The mixture of dienes (II) can be recovered in at least 60% yield by dilution of a sulfuric acid solution of I with water.

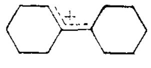
The classic freezing point depression technique[6] gives an *i*-factor of 2.08 ± 0.08 (unchanged after 24 hours) for solutions prepared by adding II to 99% sulfuric acid. This is in accord with the equation for simple protonation

$$C_{10}H_{16} + H_2SO_4 \longrightarrow C_{10}H_{17}^+ + HSO_4^-$$

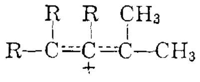
The most striking feature in infrared spectra of I (in 96% sulfuric acid or dichloromethane solutions) is an intense band at 1533 cm.$^{-1}$, the only band between 2850 and 1450 cm.$^{-1}$. This absorption is intermediate in frequency between ordinary carbon–carbon single bond and double bond stretching absorptions. The extinction of this band is approximately ten times as great as the average extinction of the two carbon–carbon double bond stretching absorptions exhibited in the infrared spectrum of the diene (II).

The ultraviolet spectrum of I (sulfuric acid) has λ_{max} 314 mμ (ϵ 9130). The equilibrium between I and II (determined spectrophotometrically) is 1:1 in 50% sulfuric acid.

The cation III and a series based on IV are half-formed in 50–75% sulfuric acid and have absorption maxima between 310 and 335 mμ. Their chemical stability is less than that of I but sufficient to allow equilibrium studies to be performed.



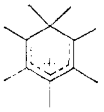
III



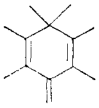
$$\mathrm{R{-}\overset{R}{C}{=}\underset{+}{\overset{R}{C}}{=}\overset{CH_3}{C}{-}CH_3}$$

IV, R = CH_3 or H

The properties of I are in excellent agreement with those of the stable cation V prepared by Doering and co-workers.[7] The bands due to α-hydrogens in n.m.r. spectra of both I and V are between 6 and 7 τ (6.15, 6.35, and 6.63 τ for V[8]). The band for the β-hydrogens of V (7.45τ) is intermediate between that for the α-hydrogens and that for the γ-hydrogens of I. The ultraviolet spectra of V[9] (λ_{max} 397 mμ, ϵ 8500, concentrated hydrochloric acid) and I exhibit comparable extinctions and have absorption maxima in agreement with the energy of the long wave length absorption calculated by simplest LCAO MO theory (β for V and $\sqrt{2}\beta$ for I).



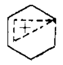
V



VI

The properties reported[10] recently for a species thought to be one of the isomeric cyclohexenyl cations VIIa or VIIb are not in agreement with those of I. There was no band comparable to the intense absorption of I at 1533 cm.$^{-1}$; a weak band at 1692 cm.$^{-1}$ was the only band reported between 2850 and 1450 cm.$^{-1}$ in infrared spectra (Nujol–Fluorolube mixed mulls) of VII. The n.m.r. spectrum of VII (a sharp band at -0.09τ and a broad band at 9.13τ with areas in the ratio of 1:2.06)[11] does not contain the expected complex absorption at about 2τ for the allylic hydrogens nor the absorption expected for α-hydrogens at 6–7τ. The extinction of 234 for the maximum at 307 mμ (dioxane) is but a shadow of the extinctions found for I and V.

VIIa



VIIb

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[6] L. P. Hammett and A. J. Deyrup, *J. Am. Chem. Soc.*, **55**, 1900 (1933).

[7] W. von E. Doering, M. Saunders, H. G. Boyton, H. W. Earhart, E. F. Wadley, W. R. Edwards, and G. Laber, *Tetrahedron*, **4**, 178 (1958).

[8] The spectrum[7] was of a hydrochloric acid solution standardized against a benzene capillary. The reported values have been converted to parts per million from benzene and 2.73 added to correct to a tetramethylsilane standard. For n.m.r. spectra of similar ions see C. MacLean, J. H. van der Waals, and E. L. Mackor, *Mol. Phys.*, **1**, 247 (1958).

