A New Entry into the Synthesis of the Nine-Membered Indole Alkaloids Related to Cleavamine. A Stereospecific Synthesis of (dl)-4α-Dihydrocleavamine and (dl)-Quebrachamine via the Thio-Claisen Rearrangement

Sir:

We wish to report a new synthesis of the nine-membered indole alkaloids related to cleavamine (8, 3,4-didehydro)[1] by employing the thio-Claisen rearrangement[2] and the stereospecific hydroboration in the key steps.

Tetracyclic thiolactam 1 (X = S),[3] prepared from lactam 1 (X = O)[4] by standard method,[5] was treated with 2-bromomethylbut-1-ene[6](EtOH, room temperature, 48 h) to give the salt 2 (R$_1$ = H, R$_2$ = Et), which on exposure to 3 mol equiv of potassium *tert*-butoxide (THF, room temperature, 3 h) underwent the Claisen rearrangement to afford 4 in 81.8% yield as a mixture of two diastereomers (1:1) through a ketene thioamino acetal (3). This mixture was separated by a preparative TLC on silica gel plates to give C-5α-ethylallyl isomer 4a (mp 190 °C dec; ν_{max}^{Nujol} 3370, 1640, 895 cm^{-1}; δ^{CDCl_3} 7.83 (1 H, br s), 5.36 (1 H, d, t, J = 12 and 4 Hz), 5.03 (1 H, br t, J = 9 Hz), 4.77, 4.67 (each, 1 H, s), 1.03 (3 H, t, J = 7 Hz)) and C-5β-ethylallyl isomer 4b (mp 188 °C dec; ν_{max}^{Nujol} 3170, 1640, 890 cm^{-1}; δ^{CDCl_3} 7.83 (1 H, br s), 5.30 (1 H, d, t, J = 10 and 4 Hz), 5.17 (1 H, t, J = 8 Hz), 4.89, 4.79 (each, 1 H, s), 1.07 (3 H, t, J = 8 Hz)). Hydroboration, followed by alkaline oxidation ((1) excess B$_2$H$_6$ in THF, room temperature 18 h, (2) H$_2$O$_2$-NaOH) of each isomer (4a and b) afforded a single identical alcohol (5 (or 6),[7] amorphous), respectively, which on desulfurization (Raney Nickel (W-2), EtOH, reflux, 30 min) gave the known amino alcohol[7,8] 5 (X = H$_2$ (or 6 (X = H$_2$));[7] ν_{mx}^{Nujol} 3380, 3175 cm^{-1}; δ^{CDCl_3} 9.3 (1 H, s, disappears with D$_2$O), 4.9 (1 H, br s, disappears with D$_2$O), 4.43 (1 H, m), 3.44 (2 H, br s), 0.82 (3 H, t, J = 6 Hz)). When the hydroboration of 4 (a and b, respectively) was carried out under more forcing condition (THF, reflux temperature) a concomitant reductive desulfurization occurred to form 5 (X = H$_2$) (or 6 (X = H$_2$)) after the oxidation with alkaline hydrogen peroxide. For the preparative purpose, therefore, the diastereomeric mixture 4 was directly treated with hot diborane solution (THF, reflux 6 h), followed by alkaline hydrogen peroxide, affording 5 (X = H$_2$) (or 6 (X = H$_2$)) exclusively in 47% yield. The structure was confirmed by converting 5 (X = H$_2$) (or 6 (X = H$_2$)) into 4α-dihydrocleavamine (8)[9] in 24.6% total yield through the quaternary salt 7 by a three-step sequence ((1) MesCl-Et$_3$N, 0 °C; (2) refluxed in CHCl$_3$; (3) Na-liquid NH$_3$) developed by Kutney and co-workers.[8]

Rather surprising stereochemical behavior encountered in the hydroboration reaction was also observed when allylthiolactam 10 (in the forms of the pure stereoisomer[10] as well as a diastereomeric mixture), prepared from 1 (R = S) through 9 ((1) allyl bromide; (2) *t*-BuOK in THF, room temperature), was subjected under the same condition above ((1) excess B$_2$H$_6$ in THF, room temperature, 18 h; (2) H$_2$O$_2$-NaOH) to give the single alcohol[7] 11 ((X = S) (or 12 (X = S)),[7] amorphous), which led to the corresponding amino alcohol 11 (X = H$_2$) (or 12 (X = H$_2$)) (amorphous, ν_{max}^{neat} 3350, 3200 cm^{-1}; δ^{CDCl_3} 8.86 (1 H, disappears with D$_2$O), 4.33 (1 H, br t), 4.13 (1 H, disappears with D$_2$O), 3.53 (2 H, t)) by the desulfurization.

