chloride (82 μM.) was isolated and crystallized as described before.[9] *Melting point:* 180–184° (authentic sample of L-glutamic acid HCl 184–188°; mixed m.p. 182–186°). *Anal.* Calcd. for $C_5H_9O_4N$ HCl: C, 32.71; H, 5.49; N, 7.63. Found: C, 32.91; H, 5.39; N, 7.67. $[\alpha]^{20}D = +31.7°$. Specific activity was calculated to be 1430 c.p.m. and 1560 c.p.m. on the basis of ninhydrin and enzymatic assays (see below), respectively (original specific activity of KA, 2460 c.p.m.). Further evidence for the identity was provided by paper chromatography[10] after and before enzymatic decarboxylation by L-glutamic decarboxylase.[11]

Preliminary experiments with KA-2-C^{14}, carboxyl-labeled KA and KA-9-C^{14} [12] indicated that glutamic acid is probably derived from the carboxyl carbon and carbon 2, 3, 4 and 10. Further studies are now in progress in order to identify other products and intermediate steps.

(9) H. Tabor and O. Hayaishi, *J. Biol. Chem.*, **194**, 171 (1952).

(10) Paper chromatographic analysis was carried out with three different solvent systems and examined with an automatic scanner and ninhydrin spray. The isolated material before and after enzymatic decarboxylation gave exactly the same R_f values as those of authentic samples of L-glutamic acid and γ-aminobutyric acid, respectively. R_f values for glutamic acid and γ-aminobutyric acid were as follows: 0.28 and 0.63 (butanol–acetic acid–water, 4:1:1), 0.15 and 0.56 (water saturated phenol), 0.35 and 0.52 (ethanol–ammonia–water, 18:1:1), respectively. DL-γ-Hydroxyglutamic acid, kindly furnished from Dr. T. Kaneko, gave R_f values of 0.14, 0.07 and 0.29, respectively.

(11) O. Schales, V. Mims and S. S. Schales, *Arch. Biochem.*, **10**, 455 (1946).

(12) KA-2-C^{14} and KA-9-C^{14} were synthesized from DL-tryptophan-2-C^{14} and DL-tryptophan-7α-C^{14}, respectively, as described above. The latter compound was a generous gift of Dr. M. Rothstein of University of California. Carboxyl-labeled KA was kindly furnished by Dr. J. M. Price of the University of Wisconsin.

DEPARTMENT OF MEDICAL CHEMISTRY
KYOTO UNIVERSITY
FACULTY OF MEDICINE
KYOTO, JAPAN

OSAMU HAYAISHI
HIROSHI TANIUCHI
MINORU TASHIRO
HIROMI YAMADA
SIGERU KUNO

RECEIVED MAY 6, 1959

α-METALLOCENYL CARBONIUM IONS[1,2]

Sir:

The results of the solvolyses reported in Table I demonstrate that α-metallocenyl carbonium ions are remarkably stable. Indeed, the rates indicate that these α-metallocenyl cations are of the same order of stability as the triphenylmethyl cation. Qualitative observations such as the solubility of ferrocenecarboxaldehyde in dilute hydrochloric acid[3] and the facile conversion of phenylferrocenylcarbinol to the corresponding methyl ether by refluxing aqueous methanol[4] previously have implied a high order of stability for such ions.

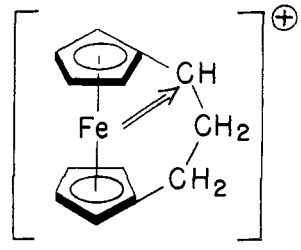
That these solvolyses indeed proceeded by alkyl-oxygen fission was conclusively shown by the ethanolysis of III and VI. Each of these acetates produced the corresponding ethyl ether and one mole of acetic acid. The addition of 7.16×10^{-3} M acetate ion reduced the solvolysis rate of III by a factor of nearly five. This was not caused simply by a change in the ionic strength of the medium as the addition of 7.24×10^{-3} M lithium perchlorate had a negligible effect on the solvolysis rate. The common ion rate depression is, therefore, further evidence for alkyl oxygen fission.[5] More importantly the large magnitude of the effect in an 80% acetone–water mixture indicates the intermediacy of an extremely stable ion which is quite selective in its recombination with nucleophiles.[6]

TABLE I[a,b]