[9] Ultraviolet spectra of similar compounds have been reported: C. Reid, *J. Am. Chem. Soc.*, **76**, 3264 (1954); G. Dallinga, E. L. Mackor, and A. A. Verrijn Stuart, *Mol. Phys.*, **1**, 123 (1958).

[10] G. A. Olah and W. S. Tolgyesi, *J. Am. Chem. Soc.*, **83**, 5031 (1961).

[11] The spectrum[10] was of a nitromethane solution standardized against water as an external reference.

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RECEIVED MARCH 2, 1962

MASS SPECTROMETRY IN STRUCTURAL AND STEREOCHEMICAL PROBLEMS. V.[1] REFRACTINE AND ASPIDOFRACTINE

Sir:

Recently structural formulas have been assigned to several complicated alkaloids[1,2,3] without resorting to any classical chemical degradations, based largely on interpretations of mass spectral fragmentation patterns, and coupled in several instances[1,3] with n.m.r. measurements. We wish now to report the application of this new approach to the structure elucidation of the hexacyclic alkaloids refractine[4] and aspidofractine isolated from the Brazilian tree *Aspidosperma refractum* Mart. Refractine[4] (polymorphic forms m.p. 157.5–159° and 191–192°, $[\alpha]_D -23°$ (all rotations in chloroform)) is a N-acetyl-7-methoxydihydroindole (with an additional carbomethoxy function) with analyses compatible with $C_{22}H_{26}N_2O_4$ or $C_{23}H_{28}N_2O_4$ (396), the latter being correct as shown by mass spectrometric molecular weight determination (found, 396). We are now proposing the hexacyclic structure IA for refractine on the basis of the following evidence.

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[1] Paper IV, C. Djerassi, S. E. Flores, H. Budzikiewicz, J. M. Wilson, L. J. Durham, J. Le Men, M.-M. Janot, M. Plat, M. Gorman and N. Neuss, *Proc. Natl. Acad. Sci. U. S.*, **48**, 113 (1962).

[2] K. Biemann, M. Friedmann-Spiteller and G. Spiteller, *Tetrahedron Letters*, 485 (1961).

[3] (a) C. Djerassi, H. W. Brewer, H. Budzikiewicz, O. O. Orazi and R. A. Corral, *Experientia*, **18**, March (1962); (b) B. Gilbert, J. M. Ferreira, R. J. Owellen, C. E. Swanholm, H. Budzikiewicz, L. J. Durham and C. Djerassi, *Tetrahedron Letters*, No. 2, 59 (1962); (c) C. Djerassi, H. Budzikiewicz, J. M. Wilson, J. Gosset, J. Le Men and M.-M. Janot, *Tetrahedron Letters*, 235 (1962).

[4] B. Gilbert, L. D. Antonaccio, A. A. P. G. Archer and C. Djerassi *Experientia*, **16**, 61 (1960).

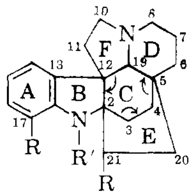
The n.m.r. spectrum[5] confirmed the aromatic substitution pattern (same signals as reported[6] for aspidospermine) and the presence of the aromatic methoxyl (3.85 p.p.m.), carbomethoxy (3.73) and N-formyl (9.47) substituents. No signals corresponding to olefinic protons, C-methyl groups *or a C-2* hydrogen[6] could be detected. Refractine cannot be hydrogenated (platinum oxide, acetic acid) and hence presumably is hexacyclic.

Warming with 1 *N* hydrochloric acid produced deformylrefractine (II) (glass, $[\alpha]_D$ −56°) which was reformylated to refractine (I). The presence of one hydrogen at C-21 was demonstrated by sodium methoxide-catalyzed epimerization to deformylisorefractine (21-iso-II) (m.p. 155–156°, $[\alpha]_D$ + 34°) and formylation to 21-isorefractine (21-iso-I) (m.p. 190–191°, $[\alpha]_D$ + 76°). Lithium aluminum hydride reduction of II led to the alcohol III (m.p. 153–154°, $[\alpha]_D$ −47°), thence to the tosylate IV (m.p. 147–148°, $[\alpha]_D$ −50°) and by exposure to alkaline alumina to the olefin V (glass, $[\alpha]_D$ −102°); IV could also be transformed into VI (glass, $[\alpha]_D$ −10°, n.m.r. doublet at 1.1 p.p.m. due to C-22 methyl). The identical sequence with deformylisorefractine (21-iso-II) proceeded *via* 21-iso-III and iso-IV to the above V, thus showing that the iso series differs only in configuration at C-21. Ozonolysis provided an oily ketone ($\lambda_{\max}^{\mathrm{CHCl_3}}$ 5.80 μ), indicating that the carbomethoxy group was attached to a strained six-membered ring.