On the contrary, an epimerization was observed when each stereoisomer of 15,[11] which was prepared from 13 (R = Et, X = S) and allyl bromide *via* the salt 14 in 82.4% overall yield, was treated under the hydroboration-oxidation condition ((1) excess B$_2$H$_6$ in THF, room temperature, 18 h; (2) H$_2$O$_2$-NaOH), giving rise to a diastereomeric mixture of the primary alcohols 16 (X = S) and 17 (X = S), respectively, which on desulfurization (Raney Ni(W-2), EtOH, reflux, 30 min),
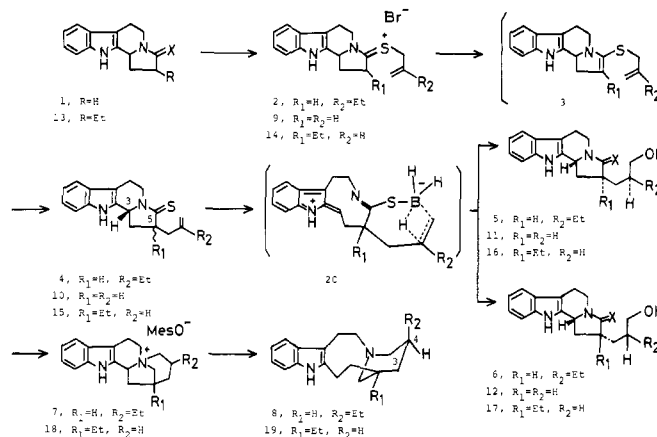
followed by a TLC separation (silica gel) afforded the known amino alcohols 16 (X = H$_2$; mp 169–171 °C (lit.[8] 169–170 °C); ν_{max}^{Nujol} 3380, 3200 cm^{-1}; δ^{CDCl_3} 7.83 (1 H), 4.27 (1 H, br t), 3.67 (2 H br), 0.68 (3 H, t, J = 6 Hz)) and 17 (X = H$_2$; mp 166–168 °C (lit.[8] 166–167 °C); ν_{max}^{Nujol} 3370, 3200 cm^{-1}; δ^{CDCl_3} 7.73 (1 H, disappears with D$_2$O), 4.23 (1 H, br t), 3.56 (2 H, t, J = 5 Hz), 0.92 (3 H, t, J = 8 Hz)). Conversion of both isomers 16 (X = H$_2$) and 17 (X = H$_2$) into dl-quebrachamine (19) through the known quaternary salts 18 was accomplished by the established method.[8,12] For the preparative purpose, the hydroboration of the diastereomeric mixture 15 was carried out under the forcing condition ((1) excess B$_2$H$_6$ in THF, reflux, 6 h; (2) H$_2$O$_2$-NaOH) promoting concomitant reductive desulfurization to give a diastereomeric mixture of amino alcohols 16 (X = H$_2$) and 17 (X = H$_2$), which without separation was converted into dl-quebrachamine (19) through a three-step reaction[8,12] in 18% total yield.

Stereochemical behavior observed during the hydroboration reaction could be rationalized by assuming the nine-membered intermediate 20 induced by the strong borane–sulfur interaction. Recyclization of 20 derived from 4, which carried only one substituent on C-5 carbon atom, would take place to form the thermodynamically most stable isomer 5 (X = S) (or 6 (X = S)) predominantly (similarly 10 afforded only 11 (X = S) (or 12 (X = S)),[7] while in the nine-membered intermediate 20 derived from 15, which carried two substituents of almost the same size on C-5 carbon atom, such a stereospecific recyclization could not take place any more and the epimerization resulted. In the intermediate 20 derived from 4, the strong borane–sulfur interaction could control not only the recyclization, but also the stereochemistry of internal hydroboration to give only one of four possible racemates.

This work allows the simple synthesis of the nine-membered indole alkaloids related to cleavamine and quebrachamine.