		Rel. rate 30° in 80% acetone/water
I	Trityl acetate	1
II	Ferrocenylcarbinyl acetate[c]	0.63
III	Methylferrocenylcarbinyl acetate[d]	6.7
IV	Methylruthenocenylcarbinyl acetate[e]	9.0
V	Methylosmocenylcarbinyl acetate[e]	34
VI	α-Acetoxy-1,1′-trimethyleneferrocene[f]	0.23

[a] The synthesis of all compounds was accomplished by standard methods from known intermediates.[c,d,e,f] Satisfactory analyses were obtained for all acetates. [b] Rates were determined by aliquot titration of the acetic acid produced. The rates followed the first order law faithfully to at least 85% completion. [c] F. S. Arimoto and A. C. Haven, Jr., THIS JOURNAL, **77**, 6295 (1955). [d] P. J. Graham, R. V. Lindsey, G. W. Parshall, M. L. Peterson and G. M. Whitman, *ibid.*, **79**, 3416 (1957). [e] Ref. 7. [f] K. L. Rinehart, Jr., and R. J. Curby, Jr., *ibid.*, **79**, 3290 (1957).

The requirement for coplanarity of the cationic center and the cyclopentadienyl ring is demonstrated by the markedly slower solvolysis rate of the bridged acetate VI (slower by a factor of 132 than the corresponding secondary acetate III). It is to be emphasized, however, that the reaction proceeded by a carbonium ion mechanism as was indicated by the occurrence of alkyl-oxygen fission. This leads us to propose the possibility that this bridged, non-planar ion is stabilized by a direct participation of the iron electrons.



Another interesting feature of the relative rates recorded in Table I is the order of effectiveness of metallocene derivatives of Group VIII metals in stabilizing adjacent carbonium ion centers; ferrocene < ruthenocene < osmocene. This is just the inverse of the order of reactivity of these sub-

(1) Presented in part at the 135th Meeting of the American Chemical Society, Boston, Mass., April 5–10, 1959, *cf.* Abstracts p. 86-O.

(2) This work was supported in part by the National Science Foundation.

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

(4) N. Weliky and E. S. Gould, THIS JOURNAL, **79**, 2742 (1957).

(5) For a general discussion, *cf.*, C. K. Ingold, "Structure and Mechanism in Organic Chemistry," Cornell University Press, Ithaca, N. Y., 1953, p. 360.

(6) C. G. Swain, C. B. Scott and K. H. Lohman, THIS JOURNAL, **75**, 136 (1953).

stances toward electrophilic substitution as judged by ease of acylation[7] and by competitive acetylations.[8] The reactivity order in this case is ferrocene > ruthenocene > osmocene.

CONTRIBUTION NO. 2461
GATES AND CRELLIN LABORATORIES JOHN H. RICHARDS
CALIFORNIA INSTITUTE OF TECHNOLOGY
PASADENA, CALIFORNIA E. ALEXANDER HILL[9]

(7) M. D. Rausch, E. O. Fischer and H. Grubert, *Chem. and Ind.*, 756 (1958).
(8) J. H. Richards and D. C. Garwood, unpublished results.
(9) National Science Foundation Predoctoral Fellow.

RECEIVED MAY 6, 1959

STEROIDS. CXXVII.[1] 6-HALO PROGESTATIONAL AGENTS

Sir:

17α-Acetoxyprogesterone 3-ethyl enol ether (I) (m.p. 160–163°, $[\alpha]_D$ −146° (all rot. in $CHCl_3$), λ_{max}^{EtOH} 241 mμ, log ϵ 4.32)[2] on reaction with N-chlorosuccinimide gave 6β-chloro-17α-acetoxyprogesterone (A = 0.5)[3] (m.p. 221–222°, $[\alpha]_D$ −10°, λ_{max} 239 mμ, log ϵ 4.19) inverted by hydrogen chloride–acetic acid to 6α-chloro-17α-acetoxyprogesterone (II) (*A* = 2–3); II ethyl enol ether (*A* = 1) (m.p. 180–181°, $[\alpha]_D$ −146° λ_{max} 251 μ, log ϵ 4.35). Similarly, progesterone, 17α-hydroxyprogesterone caproate and "S" 17,21-diacetate were converted to their respective 6α-chloro derivatives III, IV and V.

Conversion of II to its 1-dehydro analog VI was accomplished by selenium dioxide oxidation.

