was added, and the resulting solution was refluxed for one hour. This solution, if allowed to stand, precipitates out a solid resin containing phosphonic acid groups. When the solution is padded on cloth and the impregnated cloth is heated for ten minutes at 140° an insoluble, cross-linked resin condenses, which imparts flame resistance to the material. That the cloth behaves as an ion exchanger is evidenced by the following. When the cloth is treated with sodium salts, the sodium is adsorbed and the cloth loses its flame resistance. On treating the cloth with ammonium salts the flame resistance of the cloth is restored. Similarly, the flame resistance can be restored if dilute acids are used to generate the acid form of the ion exchanger.

Ion-exchange Reactions.—The titration curves of the exchange resins obtained from the condensation of formaldehyde with phenoxymethylphosphonic acid (I) and with 3-methylphenoxymethylphosphonic acid (II) are illustrated in Fig. 1. These resins behave as dibasic acids having equivalence points at *p*H values of 5.0 and 10.2.

A 2-inch column containing 24.2 g. of the acid form of I, and having a total exchange capacity of 232 milliequivalents, was tested for ion-exchange properties by passing solutions of known concentration through the column until both the break-through point (1% leakage) and the saturation point of the resin had been reached. The resin was regenerated with the theoretical amount of regenerant. Typical data are tabulated in Table II. Except for having a slightly lower exchange capacity, the ion-exchange properties of II were similar to those reported for I.

CHICAGO HEIGHTS, ILLINOIS

[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

The Structures of Grantianine and Sceleratine. A Suggested Biogenesis of the Acids in the Alkaloids from Senecio and Crotalaria Species

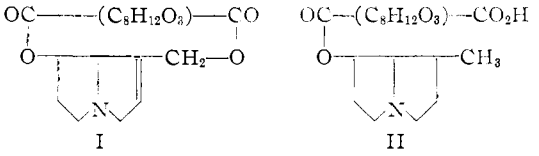
BY ROGER ADAMS AND MAURIZIO GIANTURCO

RECEIVED FEBRUARY 9, 1956

Grantianine, the alkaloid from *Crotalaria grantiana*, has been reinvestigated. Grantianic acid, which is esterified with retronecine to form the alkaloid, has been shown to be an oxidation product of trichodesmic acid. A reinterpretation of de Waal's experiments on sceleranecic acid dilactone has resulted in the postulation of a new formula for it, which conforms to those of the acid moieties of other Crotalaria alkaloids. A structure for the alkaloid sceleratine is proposed. The possible existence of a common biogenetic pathway to the formation of the various acids, which when esterified with retronecine and related bases, provide the large class of pyrrolizidine alkaloids is discussed.

The alkaline hydrolysis of the alkaloid grantianine, $C_{18}H_{23}NO_7$, extracted from *Crotalaria grantiana*, gave retronecine and an acid which could not be isolated in a pure state.[1] Upon hydrogenation over a platinum catalyst, grantianine absorbed two moles of hydrogen and formed tetrahydrograntianine, $C_{18}H_{27}NO_7$.

At the time of these earlier experiments the structure of retronecine had not been elucidated. With this structure now known,[2] the condensed formulas for grantianine and tetrahydrograntianine may be written as I and II, respectively.



I II

The infrared spectrum has now revealed that the alkaloid contains two ester carbonyl groups absorbing at 1717 and 1732 cm.$^{-1}$, a γ-lactone absorbing at 1765 cm.$^{-1}$, and an alcoholic hydroxyl group absorbing at 3520 cm.$^{-1}$. In the infrared spectrum of tetrahydrograntianine are found bands for an alcoholic hydroxyl group, a γ-lactone, an unconjugated ester, an acid (zwitterion) and a salt structure as evidenced by bands at 3380, 1767, 1736, 1615 and 2200–2400 cm.$^{-1}$, respectively.

In the introductory paper,[1] a small amount of by-product was reported with the tetrahydrograntianine after the reduction of the alkaloid. It was isolated only as a picrate, $C_{18}H_{27}NO_6 \cdot C_6H_3N_3O_7$ or $C_{18}H_{25}NO_6 \cdot C_6H_3N_3O_7$. The alkaloidal moiety has one less oxygen or one less molecule of water than tetrahydrograntianine and the infrared spectrum of the picrate shows the absence of the γ-lactone band. This by-product was probably due to the presence of an impurity of lower oxygen content in the grantianine, since the reduction of a chromatographically-pure sample of alkaloid afforded a single product as indicated by a chromatogram. Moreover, by changing slightly the isolation procedure previously described, practically a quantitative yield of tetrahydrograntianine resulted.

The possibility that the by-product picrate, $C_{18}H_{27}NO_6 \cdot C_6H_3N_3O_7$ or $C_{18}H_{25}NO_6 \cdot C_6H_3N_3O_7$, was formed by an acid-catalyzed reaction of the main product of hydrogenation, $C_{18}H_{27}NO_7$, followed by picrate formation was excluded when treatment of pure tetrahydrograntianine with aqueous picric acid yielded a characteristic picrate, $C_{18}H_{27}NO_7 \cdot C_6H_3N_3O_7$, whose infrared spectrum still showed γ-lactone, ester carbonyl and acid carbonyl bands at 1770, 1740 and 1710 cm.$^{-1}$ (shoulder), respectively, and a band for an alcoholic hydroxyl at 3420 cm.$^{-1}$.

