

A characteristic of iron pentacarbonyl is the reaction it undergoes on irradiation to produce diiron nonacarbonyl and carbon monoxide. Accordingly, the *pseudo*-iron pentacarbonyl $\text{Mn}(\text{CO})_4\text{NO}$ was irradiated in an attempt to obtain $\text{Mn}_2(\text{CO})_7(\text{NO})_2$, a compound analogous to $\text{Fe}_2(\text{CO})_9$. This treatment gave heptacarbonyldinitrosyldimanganese (30% yield) as deep red crystals (decomp. without melting at $\sim 140^\circ$), carbon monoxide, and lesser amounts of manganese carbonyl and carbonyltrinitrosylmanganese. Heptacarbonyldinitrosyldimanganese(0), very air sensitive, subliming at 25° (0.1 mm.), and exceedingly difficult to purify from manganese carbonyl, probably has a structure analogous to that of $\text{Fe}_2(\text{CO})_9$,¹⁰ *viz.*, $\text{ON}(\text{CO})_2\text{Mn}(\text{CO})_3\text{Mn}(\text{CO})_2\text{NO}$, with some metal-metal bonding between manganese atoms. The infrared spectrum⁸ shows carbonyl stretching bands at 2101 (w), 2042 (vs), 2006 (vs), 1995 (w, sh) and 1776 (s) cm^{-1} . Bands in the bridging carbonyl region and the nitrosyl stretching region occur at 1743 (m), 1735 (m), 1731 (w), 1726 (w) and 1710 (m) cm^{-1} .

(10) H. M. Powell and R. V. G. Ewens, *J. Chem. Soc.*, 286 (1939).
 (11) National Science Foundation Predoctoral Fellow.

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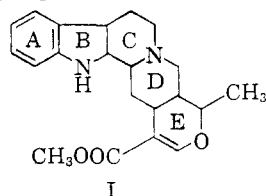
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THE TOTAL SYNTHESIS OF *dl*-AJMALICINE

Sir:

Of the numerous and widely distributed E-heterocyclic indole alkaloids, the *Rauwolfia* component ajmalicine (tetrahydroserpentine, δ -yohimbine) (I),¹ a peripheral vasodilator effective in the



treatment of angina and other physical disorders, is a notable example. In this Communication, we summarize operations leading to *dl*-ajmalicine, which represent the first synthesis of a member of this important natural product group.²

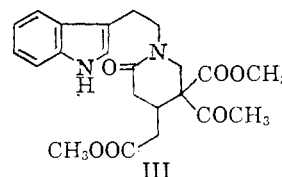
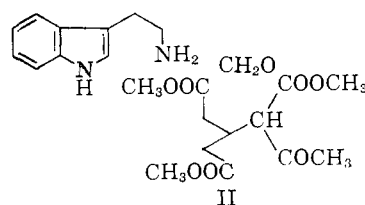
In a key step which roughly parallels the presumed biogenetic process,³ the essentials of the desired alkaloidal system are efficiently assembled at the outset: tryptamine, formaldehyde and the keto triester II⁴ undergo a Mannich condensation

(1) Isolation and characterization: (a) S. Siddiqui and R. H. Siddiqui, *J. Ind. Chem. Soc.*, **8**, 667 (1931); **9**, 539 (1932); **12**, 37 (1935); **16**, 421 (1939); (b) H. Heineman, *Ber.*, **67**, 15 (1934). Gross structure: R. Goutarel and A. LeHir, *Bull. Soc. chim.*, **18**, 909 (1951). Partial stereochemical structure: (a) E. Wenkert and D. K. Roychaudhuri, *J. Am. Chem. Soc.*, **79**, 1519 (1957); **80**, 1613 (1958); (b) N. Neuss and H. E. Boaz, *J. Org. Chem.*, **22**, 1001 (1957).

(2) First announced (March 28, 1961) at the 139th Meeting of the American Chemical Society, St. Louis, Missouri.

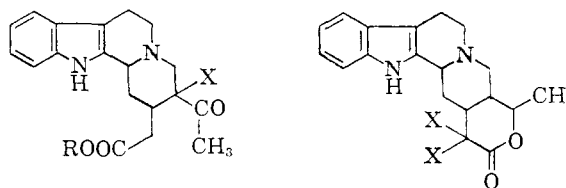
(3) E. Wenkert and N. V. Bringli, *J. Am. Chem. Soc.*, **81**, 1474 (1959).

