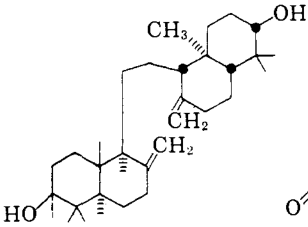
acetone–water[5] for fifteen hours at room temperature to the *dl*-acetoxyketoacid (VIII) m.p. 238–240° (found: C, 65.50; H, 8.19), hydrolyzed to the *dl*-hydroxy acid (IX) m.p. 186–187° (found: C, 67.09; H, 8.97). Resolution was effected at this point by transformation of IX into the *dl*-methyl ester-half phthalate (X) m.p. 209–210° (found: C, 66.80; H, 7.15) by treatment with diazomethane and then phthalic anhydride in pyridine. Strychnine produced an acetone insoluble salt, m.p. 225–227°, cleaved by ethyl acetate–10% hydrochloric acid to the half phthalate (+X) m.p. 185–187° $[\alpha]^{\mathrm{CHCl_3}}_{\mathrm{D}}$ + 23.5° which was hydrolyzed to the hydroxyketoacid (+IX) m.p. 174–176°, $[\alpha]^{\mathrm{CHCl_3}}_{\mathrm{D}}$ + 59.4° (found: C. 67.05; H, 8.95). The *acetone soluble* strychnine salt similarly gave the half phthalate (−X) m.p. 188–190°, $[\alpha]^{\mathrm{CHCl_3}}_{\mathrm{D}}$ − 23.5°, hydrolyzed to the hydroxyketoacid (−IX), m.p. 171–173°, $[\alpha]^{\mathrm{CHCl_3}}_{\mathrm{D}}$ − 57.8° (found: C, 67.22; H, 9.15).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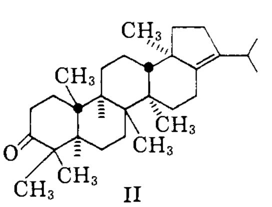
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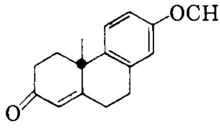
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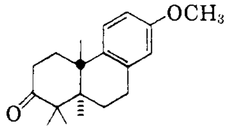
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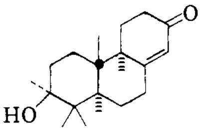
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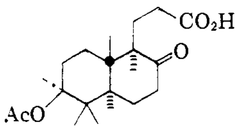
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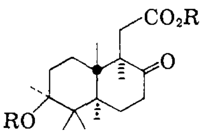

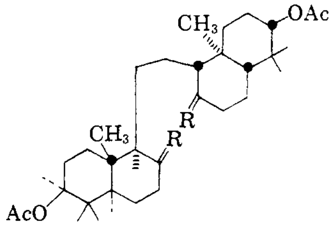

VIII, R = Ac, R′ = H

IX, R, R′ = H

X, R = $\mathrm{HO_2C{-}C_6H_4{-}\overset{O}{\overset{\|}{C}}{-}}$, R′ = $\mathrm{CH_3}$

XI, R = O

XII, R = $\mathrm{CHCO_2C_2H_5}$

The acid (−IX) on Kolbe electrolysis (platinum electrodes, methanol, trace of methoxide at 50°), followed by acetylation gave (29%) the diacetoxy dione (XI), m.p. 165–166°, $[\alpha]^{\mathrm{CHCl_3}}_{\mathrm{D}}$ − 33.9° (found: C, 72.31; H, 9.48), identical in all respects with the known substance[1] from the ozonolysis of α-onocerin diacetate (I). Reaction of the dione with ethoxyacetylenemagnesium bromide, followed by treatment with 10% methanolic–sulfuric acid at room temperature produced (35%), the di-α,β-unsaturated ester (XII) m.p. 154–155°, $\lambda^{\mathrm{EtOH}}_{\mathrm{max}}$ 224 mμ, log ε 4.60 (found: C, 71.85; H, 9.23). Hydrolysis with 10% methanolic potassium hydroxide, and then refluxing with copper chromite in quinoline for one hour and reacetylation led (30%) to α-onocerin diacetate, m.p. 220–221°, $[\alpha]^{\mathrm{CHCl_3}}_{\mathrm{D}}$ + 29.8° (found: C, 77.70; H, 10.39). This was completely identical with the diacetate of natural α-onocerin (infrared, mixed melting point).

We wish to thank Mr. Melvin Deutsch for his preparation of considerable amounts of the tricyclic ketone III used in this work and Professor F. Sondheimer for his constructive suggestions during the last stages of this synthesis.

