ture to determine the Brønsted β for the reaction of hydroxide ion with menthone and found $\beta = 0.48$, about as expected for reaction of this ketone in a purely aqueous solvent. Under the plausible assumption that the substrate SH behaves similarly to an H– indicator acid, it can be shown that a Brønsted or Eigen plot for k_{OH^-} can be replaced by a plot of this rate coefficient *vs.* the function H– + og ($[H_2O]/[OH^-]$). This procedure can give general evidence on the behavior of hydroxide ion as a base. More importantly, it permits determination of the Brønsted β in cases where "unobservable" general catalysis is suspected. In the rate studies done here, the two substrates were allowed to react with hydroxide ion at concentrations of from 0.001 to 0.05 *M* utilizing mixed solvents with mole per cent DMSO ranging from 0 to 25%. H– values were taken from Bowden.[10] The resulting Brønsted coefficient for chloroform is 1.0 within experimental error, whereas that for the 1,4-dicyanobutene is 0.7. This information, combined with the previous data, permits two conclusions. First, for the cyanocarbon acid, the degree of proton transfer to hydroxide ion is only partial, in contrast to the situation with bases like morpholine and phenolate ion, where it is virtually complete. With chloroform, the proton transfer to hydroxide is complete and this, with the other evidence, strongly indicates that this is a case of unobservable general base catalysis, *i.e.*, chloroform is behaving fully normally as an acid in the Eigen sense.

(10) K. Bowden, *Chem. Rev.*, **66**, 119 (1966).

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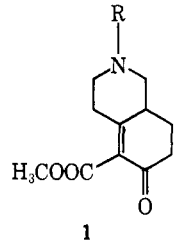
Stereoselective Total Syntheses of (±)-Yohimbine, (±)-ψ-Yohimbine, and (±)-β-Yohimbine

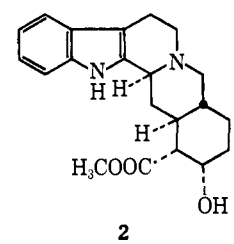
Sir:

We have for some time considered that hydroisoquinolone carboxylic acids related to **1** might make possible unusually simple syntheses of some of the yohimbe alkaloids. It is indeed this consideration that led us to develop a general method[1] for the fusion of a 2-carboxy-Δ^2-cyclohexenone system to a preexisting ring.

We now describe the synthesis of **1** and its transformation into (±)-yohimbine (**2**).[2]

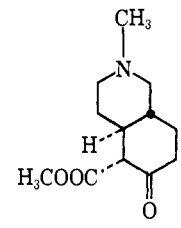


1

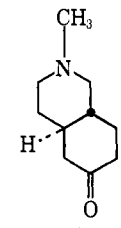


2

Reaction of the pyrrolidine enamine of *N*-methyl-4-piperidone with methyl 3-oxo-4-pentenoate[3] (3:1 benzene–methanol, reflux, 8 min) gave in ~80% yield the isoquinolone **1**,[4] R = CH_3, as an oil (ir (film) 1739, 1675, and 1634 cm^{-1}; nmr ($CDCl_3$) δ 3.81 (s, CO_2CH_3), 2.33 (s, NCH_3); λ_{max}^{EtOH} 233.5 nm (ϵ 9355)). Reduction of **1** with lithium (10% excess) in liquid ammonia–ether (4 equiv of *tert*-butyl alcohol) at −78° gave, stereospecifically, the *trans*-hydroisoquinolone ester (**3**), mp 73–74°, ir ($CHCl_3$) 1745, 1712 cm^{-1}. The expected[5] trans stereochemistry was evidenced by the nonenolic character of the β-keto ester system and by acid hydrolysis of **3** to the known *trans*-*N*-methyl decahydroisoquinolone (**4**).[6]



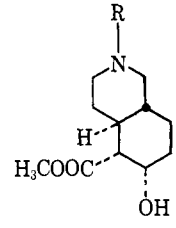
3



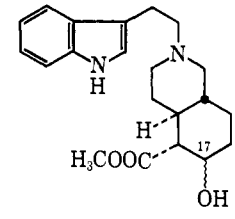
4

Stereoselective reduction of **3** could be achieved with platinum and hydrogen in acetic acid (room temperature, 40 hr) and the resulting mixture of amino alcohols was converted with cyanogen bromide (benzene, room temperature, 1.5 hr) into the mixture of axial and equatorial *N*-cyano alcohols which could be separated by chromatography.