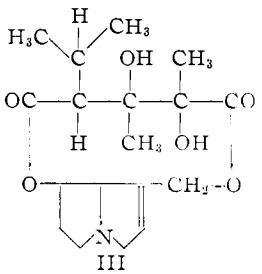
The physical properties of pure grantianine and tetrahydrograntianine, as previously determined, were confirmed in this investigation. Since grantianine is a Crotalaria alkaloid and contains the same number of carbon atoms as trichodesmine (III),[3] it is likely to be closely related in structure to the latter. A structure that fulfills all the requirements is shown in IV. Tetrahydrograntianine would then have structure V.[4]

(1) R. Adams, M. Carmack and E. F. Rogers, THIS JOURNAL, **64**, 571 (1942).

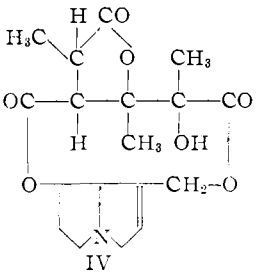
(2) R. Adams and N. J. Leonard, *ibid.*, **66**, 257 (1944).

(3) R. Adams and M. Gianturco, *ibid.*, **78**, 1922 (1956).

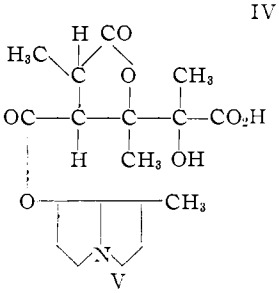
(4) A convenient microtest for determining whether by reduction of the alkaloid an intramolecular salt or an ordinary salt is formed is given in the Experimental part. Treatment of an aqueous solution with Dowex 50 in the hydrogen phase causes no change in the *p*H in the former but a change toward more acidic values in the latter.



III

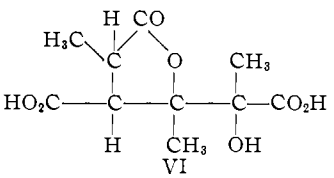


IV

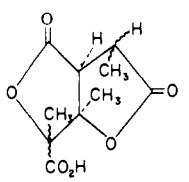


V

Grantianic acid will have structure VI or be completely lactonized as shown in VII. Unfortunately,



VI



VII

the amount of alkaloid available was too small to permit certain obvious chemical studies to confirm these postulated structures.

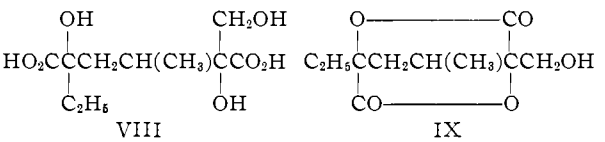
If grantianine, upon treatment with alkali, is completely saponified before degradation, it may be expected to yield the same product as would be derived from grantianic acid by similar treatment, namely, 4-methyl-5-ketohexane-2,3-dioic acid. If saponification of the lactone occurs to a certain extent first, followed by decomposition before saponification of the ester groups, some α-methyllevulinic acid should also be present. These postulated products are based on the assumption of decompositions analogous to those of trichodesmine and trichodesmic acid.[3]

The configuration of the carbon atom bearing the hydroxyl and methyl group and the orientation of the acid moiety in the alkaloid to form the two ester linkages is consistent with past findings.[3,5] The infrared spectra support these conclusions; the band at 1717 cm.$^{-1}$ in the spectrum of grantianine is probably due to the carbonyl of the ester attached to the carbon atom bearing an hydroxyl group. This appears as a carboxyl (zwitterion) band at 1615 cm.$^{-1}$ in the spectrum of tetrahydrograntianine. The other ester carbonyl band in grantianine at 1732 cm.$^{-1}$ is recognizable as the band at 1736 cm.$^{-1}$ in the spectrum of the tetrahydrograntianine. The carboxyl group with the stronger ionization constant is esterified with the less hindered and more reactive hydroxyl group of the necine.

(5) M. Kropman and F. L. Warren, *J. Chem. Soc.*, 2852 (1949); 700 (1950); R. Adams and B. L. Van Duuren, THIS JOURNAL, **75**, 4638 (1953); F. L. Warren, "Progress in the Chemistry of Organic Natural Products," Vol. XII, Springer Verlag, Vienna, 1955, p. 198.

Another alkaloid in this general class is that isolated from *Senecio sceleratus* along with retrorsine and isatidine. It is called sceleratine and is a retronecine ester which upon hydrolysis gives retronecine and the dilactone of an acid designated as sceleranecic acid. The dilactone was studied and degraded by de Waal.[6] At the time of de Waal's experiments the knowledge of the acids of the Senecio and Crotalaria alkaloids was meager. In the light of what is now known, formulas other than those of de Waal may be suggested for sceleranecic acid and its dilactone which conform more closely to the experimental results.

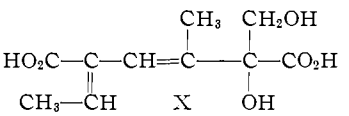
de Waal's formulas for sceleranecic acid and sceleranecic acid dilactone are shown in VIII and IX, respectively.



VIII IX

Formula IX does not satisfy completely three of the experimental facts. de Waal found that one lactone ring in the molecule is hydrolyzed slowly in water, whereas the other requires hot alkali. Such a result is suggestive of the presence of one 6- and one 5-membered lactone ring. The formation of a C_8-lactonic acid by the lead tetraacetate oxidation of the potassium salt of sceleranecic acid cannot be explained readily on the assumption of structure VIII; a C_7-molecule should result from this structure. The alkaloid from retronecine and the acid VIII should lead upon reduction to an amino acid and not to a salt of retronecanol as was found experimentally and as occurs with monocrotaline, trichodesmine and junceine. Warren[4] has summarized and interpreted de Waal's experiments on sceleranecic acid dilactone in Chart I.

