The methanol was determined by gas–liquid chromatography with a flame ionization detector. The amine and ether mixture was condensed into a tared reaction tube and treated with a known amount of hydrogen chloride. The ether and excess hydrogen chloride were distilled and the amine content was determined by the isolation of the hydrochloride salt.[2] In a partial trap-to-trap fractionation of the original mixture, both the amine and ether fractions were analyzed by infrared spectroscopy. The spectrum of the ether fraction revealed traces of amine as the only impurity.

A typical decomposition using 2 ml. of 10% tetramethylammonium hydroxide (2.20 mmoles) gave the following products.

Products	Millimoles
$(CH_3)_3N$	2.13[a]
$(CH_3)_2O$	0.97[b]
CH_3OH	0.11[c]
$(CH_2)_n$	Trace

[a] Recovered as the hydrochloride. [b] Recovered ether and HCl mixture less the HCl not used in forming the amine hydrochloride (see ref. 2). [c] Methanol and water mixture analyzed by gas–liquid chromatography with flame ionization detector.

A series of pyrolyses was carried out under a variety of conditions (a–e) without significant changes in the yield of products: (a) in an atmosphere of nitrogen, (b) in a rapid nitrogen flow system with a head pressure of 10 mm., (c) in an atmosphere of 25 mm. of water vapor, (d) in the presence of Ag^+ ion, and (e) in an initially evacuated system without continuous collection of products.

Trace amounts (0.09%) of dimethyl ether have been reported[3] as a product in the pyrolysis of cyclohexylmethyl-β-*d*-trimethylammonium hydroxide and its formation was explained by a three-step mechanism. An analogous mechanism for the decomposition of tetramethylammonium hydroxide would account for the observed products.

$$(CH_3)_4\bar{N}\bar{O}H \longrightarrow (CH_3)_3N + CH_3OH$$

$$CH_3OH + OH^- \rightleftarrows H_2O + CH_3O^-$$

$$CH_3O^- + (CH_3)_4\overset{+}{N} \longrightarrow CH_3OCH_3 + (CH_3)_3N$$

However, if methanol is formed under the present conditions it would be expected to leave the reaction zone rapidly. The formation of the methoxide ion and its subsequent reaction to form the ether in high yield would involve retaining the methanol completely but allowing the water to escape. Consequently, it is suggested that the hydroxide ion behaves as a proton-abstracting agent to give a nitrogen ylide and the observed products result from the decomposition of the ylide in various ways.

Nitrogen ylides have been shown to exhibit carbene character,[4] and carbenes have been reported[5] to react with alcohols to give ethers. Thus, the ether may be formed by the reaction of ylide with the small amount of water remaining at the decomposition temperature. Methanol may be formed either by the decomposition of the ylide in the presence of a large amount of water, or by a displacement reaction, whereas polyethylene is formed only in the latter stages of reaction when water is no longer present. The decomposition of this ylide in ether to form polyethylene and trimethylamine has been reported.[6]

From this preliminary study, it appears that in the absence of hydroxylic solvent, or after the removal of hydroxylic solvent from the reaction site, α-hydrogen abstraction by strong bases[7] (OH^-, NH_2^-, phenyl$^-$) is the favored reaction. With weaker bases (Cl^-, Br^-, etc.)[8] displacement may be the predominant reaction. It has been suggested[3] that the mechanism of the Hofmann degradation may depend on the manner in which it is carried out. However, the mechanism may change during the course of reaction. In the presence of hydroxylic solvent[9,10] or during the removal of solvent at elevated temperature, β-elimination appears to be the primary mode of decomposition. It is known that α-hydrogen abstraction occurs in the presence of these protonic solvents,[10,11] but apparently reprotonation occurs before the ylide can decompose by any competitive path and alternative mechanisms are favored.[3,9] As the solvent is removed, α-hydrogen abstraction becomes irreversible and the course of reaction depends on the mode of decomposition of the ylide.

Acknowledgment.—The author wishes to thank the National Science Foundation (GP-1704) and The University of California for supporting this research.

(2) Dimethyloxonium chloride decomposes at −2° and can be removed completely from the amine salt.

(3) A. C. Cope, N. A. LeBel, P. T. Moore, and W. R. Moore, *J. Am. Chem Soc.*, **83**, 3861 (1961).

(4) V. Franzen and G. Wittig, *Angew. Chem.*, **72**, 417 (1960).

(5) W. Kirmse, *Ann.*, **666**, 9 (1963).

(6) G. Wittig and R. Polster, *ibid.*, **599**, 1 (1956).

(7) A. C. Cope and E. R. Trumbull, *Org. Reactions*, **11**, 317 (1960).

(8) A. T. Lawson and N. Collie, *J. Chem. Soc.*, **53**, 624 (1888).

(9) G. Ayrey, E. Buncel, and A. N. Bourns, *Proc. Chem. Soc.*, 458 (1961).

