

2. Titrimetrically, the enol content of this substance is found to be 39.2% and spectrometrically 36–37%, therefore materially higher than for α -alkyl acetoacetic esters.

3. For α -phenylacetoacetic ester, in contrast to α -alkylacetoacetic ester, the direct bromine titration is just as applicable as the indirect bromine titration.

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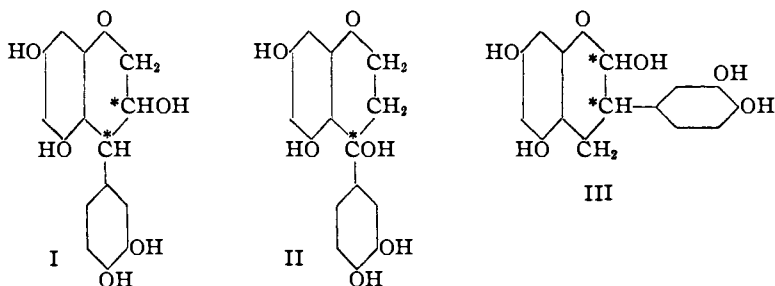
STEREOISOMERIC CATECHINS

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Six stereoisomers are to be expected from acacatechin (I) and three from iso-acacatechin (II), but so far only four have been identified in Nature, namely, *l*- and *dl*-acacatechin and *l*- and *dl*-iso-acacatechin.



The present communication describes two new stereoisomeric catechins, *d* acacatechin and *d*-iso-acacatechin. *d*-Acacatechin accompanied by *dl*-acacatechin was found in mahogany wood from South America and the West Indies and in the Australian Kinos from *Eucalyptus viminalis*, Lab., *E. Leucosylon*, Müll. and *Angophora intermedia* D. C., whereas *d*-iso-acacatechin only was identified in the heartwood of *Anarcadium occidentale*, L. Of the other plant materials investigated in the course of the present work, the Malabar Kinos from *Myristica Malabarica*, Larn. and *Pterocarpus Marsupium*, Roxb., and the Australian Kino from *Eucalyptus corymbosa*, Smith, were found to contain *l*-acacatechin and *dl*-acacatechin, whilst Chinese rhubarb, Guarana paste, Kola nuts and the leaves of *Uncaria gambir*, Roxb. and of *Uncaria acida*, Roxb. all contain *d*-gambir-catechin and *dl*-gambir-catechin.

The investigation, in view of their red-brown color suggesting the presence of catechin, was also extended to the following plant materials: oak

bark,¹ chestnut bark, quebracho wood, hemlock bark, almond skins and cured Virginian and Rhodesian tobacco. None of these materials, however, was found to contain catechin.

The identification of *d*-iso-acacatechin in Nature completes the iso-acacatechin (II) series, whereas the discovery of *d*-acacatechin (I) still leaves three more stereoisomeric acacatechins to be accounted for, since they cannot, with any degree of certainty, be identified with *d*- and *dl*-gambir-catechin.²

Whatever the interrelationship between gambir-catechin and acacatechin may prove to be, the chemistry of catechin is faced with the fact that *eight* catechins have now been identified in Nature. This, in our opinion, finally disproves the contention that all catechins are stereoisomerides of one and the same parent substance containing *two* asymmetric carbon atoms, as postulated by Freudenberg's³ hypothesis, already criticized⁴ on other grounds.

On the other hand, if one assumes that gambir-catechin is represented by Formula III, as evident from the work of Drumm, Carolan and Ryan,⁵ one realizes that *fifteen* catechins are theoretically possible, namely, six stereoisomeric acacatechins (I), three stereoisomeric iso-acacatechins (II) and six stereoisomeric gambir-catechins (III). So far only eight catechins have been identified, which still leaves seven more to be accounted for, and it is proposed to continue the work in this direction. Meanwhile reference is made to a suggestion put forward over a hundred years ago by Nees von Esenbeck,⁶ to reserve the name catechin for the substance present in the cutch of *Acacia Catechu* and to refer to the corresponding product present in the cutch of *Nauclea* (syn. *Uncaria*) *gambir* as nauclein. It is perhaps now too late to adopt this suggestion, but there is not the slightest doubt whatever that if catechin and nauclein had been dealt with separately much confusion would have been avoided. In this connection attention must be drawn to the definite line of demarcation between the occurrence of aca- and iso-acacatechin on the one hand and gambir-

¹ Casparis, *Pharm. Acta Helv.*, **4**, 181, 189 (1929), found a catechin-like substance in oak bark. This, however, has not been confirmed by Freudenberg and Oehler, *Ann.*, **483**, 140 (1930), who are of the opinion that Casparis had mistaken ellagic acid for catechin.