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RECEIVED AUGUST 24, 1959

(5) R. Pappo and A. Becker, *Bull. Res. Council Israel*, **5A**, 300 (1956); F. Sondheimer and R. Mechoulam, private communication.

PROTONATION OF FERROCENE BY STRONG ACIDS[1]

Sir:

Although the course of Friedel–Crafts acylation reactions involving ferrocene is in general analogous to that encountered with benzenoid aromatics, certain aspects of these transformations are exceptional. Thus, when equimolar quantities of ferrocene, acyl halide and aluminum chloride are employed, monoacylferrocenes are formed to the virtual exclusion of 1,1′-diacylferrocenes. These results require that the rate constant for the first acylation step (k_1) be significantly greater than that for the second step (k_2). When, however, acylation is carried out with an excess of aluminum chloride, the major products are instead the 1,1′-diacylferrocenes. Broadhead, Osgerby and Pauson[2] have attributed these latter results to an inhomogeneity of the reaction medium. We have been unable to detect, by filtration, any significant inhomogeneity in these solutions. Neither are the products interconverted under the reaction conditions.

We suggest that these results are best accounted for in terms of the *effective* removal of ferrocene from the reaction through formation of a relatively stable, non-acylable complex salt with aluminum chloride and hydrogen chloride. These observations, derived from the results of several carefully controlled acetylations (Table I), support this conclusion.

The apparent ratio of rate constants (k_2/k_1)[3] increases as reaction proceeds to completion and hydrogen chloride is generated (compare expts. 1 and 2). Prior saturation of the reaction solution with hydrogen chloride results in a marked

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(1) This investigation was supported by a research grant (RG-4772) from the National Institutes of Health, Public Health Service.

(2) G. D. Broadhead, J. M. Osgerby and P. L. Pauson, *J. Chem. Soc.*, 650 (1958).

(3) Calculated from the expression derived by W. G. McMillan, THIS JOURNAL, **79**, 4838 (1957), for second order competitive consecutive processes.

TABLE I

Expt.[a]	Reaction time, min.	Mole % acetyl chloride consumed	Mole % material recovered	Acetyl-ferrocene, g.	Diacetyl-ferrocene, g.	k_2/k_1 (apparent)
1[b]	150	72.6	72	0.090	0.480	10.9
2[c]	12	62.5	86	0.546	0.131	0.45
3[d]	150	84.0	85	1.034	None	0
4[e]	150	22.8	87	0.120	0.095	6.8
5[f]	150	92.1	91	0.660	0.280	0.40

[a] All reactions were carried out at 0°, in methylene chloride, employing one gram of ferrocene and a mole ratio of $AlCl_3$:AcCl:ferrocene of 2:1:1. [b] Average of three runs. [c] Average of two runs. [d] Reaction run under conditions of tenfold dilution. [e] Solution saturated with hydrogen chloride prior to addition of reactants; average of two runs. [f] Magnesium amalgam added prior to addition of reactants.

reduction in the mole per cent. of acyl halide consumed (compare expts. 4 and 1), while the apparent rate constant ratio is abnormally large considering the extent of reaction (compare expts. 4 and 2). Conversely, initial addition of amalgamated magnesium leads to consumption of the hydrogen chloride generated, with a consequent reduction in the apparent value of k_2/k_1 (expt. 5). The expected effect of dilution on the equilibrium concentration of the complex salt and consequently on the course and extent of reaction is well illustrated in experiment 3.

The complex salt has been isolated as a pale green solid (dec. *ca.* 125°), by precipitation with ligroin, from methylene chloride solutions. [*Anal.* Calcd. for $(C_{10}H_{10}Fe\cdot HAlCl_4)_n$: ferrocene, 52.5; Al, 7.6. Found: ferrocene, 54.0; Al, 8.1; neut. equiv., 89. Found: 86.] Decomposition of the substance with water regenerates ferrocene, accompanied by small amounts of the ferricinium cation, to which impurity the salt owes its green color.

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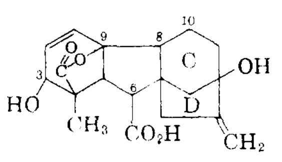
RECEIVED AUGUST 12, 1959

THE STEREOCHEMISTRY OF GIBBERELLIC ACID

Sir:

The revised structure I has been demonstrated recently for gibberellic acid by Cross, *et al.*[1] We wish to report work which extends our previous results[2] on the stereochemistry of allogibberic acid (II) to that of gibberellic acid itself.



