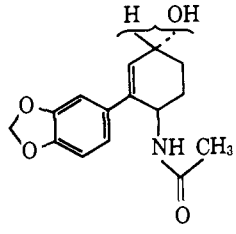
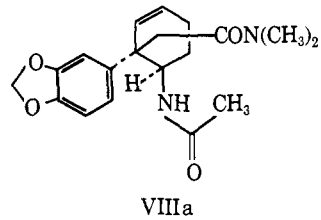
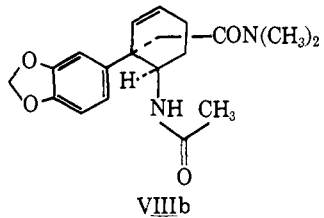
(ε) 322 (14,700) and 220 (11,300)). Treatment of the noncrystalline mixture of VIIIa and b with 10% sodium hydroxide (2-ethoxyethanol–water, 1:4, reflux) gave a 40% yield of a single lactam X (mp 206–207°) as well as some unreacted VIIIb.[11] Catalytic hydrogenation of X gave the dihydro derivative XI (mp 144–145°).



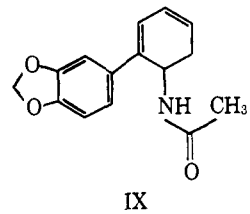
VII



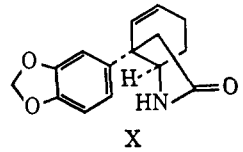
VIIIa



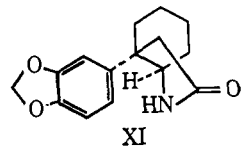
VIIIb



IX



X



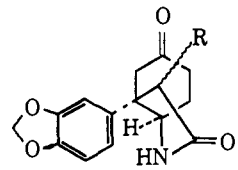
XI

Unambiguous demonstration of the configuration of X was desired. Therefore the amine VIb was prepared by treatment of VIa with Meerwein's reagent[12] followed by hydrolysis of the imino ether hydrofluoroborate in aqueous tetrahydrofuran. Reaction of VIb with carbomethoxyacetyl chloride afforded the amide VIc (mp 90–91°; $\lambda\lambda_{max}^{ethanol}$ mμ (ε) 342 (11,500), 300 (7900), 250 (13,100), and 242 (13,100)). Treatment of VIc with sodium hydride in refluxing tetrahydrofuran led in quantitative yield to XIIa (mp 183–190°; $\lambda\lambda_{max}^{ethanol}$ mμ (ε) 287 (3600) and 237 (3300)), identified by nmr as a 1:1 mixture of the C-11 epimers.[13] Kinetic and thermodynamic factors demand that the ring junction which results from an intramolecular Michael addition of VIc be *cis*. Saponification of XIIa (0.5 *N* methanolic sodium hydroxide) resulted in the quantitative formation of the acid XIIb which was not purified but decarboxylated (lithium iodide in diglyme) to XIIc (mp 179–182°). Reaction of XIIc with 1,2-ethanedithiol gave the thioketal XIII (mp 265–268°) which, upon treatment with Raney nickel (refluxing dioxane), afforded the lactam XI (mp 144–145°). This material was shown to be identical in all respects with the lactam obtained from the catalytic reduction of X. Thus the C,D ring fusion of X is established as *cis*. This was further confirmed by reduction of XI with lithium aluminum hydride followed by Pictet–Spengler cyclization (formalin, hydrochloric acid) to the previously known (±)-crinane (XIV, mp 94–97°, lit.[1a] 97–99°).

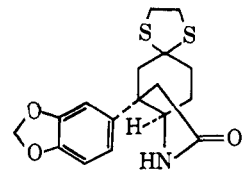
(11) The amide VIIIb (mp 200–201°) isolated from this reaction mixture could not be transformed to a lactam under the conditions mentioned above.

(12) H. Meerwein, G. Hinz, P. Hofmann, E. Kroning, and E. Pfeil, *J. Prakt. Chem.*, [2] **147**, 257 (1937).

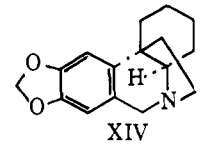
(13) All carbon atoms in the intermediates are numbered in the manner described for I.



XIIa, R = CO_2CH_3
b, R = CO_2H
c, R = H



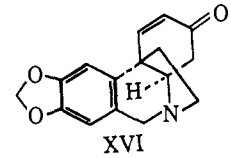
XIII



XIV

With the configuration of X firmly established, the conversion into (±)-crinine was investigated. Reduction of X with lithium aluminum hydride followed by Pictet–Spengler cyclization gave (±)-α-desoxycrinine (XV, mp 76–78°)[14] in 70% yield based on X. Oxidation of XV with selenium dioxide (acetic acid–acetic anhydride, reflux) and saponification of the resulting acetate gave (±)-crinine (I, mp 173–175°) after purification *via* its picrate (mp 203–204°). This material is identical in every respect with (±)-crinine of natural origin prepared by mixing (−)-crinine and (+)-crinine (vittatine).[15]

XV



XVI

Oxidation of I (chromium trioxide–pyridine) afforded (±)-oxocrinine (XVI, mp 172–173°, lit.[1b] 177–178°). Finally, reduction of XVI with sodium borohydride gave (±)-epicrinine (II, mp 235.5–237°, lit.[1b] 239°).

