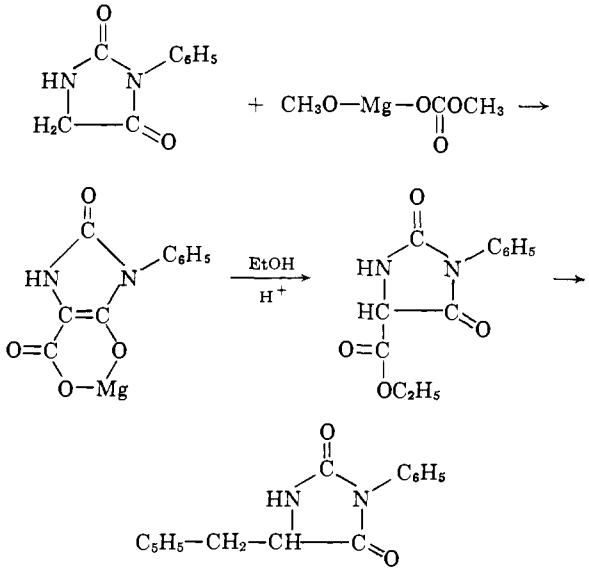
nance spectra and chemical analysis confirmed that the product was 3-phenyl-5-carbomethoxyhydantoin, yield 72%, m.p. 177–79°. *Anal.* Calcd. for $C_{11}H_{10}N_2O_4$: C, 56.40; H, 4.30; N, 11.96; mol. wt., 234.2. Found: C, 56.4; H, 4.4; N, 11.9; mol. wt., 233. The remaining proton at the 5-position of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

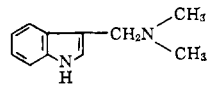
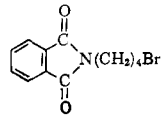
The products were identified as 3-phenyl-5-alkyl hydantoins by melting point, elemental analysis, and comparison of the infrared spectrum with that of authentic samples. Hydrolysis by the method of Gaudry[6] gave the corresponding free amino acids. Table I summarizes the data for a number of amino acids 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_3CHCH_2Br (CH₃ branch)	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	$NaOCCH_2CH_2Cl$	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

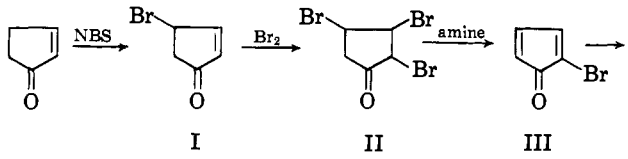
Sir:

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.

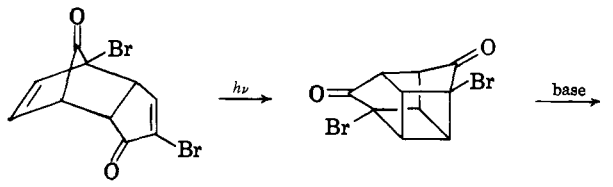
Radical-initiated reaction of N-bromosuccinimide with 2-cyclopentenone in carbon tetrachloride gives the 4-halogenated ketone I.[2] Subsequent bromination of I in pentane–methylene chloride at 0–10° with molecular bromine produces 2,3,4-tribromocyclopentanone (II). Double dehydrobromination of II in 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).

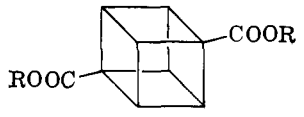
(2) C. H. DePuy, M. Isaks, and K. L. Eilers, *Chem. Ind.* (London), 429 (1961); *cf.* K. Hafner and K. Goliasch, *Chem. Ber.*, **94**, 2909 (1961).



