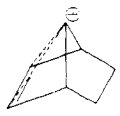
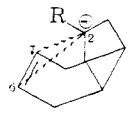
STABLE NON-CLASSICAL CARBONIUM IONS

Sir:

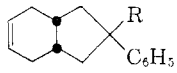
The impressive difference shown in the rate of solvolysis of the tosylates of anti-7-norbornenol and 7-norborneol[1] (a factor of 10^{11}) indicates non-classical stabilization of the intermediate carbonium ion, I, of about 15 kcal. This value is of a similar order to that involved in several other stable classical carbonium ions[2] and suggests that salts of non-classical carbonium ions might also be capable of isolation. We wish now to report the formation of such a stable non-classical carbonium ion.



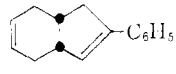
I



II



III



IV

Models indicated that in the molecular system II, a p_z orbital of carbon atom 2 could effectively overlap with the π molecular orbital of the 6:7 double bond if the ring fusion were *cis*, but could not in the corresponding *trans* isomer

Accordingly, we have synthesized the *cis* phenyl carbinol III (R = OH) and its *trans* ring fused isomer. The *cis* compound readily dissolves in strong acids giving deep yellow solutions; the ultraviolet absorption curve in 60% H_2SO_4 (Fig. 1, curve A) shows two strong peaks at 386 and

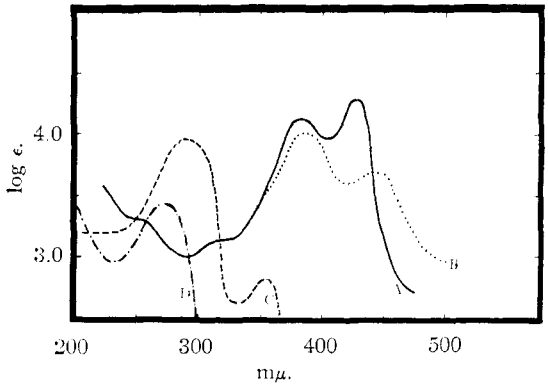


Fig. 1.

427 mμ. The *trans* isomer, however, shows no strong absorption beyond 300 mμ in 60% H_2SO_4 (curve D). The spectrum of the *cis* diene, IV, in 60% H_2SO_4 is identical with that of the *cis* carbinol; both solutions presumably contain the non-classical carbonium ion II (R = phenyl).

Treatment at 0° of the chloride III (R = Cl) with $AgClO_4$ in benzene caused immediate precipitation of AgCl together with a yellow solid. From its mode of formation and the following properties, this yellow solid is undoubtedly the perchlorate salt of the carbonium ion II (R = phenyl). The yellow solid contains the perchlorate anion, it is insoluble in hexane, $CHCl_3$, CCl_4 and benzene; it dissolves readily in nitromethane to give yellow solutions, the ultraviolet spectrum of which shows two peaks at 382 and 435 mμ (curve B), but which rapidly change with time. In 60% H_2SO_4 the spectrum is identical to that of the carbinol (curve A). Treatment of the yellow solid with water, alcohol or ether causes immediate decolorization and formation of the diene IV. The yellow solid is stable below −40° but decomposes at room temperature, especially on exposure to air.

The *cis* methylcarbinol, analogous to the phenylcarbinol, also forms stable yellow solutions in 60% H_2SO_4; these again show strong absorption beyond 200 mμ (curve C) suggesting formation of a similar non-classical carbonium ion II (R = methyl).

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(1) S. Winstein, M. Shatavsky, C. Norton and R. B. Woodward, THIS JOURNAL, **77**, 4183 (1955).

(2) For references see D. Bethell and V. Gold, *Quart. Rev.* (*London*), **12**, 173 (1958).

CHROMIUM TETRA-*t*-BUTOXIDE

Sir:

We have obtained a new tetravalent chromium compound, chromium tetra-*t*-butoxide, in the course of experiments on the catalytic action of bis-benzenechromium. Inorganic compounds of tetravalent chromium are known,[1] but tetravalent chromium with organic groups has not been isolated heretofore.

