18]The 250 MHz ^1H NMR spectrum showed clearly that the less stable *trans*-fused ketone was initially formed from Swern oxidation[17] of **20**.

[19]This conclusion assumes that the starting *cis*-relationship of the benzyloxy and ethyl groups is unaffected by the rearrangement.

[20](a) Crystal data: $P2_1/c$; a = 8.464 (1), b = 27.001 (5), c = 9.901 (1) Å, and β = 74.56 (1)°, $P_c \cong 1.22$ g/cc with z = 4 and $C_{27}H_{31}NO_2$. All diffraction maxima with $2\theta \leq 100°$ (CuKα, graphite monochromated) were recorded and 2142 (85%) of the 2513 were judged observed. Current residual is 0.063 for the observed data. (b) The library of programs used is described in *J. Am. Chem. Soc.* **103**, 1243–4 (1981). (c) Crystallographic Data have been deposited with the Cambridge Crystallographic data Centre, Lensfield Rd., Cambridge CB2 1EW.

[21]M.p.'s were determined on a Thomas Hoover apparatus and are uncorrected. ^1H NMR spectra were obtained on a Bruker WM-250 spectrometer; ^{13}C NMR spectra were obtained on a Bruker WM-250 or WH-90 spectrometer. All NMR spectra were obtained in $CDCl_3$. IR spectra were recorded on a Perkin-Elmer Model 283 spectrometer. Low resolution mass spectra (MS) were determined on a Finnigan Model 4000 GC/MS/DS by either EI (70 eV) or CI (isobutane, 100 eV) modes and are reported with their relative intensities ($\geq$ 10%). High resolution mass spectra were obtained with a Kratos MS-50 at the Midwest Center for Mass spectroscopy, University of Nebraska. Elemental analyses were performed by Galbraith Laboratories, Inc., Knoxville, TN. All reactions were conducted under an Ar atmosphere.

[22]M. S. Newman, B. Dhawan, M.M. Hashem, V. K. Khanna and J. M. Springer, *J. Org. Chem.* **41**, 3925. (1976).