Treatment of I with N-bromosuccinimide in aqueous buffered acetone yielded 6β-bromo-17α-acetoxyprogesterone (m.p. 178–180°, $[\alpha]_D$ ± 0°, λ_{max} 246 mμ, log ϵ 4.14) inverted by acid to the α-derivative VII (*A* = 1). Bromination of 1-dehydro-17α-acetoxyprogesterone[4] with N-bromosuccinimide in carbon tetrachloride gave the 6β-bromo derivative (m.p. 170–172°, $[\alpha]_D$ +23°, λ_{max} 250 mμ, log ϵ 4.24) inverted by acid to 1-dehydro-6α-bromo-17α-acetoxyprogesterone (VIII) (*A* = 6).

6-Dehydro-6-chloro-17α-acetoxyprogesterone (IX) and 6-dehydro-6-chloro-"S" diacetate (X) were obtained by chloranil oxidation[5,6] of II and V, while selenium dioxide oxidation of IX and X yielded the 6-chloro-$\Delta^{1,4,6}$-trienones XI and XII.

In multi-dose Clauberg assays[3] it was found that the progestational activity of 6α-chloro-17α-acetoxyprogesterone was increased by Δ^1- or by Δ^6-double bond introduction with the latter modification inducing the more pronounced effect. *The oral progestational activity of IX was 50× that of Norlutin or 700× that of 17α-acetoxyprogesterone and would thus appear to be the most potent*

TABLE I

Compound	M.p. °C.	$[\alpha]_{D CHCl_3}$	EtOH max. (mμ)	log ϵ	Oral progest.[4] activity (Clauberg assay)
17α-Ethynyl-19-nortestosterone					1
17α-Acetoxyprogesterone					0.07
6α-Methyl-17α-acetoxyprogesterone[a,6]					2–3
6-Dehydro-6-methyl-17α-acetoxyprogesterone[6]					12
1-Dehydro-6α-fluoro-17α-acetoxyprogesterone					6
6-Dehydro-6-fluoro-17α-acetoxyprogesterone					15
6α-Chloro-17α-acetoxyprogesterone (II)	polymor. 183–184 215–216	+40°	236	4.20	2–3
6α-Chloroprogesterone (III)	130–132	+133°	237	4.19	
6α-Chloro-17α-hydroxyprogesterone caproate (IV)	Oil	+20°	238	4.15	
1-Dehydro-6α-chloro-17α-acetoxyprogesterone (VI)	203–205	−77°	242	4.21	8
6-Dehydro-6-chloro-17α-acetoxyprogesterone (IX)	212–214	+8°	285	4.36	50
1,6-Bisdehydro-6-chloro-17α-acetoxyprogesterone (XI)	168–170	−83°	229	4.00	35
			258	4.00	
			297	4.03	
6α-Chloro-"S" diacetate (V)	197–198	+34°	237	4.19	0.5
6-Dehydro-6-chloro-"S" diacetate (X)	248–250	+37°	285	4.31	1.5
1,6-Bisdehydro-6-chloro-"S" diacetate (XII)	201–203	−36°	228	4.00	1
			260	4.03	
			295	4.07	
6α-Bromo-17α-acetoxyprogesterone (VII)	163–166	+42°	236	4.12	1
1-Dehydro-6α-bromo-17α-acetoxyprogesterone (VIII)	172–175	−7°	244	4.15	6

[a] This substance was first described by J. C. Babcock, E. S. Gutsell, M. E. Herr, J. A. Hogg, J. C. Stucki, L. E. Barnes and W. E. Dulin, THIS JOURNAL, **80**, 2904 (1958).

(1) Paper CXXVI, A Bowers, E. Denot, R. Urquiza and L. M. Sanchez Hidalgo, *Tetrahedron*, in press (1959).
(2) Correct elemental analyses were obtained for all new compounds.
(3) Clauberg assays, by the Endocrine Laboratories, *A* = oral progestational activity, 17α-ethynyl-19-nortestosterone (Norlutin) = 1.
(4) M.p. 229–230°, $[\alpha]_D$ +19°, λ_{max} 243 mμ, log ϵ 4.20.
(5) A. J. Agnello and G. Laubach, THIS JOURNAL, **79**, 1257 (1957).
(6) H. J. Ringold, J. Pérez Ruelas, E. Batres and C. Djerassi, *ibid.*, **81**, in press (1959).