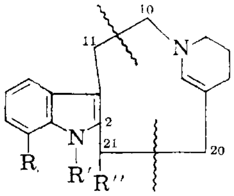
The mass spectra of all refractine and isorefractine derivatives (I–IX) exhibit a peak at M-28, characteristic[2] of the aspidospermine skeleton and ascribable[2] to expulsion of the unsubstituted bridge (C-3 and C-4) as ethylene, the driving force being aromatization of the dihydroindole moiety and relief of strain imposed by the highly fused system. These conclusions are equally applicable to refractine (see arrows in A) leading to **a** as the M-28 species. All of the above mass spectra (except V) show intense peaks at *m/e* 109 (stronger in iso-series) and 124 (stronger in "normal" series). A species such as **a** would be expected to cleave between C-10 and C-11, to yield the highly stabilized[2] $CH_2{=}N^+$—grouping (see **b** and **c**), while rupture of the 20-21 bond would afford allylically stabilized radicals leading to **c** (*m/e* 109). This allylic assistance is not possible in V. The generation of the *m/e* 124 peak (**b**?; also formed in 21-deuteriodeformylisorefractine) and its preferred formation (over **c**) in the sterically more hindered 21-normal series will be detailed in our full paper. The appearance of the *m/e* 124 (**b**) and 109 (**c**) peaks in such a diverse group (*e.g.*, I, III, VI) demonstrates that the C-21 substituent cannot be attached to that portion of the molecule encompassed by fragments **b** and **c**; furthermore, it cannot be located on the two-carbon bridge (C-3 and C-4), since this is lost in going to species **a**, which still contains that substituent. It follows that the carbomethoxy group of refractine can only be located at C-11 or C-21; we favor the latter because of the overwhelming biogenetic precedence for a carbomethoxy group in such a position among dihydroindole alkaloids.

The mass spectrum of the 21-iso-O-acetate VII offers further corroboration. In addition to the features already discussed, this spectrum is also characterized by a very strong peak at *m/e* 295 (M-87). A metastable peak at *m/e* 247 shows this to arise from M-28 (expulsion of ethylene), followed by detachment of an acetoxyl fragment (59 mass units) from species **a** (R = CH_3O; R′ = H; R″ = CH_2OAc) to give *m/e* 295 (**a**, R = CH_3O; R′ = H; R″ = $CH_2\cdot$). The strongest peak in the spectrum of VII occurs at *m/e* 109, since cleavage of the 20–21 bond is now especially favored (generation of conjugated double bond). Full confirmation was adduced by the mass spectrum of the dideuterio derivative IX where the *m/e* 295 peak has moved to 297 (**a**, R = CH_3O; R′ = H; R″ = $CD_2{}'$), while the *m/e* 109 peak remained unchanged. Consequently, the mass spectrometric and n.m.r. data, together with the "biogenetic preference" for a C-21 rather than C-11 locus of the carbomethoxy group, lead to structure IA for refractine.[7]

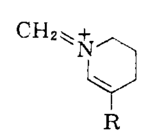
Refractine (I) is accompanied by a new alkaloid ($C_{22}H_{26}N_2O_3$), aspidofractine (X) (m.p. 193–193.5°, $[\alpha]_D$ −142°) which could be transformed into 21-isoaspidofractine (21-iso-X) (m.p. 109–110°, $[\alpha]_D$ +3°) and into an analogous series of derivatives (II–IX) as reported for refractine (I). That aspidofractine (X) and refractine (I) differ only by the absence or presence of a C-17 methoxyl group could be established through a mass spectrometric approach first developed by Biemann.[2,8] For instance, comparison of the mass spectra of deformylisorefractine (21-iso-II) and deformylisoaspidofractine (21-iso-XI) demonstrates a complete coincidence of all peaks in the lower mass range (including *m/e* 109 and 124), while those peaks still containing the aromatic portion of the molecule (*e.g.*, **a**) are all shifted by 30 mass units corresponding to the extra C-17 methoxyl group in I. It follows that aspidofractine possesses structure XA.[7]