I II III



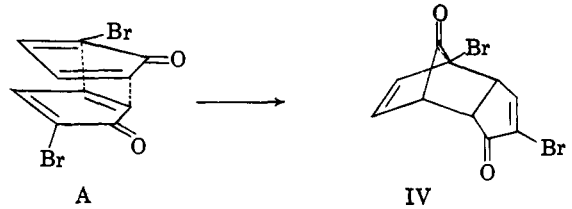
IV V



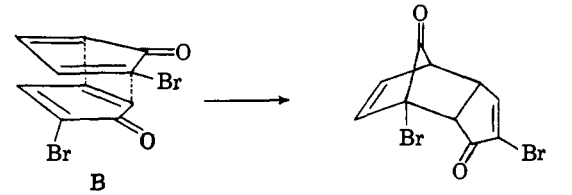
VI, R = H
VII, R = CH_3

τ_{CDCl_3} 2.33 (1*H*, d), 3.68 (2*H*, m), 6.42 (2*H*, m), and 6.79 (1*H*, m) p.p.m.

Exact structural specifications for the dimer can be arrived at *a priori*, in steps: (1) the configuration of the ring fusion should be *endo* as it is in the equivalent dimer of cyclopentadienone,[3] (2) in accord with the behavior of chlorobenzoquinone,[4] the dienophilic reactivity of III should be least at the halogen-substituted double bond, and hence one vinyl position in the dimer should bear bromine rather than hydrogen, and (3) the interactions of like dipoles should be minimized in the geometry of the transition state for Diels–Alder dimerization of III; thus, geometry A is taken as more favorable than B and, in consequence, IV as more probable than IVa.



A IV



B IVa

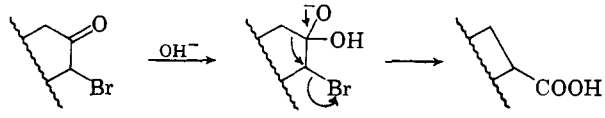
In fact, each of these predictions as to the structure of the dimer can be verified in full: (1) the *endo* configuration is essential to the subsequent light-induced ring closure (*vide infra*), (2) the n.m.r. spectrum shows only three vinyl protons; the absence of a nuclear resonance signal at τ *ca.* 4 p.p.m. confirms the substitution of halogen for hydrogen on the α-vinyl position of the cyclopentenone segment, and (3) the completed synthetic sequence leads to cubane substituted on the body diagonal vertices; this is possible only if the dimer possesses structure IV.

(3) Dicyclopentadien-1,8-dione is reduced with hydrogen over palladium to the tetrahydro derivative, which *via* Raney nickel reduction of the bisthioketal is converted to *endo*-tetrahydrodicyclopentadiene.

(4) I. G. Farbenind A.-G., French Patent 677,296.

Ultraviolet irradiation of IV in nonpolar solvents such as benzene or methylene chloride leads to polymerization rather than the familiar ring closure reaction.[5] This difficulty can be traced to the sp^2 center in the one-carbon bridge and eliminated by carrying out the irradiation in methanol containing hydrogen chloride. Under these conditions IV is converted to the sp^3 8-hemiketal which undergoes ready closure into the cage system; the ultimate product is the bishemiketal of V.[6] Deketalization is accomplished by heating with water and subsequent desiccation. The pure diketone V, crystallized from methylene chloride, melts at 232–233° dec., $\lambda_{max}^{CH_2Cl_2}$ 5.56 and 5.62 μ,[7] τ_{CDCl_3} 6.37 (4*H*, m) and 6.95 (2*H*, m).