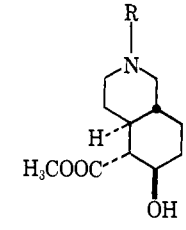
The desired axial isomer **5** (mp 125.5–127°, from benzene) was the major component of the mixture and could be isolated in 42% yield, together with ~30% of the equatorial isomer **6**, mp 152–153.5°. The stereochemistry[7] of the hydroxyl groups in **5** and **6** follows from the nmr of the related acetates (mp 105–106°, δ 5.45, J = ~7 Hz, and mp 118–120°, δ 4.98, J = ~21 Hz, respectively).



5, R = CN
7, R = H



9, 17α-OH
10, 17β-OH



6, R = CN
8, R = H

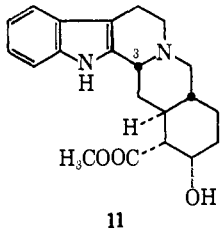
The secoyohimbane skeleton of **9** was then easily assembled *via* reductive decyanation[8] of **5** (zinc in 82% acetic acid, 100°, 3.5 hr) to the corresponding secondary amino alcohol **7**, mp 159–160° (80% yield, ir 3450 cm^{-1}), which was alkylated with tryptophyl bromide[9] (overnight reflux with 3 equiv of potassium carbonate

(1) G. Stork and R. Nath Guthikonda, manuscript in preparation.
(2) For other syntheses, see: (a) the classical work of E. E. van Tamelen, M. Shamma, A. W. Burgstahler, J. Wolinsky, R. Tamm, and P. E. Aldrich, *J. Amer. Chem. Soc.*, **91**, 7315 (1969); (b) L. Toke, K. Honty, and Cs. Szantay, *Chem. Ber.*, **102**, 3248 (1969).
(3) *Cf.* I. N. Nazarov and S. I. Zavyalov, *Zh. Obshch. Khim.*, **23**, 1703 (1953). A superior and more general synthesis of this type of substance will be described elsewhere.
(4) All substances described here were purified by chromatography on activity IV neutral alumina and gave analytical and/or spectral data in agreement with the postulated structures.
(5) G. Stork and S. D. Darling, *J. Amer. Chem. Soc.*, **86**, 1961 (1964).
(6) A. Marchant and A. R. Pinder, *J. Chem. Soc.*, 327 (1956).
(7) *Cf.* E. E. Smissman, J. Pengman Li, and M. W. Cruse, *J. Org. Chem.*, **35**, 1352 (1970).
(8) T. Fehr, P. A. Stadler, and A. Hofmann, *Helv. Chim. Acta*, **53**, 2197 (1970).
(9) T. Hoshino and K. Shimodaira, *Justus Liebigs Ann. Chem.*, **520**, 19 (1935).

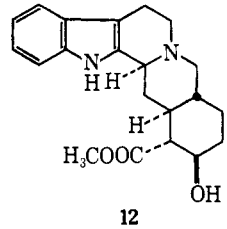
in methanol) to produce **9**, mp 143–144°, from acetonitrile (acetate mp 167–169°, nmr δ 5.43, J = 7 Hz).