All the Senecio alkaloids thus far investigated have as the acid moiety a substituted adipic acid. Since sceleratine was found in a Senecio species, search was made first for an appropriate adipic acid derivative which would fit all the experimental facts for sceleranecic acid. A structure was designed which may be considered as derived from riddellic acid (X).

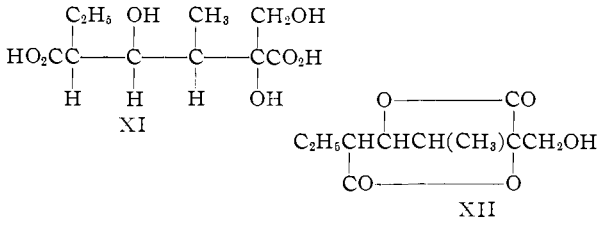


X

de Waal's structure of sceleranecic acid could stem from riddellic acid by assuming a reverse addition of water to the double bond conjugated with the carboxyl group and reduction of the other double bond. A second possibility from riddellic acid might be the reduction of the double bond conjugated with the carboxyl group and hydration of the other double bond. This would lead to formula XI which, when lactonized, would give formula XII. Both de Waal's structure and structure XII

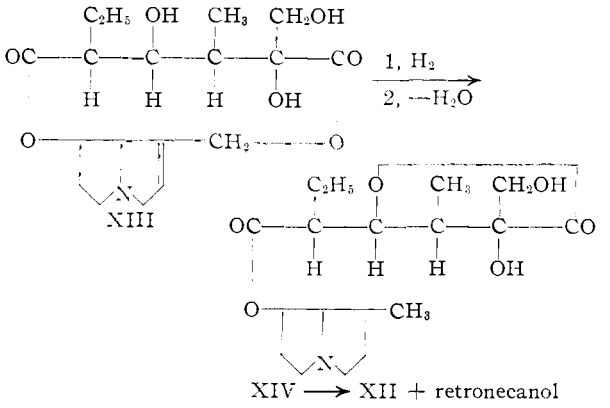
(6) (a) H. L. de Waal and T. P. Pretorius, *Onderst. J. Vet. Sci. and Animal Ind.*, **17**, 181 (1945); (b) H. L. de Waal and A. Crous, *J. South African Chem. Inst.*, **1**, 23 (1948); (c) H. L. de Waal, W. J. Serfontein and C. F. Garbers, *ibid.*, **4**, 115 (1951).

contain two C-CH_3 groups as reported by de Waal.[7]



XI XII

The structure of the alkaloid sceleratine based on formula XI for sceleranecic acid would be XIII.

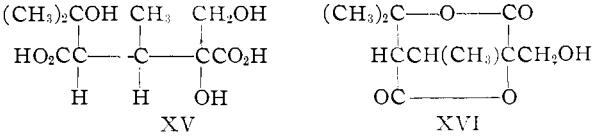


XIII XIV → XII + retronecanol

Formula XII contains both a 5- and 6-membered lactone ring and therefore fits the hydrolysis experiments. By the action of lead tetraacetate on the potassium salt of structure XI, degradation might possibly occur with formation of the same C_8-lactonic acid proposed by de Waal. The right hand part of molecule XI might be oxidized by potassium permanganate or lead tetraacetate with loss of two carbon atoms and formation of a carboxyl group from the original α-carbon; a concomitant dehydration from the secondary β'-hydroxyl and the α'-hydrogen atom might occur to give an unsaturated acid. This intermediate might then be transformed by reverse addition of water followed by lactonization to the lactonic acid end-product. These and other reactions and conversions are shown in Chart II. Structures postulated in Chart II are isomeric with those suggested by de Waal in Chart I.

The chief objection which renders formula XIII unlikely for sceleratine, besides the improbable lactonization mentioned above, is the difficulty of explaining the formation of sceleranecic acid dilactone by a hydrogenation reaction. In no case has a pyrrolizidine alkaloid derived from adipic acid undergone a 6-membered lactone transesterification after cleavage of the allyl ester group with hydrogen. A possible way to explain formation of structure XII from structure XIII would be to assume that the carboxyl group set free by the initial hydrogenolysis, lactonized with the hydroxyl in the γ-position to it and that the resulting product XIV might then transesterify to a 6-membered lactone. Models indicate that transesterification to a 6-membered lactone ring would be more facile in a chain holding the 5-membered lactone than in a chain without this ring.

In view of the two assumptions which had to be made to find a structure for sceleranecic acid having the skeleton of a Senecio-type acid and in agreement with all the experimental data, it seemed more likely that sceleranecic acid were of the Crotalaria-type. It, indeed, resembles these acids in its reaction with hydrogen and a catalyst, and may in fact be related to trichodesmic[3] and junceic[8] acids which contain the same number of carbon atoms. Alkaloids typical of both the Crotalaria and Senecio species have actually been found in the same plant, *Crotalaria juncea*.[8] The structures for the acid and dilactone postulated on this basis appear very acceptable and are shown in XV and XVI.