Several hours reflux with 50% aqueous potassium hydroxide converts V to VI, isolated and characterized as the dimethyl ester VII; over-all yield from IV, three steps, *ca.* 30%, m.p. (from hexane) 161–162°, λ_{max}^{KBr} 3.33, 3.38, 3.50, 5.80 μ, and clear from 6.0 to 6.8 μ, $\epsilon_{210\ m\mu}^{EtOH}$ 1750.[8] The extrusion of the bridge carbonyl groups in the conversion V to VI can be equated mechanistically to a Favorskii reaction formulated as a benzilic acid-type rearrangement.[9]



The n.m.r. spectrum, coupled with analytical[10] and other spectral data, establishes the structure of VII unequivocally. Over a 2000 c.p.s. sweep two and only two resonances appear, τ 5.76 and 6.28 p.p.m., equal in area and each less than one-half of one cycle wide at half-height. These dimensions are fully appropriate only to the system now in hand. The position of the higher field absorption is typical of methyl esters, and this assignment has been confirmed by comparing the separation of the sharp C^{13} satellites (146 c.p.s.)[11] with the literature value for methyl carbonate (147 c.p.s.).[12]

We have been able to observe the C^{13} satellites of the proton resonance of the ring hydrogens in VII.[11] As anticipated these are broadened badly by complex spin coupling, yet measurements made at both 60 and 100 Mc.p.s., at the former frequency on both the high- and low-field satellite partners, give an average value for $J_{C^{13}-H}$ of 160 ± 5 c.p.s. In accord with presently accepted theory,[13] this can be equated to approximately 32% s-character in the ring C–H bonds. This is to be compared to 27% for cyclobutane[14] and 32% for cyclopropane.[13a] Clearly, a substantial rehybridization of normal tetrahedral carbon occurs to accommodate the geometric requirements of the cubane skeleton.

(5) P. Yates and P. Eaton, *Tetrahedron*, **12**, 13 (1961).

(6) The course of the reaction is followed by infrared spectroscopy.

(7) The split carbonyl band can be due to either coupled asymmetric-symmetric stretchings or possibly to Fermi resonance with the vibration seen at 10.43 μ.

(8) *Cf.* the quoted ultraviolet spectrum of octaphenylcubane, λ_{max} 267 mμ (ϵ 44,600), and note the problems it engenders [Cookson and Jones, see ref. 1].

(9) *Cf.* A. C. Cope and E. S. Graham, *J. Am. Chem. Soc.*, **73**, 4702 (1951).

(10) Satisfactory analytical figures have been obtained by Mr. William Saschek, resident microanalyst, for all compounds for which physical constants are given. A Rast determination of the molecular weight of VII gives 229 (calcd., 220).

(11) The authors are grateful to Prof. Gerhard Closs of this department and to Dr. Joseph Katz and Dr. Ralph Dougherty of the Argonne National Laboratory for their willing collaboration on the measurement of the C^{13} coupling constants.

(12) N. Muller, *J. Chem. Phys.*, **36**, 359 (1962).

(13) (a) N. Muller and D. E. Pritchard, *ibid.*, **31**, 768, 1471 (1959); (b) J. N. Shoolery, *ibid.*, 1427 (1959); (c) C. Juan and H. S. Gutowsky, *ibid.*, **37**, 2198 (1962).

(14) C. S. Foote, *Tetrahedron Letters*, 579 (1963).

Work continues in these laboratories both on further syntheses of cubically symmetric molecules and, now more important, on the chemical reactions of such systems.

Acknowledgment.—The National Science Foundation, the National Institutes of Health, the Alfred P. Sloan Foundation, and the General Chemical Division of Allied Chemical Corporation each contributed generously to the support of this work.

(15) Alfred P. Sloan Foundation Fellow.

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THOMAS W. COLE, JR.

RECEIVED JANUARY 30, 1964

Studies in Organophosphorus Chemistry. I. Conversion of Alcohols and Phenols to Halides by Tertiary Phosphine Dihalides

Sir:

We wish to report the preparation of a variety of alkyl and aryl halides in high yields using phosphorus reagents of the type R_3PX_2.[1,2] The method is outlined in eq. 1.

$$R_3P: + X_2 \longrightarrow R_3PX_2 \xrightarrow{R'OH} R_3PO + HX + R'X \quad (1)$$

R = C_6H_5 or n-C_4H_9; X = Br, Cl, I R'; = alkyl or aryl

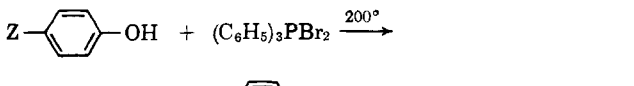
Our interest in these reagents was stimulated by the consideration that only two replaceable groups are necessary *and desirable* in reactions of compounds of the PX_5-type with alcohols.

