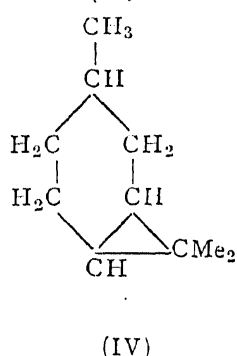
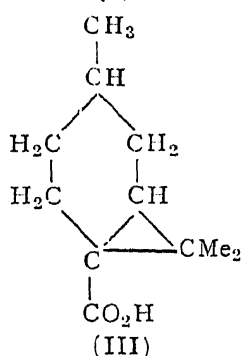
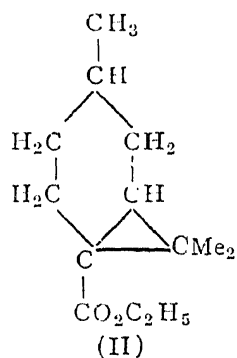
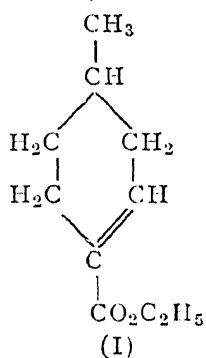


Synthesis of Carane.

IN the present communication, the synthesis of carane starting from a *cyclohexene* derivative, possessing a methyl group in position 1, and a double bond between the carbon atoms in positions 3 and 4, is described. The starting substance was ethyl Δ^1 -tetrahydro-*p*-toluate, obtained in an improved yield according to the method of



Bardhan¹ starting from *p*-methyl *cyclohexanone*. The unsaturated compound (I) reacts with dimethyl-diazomethane on being allowed to stand at 0° during two weeks to yield the bicyclo (0 : 1 : 4)-heptane derivative (II) (b.p. 150 – 160°/6 mm.) giving on hydrolysis with 5 per cent. alcoholic potassium hydroxide the corresponding carboxylic acid (III), m.p. 104–105°; Eq. Wt. Found : 181.2; required, 182. The acid on being distilled with ZnO–BaO under reduced pressure gives a compound which from its boiling point (Found : 161°/684 mm.; known, 169°/750 mm.), refractive index (Found : 1.4553; known, 1.4567) and the characteristic smell appears to be carane (IV). It is to be mentioned that the present synthesis constitutes the first total synthesis of a bicyclic compound of the carane series.

P. C. GUHA.

D. K. SANKARAN.

Department of Organic Chemistry,
Indian Institute of Science,
Bangalore,
May 3, 1938.

Rottlerin—Part IV.

IN Part III, we have advocated the view that rottlerin is best represented by the formula $C_{31}H_{30}O_8$ containing five hydroxyl groups which are methylated by dimethyl sulphate and potassium bicarbonate in acetone solution. Since then, McGookin, Percival and Robertson¹ have stated that all their previous published data are equally explainable on the basis of $C_{30}H_{28}O_8$ (pentahydroxy) formula as against $C_{33}H_{30}O_9$ (hexahydroxy) formula which they once considered to be possible.² Although it is difficult to pronounce a final opinion on this question, yet our results, notably the oxide and the nitrosite, are best explained on the basis of a C_{31} formula for rottlerin. Hoffmann and Fari³ advocated a C_{31} formula mainly on the analysis of the sodium salt. Therefore, the present indications are that probably rottlerin is C_{31} but as we have already mentioned this question will not be solved finally before more data accumulates.

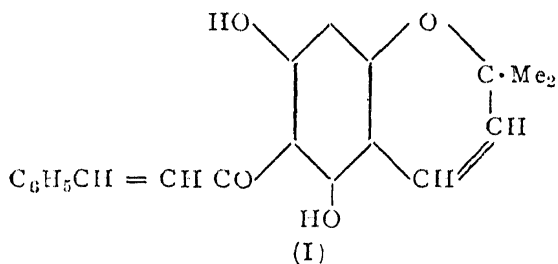
Robertson *et al*¹ described a substance $C_{20}H_{18}O_4$ obtained by the alkaline hydrolysis (barium hydroxide) of rottlerin, which they called rottlerone. We found⁴ that the hydrolysis of tetrahydrorottlerin with aqueous alcoholic hydrochloric acid gave a substance $C_{20}H_{22}O_4$ ($\pm 1 CH_2$) which we suggested might be identical with tetrahydrorottlerone described by Robertson *et al*. We have now methylated our product and find it to be so. In this connection we wish to state that this substance $C_{20}H_{22}O_4$ is obtained in a much greater yield by the acid hydrolysis described by us (3.2 g. from 8.0 g. of tetrahydrorottlerin) whilst Robertson *et al* obtained 5 to 6 gr. from 20 g. of tetrahydrorottlerin by the sodium hydroxide hydrolysis. Under the following conditions, the yield stated above can be easily obtained.