Acknowledgment. The authors are grateful to Professor W. C. Wildman for an authentic sample of (±)-crinine and to the National Science Foundation (Grant No. GP-3696) for generous financial support.

(14) H. M. Fales and W. C. Wildman, *J. Am. Chem. Soc.*, **80**, 4395 (1958). Professor W. C. Wildman has confirmed the identity of XV with a sample of α-desoxycrinine previously known as a degradation product of powelline.

(15) H. G. Boit and H. Ehmke, *Chem. Ber.*, **90**, 369 (1957).

(16) National Institutes of Health Predoctoral Fellow, 1963–1966.

(17) National Aeronautics and Space Administration Trainee, 1964–1966.

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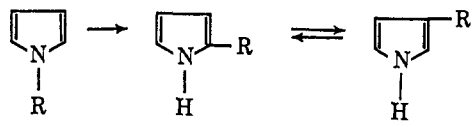
The Stereochemistry of the Thermally Induced Isomerization of N-Substituted Pyrroles

Sir:

Recent kinetic studies on the thermal isomerization of N-alkylpyrroles have indicated that the isomerization is a homogeneous unimolecular process[1] in which the 2

(1) (a) I. A. Jacobson, Jr., H. H. Heady, and G. V. Dinneen, *J. Phys. Chem.*, **62**, 1563 (1958); (b) I. A. Jacobson, Jr., and H. B. Jensen, *ibid.*, **66**, 1245 (1962); (c) I. A. Jacobson, Jr., and H. B. Jensen, *ibid.*, **68**, 3068 (1964).

isomer is irreversibly formed from the N isomer while the 3 isomer is reversibly formed from the 2 isomer. Furthermore, the negative entropies of activation calcu-



lated from the kinetic data have been interpreted as requiring a cyclic activated complex. Similar results were obtained by Pine[2] in the substituted N-benzylpyrrole series. Since all substituents (F, Cl, CH_3O, CH_3 (*para*)) facilitated isomerization and since activation energies were close to the estimated bond dissociation energies, it was concluded[2] that homolytic dissociation had occurred to the extent of about 90% in the transition state.

We wish to report that the isomerization of N-(*sec*-butyl)pyrrole to the 2 isomer occurred with retention of configuration both above and below the isokinetic temperature of 589°;[3] at 575°, 79% retention; and at 600°, 77% retention. The migration of the phenylethyl group in (+)-N-(1-phenylethyl)pyrrole to the 2 position likewise occurred with 72% retention of configuration at 550°. The 3 isomers, 3-*sec*-butylpyrrole (600° experiment) and 3-(1-phenylethyl)pyrrole, were both formed with an estimated 10% retention of configuration.

N-(*sec*-Butyl)pyrrole,[4] bp 156–156.5°, $n^{25}D$ 1.4687, $[\alpha]^{25}D$ +10.2° (neat), synthesized by an adaptation of the method of Elming and Clauson-Kaas[5] from (+)-*sec*-butylamine, $[\alpha]^{25}D$ +2.5° (neat) (31% optical purity),[6] was pyrolyzed at 575 and 600°. At 575°, 23%[7] of 2-(*sec*-butyl)pyrrole, $n^{25}D$ 1.4910, $[\alpha]^{25}D$ +6.38° (neat, 24.4% optical purity) (lit.[8] $n^{25}D$ 1.4900, $[\alpha]^{25}D$ +11.24° (43% optical purity)), and 4% of 3 isomer were obtained. At 600°, 31%[7] of 2-(*sec*-butyl)pyrrole, $n^{25}D$ 1.4910, $[\alpha]^{25}D$ +6.16° (neat, 23.6% optical purity), and 12%[7] of 3 isomer were obtained. After separation, the 3 isomer was 81% pure, $n^{25}D$ 1.5010, $\alpha^{24}D$ +3.92°. Further purification by glpc on an 8 ft × 3/8 in. 30% SE-30 column gave a pure compound, $n^{25}D$ 1.4870, $[\alpha]^{25}D$ +8.0° (*c* 2.87, ethanol) (lit.[8] $n^{25}D$ 1.4878, $[\alpha]^{25}D$ +11.98° (43% optical purity)). The (+)-*sec*-butylpyrrole has been shown to have the same configuration as (+)-*sec*-butyl bromide[8] and the (+)-*sec*-butyl bromide the same configuration as (+)-*sec*-butylamine.[9]

The pyrolysis of (+)-N-(1-phenylethyl)pyrrole, $n^{25}D$ 1.5581, $[\alpha]^{25}D$ +48.15° (neat), synthesized as for the *sec*-butyl compound from (−)-1-phenylethylamine, $n^{25}D$ 1.5235, $[\alpha]^{25}D$ −39.7° (neat, 98% optical purity),[10] produced 39.9%[7] of (+)-2-(1-phenylethyl)pyrrole, bp 138–140° (10 mm), $n^{25}D$ 1.5715, $\alpha^{25}D$ +62.1°, and 10.9%[7] of (+)-3-(1-phenylethyl)pyrrole, bp 153° (10 mm), $n^{25}D$ 1.5729, $\alpha^{25}D$ +9.18°.