A solution of bis-benzenechromium in benzene (or petroleum ether) was heated with di-*t*-butyl peroxide in a sealed tube at 90° for 20 hr. After solvent had been removed, the green residues were sublimed under reduced pressure at 70–90°. The sublimed deep blue crystals (80% yield based on $Cr(C_6H_6)_2$) melt at 30–35° and give *t*-butyl alcohol on decomposition with dilute sulfuric acid. These crystals contain a small amount of biphenyl as an impurity. The experimental results strongly indicate that this biphenyl is derived from the benzene in bis-benzenechromium. It is interesting that π-bonded benzene shows a different chemical behavior from that of benzene itself. The contaminated biphenyl was freed from the blue crystals by means of the formation of adduct with 2,4,7-trinitrofluorenone. The purified blue crystals showed no characteristic absorption bands of biphenyl in the infrared spectrum.

Analytical results of the purified blue crystals are as follows. Calcd. for $C_{16}H_{26}O_4Cr$: Cr, 15.1; C, 55.79; H, 10.56; mol. wt., 345. Found: Cr, 15.2; C, 55.57; H, 10.27; mol. wt., 330. This compound has been found to be paramagnetic to the extent of 2.88 Bohr magnetons, suggesting the presence of two unpaired electrons in the molecule.[2]

From these results, the blue crystals should be chromium tetra-*t*-butoxide, $Cr[OC(CH_3)_3]_4$. This

(1) E. Huss and W. Klemm, *Z. anorg. u. allgem. Chem.*, **262**, 25 (1950); H. Bode and E. Voss, *ibid.*, **286**, 136 (1956); R. Scholder and W. Klemm, *Angew. Chem.*, **66**, 461 (1954).

(2) We are indebted to Drs. H. Takagi and M. Mekata of Kyoto University for this magnetic measurement.

compound is sensitive to moisture and oxygen, m.p. 37–38°, b.p. 105° (15 mm.). The infrared spectrum of this compound shows an absorption band at 12.8 μ. It is soluble in most organic solvents in all proportions, but reacts with alcohol forming an insoluble solid.

It is remarkable that the tetravalent chromium compound was isolated. Additional evidence for the tetravalent state of chromium was found in another experiment. An acid solution of potassium iodide was treated with a weighed amount of this compound and the liberated iodine titrated. Thus 0.638 g. of chromium tetra-*t*-butoxide liberated 1.89 mmol. of iodine. Assuming that one electron transfer occurred as shown in equation (1), the molecular weight was calculated as 338 in good agreement with the molecular weight determined cryoscopically.

$$Cr^{4+} + I^- \longrightarrow Cr^{3+} + {}^1/_2I_2 \qquad (1)$$

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RECEIVED FEBRUARY 11, 1959

GROSS STRUCTURE OF HEMOGLOBIN H

Sir:

Human hemoglobin H has been described in some detail by Rigas, Koler and Osgood.[1] Chemical investigations of chromatographically purified[2] hemoglobin H, here presented, lead to a further understanding of its structure and of its relation to other human hemoglobins.

When DNP-globin H was prepared and examined by methods previously described,[3,4,5] the result was approximately four N-terminal valyl residues per molecule of 66,000 molecular weight[1] but only one kind of N-terminal sequence: val-his-leu. This N-terminal sequence defines β chains[5] and suggests that hemoglobin H may be represented[6] as β_4^H.

"Fingerprints"[10] of tryptic hydrolysates of hemoglobins H and A differed markedly. Peptides numbered[10] 5, 10, 11, 13, 17, 18, 23, and probably several others in regions normally poorly resolved were absent on the fingerprint of H but no new peptides were apparent. The absent peptides were present on fingerprints of isolated α^A chains. The likely conclusion that the sequence in β^H and β^A chains is identical was substantiated by the following hybridization experiment.[8,11]

(1) D. A. Rigas, R. D. Koler and E. E. Osgood, *J. Lab. Clin. Med.*, **47**, 51 (1956).