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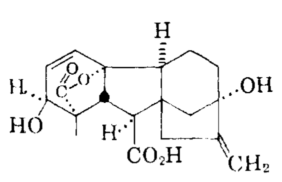

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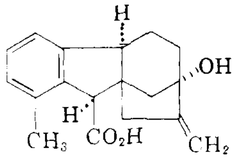

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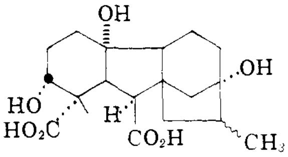

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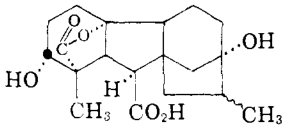

IV

1. **The Lactone Ring.**—Its relationship to the β-oriented two carbon bridge of ring D follows from the demonstration that the lactone is α-oriented. Tetrahydrogibberellic acid, m.p. 273–275° (reported[3] m.p. 273–274°), was hydrolyzed at room temperature for eighteen hours with 20% sodium hydroxide solution. This resulted in a diacid (III), the dimethyl ester of which, m.p. 185–187° (found: C, 63.60; H, 8.32), has $[\alpha]^{EtOH}_D$ − 40.3°. Refluxing the diacid for two hours with ethyl acetate containing a drop of concentrated hydrochloric acid gave a lactonic acid (IV) isomeric with tetrahydrogibberellic acid. IV had m.p. (285) 293–295° and gave a methyl ester, m.p. (185) 196–200°, $\gamma^{CHCl_3}_{max}$ 5.7, 5.8 μ (found: C, 66.15; H, 7.72), $[\alpha]^{EtOH}_D$ + 34.4°. The lactonic acid (IV) *has the same lactone ring system as gibberellic acid:* oxidation of methyl gibberellate with managanese dioxide gave the corresponding ketone, m.p. 186–188.7°, λ^{EtOH}_{max} 228 mμ (7500) (found: C, 66.72; H, 6.05). Reduction of the unsaturated ketone with platinum oxide in acetic acid gave a substance identical (infrared, mixed melting point) with V-methyl ester. This establishes that V differs from tetrahydrogibberellic acid *only* at the C_3 secondary hydroxyl. The large positive rotation difference between the lactonic ester V and the conformationally related diester III establishes the α-orientation of the lactone ring.[4]

2. **The C_5 Hydrogen.**—This hydrogen must be β-oriented for the following reason: Should the C_5 hydrogen be α, C_6 would be axial to ring A and the C_6 carboxyl group, which is known to be β,[2] would have the less stable of the two possible orientations. Base hydrolysis of the *methyl ester* of tetrahydrogibberellic acid followed by relactonization gave the same 3-epitetrahydrogibberellic acid (IV) obtained from hydrolysis of the acid itself. Since IV has the original orientation of the carboxy group, no epimerization has taken place and C_6 must be equatorially linked to ring A.

3. **The C_3 Hydroxyl.**—Our observation (*vide supra*) that the 3-epi configuration of IV is formed on catalytic hydrogenation of the 3-ketone from gibberellic acid implies α-stereochemistry for the 3-epi series (adsorption from the β-side, *trans* to the lactone). Consequently, gibberellic acid must have a 3-β-hydroxyl. The same conclusion is reached[5] by noting that the base epimerization at C_3 must imply axial → equatorial transformation (presumably *via* dealdolization–realdolization).

4. **The C_8 Hydrogen.**—The α-oriented C_1 hydrogen of allogibberic acid (II) is not the same as the original C_8 hydrogen of gibberellic acid: Transformation of I into II with hydrogen chloride in

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(1) B. E. Cross, J. F. Grove, J. MacMillan, J. S. Moffatt, T. P. C. Mulholland, J. C. Seaton and N. Sheppard, *Proc. Chem. Soc.*, in press.

(2) G. Stork and H. Newman, THIS JOURNAL, **81**, 3168 (1959).

(3) Y. Sumiki, A. Kawarada, H. Kitamura, Y. Seta and N. Takahashi, Abstract No. 460 in F. H. Stodola, "Source Book on Gibberellin 1828–1957," U. S. Dept. of Agriculture, 1958.

(4) W. Klyne, *Chem. and Ind.*, 1198 (1954).

(5) B. E. Cross, J. F. Grove, J. MacMillan, T. P. Mulholland and N. Sheppard, *Proc. Chem. Soc.*, 221 (1958).