(10) V. J. Shiner and M. L. Smith, *J. Am. Chem. Soc.*, **80**, 4095 (1958).

(11) W. von E. Doering and A. K. Hoffmann, *ibid.*, **77**, 521 (1955).

UNIVERSITY OF CALIFORNIA
DEPARTMENT OF CHEMISTRY
DAVIS, CALIFORNIA
W. KENNETH MUSKER

RECEIVED NOVEMBER 25, 1963

Chelation as a Driving Force in Organic Reactions.[1] A Generic Synthesis of Amino Acids by the Carboxylation and Alkylation of 3-Phenylhydantoin

Sir:

In the course of our work on the carboxylation of compounds containing activated methylene positions, we became interested in 3-phenylhydantoin. Wheeler and Hoffman[2] showed that the methylene position of hydantoin is sufficiently activated to condense with aromatic aldehydes, and thus hydantoin might be a member of the group of compounds which react with magnesium methylcarbonate.[1]

When 3-phenylhydantoin[3] was heated at 80° with magnesium methyl carbonate and the reaction mixture sampled periodically by diluting 1-ml. portions with methanol, a new absorption peak in the ultraviolet was observed at 278 mμ. A basic solution of 3-phenylhydantoin does not absorb in this region. This suggested that the 5-position of 3-phenylhydantoin has been carboxylated and the chelate formed. The new absorption peak immediately disappeared on addition of a trace of aqueous acid.

The identity of the carboxylation product was established by isolation of 3-phenyl-5-carbomethoxyhydantoin. The product was precipitated by pouring the reaction mixture into ether. After decanting the liquid phase, methanolic hydrogen chloride, at −50°, was added. After 2 days at room temperature most of the methanol was removed and the remainder poured into water. The infrared and nuclear magnetic reso-

(1) Previous related papers: H. L. Finkbeiner and M. Stiles, *J. Am. Chem. Soc.*, **85**, 616 (1963); H. L. Finkbeiner and G. W. Wagner, *J. Org. Chem.*, **28**, 215 (1963), and references cited.

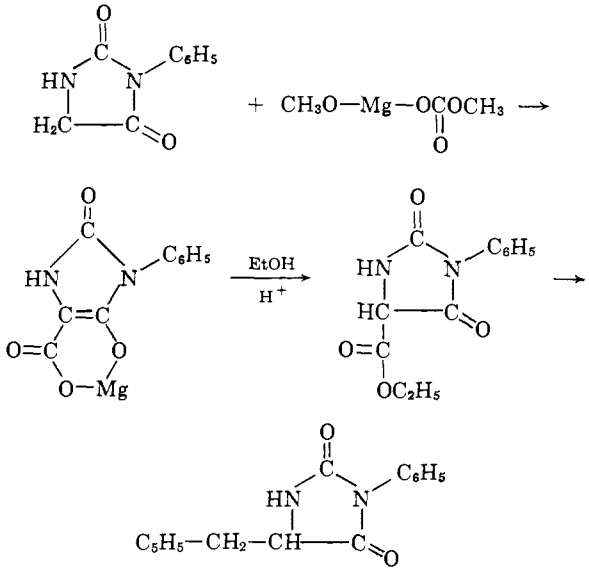
(2) H. L. Wheeler and C. Hoffman, *Am. Chem. J.*, **45**, 368 (1911). Subsequent work on hydantoins, their synthesis, and utility has been reviewed by E. Ware, *Chem. Rev.*, 403 (1950).

(3) This compound is prepared from the direct reaction of glycine with phenylisocyanate [J. R. Bailey and C. P. Randolph, *Ber.*, **41**, 2499 (1908)].

nance spectra and chemical analysis confirmed that the product was 3-phenyl-5-carbomethoxyhydantoin, yield 72%, m.p. 177–79°. *Anal.* Calcd. for $C_{11}H_{10}N_2O_4$: C, 56.40; H, 4.30; N, 11.96; mol. wt., 234.2. Found: C, 56.4; H, 4.4; N, 11.9; mol. wt., 233. The remaining proton at the 5-position of 3-phenyl-5-carboethoxyhydantoin has a pK_a of 7.75 or about six orders of magnitude more acidic than diethyl malonate.

The 3-phenyl-5-carbomethoxyhydantoin was alkylated by dissolving in excess methanolic sodium methoxide and adding benzyl chloride. After the alkylation was complete, aqueous hydrochloric acid was added to hydrolyze and decarboxylate the ester. The product had an infrared spectrum identical with that of an authentic sample of 3-phenyl-5-benzylhydantoin, m.p. 166–168°, lit.[4] 170–172°.

These reactions are summarized as



Stiles has shown that the chelates of β-ketoacids, prepared from ketones and magnesium methyl carbonate, could be alkylated directly.[5] To investigate this technique a number of experiments were carried out in which 0.25 mole of 3-phenylhydantoin was heated to 80° in 370 ml. of 2 *M* magnesium methyl carbonate for 2 hr. The appropriate alkylating agent was then added and the reaction mixture heated to 100° (or reflux if the alkylating agent was of low boiling point) for 5 hr. Hydrolysis was accomplished by pouring the reaction mixture into ice and hydrochloric acid.