² See Freudenberg and Cohn, *Ber.*, **56**, 2127 (1923); Freudenberg, Carrara and Cohn, *Ann.*, **446**, 87 (1925); Carrara and Cohn, *Gazz. chim. ital.*, **56**, I, 134 (1926); Baker, *J. Chem. Soc.*, 1593 (1929); Drumm, Carolan and Ryan, *Proc. Royal Irish Acad.*, [B] **39**, 114 (1929).

³ Freudenberg, Böhme and Beckendorff, *Ber.*, **54**, 1204 (1921); Freudenberg, Böhme and Purrmann, *ibid.*, **55**, 1734 (1922); Freudenberg and Purrmann, *Ann.*, **437**, 274 (1924).

⁴ Hüchel, Neunhöffer, Gercke and Frank, *ibid.*, **477**, 159 (1929).

⁵ Drumm, Carolan and Ryan, *Proc. Royal Irish Acad.*, [B] **39**, 114 (1929).

⁶ Nees von Esenbeck, *Büchner's Report*, **33**, 171 (1829).

catechin on the other, although it must be noted that Freudenberg and Oehler⁷ report the presence of *l*-acacatechin and *d*-gambir-catechin in the Kola nut, a point not confirmed by us, since we only found *d*- and *dl*-gambir-catechin in the material investigated by us, and also in a specimen of Kola nut catechin kindly sent us by Dr. Ultée.

Historical

Some of the materials investigated by us have already been studied by previous workers. Thus mahogany wood was found by Latour and Caseneuve⁸ to contain a catechin-like substance, and this was confirmed by Freudenberg, Böhme and Purrmann,⁹ who showed it to be dextro-rotatory.

Catechin-like substances were also found in the Kinos of *Eucalyptus viminalis* and *Eucalyptus Leucoxyton* by Heckel and Schlagdenhauffen,¹⁰ whereas Maiden¹¹ and Smith¹² reported the presence of such substances in the Kinos of *Angophora intermedia* and *Pterocorpus Marsupium*, respectively.

The catechin in Chinese rhubarb was investigated by Gilson,¹³ who proved it to be *d*-gambir-catechin. This was confirmed by Freudenberg, Böhme and Purrmann,⁹ and now also by us. As regards the presence of catechin in Guarana paste, it must be noted that Kirmsse¹⁴ and Freudenberg and his collaborators¹⁵ have investigated it with no definite success, and similar indefinite results were obtained by Goris¹⁶ and Goris and Fluteaux,¹⁷ and by Casparis¹⁸ in the case of the Kola nut. The results of Freudenberg and Oehler on the catechins present in the Kola nut have already been mentioned.

Experimental

The Kinos, the Guarana paste and the different kinds of wood, in the form of sawdust, were exhaustively extracted with ethyl acetate in a large Soxhlet apparatus. The Kinos and the Guarana paste were finely powdered, passed through a 30-mesh sieve and mixed with ten times their own weight of sand.¹⁹ The ethyl acetate extracts were evaporated to dryness under

⁷ Freudenberg and Oehler, *Ann.*, **483**, 140 (1930).

⁸ Latour and Caseneuve, *Ber.*, **8**, 828 (1875); *Arch. Pharm.*, **208**, 558 (1876).

⁹ Freudenberg, Böhme and Purrmann, *Ber.*, **55**, 1743 (1922).

¹⁰ Heckel and Schlagdenhauffen, *J. pharm. chim.*, [5] **26**, 152 (1892).

¹¹ Maiden, *Pharm. J.*, [3] **20**, 27 (1890).

¹² Smith, *Am. J. Pharm.*, **68**, 676 (1896).

¹³ Gilson, *Acad. méd. belg.*, [4] **16**, 827 (1902).

¹⁴ Kirmsse, *Arch. Pharm.*, **236**, 122 (1898).

¹⁵ Freudenberg, Böhme and Purrmann, *Ber.*, **55**, 1744 (1922).

¹⁶ Goris, *Compt. rend.*, **144**, 1162 (1907).

¹⁷ Goris and Fluteaux, *Bull. soc. pharmacol.*, **17**, 599 (1910).

¹⁸ Casparis, *Pharm. Acta Helv.*, **4**, 181, 189 (1929).