Tetrahydrorottlerin (8 g.) in alcohol (400 c.c.), hydrochloric acid (d. 1.14, 80 c.c.) and water (40 c.c.) was heated for 26 hours. The substance was obtained by filtering the mixture hot as an insoluble powder which crystallised from ethyl acetate. If in the above experiment the reaction mixture is cooled and diluted after 8 hours heating, a light brown substance is precipitated which is soluble in sodium bicarbonate and behaves like an unstable acid. Owing to the ease of decomposition, it has not been possible to get it in a pure form but it is certain that it is an acid and also this very substance

¹ J.C.S., 1935, 478.

in alcoholic hydrochloric acid solution on further heating becomes converted to tetrahydrorottlerone. This fact is significant and it will not do to ignore it in assigning a structure to rottlerin. Along with this, we have also to remember that rottlerin is never recovered completely back from its alkaline solution indicating some kind of lactonic or ester linking.

Robertson *et al* have advanced the formula (I) for rottlerone.

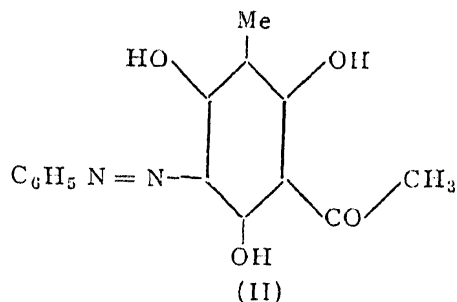


We are unable to subscribe to this view on the following grounds:—

(a) We could not get any evidence of a ketonic group in tetrahydrorottlerone methyl ether.

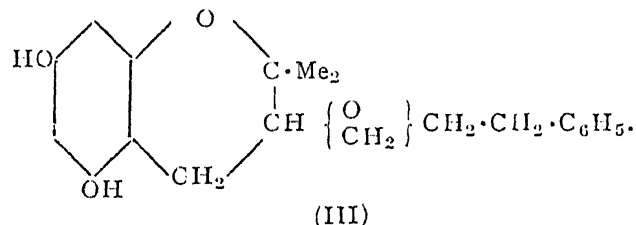
(b) We obtained no indications of the formation of pyrrilium salt when tetrahydrorottlerone methyl ether was saturated with hydrogen chloride at 0° in ether solution along with salicylaldehyde.

Robertson *et al* have suggested a tentative formula for rottlerin in which an additional CO·CH₃ has been postulated in the second part of the molecule. This again we consider to be most improbable in view of our failure to get an oxime or a semicarbazone. We have treated pentamethoxy rottlerin and pentamethoxy tetrahydrorottlerin with sodium hypobromite and obtained no indication of the formation of bromoform. Under these circumstances we cannot accept the presence of a CO·CH₃ group. Brockman and Maier⁵ have obtained an azo-derivative (II) by the action of diazobenzene chloride on rottlerin. This would indicate that there exists a CO·CH₃ group in the rottlerin molecule but

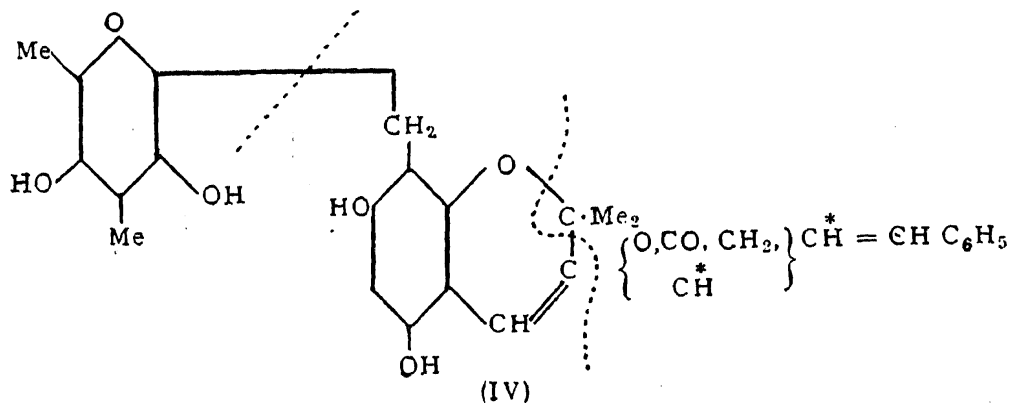


we think that this substance is formed by the simultaneous hydrolysis of the chromene ring and the extrusion of the second half of the rottlerin molecule.