(4) Secured through Michael addition of methyl acetoacetate to dimethylglutaconate (*cf.* M. H. Dreifuss and C. K. Ingold, *J. Chem. Soc.*, **123**, 2964 (1923).



in *tert*-butyl alcohol, providing the lactam III in nearly quantitative yield.⁵ Although the lactam was found to be neither distillable nor crystallizable, it could be purified by column chromatography; material so obtained displayed consonant spectral properties (infrared absorption at 2.88, 5.75, 5.80 and 6.09 μ) (λ_{max} 221, 276, 284 and 292 $\text{m}\mu$) and was suitable for the succeeding steps.

First of all, ring-C was fashioned, carried out by means of phosphorus oxychloride closure to the tetracyclic Δ^3 -dehydro base (PO_2Cl_2^- salt, m.p.



IVa (X = $-\text{COOCH}_3$;
 R = $-\text{CH}_3$)

IVb (X = $-\text{H}$; R = $-\text{H}$)

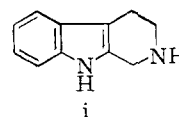
Va (X = $-\text{H}$)
 Vb (X = $=\text{CHOH}$)

148–150°) (λ_{max} 247, 358 $\text{m}\mu$, $\epsilon = 11,900$; 23,500) and then reduction over palladium-on-carbon in ethanol to the keto diester IVa (HCl salt, m.p. 152.5–154°).

Removal of the ester function from the β -keto ester moiety was accomplished next, effected by prolonged heating of the keto diester IVa in refluxing dilute hydrochloric acid. The resulting keto acid IVb, isolated and purified as the hydrochloride (m.p. 236.5–238°), was accompanied by varying amounts of *diacid* (m.p. 268–269°) formed by acid-catalyzed deacetylation of IVa.

In preparation for the construction of the E-ring, keto acid IVb was reduced with sodium borohydride to the hydroxy acid (m.p. 248–251°), which, on treatment with *N,N'*-dicyclohexylcarbodiimide in pyridine, was converted to the δ -lactone Va (HCl salt, m.p. 236–238°) (infrared absorption

(5) Use in this case of traditional Mannich conditions, *viz.*, formaldehyde, active hydrogen component and amine in an *acidic* medium, leads to formation of tetrahydro- β -carboline (i), but no product of the type III. When the reaction is carried out in *tert*-butyl alcohol and



in the absence of added acid, formation of tetrahydro- β -carboline is suppressed, and lactam III is produced instead. These observations will be treated appropriately in the future full publication.

at 2.90 and 5.78 μ). Conversion to the α -hydroxy-methylene- δ -lactone Vb (not purified) was managed by treatment of Va with methyl formate in the presence of excess sodium triphenylmethyl in dioxane. Upon being heated in refluxing methanolic hydrogen chloride,⁶ the hydroxymethylene lactone was transformed readily to the dihydropyran carboxylic ester (m.p. 222–225°). Infrared spectral comparison (chloroform solution) of authentic ajmalicine with the base thus produced demonstrated the latter to be *dl*-ajmalicine.⁷

Proper utilization of certain intermediates described above should permit establishment of the complete stereochemistry of ajmalicine and other hetero-ring E indole alkaloids, and such studies are now under way in this Laboratory.

Acknowledgment.—The authors are grateful to the National Institutes of Health (RG3892) and to the Wisconsin Alumni Research Foundation for financial support; to Mr. Ian G. Wright for the preparation of starting materials; and to Dr. Thomas A. Spencer, Jr., who first isolated intermediate IVb.

(6) F. Korte and K. H. Büchel, *Angew. Chem.*, **71**, 709 (1959).

(7) Complete spectral, physical, and analytical data will be recorded in the full paper to be published.

(8) Allied Chemical Corporation (Plastics Division) Fellow, 1959–1960.

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CYCLOPROPANES. X. AN OPTICALLY ACTIVE GRIGNARD REAGENT¹

Sir:

To date, all previous attempts to prepare optically active Grignard reagents from optically active halides have been unsuccessful². We wish at this time to report that optically active (+)-1-bromo-1-methyl-2,2-diphenylcyclopropane³ reacts with magnesium to form a Grignard reagent which on carbonation followed by hydrolysis produces optically active (–)-1-methyl-2,2-diphenylcyclopropane-carboxylic acid (II)⁵ and (–)-1-methyl-2,2-diphenylcyclopropane. This result represents the first example of an optically active Grignard reagent.⁵

Magnesium powder (0.5 g.) and 2.30 g. of I, [α]_D²⁵ +106 \pm 1° (*c*, 2.229)⁶, were placed in 12 ml. of tetrahydrofuran and a solution of 0.5 ml. of ethylene dibromide⁷ in 2.5 ml. of tetrahydrofuran

(1) This work was supported in part by a grant from the National Science Foundation and in part by a grant from the U. S. Army Research Office (Durham).