¹⁹ The sand used was at first treated with dilute hydrochloric acid, then washed with water, alcohol and ether. It was then dried at 100° and powdered.

reduced pressure and the remaining solid powdered and mixed with ten times its own weight of sand. It was then extracted in a Soxhlet apparatus with ether free from alcohol. Extraction was continued until no solid was obtained on evaporation of the ether. The solids obtained on evaporation of the ether were dissolved in hot water slightly acidulated with acetic acid,²⁰ and the solid collected after standing for some time, when as a rule the *dl*-forms separated first. The catechin fractions thus obtained were recrystallized from water, dried in a vacuum desiccator over concentrated sulfuric acid for several days and acetylated by heating with acetic anhydride. The solid obtained on precipitation with water crystallized from alcohol and a few drops of acetone. The filtrates of the crude catechins were evaporated by standing over concentrated sulfuric acid, the solids thus obtained were then powdered and mixed with sand, again extracted with ether and worked up in the manner described above. The aqueous filtrates were then again solidified and examined in the same way. It was generally found that these third solids contained little or no catechin.

In the case of the leaves of the *Uncaria* species and the Chinese rhubarb, no ethyl acetate extractions were carried out, but the materials were at first exhaustively extracted in a Soxhlet apparatus with chloroform so as to remove chlorophyll, and in the case of Chinese rhubarb chrysophanic acid and such-like substances. The removal of chrysophanic acid from Chinese rhubarb was very tedious, and required continuous extraction for nearly two months. After the extraction with chloroform, the leaves and rhubarb were powdered in a mill and extracted with ether as described. In the case of the Kola nut it was also found necessary to subject the finely broken up material to chloroform extraction before extraction with ether.

In the identification of the different catechins, reliance was laid on the pentaacetyl derivatives, which are remarkable for the ease with which they crystallize and for the sharpness of their melting points. Nearly thirty years' experience with catechin has convinced Nierenstein²¹ that very little reliability can be placed on the melting points of the catechins themselves, as these are greatly affected by moisture. This is best illustrated in the case of gambir-catechin,²² which is reported to melt at 96, 175-177 and 210°, respectively, these variations being due to water of crystallization. In a similar manner, Nierenstein²³ has come to the conclusion that not much confidence can be attached to the melting points of the methoxy derivatives if prepared in the usual way by the action of dimethyl sulfate

²⁰ Nierenstein, *J. Chem. Soc.*, 121, 609 (1922).

²¹ Nierenstein, *J. Indian Chem. Soc.*, 7, 279 (1930).

²² See Kostanecki and Tambor, *Ber.*, 35, 1867 (1902); Clauser, *ibid.*, 36, 101 (1903); Perkin, *J. Chem. Soc.*, 87, 398 (1905).

²³ Nierenstein, *THIS JOURNAL*, 48, 1964 (1926); 52, 4012 (1930).

and alkali, since these derivatives are generally contaminated with by-products, formed through fission of the chromane ring. The following summary gives the melting points and rotations in tetrachloroethane of the pentaacetyl derivatives as used by us as evidence of identity and purity.

	M. p., °C.	$[\alpha]_D$
Pentaacetyl- <i>l</i> -acacatechin	151	-12.0°
Pentaacetyl- <i>d</i> -acacatechin	151	+12.0°
Pentaacetyl- <i>dl</i> -acacatechin	160
Pentaacetyl- <i>l</i> -iso-acacatechin	171	-29.3°
Pentaacetyl- <i>d</i> -iso-acacatechin	171	+29.3°
Pentaacetyl- <i>dl</i> -iso-acacatechin	193	...
Pentaacetyl- <i>d</i> -gambir-catechin	137	+37.6°
Pentaacetyl- <i>dl</i> -gambir-catechin	156	...

As a check on our melting points of pentaacetyl-*dl*-acacatechin and pentaacetyl-*dl*-iso-acacatechin obtained from the naturally occurring *dl*-catechins, these pentaacetates were also prepared by admixture of equal parts of pentaacetyl-*l*-acacatechin with pentaacetyl-*d*-acacatechin and of pentaacetyl-*l*-iso-acacatechin with pentaacetyl-*d*-iso-acacatechin. These synthetic pentaacetates proved to be in every respect identical with the pentaacetates of natural origin. Unfortunately, no such check could be carried out on pentaacetyl-*dl*-gambir-catechin, as only pentaacetyl-*d*-gambir-catechin has so far been identified in Nature.