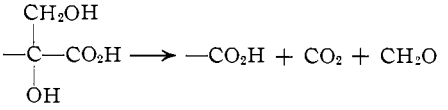
XV XVI

Formula XVI contains both a 5- and a 6-membered lactone ring. By the action of lead tetraacetate on the potassium salt of the corresponding acid XV, a C_8-lactonic acid, isomeric with the one proposed by de Waal, can be derived by a more likely series of reactions. The fact that no acetone was detected by oxidation of sceleranecic acid dilactone with chromic acid in glacial acetic acid[9] does not disqualify structure XVI. This structure would be expected to yield acetone on oxidation only after the opening of the lactone ring. de Waal has shown that the lactone rings in sceleranecic acid dilactone are very resistant to oxidation in acidic media.[6b] The most likely interpretation of the reactions of sceleranecic acid is shown in Chart III. The postulated structures in all instances are isomeric with those proposed by de Waal in Chart I.

The structure of the alkaloid sceleratine would then be represented by XVII. Such a structure would be expected upon hydrogenation with a platinum catalyst to absorb two moles of hydrogen

(7) The question concerning the number of C-CH_3 groups in sceleranecic dilactone is confused. de Waal[6b] reports in the text of a Communication that sceleranecic acid dilactone contains two C-CH_3 groups. He made this deduction from a C-CH_3 determination on the acid obtained by nitric oxidation of sceleranecic acid dilactone which involves merely the conversion of a primary methylol group to a carboxyl group. The actual analysis showed 2.5 C-CH_3 groups which ordinarily would indicate the presence of three C-CH_3 groups.

When sceleranecic dilactone is converted to the potassium salt and oxidized, two carbon atoms are lost, as formaldehyde and carbon dioxide, and an acid, $C_8H_{12}O_4$, results. The normal mode of attack by lead tetraacetate, one of the oxidizing agents used, is indicated below.



No C-CH_3 groups would thus be lost in the conversion. A C-CH_3 determination on this acid gave a value of 1.5 C-CH_3 groups, thus indicating two groups of this kind in the molecule and hence also in sceleranecic acid dilactone. With these conflicting results and without material to repeat the C-CH_3 determination, the present authors chose de Waal's conclusion that two C-CH_3 groups were present in sceleranecic acid dilactone as probably correct.

(8) R. Adams and M. Gianturco, THIS JOURNAL, **78**, 1919, 1926 (1956).

(9) C. Rimington, *Onderst. J. Vet. Sci. and Animal Ind.*, **4**, 89 (1935).

CHART I

Postulated Structures of Sceleranecic Dilactone and Derivatives (de Waal)

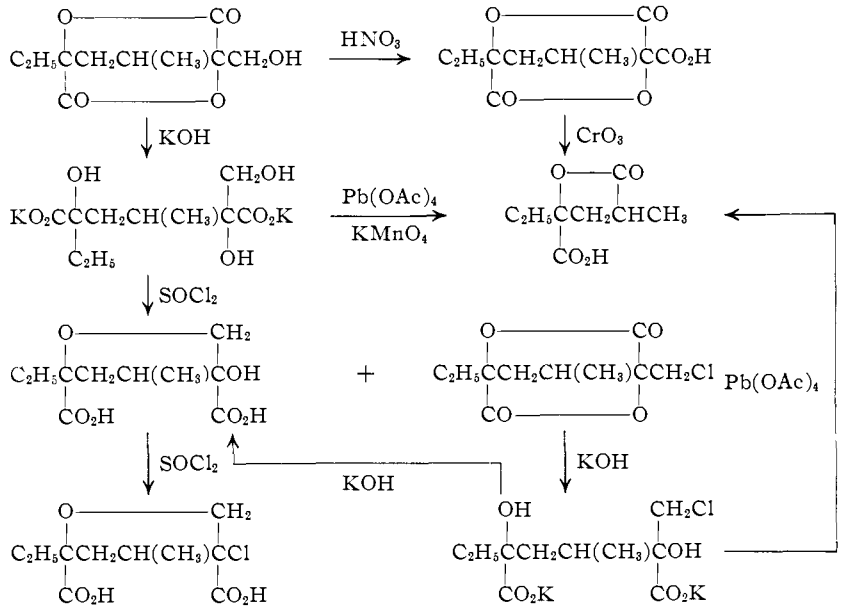
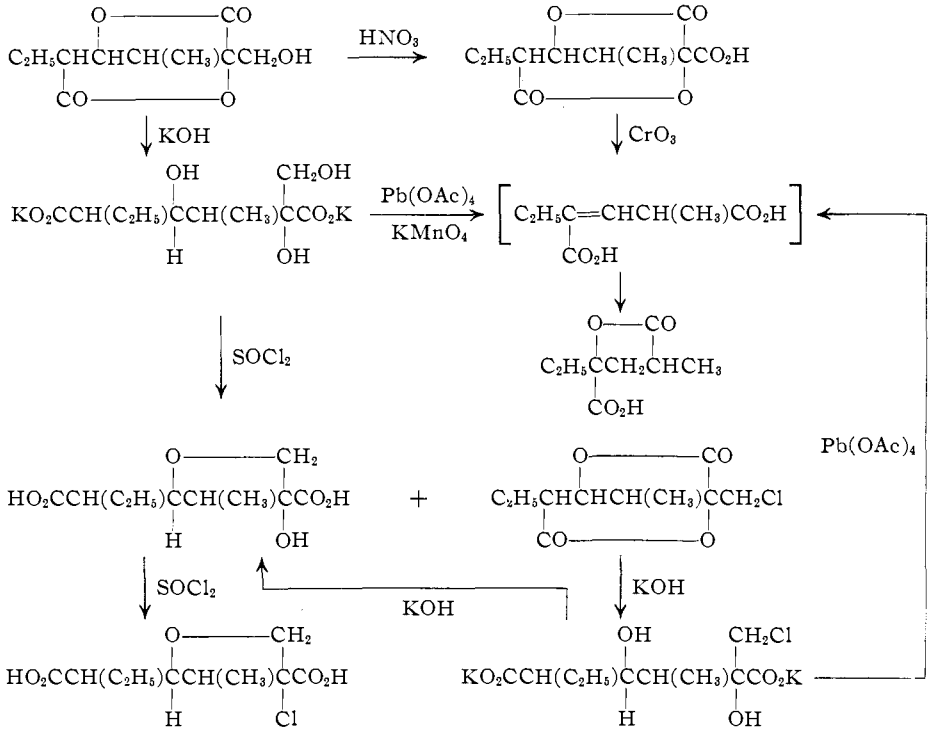
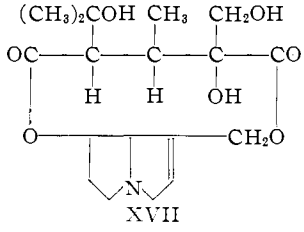