In one experiment we obtained phthalic acid as one of the products when we oxidised methyl ether of rottlerin with chromic acid but the exact conditions were not known and since then we have failed to repeat this experiment. If phthalic acid is an oxidation product, it can only be indirectly formed. Therefore we are inclined to remove the group Ph·CH = CH·CO of Robertson's formula (I) from the phloroglucinol ring and place it adjacent to the chromene ring. Moreover in absence of any proof for the existence of the CO group we are inclined to think that there is a lactonic grouping in association with the chromene ring. Therefore, we suggest tentatively that tetrahydrorottlerone has an arrangement similar to III.

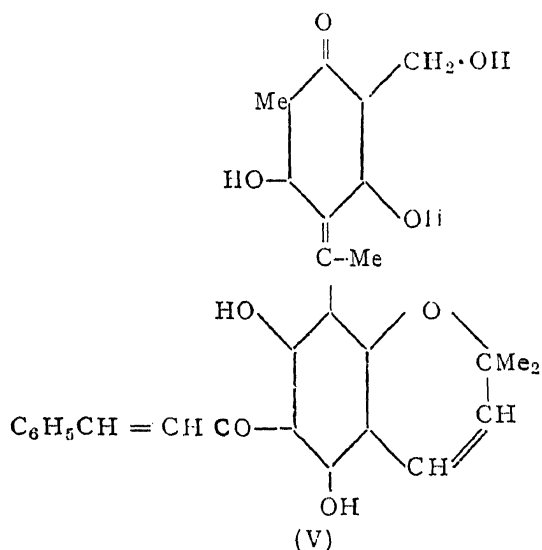


The analytical data (C and H values) for the methyl ether of tetrahydrorottlerone agrees with a trimethyl ether but difficulties are experienced in the formulation of the acetyl derivative. In our opinion the part in bracket arises from the opening up of a lactone ring and we think that rottlerin has an arrangement similar to (IV). If ultimately



rottlerin is proved to be C_{30} then the CH and H marked with * will have to be taken off from the formula. The product (II) of Brockman is formed by scission along the dotted lines.

Prof. Robinson, to whom we wrote about the rottlerin problem, has very kindly suggested to us in a letter dated 23rd April 1938 the following as the probable constitution (V) of rottlerin based mainly on the rottlerone work of Robertson.



We are engaged in testing the validity of the formula so kindly suggested by Prof. Robinson.

K. S. NARANG.
J. N. RAY.
B. S. ROY.

The University,
Lahore,
May 7, 1938.

¹ *J.C.S.*, 1938, 309.

² *Ibid.*, 1937, 748.

³ *Arch. Pharm.*, 1933, 99.

⁴ *J.C.S.*, 1937, 1862.

⁵ *Naturwiss.*, 1937, 460.

The Chemotherapy of Tuberculosis.

THE recent discovery of the specific action of Prontosil (I), sulphanilamide (II) and the diacetyl derivative of 4:4'-diaminodiphenyl sulphone (III) in infections due to the *cocci* and other bacteria¹ led the present author to try some of the derivatives of the above compounds in the case of tuberculosis also. The general procedure adopted is to react the amino-groups of the compounds (I), (II) and (III)—as such

and also their derivatives—with allyl mustard oil to yield compounds (with allylthiourea groupings) resembling 'lopion' (the gold salt of IV) which is known to be least toxic and not deranging the kidneys.

Thus *para*-aminobenzene sulphonamide (II), *para*-aminocinnamic acid, *para*-amino mandelic acid and 4:4'-diaminodiphenylsulphon (III), yielded the corresponding allylthiourea derivatives with allyl mustard oil. Sulphanilic acid, however, did not undergo a similar condensation. It furnished with *p*-acetaminobenzenesulphonic chloride in alkaline solution *p*-acetaminobenzene sulphonamino benzene sulphonic acid (V) which was hydrolysed to the corresponding amine and the latter with allyl mustard oil yielded the allylthiourea derivative.

Prontosil (I) condensed with allyl-mustard oil to yield the allylthiourea derivative. Though *meta*- and *para*-phenylenediamines yield only monothioureas with one molecule of potassium thiocyanate, it has now been found that even with one molecule of allyl mustard oil the above diamines furnished almost exclusively phenylene di-allylthioureas. However *m*- and *p*-acetphenylenediamines condensed with allyl mustard oil to the corresponding acetaminophenyl allylthiourea derivatives (VI) which were hydrolysed with hydrochloric acid (6N) to the corresponding hydrochlorides of aminophenyl allylthioureas (VII). Of these, the *meta*-isomer coupled with diazotised *p*-aminosulphanilamide to yield the dyestuff (VIII) related to prontosil (*vide* preparation from prontosil), while the *para*-isomer did not undergo a similar coupling. *p*-aminocinnamic acid also failed to couple with diazotised *p*-sulphanilamide while 4-aminothiouracil with the same reagent yielded the dyestuff (IX). Similar dyes are being prepared by using the compound (III) in place of (II) in the above reactions.

