The protected heptapeptide was decarbobenzoxylated on exposure to HBr in acetic acid and subjected to paper chromatography; R_f^1 0.89, R_f^2 4.85 × his, single ninhydrin-positive spot. A sample of the decarbobenzoxylated heptapeptide was digested with LAP. Paper chromatography of the digest in the Partridge system showed the presence of only six ninhydrin-positive spots with R_f's 0.23, 0.28, 0.46, 0.50, 0.64, and 0.71, identical with the R_f's of authentic sample of glycine, alanine, tyrosine, valine, leucine, and S-benzylcysteine, respectively.

Amino acid analysis of an acid hydrolysate of the deblocked heptapeptide showed the expected composition expressed in molar ratios: $gly_{0.95}ala_{0.91}val_{1.05}leu_{2.0}tyr_{0.95}$. S-Benzylcysteine present in a paper chromatogram of the hydrolysate (R_f^1 0.71) was not determined.

N-Carbobenzoxy-γ-benzyl-L-glutamyl-L-alanyl-L-leucyl-L-tyrosyl-L-leucyl-L-valyl-S-benzyl-L-cysteinylglycine (VII).—N-Carbobenzoxy-L-alanyl-L-leucyl-L-tyrosyl-L-leucyl-L-valyl-S-benzyl-L-cysteinylglycine (1.42 g.) was dissolved in acetic acid (15 ml.) and treated with 4 *N* HBr in acetic acid (15 ml.). After 1 hr. at room temperature, the solvent was removed *in vacuo* and the remaining peptide hydrobromide was triturated with ether and dried over KOH. To a solution of this product in dimethylformamide (20 ml.) was added N-carbobenzoxy-γ-benzyl-L-glutamic acid *p*-nitrophenyl ester (0.76 g.) dissolved in dimethylformamide (10 ml.) and triethylamine (0.4 ml.). The solution was stirred for a few minutes and the excess of base was neutralized with acetic acid (*ca.* 0.2 ml.). The reaction mixture was stirred for 24 hr. at 0° and for 48 hr. at room temperature. Some insoluble material was removed by filtration and the filtrate was poured into 1 *N* HCl (500 ml.). The precipitated product was isolated by filtration, washed with water, and dried; wt. 1.39 g. (78%), m.p. 248–250°. A sample for analysis was reprecipitated from dimethylformamide–ether; m.p. 251–252°, $[\alpha]^{28}D$ −38° (*c* 1.12, acetic acid).

Anal. Calcd. for $C_{61}H_{80}N_8O_{14}S$: C, 62.0; H, 6.82; N, 9.5. Found: C, 61.5; H, 6.71; N, 9.4.

For paper chromatography a sample was decarbobenzoxylated on exposure to HBr in acetic acid; R_f^1 0.86, R_f^2 3.91 × his, single ninhydrin-positive spot. Amino acid analysis of an acid hydrolysate showed the expected composition expressed in molar ratios: $gly_{0.98}glu_{0.80}ala_{0.98}val_{1.1}leu_{2.0}tyr_{0.60}$. S-Benzylcysteine present in a paper chromatogram of the hydrolysate (R_f^1 0.71) was not determined.

N-Carbobenzoxy-L-alanyl-L-leucyl-L-tyrosyl-L-leucyl-L-valyl-S-benzyl-L-cysteinylglycyl-γ-benzyl-L-glutamyl-Nω-tosyl-L-arginylglycyl-L-phenylalanyl-L-phenylalanyl-L-tyrosyl-L-threonyl-L-prolyl-Nε-tosyl-L-lysyl-L-alanine Methyl Ester (VIII). A.—A solution of N-carbobenzoxy-γ-benzyl-L-glutamyl-Nω-tosyl-L-arginylglycyl-L-phenylalanyl-L-phenylalanyl-L-tyrosyl-L-threonyl-L-prolyl-Nε-tosyl-L-lysyl-L-alanine methyl ester[5] (1.76 g.) in acetic acid (15 ml.) was treated with 4 *N* HBr in acetic acid (12 ml.). After 45 min. at room temperature, the reaction mixture was poured into anhydrous ether (100 ml.). The precipitated decapeptide ester hydrobromide was isolated by filtration, washed with ether, and reprecipitated from methanol–ether. This product was subsequently used for condensation with the heptapeptide VI. To a cooled (0°) solution of compound VI (0.99 g.) in dimethylformamide (15 ml.) containing triethylamine (0.15 ml.) was added 2-ethyl-5-phenyloxazolium-3′-sulfonate (0.26 g.). The reaction mixture was stirred at 0° for 1 hr. and then diluted with a solution of the decapeptide ester in dimethylformamide prepared as noted: the hydrobromide salt of the decapeptide ester which was made as described above was dissolved in dimethylformamide (12 ml.) containing triethylamine (0.18 ml.) and then added to the activated carboxyl component prepared as described previously. After 24 hr. at room temperature, the reaction mixture was cooled and diluted with a mixture consisting of saturated $KHCO_3$ (10 ml.), water (150 ml.) and methanol (40 ml.). The precipitated product was isolated by centrifugation and washed on the centrifuge successively with a mixture of dimethylformamide–methanol–water (1:1:7), and 20% aqueous methanol. On reprecipitation from 50% aqueous acetic acid, 1 g. (38%) of product was obtained, m.p. 265–268°, $[\alpha]^{27}D$ −33.6° (*c* 0.36, dimethylformamide).