CHART II

Postulated but Unlikely Structures of Sceleranecic Dilactone and Derivatives (Formulated as a Senecio-type)



and then to transesterify to give retronecanol and a compound with structure XVI, assigned to



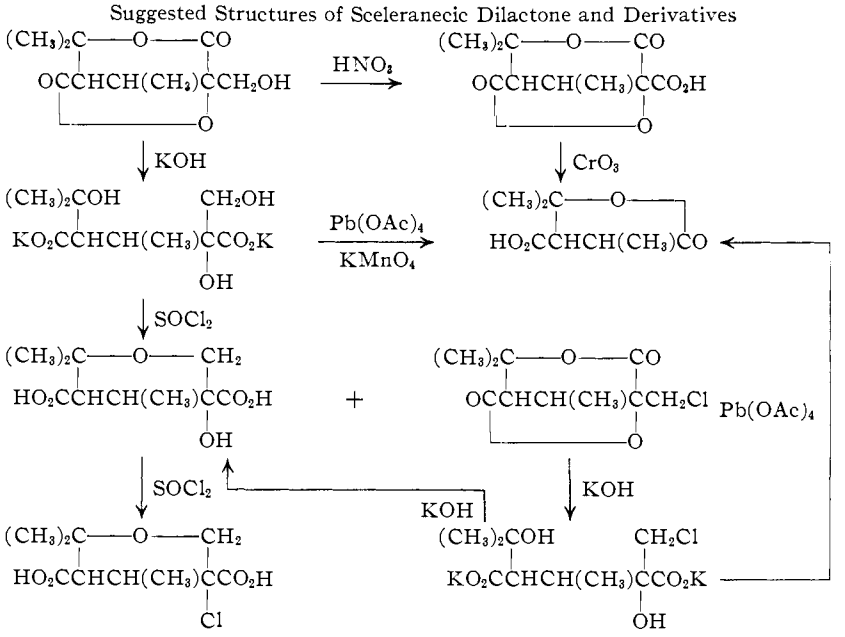
XVII

sceleranecic acid dilactone. Only in the pyrrolizidine alkaloids with acid moieties derived from a substituted glutaric acid has reduction led to transesterification following an ester cleavage, to provide a salt of retronecanol.

Biogenetic Relationships of the Necic Acids.—The isolation from plants of various genera of the families of the *Boraginaceae*, *Compositae* and *Leguminosae* of alkaloids which are esters of retronecine, or related bases, with a variety of acids having skeletons of 5, 6, 7, 8 or 10 carbon atoms, sug-

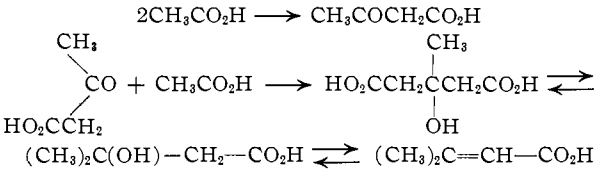
CHART III

Suggested Structures of Sceleranecic Dilactone and Derivatives



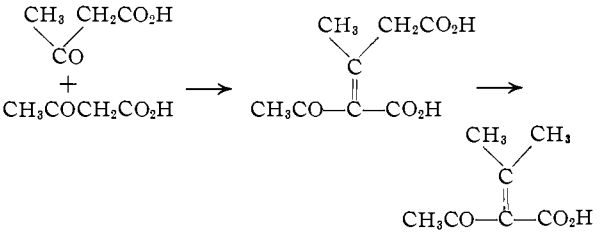
gested that the biogenesis of the latter may proceed through similar intermediates and that all the acids may, indeed, be products of multiple condensations of acetate units with themselves or with simple three-carbon units commonly occurring in plants.