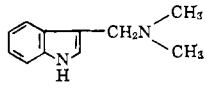
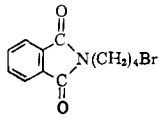
The products were identified as 3-phenyl-5-alkyl hydantoins by melting point, elemental analysis, and comparison of the infrared spectrum with that of authentic samples. Hydrolysis by the method of Gaudry[6] gave the corresponding free amino acids. Table I summarizes the data for a number of amino acids prepared in this fashion.

The preparation of proline was made possible when it was found the excess alkylating agent would react with the nitrogen in the 1-position of 3-phenylhydantoin. Excess methyl iodide gave 1,5-dimethyl-3-phenylhydantoin, m.p. 145–147°, yield 68%. Substitution of 1,3-dibromopropane for the methyl iodide led directly to 1,5-trimethylene-3-phenylhydantoin.

Although 3-phenyl-5-methylhydantoin did not react with magnesium methyl carbonate, hydantoin itself and the sodium salt do undergo reaction. In this case,

(4) M. Bergmann and D. Delis, *Ann.*, **458**, 89 (1927).
(5) M. Stiles, *J. Am. Chem. Soc.*, **81**, 2598 (1959).
(6) R. Gaudry, *Can. J. Res.*, **26B**, 773 (1948).

TABLE I

Amino acid	Alkylating agent	3-Phenyl-5-alkylhydantoin[a] Yield, %	M.p., °C.	Yield of amino acid, %[b]
DL-Valine	$CH_3CHBrCH_3$	40	123–125	38
DL-Leucine	$CH_3CH(CH_3)CH_2Br$	66	126–127	46
DL-Phenylalanine	$C_6H_5CH_2Cl$	98	170–172	97
DL-Tryptophan		55	173–175	53
DL-Proline	$BrCH_2CH_2CH_2Br$	48	117–119	45
DL-Lysine		53	205–207	45[c]
DL-Glutamic	$NaOC(=O)CH_2CH_2Cl$	56	168–169	~30[d]

[a] Satisfactory analyses and n.m.r. data were obtained in each case. [b] Based on the starting 3-phenylhydantoin. [c] Isolated as the hydrochloride. [d] The hydrolysis was very slow and incomplete.

the initial alkylation takes place at the 3-position followed by alkylation at the 5-position. For example, if hydantoin is treated with magnesium methyl carbonate followed by benzyl chloride the product obtained is 3,5-dibenzylhydantoin, 93% yield, m.p. 145–146°. The synthetic possibilities of this multiple alkylation are being investigated.

GENERAL ELECTRIC RESEARCH LABORATORY
SCHENECTADY, NEW YORK HERMAN FINKBEINER
RECEIVED JANUARY 4, 1964

The Cubane System

Sir:

It is with pleasure that we report the first tactical synthesis of the cubane carbon skeleton[1] and present the first observation on the electronic hybridization intrinsic to this system.

Radical-initiated reaction of N-bromosuccinimide with 2-cyclopentenone in carbon tetrachloride gives the 4-halogenated ketone I.[2] Subsequent bromination of I in pentane–methylene chloride at 0–10° with molecular bromine produces 2,3,4-tribromocyclopentanone (II). Double dehydrobromination of II in absolute ether at −20° with diethylamine leads to the transient bromocyclopentadienone III which, as with the unsubstituted case, undergoes spontaneous Diels–Alder dimerization. A single dimer is obtained: over-all yield from cyclopentenone, three steps, *ca.* 40%, m.p. (from carbon tetrachloride) 154–155° dec.; $\lambda_{max}^{CH_2Cl_2}$ 5.50, 5.54, 5.59 (sh), 5.77, 6.32, and 6.42 μ;

(1) Only serendipitous syntheses of octaphenylcubane have been reported previously: H. H. Freedman, *J. Am. Chem. Soc.*, **83**, 2195 (1961); H. H. Freedman and D. R. Petersen, *ibid.*, **84**, 2837 (1962); G. Büchi, C. W. Perry, and E. W. Robb, *J. Org. Chem.*, **27**, 4106 (1962); M. Tsutsui, *Chem. Ind.* (London), 780 (1962). The encumbering phenyl groups have prevented examination of the properties of the skeleton and indeed have left the proof of structure tenuous: R. C. Cookson and D. W. Jones, *Proc. Chem. Soc.*, 115 (1963); H. H. Freedman and R. S. Gohlke, *ibid.*, 249 (1963).

(2) C. H. DePuy, M. Isaks, and K. L. Eilers, *Chem. Ind.* (London), 429 (1961); *cf.* K. Hafner and K. Goliasch, *Chem. Ber.*, **94**, 2909 (1961).