Table I and eq. 2 give some indication of the scope of the reaction.

TABLE I

Alcohol	$(C_6H_5)_3PBr_2$ % yield of RBr[a]	$(n\text{-Bu})_3PBr_2$ % yield of RBr[a]	$(C_6H_5)_3PCl_2$ % yield of RCl[a]
n-Butyl	91	93	~99[b]
Isobutyl	89		
Neopentyl	79	91	92
2-Butyl	90	89	
2-Octyl	86		
2-Pentyl	~99[b,c]	~99[b,c]	
3-Pentyl	~99[b,c]	~99[b,c]	
Cyclopentyl	83	84	
Cyclohexyl	88	45 (41% olefin)[e]	~99[b]
α-Phenethyl	79		
Ethyl lactate	75		
t-Butyl	49 (25% side product)[d,e]		90[b] (10% olefin)

[a] These are yields of isolated products unless otherwise indicated. Gas chromatographic analyses of crude reaction mixtures showed no side products except as indicated. [b] Gas chromatographic analysis only. [c] The isomeric bromides were separated on a 20-ft. Carbowax column. No isomer contamination was found (<1% would be detectable). [d] Isobutylene or its dibromide was isolated depending on whether R_3PBr_2 was preformed or generated *in situ*. [e] The alkyl halide was found to eliminate under reaction conditions.



$$Z\text{-}C_6H_4\text{-}OH + (C_6H_5)_3PBr_2 \xrightarrow{200°} Z\text{-}C_6H_4\text{-}Br + HBr + (C_6H_5)_3PO \quad (2)$$

Z = H, 92%; Cl, 90%; NO_2, 60%; CH_3O, 59%

An important characteristic of these reagents is their tendency to induce substitution without elimination or rearrangement. The cyclic halide preparations best illustrate the former point.[3] The conversions of secondary pentyl and neopentyl alcohols to halides without rearrangement illustrate the latter.[4] Phenols are converted at elevated temperatures without position isomers being formed.[5]

The stoichiometry shown in eq. 1 was confirmed for n-butyl bromide formation. Triphenylphosphine oxide was isolated in 92% yield and tributylphosphine oxide hydrobromide obtained in 95% yield.[6] The HBr was determined titrimetrically.

Though results reported here are for chlorides and bromides, the method may be used for iodides as well.[7] Dimethylformamide (DMF) or acetonitrile were the most satisfactory solvents.

n-Butyl Bromide.—Dry n-butyl alcohol (9.2 ml., 0.1 mole) was mixed with 28 g. (0.107 mole) of dry distilled triphenylphosphine[8] in 100 ml. of dry DMF in a nitrogen atmosphere. Baker "purified" bromine was added over a 15-min. period while flask temperature was maintained below 55°. The addition was stopped when 2 drops persisted in giving the solution an orange tint. All volatile material was then removed by distillation at 5 mm. into a receiver cooled in a Dry Ice bath. Cold water (500 ml.) was added and 9.8 g. (91%) of n-butyl bromide separated. It was carefully removed and dried and gave b.p. 100.5–102.2° and $n^{29}D$ 1.436 (lit.[9] b.p. 100.4–100.6°, $n^{20}D$ 1.43784). The product showed one peak in the gas chromatography, which was identical in retention time with that of a reference sample of n-butyl bromide.

Neopentyl Bromide.—The reaction was performed as above employing 22.0 ml. (0.088 mole) of distilled tributylphosphine,[8] 6.95 g. (0.079 mole) of dry neopentyl alcohol, and 4.1 ml. (0.082 mole) of bromine in 75 ml. of DMF.