Senecioic acid, β,β-dimethylacrylic acid, occurring in the rhizomes of *Senecio kaemperi* Sieb,[10] and dicrotalic acid, β-hydroxy-β-methylglutaric acid, which is the acid moiety of dicrotaline,[11] the alkaloid from *Crotalaria dura* and *Crotalaria globifera*, are of great biological significance; they have been postulated as intermediates in the synthesis of cholesterol in the human body,[12] of terpenes[13] and in the metabolism of leucine.[14] Furthermore, senecioic acid has been shown to enhance rubber formation in stem-section cultures of the guayule plant.[15] These acids are most likely formed from acetate units through acetylco-A and acetoacetylco-A



The C_7-necic acids, in the skeleton of which may be recognized an isopentane unit joined at the 3-carbon atom with a two-carbon unit, are represented by the general formula

where R,R′,R″ = H (trachelanthic and viridifloric acid) or R,R′ = H and R″ = OH (acid moiety in macrotamine). These acids probably arise, through simple reactions commonly occurring in plants, from α-isopropylideneacetoacetic acid, which in turn may be formed by condensation of two moles of acetoacetic acid, followed by elimination of a mole of carbon dioxide



The skeleton of monocrotalic acid, the only C_8-necic acid, is likewise formed of an isopentane unit, joined at the 3-carbon atom with the 2-carbon atom of a three-carbon fragment. The acid may be formed by condensation of propionate with α-acetolactic (or acetoglyceric) acid. α-Acetolactic acid is probably synthesized in nature from pyruvic acid and acetaldehyde[16] and it has frequently been assumed to take part in bacterial reactions.[17]

In the skeleton of the C_{10}-crotalaria acids, two isopentane units are obvious, joined through the 3-carbon atoms of each. These acids may arise from the condensation of α-acetolactic (or acetoglyceric) acid with isovalerate, β-hydroxyisovalerate, methylsuccinate or their equivalents. The

(10) Y. Asahina, *Arch. Pharm.*, **251**, 355 (1913).

(11) R. Adams and B. L. Van Duuren, THIS JOURNAL, **75**, 2377 (1953).

(12) K. Block, Harvey Lectures, Academic Press, New York, 1952–53, p. 868; L. C. Clark, T. Harary, O. Reiss and K. Block, *Federation Proc.*, **13**, 192 (1954).

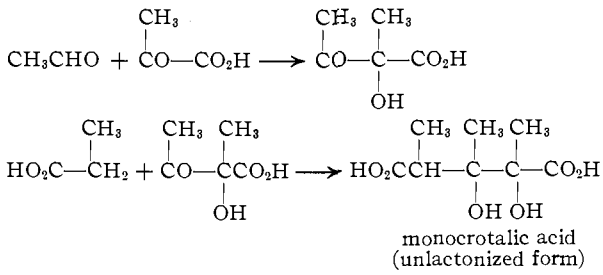
(13) R. Robinson, "The Structural Relations of Natural Products," The Clarendon Press, Oxford, 1955, p. 16.

(14) J. Coon, W. G. Robinson and B. K. Bachawat, "Amino Acid Metabolism," Johns Hopkins Press, Baltimore, 1955, p. 431.

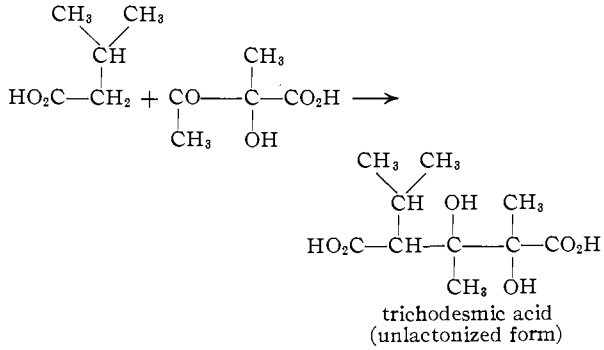
(15) B. Arreguin, J. Bonner and B. J. Wood, *Arch. Biochem.* **31**, 234 (1951); J. Bonner and B. Arreguin, *ibid.*, **21**, 109 (1949); J. Bonner, M. W. Parker and J. C. Montermoso, *Science*, **120**, 549 (1954).

(16) R. Strassman, A. J. Thomas and S. Weinhouse, THIS JOURNAL, **75**, 5135 (1953); P. P. Singer and J. Pensky, *Biochim. et Biophys. Acta*, **9**, 316 (1952).

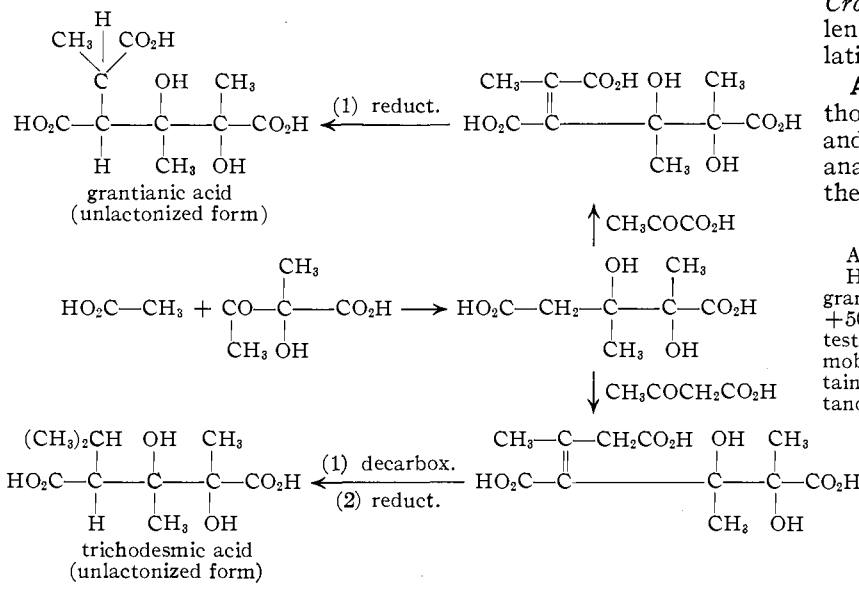
(17) E. Juin, *J. Biol. Chem.*, **195**, 715 (1952); D. Watt and L. O. Krampitz, *Federation Proc.*, **6**, 301 (1947).