In the identification of the different pentaacetyl derivatives, we strongly adhered to the constants given above. Where lower melting points or lower rotations were observed, the products were repeatedly recrystallized until these constants were reached. In this we have succeeded in every case. With the single exception of pentaacetyl-*d*-iso-acacatechin, which has so far only been found in *Anarcadium occidentale*, mixed melting points were taken, and in no case could depressions be observed. All the pentaacetates, dried at 110°, were analyzed in duplicate and were found to agree within the limits of experimental error for $C_{15}H_9O_6(COCH_3)_5$.

We append the following summary showing the quantities of material investigated and the approximate yields of the different catechins obtained.

- (1) 56 Kilos mahogany wood from South Africa: 12 g. *d*-acacatechin and 3.5 g. *dl*-acacatechin
- (2) 42 Kilos mahogany wood from the West Indies: 6 g. *d*-acacatechin and 6 g. *dl*-acacatechin
- (3) 8 Kilos Australian Kino from *Eucalyptus viminalis*: 16 g. *d*-acacatechin and 22 g. *dl*-acacatechin
- (4) 6 Kilos Australian Kino from *Eucalyptus Leucoxydon*: 5 g. *d*-acacatechin and 10 g. *dl*-acacatechin
- (5) 9 Kilos Australian Kino from *Angophora intermedia*: 14 g. *d*-acacatechin and 8 g. *dl*-acacatechin
- (6) 86 Kilos heartwood of *Anarcadium occidentale*: 29 g. *d*-iso-acacatechin

- (7) 4 Kilos Malabar Kino from *Myristica Malabarica*: 3 g. *l*-acacatechin and 11 g. *dl*-acacatechin
- (8) 7 Kilos Malabar Kino from *Pterocarpus Marsupium*: 9 g. *l*-acacatechin and 17 g. *dl*-acacatechin
- (9) 6 Kilos Australian Kino from *Eucalyptus corymbosa*: 4 g. *l*-acacatechin and 9 g. *dl*-acacatechin
- (10) 28 Kilos *Uncaria gambir* leaves: 56 g. *d*-gambir-catechin and 6 g. *dl*-gambir-catechin
- (11) 2.8 Kilos *Uncaria acida* leaves: 9 g. *d*-gambir-catechin and 4.5 g. *dl*-gambir-catechin
- (12) 11 Kilos Chinese rhubarb: 17 g. *d*-gambir-catechin and 3 g. *dl*-gambir-catechin
- (13) 2 Kilos Guarana paste: 5 g. *d*-gambir-catechin and 4 g. *dl*-gambir-catechin
- (14) 19 Kilos Kola nuts: 58 g. *d*-gambir-catechin and 8 g. *dl*-gambir-catechin

In conclusion, the authors wish to express their thanks to the Colston Research Society of the University for many generous grants, without which this investigation would not have been possible.

Summary

Eight stereoisomeric catechins have been shown to exist in Nature, of which *d*-acacatechin and *d*-iso-acacatechin have been discovered in the course of the present investigation.

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[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE OHIO STATE UNIVERSITY]

NUCLEAR SYNTHESSES IN THE OLEFIN SERIES.

II. 1,4-DIOLEFINS¹

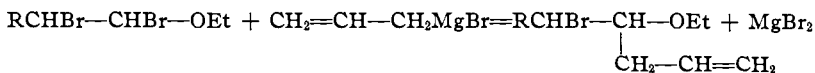
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The nuclear synthesis of unsaturated hydrocarbons previously described³ has been extended to the synthesis of 1,4-diolefins. This extension has been made possible through the preparation of allylmagnesium bromide by the method described by Gilman and McGlumphy.⁴

The addition of an α,β -dibromoalkyl ethyl ether to a slight excess of allylmagnesium bromide in ether solution leads to the formation of an α -allyl- β -bromoalkyl ethyl ether. It has been found in general that β -bromo



¹ Presented before the Organic Division of the American Chemical Society, at Atlanta, Georgia, April, 1930.

² Abstracted from the dissertation presented by Bernard H. Shoemaker in partial fulfillment of the requirements for the Ph.D. degree to the Faculty of the Graduate School of The Ohio State University, June, 1930.

³ Dykstra, Lewis and Boord, *THIS JOURNAL*, **52**, 3396 (1930).

⁴ Gilman and McGlumphy, *Bull. soc. chim.*, [4] **43**, 1322 (1928).