Anal. Calcd. for $C_{129}H_{167}N_{21}O_{29}S_3 \cdot 3H_2O$: C, 59.0; H, 6.52; N, 11.20. Found: C, 58.6; H, 6.80; N, 11.40.

The protected heptadecapeptide was decarbobenzoxylated on exposure to 2 *N* HBr in acetic acid and chromatographed on paper; R_f^1 0.95, R_f^3 0.82, single sharp ninhydrin-positive spots. Amino acid analysis of an acid hydrolysate of the protected heptadecapeptide by the automatic analyzer showed the following composition expressed in molar ratios: $lys_{0.92}arg_{1.00}$ S-benzylcysteine$_{0.84}thr_{0.96}glu_{1.12}pro_{1.04}gly_{2.08}ala_{1.84}val_{1.08}leu_{2.16}tyr_{1.88}phe_{2.00}$. Average amino acid recovery was 96% of theory.

B.—To a precooled (0°) solution of VI (0.5 g.) in dimethylformamide (15 ml.), N,N′-carbonyldiimidazole (0.12 g.) was added. The reaction mixture was stirred at 0° for 1.5 hr. and then diluted with a solution of the decapeptide ester hydrobromide in dimethylformamide (10 ml.) containing triethylamine (0.12 ml.). The decapeptide ester hydrobromide was prepared, as described in A, from 1.1 g. of the carbobenzoxy derivative and 20 ml. of 2 *N* HBr in acetic acid. After 2 hr. at 0° and 20 hr. at room temperature, the reaction mixture was treated as in A and yielded 0.74 g. (56%) of product, m.p. 265–268°.

Acknowledgments.—The authors wish to thank Mrs. Jemele Hudson for the enzymatic analysis and amino acid analyses reported in this work.

COMMUNICATIONS TO THE EDITOR

cis- and *trans*-1,2-Diphenylnaphtho[*b*]cyclobutenes. A Novel Synthesis of a Naphthalene Nucleus

Sir:

In order to effect the synthesis of a stabilized aromatic-fused cyclobutadiene,[1] it was necessary to develop practical routes to the 1,2-diphenylnaphtho[*b*]cyclobutene system. Two entirely unrelated approaches are described below.

Reaction of 3-benzyl-2-naphthoic acid (I)[2] with thionyl chloride in methylene chloride–benzene gives the corresponding acid chloride which, without isolation, is converted directly by gaseous ammonia into 3-benzyl-2-naphthamide (II),[3] m.p. 197.5–198.5°, in 93% yield. Phosphorous oxychloride dehydration of amide II affords 3-benzyl-2-cyanonaphthalene (III), m.p. 111–112°, in 78% yield. Addition of phenylmagnesium bromide to nitrile III gives, after acid hydrolysis of the intermediary imine, 3-benzyl-2-benzoylnaphthalene (IV), m.p. 82–83°, in 69% yield. Sodium borohydride reduction of ketone IV gives the alcohol V which, without purification, is converted by thionyl chloride into the corresponding chloride VI; reaction of crude VI with potassium *t*-butoxide affords, in 78% yield (based on IV), *trans*-1,2-diphenylnaphtho[*b*]cyclobutene (VII), m.p. 158–159°.[4] Although VII is more stable thermally than the related *trans*-1,2-diphenylbenzocyclobutene,[5] it undergoes rearrangement in good yield (83%) in boiling dimethylformamide (*ca.* 150°) to give 5-phenyl-5,12-dihydronaphthacene (VIII), m.p. 149–150°; fusion of a mixture of VII and N-phenylmaleimide at 150° gives a Diels–Alder adduct (IX), m.p. 276–278°, in 50% yield. Free-radical

(1) M. P. Cava, B. Hwang, and J. P. Van Meter, *J. Am. Chem. Soc.*, **85**, 4032 (1963).