The synthesis of yohimbine was completed by regiospecific cyclization, effected by heating the seco alcohol **9** with 2 equiv of mercuric acetate–ethylenediaminetetraacetic acid disodium salt (EDTA)[10] (1:1) at 125° for 2 hr in aqueous 1% acetic acid, followed by reduction of the crude intermediate with sodium borohydride (1 equiv, 0°, 15 min in methanol). (±)-Yohimbine (**2**) was thus obtained in ~32% yield from **9** as the only isolatable product (mp 214–216° from methanol, lit.[2b] mp 218–220°). The nmr, ir, and mass spectra (*m/e* 354.1947) were indistinguishable from those of the natural substance.

The stereoselective route to yohimbine which has just been described can be modified to lead to (±)-ψ-yohimbine (**11**) or to (±)-β-yohimbine (**12**).



11



12

Treatment of **9** with 10 equiv of mercuric acetate in aqueous 5% acetic acid at 120° for 3.5 hr, followed by removal of mercury salts and interfering by-products (with hydrogen sulfide, and then sodium borohydride in methanol for 15 min at 0°), gave (±)-ψ-yohimbine (**11**), mp 248–251° (from methanol; lit.[2a] mp 252–256°) in 27% yield.[11] No yohimbine appeared to be produced under these conditions.[12]

The synthesis of β-yohimbine (**12**) was effected simply by cleavage of **3** with cyanogen bromide, followed by reduction with sodium borohydride in methanol. The mixture of the *N*-cyano alcohols **5** and **6** was now predominantly the equatorial isomer **6** (**5**:**6** = 11:89) which was easily separated to give pure **6** (*vide supra*), mp 152–153.5°. Removal of the cyano group and alkylation with trytophyl bromide were performed as described above for the epimeric **5**, leading successively to **8**, mp 153–155° (65%, ir 3120 cm^{-1}), and **10**, mp 78–84° (acetate mp 153–154°, nmr δ 4.98, J = 21 Hz). The latter was finally cyclized (as described above for (±)-yohimbine) to (±)-β-yohimbine (**12**), mp 132–137 and 227–232°[2b] (lit. mp 130–140 and 232–236°) in 31% yield.[11,13]

(10) Only 2 equiv of mercuric acetate is required since mercury, rather than mercurous acetate, is produced in the presence of EDTA; *cf.* J. Knabe and H. P. Herbort, *Arch. Pharm.*, **300**, 774 (1967). Closely related observations in another series have appeared since the completion of our work (*cf.* J. Gutzwiller, G. Pizzolato, and S. M. Uskokovic, *J. Amer. Chem. Soc.*, **93**, 5907 (1971)).

(11) The ir, nmr, and mass spectra of the synthetic (±) material were identical with those of an authentic sample of the natural substance. We thank Professor E. Wenkert (Indiana) and Dr. R. A. Lucas (Ciba) for samples of natural ψ- and β-yohimbine, respectively.

(12) The oxidation of 9 by mercuric acetate with and without EDTA gives strikingly different results. The kinetic formation of the ψ stereochemistry at C_3 is not unexpected (*cf.* ref 2a) while the stability of the resulting ψ-yohimbine to oxidation by mercuric acetate either alone (F. L. Weisenborn and P. A. Diassi, *J. Amer. Chem. Soc.*, **78**, 2022 (1956); E. Wenkert and D. K. Roychaudhuri, *J. Org. Chem.*, **21**, 1315 (1956)), or in the presence of EDTA at 70° (L. Bartlett, N. J. Dastoor, J. Hrbek, Jr., W. Klyne, H. Schmid, and G. Snatzke, *Helv. Chim. Acta*, **54**, 1238 (1971)), is well documented. The implication of our work on the transformation of **9** to yohimbine is that at 120° in the presence of EDTA, the kinetically produced ψ-yohimbine must be oxidized to the iminium salt, which then gives the expected yohimbine stereochemistry at C_3 on borohydride reduction. We indeed were able to show that (±)-ψ-yohimbine could be oxidized with mercuric acetate–EDTA under more rigorous conditions (120°, 3 hr) than described by Bartlett, *et al.* (*vide supra*), to an intermediate (which was then reduced with sodium borohydride) to (±)-yohimbine in 41% overall yield.

