Diazepines II. A New Synthesis of 4*H*-Pyrrolo[1,2-*a*]-[1,4]benzodiazepine (1)

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A convenient synthesis of a 4*H*-pyrrolo[1,2-*a*][1,4]benzodiazepine is described. 2,5-Dimethoxy-2-methyl-5-phthalimidomethyltetrahydrofuran (**3**) was prepared starting from 2-methyl-5-phthalimidomethylfuran (**1**). The condensation of 2-amino-5-chlorobenzophenone with **3** to give 5-chloro-2-(2-methyl-5-phthalimidomethylpyrrol-1-yl)benzophenone (**4**), the treatment of which with hydrazine hydrate afforded 8-chloro-1-methyl-4*H*-pyrrolo[1,2-*a*][1,4]benzodiazepine (**5**).

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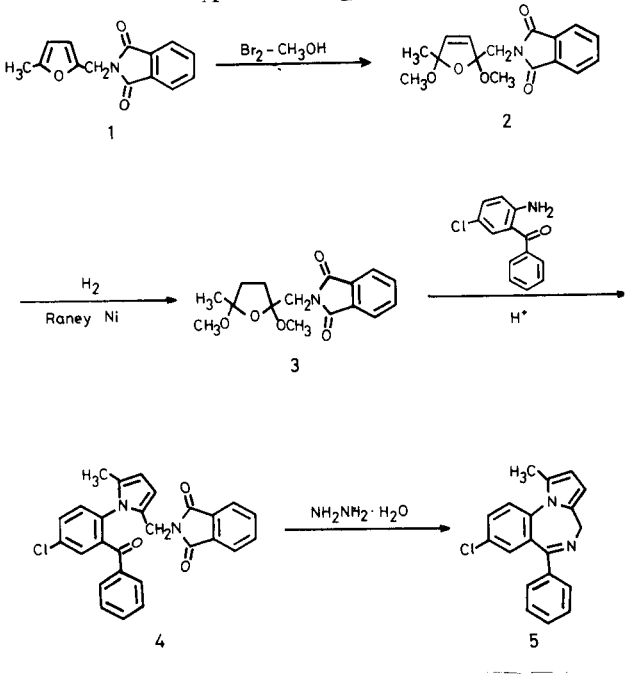
Sir:

Although there is considerable work (3,4) in recent years for the synthesis of tricyclic diazepine compounds having anxiolytic activity, but a single synthesis of the heterocyclic system, 4*H*-pyrrolo[1,2-*a*][1,4]benzodiazepine has thus far been reported (5). We now wish to report the efficient synthesis of 8-chloro-1-methyl-6-phenyl-4*H*-pyrrolo[1,2-*a*][1,4]benzodiazepine.

Treatment of 2-methyl-5-phthalimidomethylfuran (**1**) with bromine in a mixture of methylene chloride and absolute methanol at -40~-50° followed by introduction of gaseous ammonia (6) gave the dihydrofuran **2** in 96% yield. The nmr spectrum (7) of **2** showed that it was an approximately equimolar mixture of *trans* and *cis* isomers, which could be separated by fractional recrystallization from ether-*n*-hexane. The physical, analytical and spectral data for each of the isomers are as follows: m.p. 119.5-120.5°. *Anal.* Calcd. for $C_{16}H_{17}NO_5$: C, 63.36; H, 5.65; N, 4.62. Found: C, 63.63; H, 5.53; N, 4.83; nmr 1.51 (3H, s, 1-CH_3), 3.08 (3H, s, OCH_3), 3.19 (3H, s, OCH_3), ν_A 4.01 and ν_B 3.96 (2H, AB system, J = 14.0 Hz, CH_2N), 5.86 (2H, s, CH=CH), 7.55~7.88 (4H, m, C_6H_4); m.p. 89.5-91.0°; nmr: 1.27 (3H, s, 1-CH_3), 3.29 (3H, s, OCH_3), 3.33 (3H, s, OCH_3), 3.97 (2H, s, CH_2N), 5.89 (2H, s, CH=CH), 7.59~7.93 (4H, m, C_6H_4).

Catalytic hydrogenation of **2** with the higher melting point using Raney nickel in ethanol afforded the tetrahydrofuran **3** in 96% yield (8) [m.p. 113.4-114.5° (recrystallized from ether-*n*-hexane). *Anal.* Calcd. for $C_{16}H_{19}NO_5$: C, 62.94; H, 6.27; N, 4.59. Found: C, 62.88; H, 6.29; N, 4.74; nmr: δ 1.47 (3H, s, 1-CH_3, 1.77~2.56 (4H, m, CH_2CH_2), 3.16 (3H, s, OCH_3), 3.33 (3H, s, OCH_3), ν_A 4.06 and ν_B 3.84 (2H, AB system, J = 14.0 Hz, CH_2N), 7.60~7.91 (4H, m, C_6H_4).

Condensation of 2-amino-5-chlorobenzophenone with **3** in benzene with *p*-toluenesulfonic acid as catalyst gave the pyrrolylbenzophenone **4** in 87% yield [m.p. 148.5-149.5° (recrystallized from ether-*n*-hexane). *Anal.* Calcd. for $C_{27}H_{19}ClN_2O_3$: C, 71.29; H, 4.21; N, 6.16. Found: C, 71.27; H, 3.97; N, 6.18; nmr: δ 1.89 (3H, s, CH_3), ν_A 4.57 and ν_B 4.39 (2H, AB system, J = 15.0 Hz, CH_2N), ν_A 6.03 and ν_B 5.69 (2H, AB system, J =



benzene rings)].

Removal of the phthaloyl group from **4** and ring closure to 8-chloro-1-methyl-6-phenyl-4*H*-pyrrolo[1,2-*a*][1,4]benzodiazepine (**5**) was effected by heating at reflux a solution of **4** in ethanol with hydrazine hydrate (in 67%). Most of the phthalazine generated in the reaction could be removed as solid by filtration from the cooled reaction mixture. Chromatographic isolation followed by recrystallization from ether-*n*-hexane gave **5** as slightly yellow prisms showing m.p. 142.5-143.5°. Infrared absorption was recorded at 1607, 1480, 1444, 1410 and 1299 cm^{-1}. The nmr spectrum had δ 2.33 (3H, s, CH_3), ν_A 4.97 and ν_B 3.95 (2H, AB system, J = 12.5 Hz, CH_2N), 7.02 (2H, m, =CH-CH=), 7.18~7.60 (8H, m, protons on two benzene rings). *Anal.* Calcd. for $C_{19}H_{15}ClN_2$: C, 74.39; H, 4.93; N, 9.13; Cl, 11.56. Found: C, 74.29; H, 4.76; N, 9.06; Cl, 11.55.

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(7) All the nmr spectra were recorded by a JOEL JNM-MH-100 nuclear magnetic resonance spectrometer in deuteriochloroform with tetramethylsilane as an internal standard.

(8) As either *trans* or *cis* isomer of **3** can be equally employed for the present synthesis, the separation of the isomers of **2** is not necessary for the synthetic purpose. A mixture of *trans* and *cis* isomers of **2** was successfully transformed to a mixture of the stereoisomers of **3**, and then to compound **4**.