(2) E. de B. Barnett and R. A. Lowry, *Ber.*, **65**, 1649 (1932).

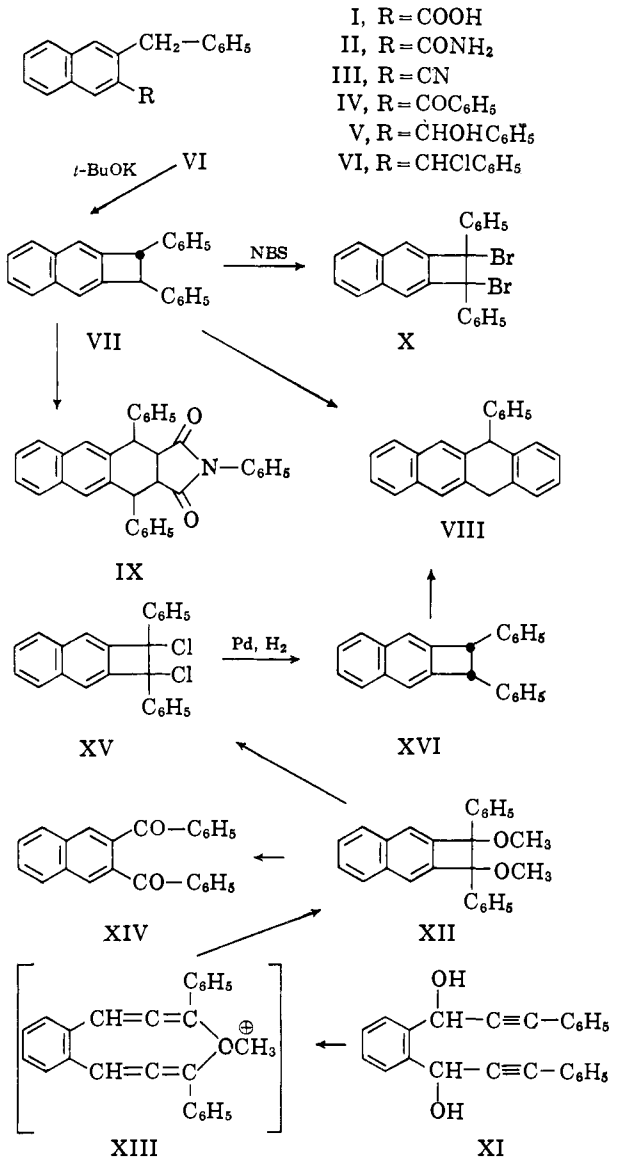
(3) Melting points are uncorrected. Satisfactory analyses were obtained for all new compounds, the spectra of which were also consistent with the assigned structures.

(4) The analogous dehydrohalogenation of an α-halo-α,α′-diphenyl-*o*-xylene to *trans*-1,2-diphenylbenzocyclobutene was first reported in 1958 (see ref. 5). We are grateful to Dr. A. J. Berlin for valuable suggestions concerning improvements in this type of reaction.

(5) F. R. Jensen and W. E. Coleman, *J. Am. Chem. Soc.*, **80**, 6149 (1958).

bromination of VII with N-bromosuccinimide in carbon tetrachloride proceeds smoothly in the presence of benzoyl peroxide to give, in 89% yield, 1,2-dibromo-1,2-diphenylnaphtho[*b*]cyclobutene (X), m.p. 180–183° dec.[6]

The second entry into the 1,2-diphenylnaphtho[*b*]-cyclobutene system employs a novel two-step route from a simple benzene derivative. Thus, *o*-phthalaldehyde reacts with phenylethynylmagnesium bromide to give, in 66% yield, the bispropargylic alcohol XI, m.p. 109–110°. Reaction of diol XI with warm dry methanolic hydrogen chloride affords, in 35–40% yield, 1,2-dimethoxy-1,2-diphenylnaphtho[*b*]cyclobutene (XII)[6] as colorless crystals, m.p. 150–151° dec.; a diallenic compound such as XIII is assumed to be an intermediate in this cyclization.[7] The presence of a naphthalene nucleus in XII is indicated not only by the similarity of its ultraviolet spectrum (λ_{max} 230, 272, 283, 293, 307, 320 mμ) to that of naphtho[*b*]-cyclobutene[8] but also by its slow reaction with bromine in carbon tetrachloride to give (65% yield) 2,3-dibenzoylnaphthalene (XIV), identical with authentic material.[1]



(6) The stereochemistry of this compound is as yet undetermined.

