Department of Chemistry, Louisiana State University in New Orleans

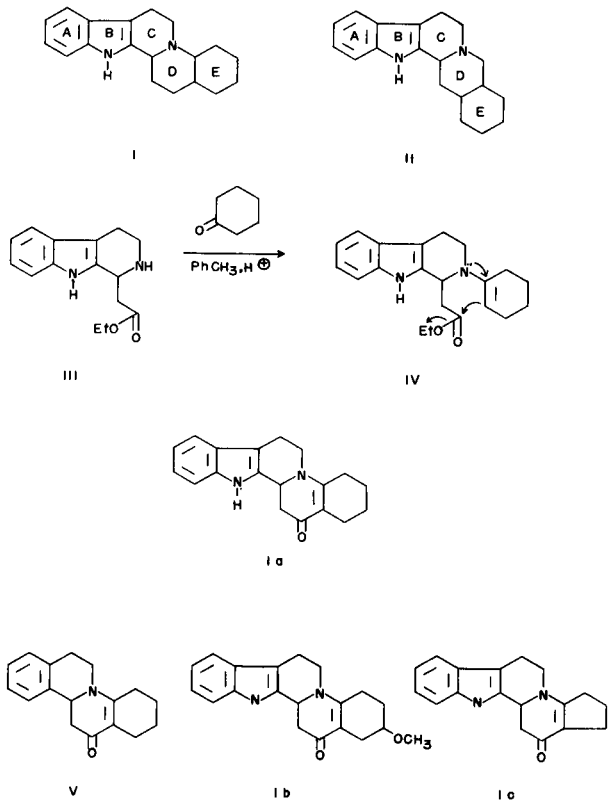
Cycloalkeno[f]indolo[2,3-a]quinolizinones. A New Pentacyclic System Isomeric with Yohimbane (1)

A. I. Meyers and J. C. Sircar

Sir:

We wish to report a facile route to a new pentacyclic ring system (I) which bears an interesting relationship to the well known yohimbane skeleton, (II). The main difference between I and II lies in the fusion point of the E-ring. It is noteworthy that there is a conspicuous absence in the literature of I or any of its derivatives, although one report describes an attempt to prepare this system (2). The synthesis of the first member of this system (Ia) was readily accomplished by treating the carboline derivative, III (3) with cyclohexanone in refluxing toluene containing a trace of trifluoroacetic acid. Instead of obtaining the expected enamine, IV, the pentacyclic system was isolated in 40% yield [m.p. > 300° (EtOH); λ (Nujol), 3.03, 6.18, 6.50 μ; λ (EtOH) (ε) 336 (13,910), 292 (7,271), 282 (8,029), 224 (37,300)]. Also recovered from the reaction was approximately 50% of the starting carboline, III. The NMR spectrum of Ia could not be recorded due to its lack of solubility in the common organic solvents. Nevertheless, the ultraviolet spectrum was in excellent agreement with other compounds (4) containing the enaminoketone chromophore, V [λ max (EtOH) 335 mμ (13,400)]. This reaction represents still another example of intramolecular enamine acylation by an ester function (4). Similar treatment of III with 4-methoxycyclohexanone gave Ib [m.p. > 300° (EtOH), λ (nujol) 3.04, 6.18, 6.43 μ; λ max (EtOH) (ε) 336 (17,150), 292 (8,574), 278 (11,320), 224 (33,160)] whereas the use of cyclopentanone resulted in Ic [m.p. > 300° (EtOH); λ (nujol) 3.04, 6.15, 6.40 μ; λ max (EtOH) (ε) 334 (15,440), 292 (8,341), 280 (8,774), 224 (33,670)]. The insoluble nature of both Ib and Ic also prohibited their NMR spectra from being recorded (5).

This reaction allows for the first time, a route to pentacyclic heterocycles isomeric to the indole alkaloids and this altered skeleton may prove to possess the important biological activity usually absent from the pentacyclic indole alkaloids. We are planning to further investigate the scope and the utility of this reaction in hope of acquiring interesting and new heterocyclic systems.



REFERENCES

(1) This study supported by the National Institutes of Health (GM-06248-06).

(2) Y. Kanaok, *Chem. Pharm. Bull.* (Tokyo), 7, 589 (1959).

(3) G. B. Kline, *J. Am. Chem. Soc.*, 81, 2251 (1959).

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(5) The elemental analyses for the three products described were in total agreement with the calculated values. All three compounds, after recrystallization from ethanol were highly crystalline and colorless to off-white.

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