A



a



b R = C_2H_5
c R = $CH_2\cdot$

	R	R′	R″		R	R′	R″
I	CH_3O	CHO	CO_2CH_3	VII	CH_3O	H	CH_2OAc
II	CH_3O	H	CO_2CH_3	VIII	CH_3O	H	CD_2OH
III	CH_3O	H	CH_2OH	IX	CH_3O	H	CD_2OAc
IV	CH_3O	H	CH_2OTs	X	H	CHO	CO_2CH_3
V	CH_3O	H	$=CH_2$	XI	H	H	CO_2CH_3
VI	CH_3O	H	$-CH_3$	XII	H	H	CH_2OH

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(5) Measured by Dr. J. N. Shoolery (Varian Associates) or Dr. Lois J. Durham (Stanford University) in deuteriochloroform with tetramethylsilane as internal standard; signals reported as δ units in p.p.m. (δ = c.p.s./60).

(6) C. Djerassi, A. A. P. G. Archer, T. George, B. Gilbert, J. N. Shoolery and L. F. Johnson, *Experientia*, **16**, 532 (1960).

(7) The alternatives (ref. 3b) with 2–19 and 3–12 or 5–12 and 4–19 linkages are excluded because ring E is six-membered (see also ref. 10).

(8) K. Biemann, *Tetrahedron Letters*, **15**, 9 (1960); K. Biemann and G. Spiteller, *ibid.*, 299 (1961).

After preparation of this manuscript, there appeared an article[9a] describing the isolation of certain *Pleiocarpa* alkaloids with properties similar to those of aspidofractine (XA). Subsequent correspondence with Prof. H. Schmid (Zürich) and Dr. A. R. Battersby (Bristol) revealed that they had arrived independently at skeleton A for their alkaloids. Direct comparison of kopsinine[9] and XI, kopsinyl alcohol[9] and XII, and synthetic N-formylkopsinine and aspidofractine (X) established the identity of the two series. As reported elsewhere,[10] the British and Swiss investigators have been able to prove chemically the C-21 attachment of the carbomethoxy group; their other studies as well as our results mutually support the novel skeleton A for this group of alkaloids.

All of the substances recorded in this communication gave satisfactory elementary analyses and correct mass spectral molecular ion peaks. We are indebted to the National Institutes of Health (grants 2G-682 and A-4257) and to the Rockefeller Foundation for financial aid, and to Prof. K. Biemann for a stimulating discussion.

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[9] (a) W. G. Kump and H. Schmid, *Helv. Chim. Acta*, **44**, 1503 (1961); (b) W. D. Crow and M. Michael, *Australian J. Chem.*, **8**, 129 (1955).

[10] W. D. Kump, D. J. Le Count, A. R. Battersby and H. Schmid, *Helv. Chim. Acta*, **45**, in press (1962).

[11] The contents of this paper were first reported at the Golden Jubilee Phytochemistry Symposium of the University of Hong Kong, September 12, 1961.

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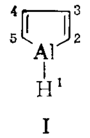
THE NOVEL SYNTHESIS OF ALUMINOLES BY THE METALATIVE CYCLIZATION OF UNSATURATED ORGANOALUMINUM COMPOUNDS