(7) Several instances have been recorded of the intermolecular dimerization of acetylenic alcohols to unsaturated cyclobutanes, presumably *via* allenic intermediates: (a) T. Nagase, *Bull. Chem. Soc. Japan*, **34**, 139 (1961); (b) P. D. Landor and S. R. Landor, *Proc. Chem. Soc.*, 77 (1962)

(8) M. P. Cava and R. L. Shirley, *J. Am. Chem. Soc.*, **82**, 654 (1960).

Reaction of ether XII with acetyl chloride at room temperature affords, in 66% yield, 1,2-dichloro-1,2-diphenylnaphtho[*b*]cyclobutene (XV),[6] m.p. 149–150° dec. Catalytic reduction of dichloride XV in the presence of palladium–charcoal and triethylamine gives, in 95% yield, *cis*-1,2-diphenylnaphtho[*b*]cyclobutene (XVI), m.p. 141–141.5°. When a solution of XVI in dimethylformamide is refluxed, the compound rearranges (90% yield) to the *identical hydrocarbon VIII*, formed by thermolysis of the *trans* isomer VII.

As with the corresponding *cis* and *trans* isomers of 1,2-diphenylbenzocyclobutene,[9] the stereochemistry of XVI and VII may be assigned on the basis of the positions of their benzylic protons in the n.m.r. Thus, the benzylic protons of the *trans* isomer VII are more shielded (4.67 δ) than those of the *cis* isomer XVI (5.34 δ).

The conversion of dihalides XV and X into a stable naphthocyclobutadiene is described in the following communication.

Acknowledgment.—We are grateful to the National Science Foundation for a grant in support of this work. We also express thanks to Mr. R. H. Schlessinger for determining the n.m.r. spectra of compounds in this series.

(9) L. A. Carpino, *ibid.*, **84**, 2196 (1962).

EVANS CHEMICAL LABORATORY
THE OHIO STATE UNIVERSITY
COLUMBUS 10, OHIO

M. P. CAVA
B. HWANG
J. P. VAN METER

RECEIVED OCTOBER 21, 1963

A Stable Naphtho Derivative of Cyclobutadiene

Sir:

No example has yet been recorded of a compound containing a cyclobutadiene nucleus which is neither stabilized as a transition metal complex nor fused on both sides, as in biphenylene, to aromatic rings. Attempts to stabilize cyclobutadiene by substituting phenyl groups for all four of its hydrogens,[1] or by fusing one side only of the four-membered ring to a benzene[2] or a naphthalene[3] nucleus, have not led to the formation of isolable monomeric hydrocarbons. We now report the synthesis of 1,2-diphenylnaphtho-[*b*]cyclobutadiene (I), a stable crystalline analog of the transient molecule benzocyclobutadiene.

The reaction of 1,2-dichloro-1,2-diphenylnaphtho-[*b*]cyclobutene (II)[4] with zinc dust in boiling benzene for 3 min., followed by chromatography on alumina, affords in 60% yield, bright red needles of 1,2-diphenylnaphtho[*b*]cyclobutadiene (I), m.p. 137–138°: λ_{max}^{EtOH} 209 mμ (log ε 4.71), 257 (4.68), 289 (4.85), 300 (4.87), 436 (3.71), 455 (3.71). The 2,4,7-trinitrofluorenone complex I forms black needles, m.p. 182–183°. Hydrocarbon I is obtained also, in 49% yield, by zinc debromination of 1,2-dibromo-1,2-diphenylnaphtho-[*b*]cyclobutene (III).[4] In the presence of palladium-on-charcoal catalyst a solution of I in benzene–ethanol is reduced rapidly at room temperature to *cis*-1,2-diphenylnaphtho[*b*]cyclobutene (IV)[4] in 95% yield. Further confirmation of the structure of I results from its behavior on oxidation with potassium permanganate in acetone, which affords 2,3-dibenzoylnaphthalene (V) in 80% yield; an authentic sample of diketone V (m.p. 143–145°) was synthesized for comparison purposes in 87% yield by the pyridine–chromic oxide oxidation of the previously described lactol VI.[5]

(1) H. H. Freedman, *J. Am. Chem. Soc.*, **83**, 2194 (1961).

(2) M. P. Cava and D. R. Napier, *ibid.*, **79**, 1701 (1957).

(3) C. D. Nenitzescu, M. Avram, I. G. Dinulescu, and G. Mateescu, *Ann.*, **653**, 79 (1962).

(4) M. P. Cava, B. Hwang, and J. P. Van Meter, *J. Am. Chem. Soc.*, **85**, 4031 (1963).

(5) M. P. Cava and J. P. Van Meter, *ibid.*, **84**, 2008 (1962).