postulated formation of trichodesmic acid will serve as an example

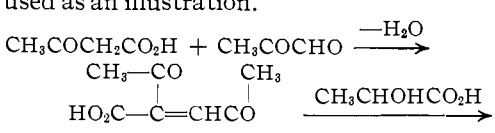


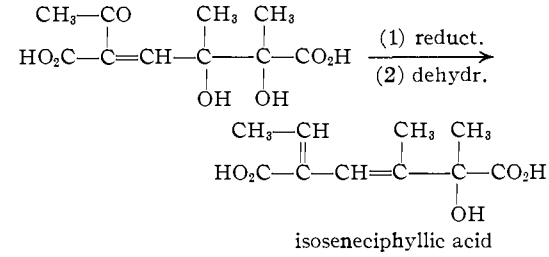
The synthesis could, of course, occur stepwise from α-acetolactic acid and acetate, as exemplified for grantianic and trichodesmic acid.



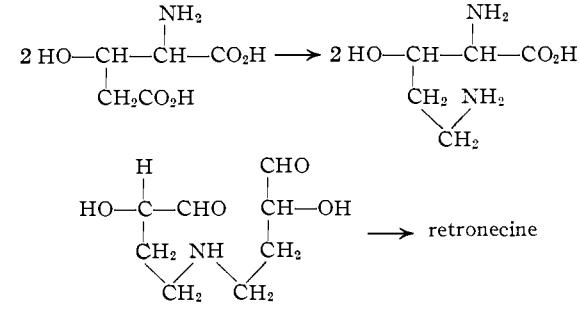
Similarly, the C_{10}-senecio acids, whose skeletons contain two isopentane units with a 3-carbon and a 1-carbon junction, may arise by a condensation of acetoacetate with a simple three-carbon unit, like pyruvic aldehyde, followed by a second condensation with lactate or glycerate or their equivalents and by the usual reactions of dehydration, reduction and the like.

The synthesis of isoseneciphyllic acid may be used as an illustration.





It is noteworthy that Robinson[18] has suggested that retronecine might be formed from two molecules of hydroxyornithine, derived from 2-hydroxyglutamic acid, according to the scheme



The amino acid, D,L-β-hydroxy-N-methylnorvaline, with a structure rather closely related to hydroxyornithine, has been actually obtained from *Crotalaria juncea*[19] and this may lend support to Robinson's postulation.

Acknowledgement.—The authors are indebted to Mr. J. Nemeth and Mrs. M. Benassi for the microanalysis and to Mr. J. Brader for the infrared spectra.

Experimental

All melting points are corrected.

Hydrogenation of Grantianine.—The grantianine, m.p. 204–205°, $[\alpha]^{30}D$ +50.6° ($CHCl_3$), used for reduction was tested by a paper chromatogram. The mobile phase was the upper layer obtained by shaking equal volumes of butanol and 5% acetic acid. The same solvent system was employed throughout the present investigation. At a temperature of 27 ± 1°, the R_f of grantianine was 0.45 as compared with R_f 0.40 for monocrotaline.

A solution of 0.050 g. of grantianine in 5 ml. of 95% ethanol and 3 ml. of glacial acetic acid was hydrogenated at room temperature and atmospheric pressure in presence of 0.025 g. of platinum oxide catalyst. Two mole equivalents of hydrogen were absorbed in 7 min. A sample was taken to dryness and a quantitative solution in chloroform was prepared. Aliquot parts containing 50 and 150 γ, respectively, were used for a paper chromatogram. The presence of only one compound was indicated.

The reduction solution was then filtered, the catalyst was thoroughly washed with ethanol containing 1% acetic acid, and the combined solutions taken to dryness at room temperature. The yield was 0.047 g. (92%) of white crystals, m.p. 242–242.5°, R_f 0.29. Rotation: 0.023 g. made up to 1.5 ml. with 50% aqueous acetic acid at 27° gave αD −0.87°, l 1; $[\alpha]^{27}D$ −56.8°.

(18) Ref. 11, p. 72.

(19) R. Adams and M. Gianturco, THIS JOURNAL, **78**, 1919 (1956).

Anal. Calcd. for $C_{18}H_{27}NO_7$: C, 58.52; H, 7.37; N, 3.79. Found: C, 58.63; H, 7.26; N, 3.87.

In order to establish the stability of the tetrahydrograntianine to strong acid, the rotation solution was acidified with 0.1 ml. of concentrated hydrochloric acid and the rotation determined immediately, $[\alpha]^{27}D$ −54.0°. The rotation did not change after the solution stood at room temperature for 20 hr. A paper chromatogram of a sample of this solution, after treatment on the paper with ammonia vapors to set the base free, gave only one spot, R_f 0.29.

Reduction of a second sample of grantianine, which was permitted to remain in contact with hydrogen and the catalyst for 24 hr., gave the same product.