(2) R. H. Pickard and J. Kenyon, *J. Chem. Soc.*, **99**, 45 (1911); A. M. Schwartz and J. R. Johnson, *J. Am. Chem. Soc.*, **53**, 1063 (1931); C. W. Porter, *ibid.*, **57**, 1436 (1935); H. L. Goering and F. H. McCarron, *ibid.*, **80**, 2287 (1958).

(3) H. M. Walborsky and F. J. Impastato, *ibid.*, **81**, 5835 (1959).

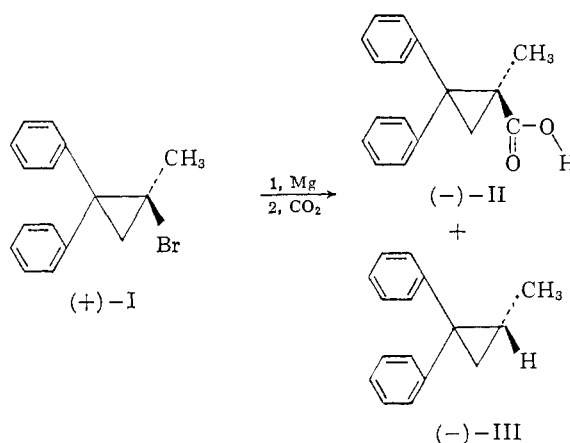
(4) F. J. Impastato, L. Barash and H. M. Walborsky, *ibid.*, **81**, 1514 (1959).

(5) For the constitution of Grignard Reagents see, R. E. Dessy and G. S. Handler, *ibid.*, **80**, 5824 (1958).

(6) All rotations were taken in chloroform solution.

(7) D. E. Pearson, D. Cowan and J. D. Beckler, *J. Org. Chem.*, **24**, 504, (1958).

was added over a period of ten minutes. The exothermic reaction brought the solution to reflux temperature (65°) and this temperature was maintained for an additional ten minutes. The reaction mixture was poured into Dry Ice and worked up in the usual manner to yield the optically active acid II (0.766 g., 38%), [α]_D²⁵ 5.3 \pm 1.2° (*c*, 2.173). The infrared spectrum of the acid was identical in all respects with that of an authentic sample⁴ and its rotation represents an optical purity of 14 \pm 2%. A neutral fraction (0.624 g., 38%) was obtained and shown to be 1-methyl-2,2-diphenylcyclopropane (III)³ by its b.p., infrared spectrum and retention time on vapor phase chromatography. The hydrocarbon III, [α]_D²⁵ –13.6 \pm 1.2°, was 11 \pm 2% optically pure.



In another experiment an excess of magnesium powder was treated with a solution of ethylene dibromide in tetrahydrofuran until gas evolution ceased and then a solution of I in tetrahydrofuran was added slowly, over a period of 40 minutes, in order to maintain the temperature between 25–27°. Carbonation of the reaction mixture gave these results: Acid II was isolated in 45% yield and was 12 \pm 2% optically pure; Hydrocarbon III was obtained in 36% yield with an optical purity of 10 \pm 2%.

Since (+)-I has been related to (–)-II and (–)-III the stereochemistry of the over-all reaction is that of retention of configuration.^{3,8} A similar stereochemical result is obtained when 1-methyl-2,2-diphenylcyclopropyllithium³ (by reaction of butyllithium with (+)-I) is carbonated to yield (–)-II and (–)-III.⁹ There is, however, an important difference in these two reactions. Whereas carbonation of the lithium reagent gives 100% retention of configuration and activity, the Grignard reagent yields only *ca.* 12% retention of activity and 56% retention of configuration. Since a carbon–magnesium bond has less ionic character associated with it than does the carbon–lithium bond,¹⁰ one might have expected a high retention

(8) H. M. Walborsky, L. Barash, A. E. Young and F. J. Impastato, *J. Am. Chem. Soc.*, **83**, 2517 (1961).

(9) It has been demonstrated that (–)-III is formed by reaction of 2,2-diphenylcyclopropyllithium with the solvent (unpublished results).

(10) L. Pauling, "The Nature of the Chemical Bond," Cornell University Press, Ithaca, N. Y., 1960.