The (±)-2- and (±)-3-(1-phenylethyl)pyrroles were synthesized from pyrrylmagnesium bromide and 1-phenylethyl bromide.

The configuration and optical purity of the 2 isomer were established by permanganate oxidation[8] to (+)-hydratropic acid, which in turn was converted into methyl hydratropate and purified by glpc, $n^{25}D$ 1.4993 (authentic sample, $n^{25}D$ 1.5000), $[\alpha]^{25}D$ +79.8° (*c* 4.05, ethanol), 70.5% optical purity. Bonner and Zderic[11] report $[\alpha]^{23}D$ +108.7° (*c* 5.5, ethanol) for ester prepared from 96% optically pure hydratropic acid. It has been shown by Bernstein and Whitmore[12] that (+)-hydratropic acid and (−)-phenylethylamine have the same configuration.

The configurations of 2-(1-phenylethyl)pyrrole and 3-(1-phenylethyl)pyrrole are probably the same since both isomers give very similar optical rotatory dispersion curves.

It is tentatively concluded that migrations involving considerable free radical character can occur with retention of configuration and that a cyclic transition state is involved in which homolytic bond breaking has progressed to a greater extent than bond formation.

Acknowledgment. The authors thank Dr. E. D. Rees and Mrs. H. Ades for the ORD measurements. The research was supported byt he U. S. Army Research Office, Durham.

(2) L. A. Pine, *Dissertation Abstr.*, **24**, 522 (1963).
(3) From ref 1. It is assumed that *sec*-butyl group migration follows the same mechanism as do methyl, *n*-butyl, and isopropyl groups.
(4) All new compounds gave satisfactory elemental analyses and all structural assignments were consistent with nmr and infrared spectra.
(5) N. Elming and N. Clauson-Kaas, *Acta Chem. Scand.*, **6**, 867 (1952).
(6) Based on the rotation $[\alpha]^{25}D$ +8.1° reported by H. E. Smith, S. L. Cook, and M. E. Warren, Jr., *J. Org. Chem.*, **29**, 2265 (1964).
(7) Area per cent obtained from glpc analysis on a 6 ft × 1/8 in. 10% SE-30 column. Separations by glpc on an 8 ft × 3/8 in. 30% Carbowax 20M column.
(8) P. S. Skell and G. P. Bean, *J. Am. Chem. Soc.*, **84**, 4660 (1962).
(9) P. Brewster, F. Hiron, E. D. Hughes, C. K. Ingold, and P. A. D. S. Rao, *Nature*, **166**, 179 (1950).
(10) Based on the rotation $[\alpha]^{15}D$ +40.7° reported by W. Leithe, *Monatsh.*, **51**, 381 (1929).
(11) W. A. Bonner and J. A. Zderic, *J. Am. Chem. Soc.*, **78**, 3218 (1956).
(12) H. I. Bernstein and F. C. Whitmore, *ibid.*, 61, 1324 (1939).

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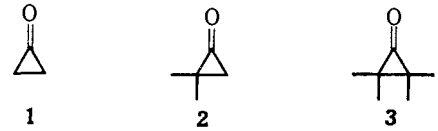
Received May 16, 1966

Cyclopropanone[1]

Sir:

The chemistry of small unsaturated molecules of unusual structure is of considerable interest because of both the theoretical predictions concerning the properties of these compounds and their great potential as intermediates in organic syntheses. We report now a relatively simple, high yield synthesis of such a compound, cyclopropanone (**1**). The preparations and reactions of the alkylated cyclopropanones, **2** and **3**, have been reported recently.[1,2]



1 **2** **3**

Addition of a cold (−78°) methylene chloride (10 ml) solution of diazomethane[3a] (10 mmoles) to a methyl-

(1) Cyclopropanones. IV. See W. B. Hammond and N. J. Turro, *J. Am. Chem. Soc.*, **88**, 2880 (1966), for paper III is this series.
(2) N. J. Turro, W. B. Hammond, and P. A. Leermakers, *ibid.*, **87**, 2774 (1965).
(3) (a) G. L. Closs and J. J. Coyle, *ibid.*, **87**, 4270 (1965), (b) W. E. Hanford and J. C. Sauer, *Org. Reactions*, **3**, 136 (1946).