(13) We thank the National Science Foundation and the National Institutes of Health for their support of this work.

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Semiconducting Polymers. Mixed Valence Ferrocene–Ferricenium Polymers[1]

Sir:

The mixed valence compound, biferrocene [Fe(II)-Fe(III)] picrate (**1**) exhibits properties which are not the sum of the properties of ferrocene and ferricenium picrate.[2] The single-crystal conductivity of **1** was six orders of magnitude greater than either of its components, and a new electronic transition (1900 nm), ascribed to an electron-transfer band, was observed for **1**. We proposed that it should be possible to alter the electrical properties of ferrocene polymers by the partial oxidation of these compounds.[2] Recently several ferrocene–ferricenium polymers have been prepared and characterized,[3,4] and we now report on the electrical properties of three structurally different mixed valence ferrocene polymers.

Poly(vinylferrocene) (**2**),[3,5] ferrocene-*o*-anisaldehyde condensation polymer **3**,[6] and polyferrocenylene (**4**)[7,8] were prepared by published methods and then oxidized with benzoquinone, HBF_4, and also with 2,3-dichloro-5,6-dicyanoquinone (DDQ) and 3,4,5,6-tetrachloro-1,2-benzoquinone (*o*-CA). The oxidized polymers **5**–**7** were blue-green or black in color due to the ferricenium 620-nm $^2E_{2g} \rightarrow {}^2E_{1u}$ transition. No absorption in the 1900-nm region was observed for **5** and **6** but a weak long wavelength transition was observed for **7**. For every mole of DDQ, *o*-CA, or BF_4^- incorporated into the polymers, 1 mol of ferrocene units was oxidized. This could be rigorously established by the comparison of the elemental analysis and the Fe(II)/Fe(III) ratio determined by infrared,[3] Mössbauer,[3,9] and X-ray photoelectron spectroscopy[10] studies as described previously.

(1) The Organic Solid State. VII. For part VI see D. O. Cowan J. Park, M. Barber, and P. Swift, *Chem. Commun.*, 1444 (1971). Also, Organometallic Polymers. XVII. For part XVI, see C. U. Pittman, Jr., T. L. Grube, O. E. Ayers, S. T. McManus, M. D. Rausch, and G. A. Mosher, *J. Polym. Sci., Part A-1*, **10**, 379 (1972).

(2) D. O. Cowan and F. Kaufman, *J. Amer. Chem. Soc.*, **92**, 219 (1970); F. Kaufman and D. O. Cowan, *ibid.*, **92**, 6198 (1970).

(3) C. U. Pittman, Jr., J. C. Lai, T. D. Rounsefell, D. Vanderpool, M. Good, and R. Prados, *Macromolecules*, **3**, 746 (1970); C. U. Pittman, Jr., J. C. Lai, D. P. Vanderpool, M. Good, and R. Prados in "Polymer Characterization: Interdisciplinary Approaches," C. D. Carver, Ed., Plenum Press, New York, N. Y., 1971.

(4) C. U. Pittman, Jr., *Chem. Technol.*, **1**, 416 (1971).

(5) F. S. Arimoto and A. C. Haven, *J. Amer. Chem. Soc.*, 77, 6295 (1955).

(6) E. W. Neuse and K. Koda, *J. Organometal. Chem.*, 4, 475 (1965).

(7) Samples of **4** were prepared by the polyrecombination technique (ref 8). Additionally, several samples were generously provided by Dr. N. Bilow, Hughes Aircraft Corp., Culver City, Calif.

(8) N. Bilow, A. L. Landis, and H. Rosenberg, *J. Polym. Sci., Part A-1*, 7, 2719 (1969).

(9) D. O. Cowan, R. L. Collins, and F. Kaufman, *J. Phys. Chem.*, **75**, 2025 (1971).

(10) D. O. Cowan and J. Park, *Chem. Commun.*, 1444 (1971).