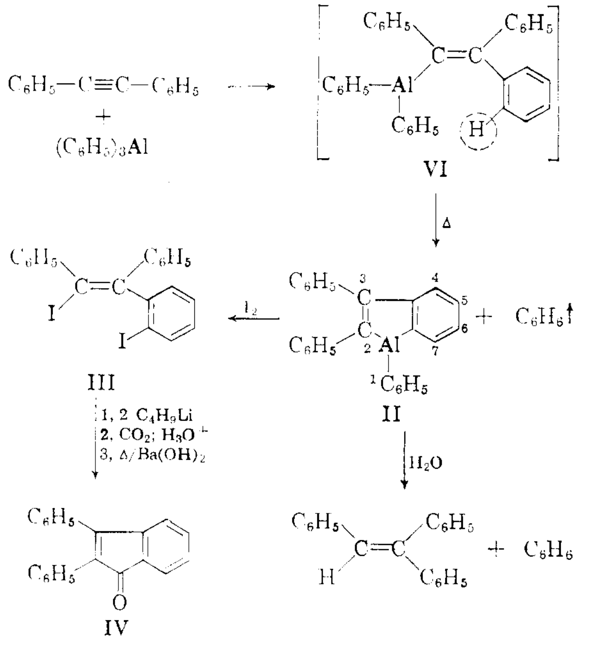
Sir:

We wish to report the novel cyclization of certain unsaturated organoaluminum compounds, leading to the formation of the unsaturated, five-membered aluminum heterocyclic system shown in I. Representing the first reported example of an aluminum heterocycle, I may be designated as the aluminole nucleus.[1] Interaction of triphenylaluminum with diphenylacetylene in a melt at 200° led to the evolution of benzene (identified as its *m*-dinitro derivative) and the deposition of a yellow solid (II). The reaction proceeded more smoothly in phenyl ether solution. After washing II with benzene and recrystallizing from toluene the pale yellow solid II melted at 285–288°.[2] *Anal.* Calcd. for $C_{26}H_{19}Al$: Al, 7.53. Found: Al, 7.40. Upon hydrolysis II yielded benzene and triphenylethylene. Treatment of II with iodine provided iodobenzene and a pale yellow, iodine-containing solid III, m.p. 174–175°. The latter product was shown to be 1-iodo-*cis*-1,2-diphenyl-2-(2-iodophenyl)ethene by the results of analysis (Calcd. for $C_{20}H_{14}I_2$: C, 47.27; H, 2.78; I, 49.95. Found: C, 47.26; H, 2.90; I, 49.80) and its transformation into the known 2,3-diphenylindone (IV).[3] The latter conversion was effected by treating III with two equivalents of *n*-butyllithium in ether to exchange the iodine for lithium.[4] Carbonation of the resulting dilithio compound produced the diacid V, 3-(2-carboxyphenyl)-*cis*-2,3-diphenylpropenoic acid, m.p. 208–210° (*Anal.* Calcd. for $C_{22}H_{16}O_4$: neut. equiv., 172. Found: neut. equiv., 173) and some IV. Heating the diacid V with $Ba(OH)_2$ also afforded IV (mixture m.p. with authentic 2,3-diphenylindone undepressed). This therefore proves both the structure of III and the *cis*-relationship of the two phenyl groups about the ethylenic linkage. By heating diphenylacetylene with triphenylaluminum in phenyl ether solution at 200° and then treating with iodine pure yields of 65% of this interesting and otherwise difficultly accessible diiodo compound have been achieved.[5]



I

Thus the course of the formation and structure-proof of 1,2,3-triphenylbenzaluminole (II) can be viewed as shown



Although the adduct VI has not been isolated as yet, there can be no doubt that reactive aryl organometallics are able to add across the C≡C linkage. We have observed, for example, that the heating of diphenylacetylene with phenyllithium in ether solution and subsequent carbonation yields

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[1] The authors are grateful for the guidance of Dr. Leonard T. Capell of Chemical Abstracts Service in the choice of suitable nomenclature for this novel system.

[2] Due to the sensitivity of organoaluminum compounds to oxidation and hydrolysis all operations were conducted under an atmosphere of dry, oxygen-free nitrogen.

[3] C. F. Koelsch, *J. Am. Chem. Soc.*, **54**, 2045 (1932).

[4] *Cf.* R. G. Jones and H. Gilman, "Organic Reactions," John Wiley and Son, Inc., New York, N. Y., Chap. 7, 1951.

[5] Utilization of such an appropriate intermediate for the synthesis of the benzocyclobutadiene system is under consideration in this Laboratory.