References and Notes

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(9) Identical with the authentic material prepared by degradation of cathar-

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(10) Separated by preparative TLC (silica gel); isomer A[7] (oil, ν_{max}^{neat} 3370, 3230, 1634, 910 cm^{-1}, δ^{CDCl_3} 8.3 (1 H, br s), 6.05–5.55 (1 H, m), 5.5–4.95 (4 H, m)) and isomer B[7] (oil, ν_{max}^{neat} 3360, 3230, 1634, 910 cm^{-1}, δ^{CDCl_3} 8.1 (1 H, br s), 6.05–5.50 (1 H, m), 5.5–4.8 (4 H, m)).

(11) Preparative TLC (silica gel) separation furnished α-ethyl isomer (mp 157–158 °C; ν_{max}^{Nujol} 3300, 1638, 908 cm^{-1}; δ^{CDCl_3} 7.9 (1 H), 6.03–5.6 (1 H, m), 5.5–4.98 (3 H, m), 0.72 (3 H, t, J = 7 Hz)) and β-ethyl isomer (oil, ν_{max}^{neat} 3250, 1636, 910 cm^{-1}; δ^{CDCl_3} 8.1 (1 H), 5.83–4.8 (3 H, m), 0.97 (3 H, t, J = 7 Hz)).

(12) S. Takano, S. Hatakeyama, and K. Ogasawara, *J. Am. Chem. Soc.*, **98**, 3022 (1976).

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The Ferraborane B₅H₉Fe(CO)₃ and Its Conjugate Base B₅H₈Fe(CO)₃⁻

Sir:

We have isolated an unstable ferraborane, $B_5H_9Fe(CO)_3$, which appears to be the precursor of $B_4H_8Fe(CO)_3$.[1] The reaction of B_5H_9 with $Fe(CO)_5$ in a hot–cold reactor maintained at 220 °C/20 °C for ca. 3 days with frequent removal of evolved CO yielded $B_5H_9Fe(CO)_3$, which was separated from other products by low-temperature fractionation. This compound is a red liquid and is sensitive to both light and heat. Its mass spectrum exhibited a high mass cutoff at m/e = 204 with fragment ions corresponding to the successive loss of three CO molecules. Relative intensity distributions of the parent ion cluster and those fragments due to loss of CO were characteristic of a compound containing five boron atoms (obsd 87:100:59:21; calcd 80:100:49:12).[2] Precise mass measurements on the m/e 204 ion yielded a composition of $^{11}B_5{}^1H_9{}^{-}$ $^{12}C_3{}^{16}O_3{}^{56}Fe$ (obsd 204.036 ± 0.002 amu; calcd 204.037 amu).

Structural information from ^{11}B and ^1H NMR spectra are consistent with a pyramidal structure which contains an $Fe(CO)_3$ group at a basal vertex (Figure 1). For reasons given below, the hydrogen which is bound to Fe is not clearly a bridging hydrogen. Boron-11 NMR spectra in CH_2Cl_2 at ambient temperature are indicative of C_s symmetry, showing two basal doublets of intensity ratio 2:2 at −46.1 ppm (J, 150 Hz) and −8.6 ppm (J, 150 Hz), compared to an apical resonance of intensity 1 at 47.2 ppm (J, 140 Hz) relative to BF_3OEt_2 at 0 ppm. Severe broadening of these resonances occurred at lower temperatures. The most striking feature of ^1H NMR spectra is the presence of a temperature invarient resonance over the range studied (30 to −100 °C), which appeared as a single broad peak at τ 26.82 (Me₄Si τ 10.00). This resonance can only be due to a proton which is bound to Fe.[3] Boron-11 spin-decoupling causes this resonance to sharpen. While these results suggest a possible static Fe–H–B bridging system[4] on the NMR time scale, the proton NMR spectra of the remaining basal protons and ^{13}C NMR are clearly consistent with a fluxional system. At −35 °C a single averaged resonance for protons bridging boron atoms (τ 9.90) and two averaged resonances representing the two sets of terminal basal protons are observed (τ 3.60, 5.81). Below −70 °C the bridge resonance splits into three peaks of equal intensity (τ 9.18, 9.92, 10.72) and each basal terminal resonance splits into two resonances of equal intensity (τ 3.16, 4.03, 5.48, 6.14). The apical resonance is temperature independent (τ 11.19). The ^{13}C NMR spectrum reveals a single resonance at −30 °C (207.9 ppm downfield of Me₄Si) which splits into three resonances of equal intensity below −120 °C (210.5, 207.7, 206.6 ppm).
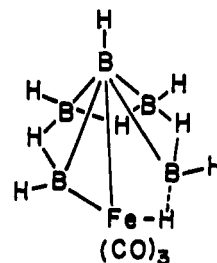