The mixture was distilled at 2 mm. until no more material came over below 84°. Dilution of the distillate with cold water gave 10.89 g. (91%) of neopentyl bromide, $n^{31.5}D$ 1.4310 (lit.[10] b.p. 104.8 at 732 mm., $n^{20}D$ 1.4370). It showed a single peak in gas chromatography with retention time identical with that of an authentic sample. It gave no precipitate with alcoholic silver nitrate.

Neopentyl Chloride.—Triphenylphosphine dichloride was prepared by chlorination of 10.0 g. (0.037 mole) of

(1) These reagents do not appear to have been exploited. For a few examples see ref. 2b,c. Landauer, Rydon, and co-workers have developed a related series of reagents, $(C_6H_5O)_3PRX$, where X = halogen and R = alkyl, H, or halogen.[2d,e] These appear to be useful reagents for the preparation of many alkyl and aryl halides. For descriptions of preparations and properties of R_3PX_2 see ref. 2f, 2g, and citations therein.

(2) (a) F. Fleissner, *Chem. Ber.*, **13**, 1665 (1880); (b) L. Horner, H. Oediger, and H. Hoffmann, *Ann.*, **626**, 26 (1959); (c) H. Hoffmann, L. Horner, H. G. Wippel, and D. Michael, *Chem. Ber.*, **95**, 523 (1962); (d) S. R. Landauer and H. N. Rydon, *Chem. Ind.* (London), 313 (1951); *J. Chem. Soc.*, 2224 (1953); D. G. Coe, S. R. Landauer, and H. N. Rydon, *ibid.*, 2281 (1954); (e) D. G. Coe, H. N. Rydon, and B. L. Tonge, *ibid.*, 323 (1957); (f) V. K. Issleib and W. Seidel, *Z. anorg. allgem. Chem.*, **288**, 201 (1956); (g) G. M. Kosolapoff, "Organophosphorus Compounds," John Wiley and Sons, Inc., New York, N. Y., 1950, p. 73.

(3) P. Carré and D. Libermann, *Bull. soc. chim. France*, [4] **53**, 1051 (1933); C. E. Wood and M. A. Comley, *J. Chem. Soc.*, **125**, 2636 (1925); E. P. Kohler and M. C. Burnley, *Am. Chem. J.*, **43**, 413 (1910).

(4) (a) F. C. Whitmore and H. S. Rothrock, *J. Am. Chem. Soc.*, **54**, 3431 (1932); (b) L. H. Sommers, H. D. Blankman, and D. C. Miller, *ibid.*, **73**, 3542 (1951); (c) the preparations of 2- and 3-pentyl bromides from the corresponding alcohols reported here appear to be the first direct conversions in this series without isomerization, *cf.* H. Pines, A. Rudin, and V. N. Ipatieff, *J. Am. Chem. Soc.*, **74**, 4063 (1952).

(5) (a) Similar transformations have been described using $(C_6H_5)_3PCl_2$[2c] and $(C_6H_5O)_3PCl_2$,[2e] the latter being limited to negatively substituted phenols.[2e] (b) This reaction was not attempted using $(n\text{-Bu})_3PX_2$ since at high temperatures a similar substance is reported to decompose to alkyl halide and halophosphine [J. N. Collie and G. N. White, *J. Chem. Soc.*, **107**, 367 (1915)].

(6) This substance analyzed for $(n\text{-Bu})_3PO \cdot {}^2/_3HBr$.

(7) R. L. Hershkowitz, unpublished results.

(8) Metal and Thermit Co., 100 Park Avenue, New York, N. Y.

(9) C. P. Smyth and E. W. Engel, *J. Am. Chem. Soc.*, **51**, 2651 (1929).

(10) F. C. Whitmore, E. L. Whittle, and B. R. Harriman, *ibid.*, **61**, 1585 (1939).