The picrate of tetrahydrograntianine was prepared from equivalent amounts of the base and picric acid in water. The product was purified from ethanol by addition of a little ether, m.p. 195–196°. *Anal.* Calcd. for $C_{18}H_{27}NO_7 \cdot C_6H_3N_3O_7$: C, 48.16; H, 5.01. Found: C, 48.36; H, 5.23.

Microtest for Character of Alkaloid Reduction Products. – Two types of reduction products have been obtained from pyrrolizidine alkaloids, dependent on the structure of the alkaloids. The one is represented by salts where both ester linkages have been cleaved; the second by intramolecular salts formed by cleavage of only one ester group.

A few mg. of the hydrogenated product is dissolved in 1–2 ml. of water and the *p*H of the solution is tested. The *p*H is tested again after a few mg. of Dowex 50 in the hydrogen phase is added. If the compound corresponds to the first type, the *p*H changes toward more acidic values; if it corresponds to the second type no change in *p*H is observed.

URBANA, ILLINOIS

[CONTRIBUTION FROM THE DEPARTMENT OF ORGANIC CHEMISTRY, UNIVERSITY OF PRETORIA AND THE POST GRADUATE MEDICAL SCHOOL, NEW YORK UNIVERSITY]

The Structure of Sceleratine, an Alkaloid from *Senecio sceleratus*

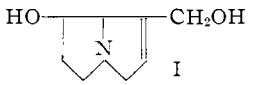
BY H. L. DE WAAL AND BENJAMIN L. VAN DUUREN[1]

RECEIVED FEBRUARY 9, 1956

Structural studies earlier conducted on sceleratine, sceleranecic dilactone and sceleratinic dilactone are re-evaluated. Sceleranecic dilactone is shown to be α,δ-dihydroxy-α-hydroxymethyl-γ-carboxy-β,γ-dimethylcaproic acid, γ,δ-dilactone (VI) and sceleratinic dilactone is the corresponding chloride X. Infrared data supporting these structures are discussed.

The toxic plant *Senecio sceleratus* which occurs in the Northern Transvaal region of South Africa has been known for many years to be responsible for cattle poisoning.[2] Chemical investigations revealed the presence of three alkaloids in this plant.[2] The structures of two of these alkaloids, retrorsine (β-longilobine) and its N-oxide isatidine have since been elucidated.[3] The third alkaloid, $C_{18}H_{27}O_7N$, was named sceleratine.

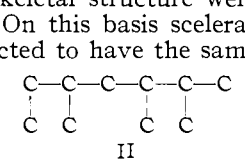
Aqueous alkaline hydrolysis of sceleratine gave retronecine (I) which is obtained by the hydrolysis



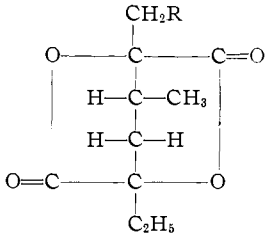
I

of many pyrrolizidine alkaloids[3] and a new optically active substance, $C_{10}H_{14}O_5$, which was named sceleranecic dilactone. Hydrogenolysis of the alkaloid with platinum as catalyst gave the known base retronecanol (Ia) and the same dilactone. Sceleranecic dilactone was later found to occur as such in *Senecio sceleratus*, together with an apparently closely related compound, $C_{10}H_{13}O_4Cl$, which was named sceleratinic dilactone.[4]

In previous studies of pyrrolizidine alkaloids only those alkaloids containing acid moieties with the same carbon skeletal structure were found in the same plant.[3] On this basis sceleranecic dilactone would be expected to have the same carbon skeleton, II, as retronecic acid, the acid moiety in the alkaloid retrorsine. Combining this assumption with the available experimental evidence,[2,4–6] structures IIIa and IIIb were suggested[6] for sceleranecic and sceleratinic dilactones, respectively.



II



IIIa, R = OH
b, R = Cl

Several objections can be raised to these structures. Thus an examination of the Kuhn–Roth carbon–methyl results[2,4–6] indicates the presence of three rather than two CH_3–C groups in IIIa and IIIb. It is known that these values are often too low.[7] In addition the behavior of sceleranecic and sceleratinic dilactones on neutralization with alkali cannot be satisfactorily accounted for by a structure containing two six-membered lactone groupings. Furthermore, the α,α′-dihydroxyadipic acid structure III would be expected to give, on oxidation with alkaline potassium permanganate or aqueous lead tetraacetate, a smaller molecule than the C-8 acid actually obtained from IIIa and IIIb by these oxidation procedures.

In view of these considerations it seemed desirable to re-evaluate the experimental results presented in the earlier papers without making any assumptions with respect to carbon-skeletal structure.

(1) To whom inquiries should be sent at 550 First Avenue, New York 16, N. Y.

(2) H. L. de Waal and T. P. Pretorius, *Onderstepoort J. Vet. Sci. Animal Ind.*, **17**, 181 (1941).

(3) For a recent review see: R. Adams, *Angew. Chem.*, **65**, 433 (1953).

(4) H. L. de Waal and D. F. Louw, *Tydskrif vir Wetenskap en Kuns*, **10**, 171 (1950).

(5) H. L. de Waal and A. Crous, *J. S. African Chem. Inst.*, **1**, 23 (1948).

(6) H. L. de Waal, W. J. Serfontein and C. F. Garbers, *ibid.*, **4**, 115 (1951).

(7) E. J. Eisenbraun, S. M. McElvain and B. F. Aycock, THIS JOURNAL, **76**, 607 (1954).