**Figure 1.** Proposed structure of $Fe(CO)_3B_5H_9$.

The fluxionality is believed to arise from movement of the H on iron between the two possible bridging sites either through rotation or pseudorotation of the $Fe(CO)_3H$ group. If the H on Fe is involved in three-center bonding with boron, the breaking of this bond occurs as Fe–HB rather than the commonly observed M H–B in other fluxional metalloboranes.[5] Thus hydrogen on iron might be termed a "pseudo" terminal hydrogen, since it appears always to be associated with Fe throughout the fluxional process.

The following deprotonation reaction was observed.[6]

$$B_5H_9Fe(CO)_3 + KH \xrightarrow[-78\ °C]{(CH_3)_2O} K^+ B_5H_8Fe(CO)_3{}^- + H_2$$
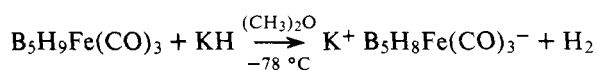
Boron-11 and proton NMR spectra of $KB_5H_8Fe(CO)_3$ in $(CD_3)_2O$ are very similar to the spectra of $B_5H_9Fe(CO)_3$ with respect to appearance and temperature dependence except that the low temperature (−140 °C) ^1H NMR spectrum of $B_5H_8Fe(CO)_3{}^-$ reveals only two bridge resonances (1:1 relative areas), rather than the three bridge resonances observed in the ^1H NMR spectrum of $B_5H_9Fe(CO)_3$. This indicates that a B–H–B bridging proton has been removed in the deprotonation process. Furthermore, a temperature-independent resonance at τ 26.0 indicates that an H associated with Fe exists in the anion as well as in the neutral molecule. Boron-11 spin decoupling causes this resonance to sharpen.

From the following metathesis reaction, crystals of $N(n-C_4H_9)_4{}^+B_5H_8Fe(CO)_3{}^-$ were obtained.

$$K^+\ B_5H_8Fe(CO)_3{}^- + N(n-C_4H_9)_4{}^+\ Br^-$$

$$\xrightarrow[-23\ °C]{CH_2Cl_2} N(n-C_4H_9)_4{}^+\ B_5H_8Fe(CO)_3{}^- + KBr$$
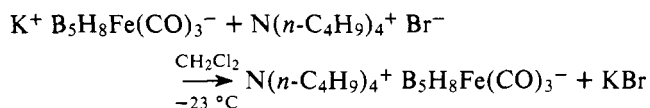
The crystals are monoclinic (space group $P2_1/b$): a = 11.108 (6), b = 15.462 (12), c = 15.443 (9) Å, γ = 95.87 (5)°. Assuming Z = 4, d calcd = 1.10 g/cm³. Of the 3893 independent reflections measured 1557 had $I \geq 3\sigma(I)$ and were considered observed. Patterson and Fourier[8] techniques gave the positions of the nonhydrogen atoms. Methylene hydrogen atoms of the cation were placed at their calculated positions and the weighting scheme of Clayton, Mangion, and Meyers[8] was employed to obtain a weighted difference electron density synthesis from which approximate coordinates of hydrogens on the anion were obtained. Due to the limited number of observed reflections the hydrogens were not refined and anisotropic refinement of heavier atoms was not attempted. Full matrix least-squares refinement converged with a conventional R of 0.080 and a weighted R of 0.092.[7]

The structure of $B_5H_8Fe(CO)_3{}^-$ is given in Figure 2. This structure is like the proposed structure of $B_5H_9Fe(CO)_3$ except that the bridging H between B3 and B4 is absent. The three Fe–B distances are B1–Fe = 2.16 (1), B3–Fe = 2.08 (2), and B6–Fe = 2.13 (2) Å. These distances appear shorter than the B–Fe distances of 2.22 (1) and 2.20 (1) Å for iron in a bridging position in μ-Fe(CO)_4-B_7H_{12}{}^-$.[9] The angle B3–Fe–B6 = 83.5 (6)° is much wider than is observed for Fe in a bridging position, B–Fe–B = 47.4 (3)°, in μ-Fe(CO)_4-B_7H_{12}{}^-$.[9] Within the boron framework the distances appear normal.[10] The position