(2) Extension of methods of D. W. Allen, W. A. Schroeder and J. Balog, THIS JOURNAL, **80**, 1628 (1958).

(3) H. S. Rhinesmith, W. A. Schroeder and L. Pauling, *ibid.*, **79**, 609 (1957).

(4) *Ibid.*, **79**, 4682 (1957).

(5) H. S. Rhinesmith, W. A. Schroeder and N. Martin, *ibid.*, **80**, 3358 (1958).

(6) The N-terminal sequence[5] defines the chain as α or β, the superscript denotes the hemoglobin that is the source of the chain, and the subscript has the usual chemical significance. The glycyl chains[7] of hemoglobin F are termed γ chains. Thus, hemoglobin A and S are $\alpha_2^A\beta_2^A$ and $\alpha_2^A\beta_2^S$ inasmuch as the α chains are identical.[8,9]

(7) W. A. Schroeder and G. Matsuda, THIS JOURNAL, **80**, 1521 (1958).

(8) J. R. Vinograd, W. D. Hutchinson, and W. A. Schroeder, *ibid.*, in press.

(9) V. M. Ingram, personal communication.

(10) V. M. Ingram, *Biochem. Biophys. Acta*, **28**, 539 (1958).

(11) J. Vinograd and W. D. Hutchinson, *Nature*, to be submitted.

Following hybridization of carbonmonoxyhemoglobin H and radioactive carbonmonoxyhemoglobin S at *p*H 11.0 at 3° for 24 hr., four hemoglobins were chromatographically isolated. These data are pertinent:

	Reactants		Products			
Zone	...	...	1	2	3	4
Mg.	22	22	5[a]	2[a]	15	7
C.p.m./mg.	0	1200	70	1100	600	1200
Identity of material	Hb-H	Hb-S*	Hb-H	β_4^S*	Hb-A*	Hb-S*
Formula	β_4^A	α_2^A*β_2^S*	β_4^A	β_4^S*	α_2^A*β_2^A	α_2^A*β_2^S*

[a] Precipitation that occurred during hybridization must have consisted of β^A and β^S* chains because α chains are conserved.

Identification of the products involved chromatographic studies and determination of radioactivity and for hemoglobin A also the study of sedimentation velocity and examination of N-terminal peptides[3,4,5] to show that only the α chains were radioactive. Thus, hemoglobin A and β_4^S* were formed during hybridization but there was no evidence for $\beta_2^A\beta_2^S$*. On the basis of the radioactive and material balance, it was concluded that the four β chains of hemoglobin H are identical with each other and with β^A chains.

Hemoglobin H is the first observed example of a hemoglobin composed of a single kind of polypeptide chain. Possibly, other abnormal hemoglobins or minor components in normal hemoglobin may be built on the scheme α_4, $\alpha_3\beta$, $\beta_2\gamma_2$, etc. Biologically, it suggests that hemoglobin H disease results from an imbalance in the relative production of α and β chains and hence that α and β chains are under separate biosynthetic and genetic control. This latter suggestion is further supported by experiments now in progress which show that the α^A and α^F chains are identical and that β chains are present in several minor hemoglobin components normally associated with hemoglobin A and S.

These experiments were made possible by the interest and generosity of Dr. D. A. Rigas and Dr. R. D. Koler. This investigation was supported in part by grants H-2258 and H-3394 from the National Institutes of Health, United States Public Health Service.

(12) National Research Fellow in the Medical Sciences.

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RECEIVED APRIL 14, 1959

THE SYNTHESIS OF TIGOGENIN AND NEOTIGOGENIN

Sir:

We wish to report the synthesis of tigogenin (VIa) and neotigogenin (VIb), typical members of the large and important family of steroidal sapogenins.[1]

(1) *Cf.* L. F. Fieser and M. Fieser, "Natural Products Related to Phenanthrene," Reinhold Publishing Corp., New York, N. Y., 3rd Edition, 1949, Chapter VIII.