In a similar experiment, tensimetric titration of triphenylmethyl methyl ether in toluene solution with the acid showed the formation of a 1:1 complex. The resulting yellow compound was less stable in methylene chloride solution than the product of eq 1. Equilibrium measurements in dilute methylene chloride solutions indicate that at low $F_2B-CH_2-CH_2-BF_2$ concentrations a 2:1 adduct forms, but in the presence of a large excess of acid the 1:1 complex predominates.

$$C_2H_4B_2F_4 \cdot 2(C_6H_5)_3C-O-CH_3 + C_2H_4B_2F_4 = 2[(C_6H_5)_3C]^+ \left[CH_3-O(BF_2-CH_2)_2 \right]^- \quad (2)$$

The true nature of the anion was not elucidated by the form of the equilibrium constant because ion clusters formed in the low dielectric constant solvent are not distinguishable from high molecular weight substances.

To circumvent the complications introduced by the equilibrium shown in eq 2, a tropenium (tropylium) derivative was prepared *via* hydride exchange (eq 3).[4] A 0.357-mmole sample of the acid was added to a

$$[(C_6H_5)_3C]^+ \left[CH_3-O(BF_2-CH_2)_2 \right]^- + \bigcirc\!\!=\!\!\bigcirc \rightarrow \left[\bigcirc\!\!=\!\!\bigcirc \right]^+ \left[CH_3-O(BF_2-CH_2)_2 \right]^- + (C_6H_5)_3CH \quad (3)$$

solution of 0.308 mmole of triphenylmethyl methy ether in methylene chloride. An excess of 1,3,5-cycloheptatriene was added, whereupon a white crystalline precipitate formed. The reaction mixture was filtered and washed with pentane. Vacuum evaporation of the solvent and excess reagents from the filtrate gave 0.309 mmole of triphenylmethane which was characterized by an infrared spectrum and melting point: mp 92.0°, lit. 92.5°. Also, a flame test on this methylene chloride soluble product indicated the absence of boron. The infrared and ultraviolet spectra of the precipitate matched those cited in the literature for the $C_7H_7^+$ cation.[5,6] Significantly, the only infrared absorption frequencies characteristic of B–F stretching motions were in the 1000-cm^{-1} region which is symptomatic of four-coordinated boron. Thus, the general correctness of reaction 3 is established, but just as in reactions 1 and 2 there is the possibility of a polymeric anion.

To settle this question, cryoscopic molecular weight measurements were performed on freshly prepared tetramethylene sulfone solutions of the tropylium salt.[7] The resulting solutions slowly decomposed as indicated by changes in freezing point depression and the development of a yellow coloration. Therefore, it was not possible to obtain sufficiently accurate data to establish a reliable ion-pairing constant. However, an average molecular weight of 211 ± 31 was determined for four solutions in the 0.05 to 0.20 *m* range; the formula weight is 248. For comparison, the apparent molecular weight of a similar salt, tetrapropylammonium tetrafluoroborate, was investigated and found to be 207 in a 0.101 *m* tetramethylene sulfone solution. The formula weight of this salt is 273. Thus, molecular weight and infrared data indicate a chelate structure for the tropenium salt and a similar structure is inferred for the other salts.

While the foregoing observations establish a *chelate structure*, they do not prove a *chelate effect*. In our current work we are employing displacement experiments to test for this effect.

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Synthesis of Tyrocidine A

Sir:

Tyrocidine A is an antibiotic cyclic peptide isolated as its hydrochloride in 1952 by Battersby and Craig[1] from the cultured filtrate of *Bacillus brevis*. Its structure has been proposed by Craig and his colleagues to be I_n.[2] It is of interest to note that the pentapeptide sequence L-Val-L-Orn-L-Leu-D-Phe-L-Pro

L-Val-L-Orn-L-Leu-D-Phe-L-Pro
↑ ↓
L-Tyr-L-Gln-L-Asn-D-Phe-L-Phe
I_n

is also found in gramicidin S[3] and tyrocidines B[4] and C.[5] Although the partial syntheses of the open-chain peptides related to tyrocidine A have been reported,[6] the complete synthesis has not been accomplished.

We wish to report the synthesis of the cyclic decapeptide (I_s) having the structure of I_n and on the identity of I_s with natural tyrocidine A in chemical and biological properties.[7] *p*-MZ-L-Phe-D-Phe-OEt (II), mp 126–128°, $[\alpha]_D$ −2.8°, was prepared, in a yield of 79%, by coupling *p*-methoxybenzyloxycarbonyl-L-phenylalanine with D-phenylalanine ethyl ester by the mixed anhydride method.[8] II was treated with hydrazine to

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(7) Satisfactory analyses and chromatographic data were obtained for all crystalline compounds described here. Melting points were uncorrected. $[\alpha]_D$ refers to a solution in dimethylformamide at 20° except the cyclic decapeptide hydrochlorides, $I_s \cdot HCl$ and $I_n \cdot HCl$. The abbreviations are as follows: Z, benzyloxycarbonyl; *p*-MZ, *p*-methoxybenzyloxycarbonyl; BOC, *t*-butyloxycarbonyl; $NHNH_2$, hydrazide.
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afford *p*-MZ-L-Phe-D-Phe-$NHNH_2$ (III), 96%, mp 194–195°, $[\alpha]D$ −3.4°. Condensation of benzyloxycarbonyl-L-glutamine *p*-nitrophenyl ester[9] with L-tyrosine ethyl ester gave Z-L-Gln-L-Tyr-OEt (IV), 70%, mp 197–199°, $[\alpha]D$ +1.8°, which was treated with hydrogen bromide in acetic acid to produce oily H-L-Gln-L-Tyr-OEt·HBr (V) in a yield of 94%. Z-L-Asn-L-Gln-L-Tyr-OEt (VI), 72%, mp 224–225°, $[\alpha]D$ −11.6°, obtained from benzyloxycarbonyl-L-asparagine *p*-nitrophenyl ester[9] and V, was converted to oily H-L-Asn-L-Gln-L-Tyr-OEt·HBr (VII) in a yield of 98%. *p*-MZ-L-Phe-D-Phe-L-Asn-L-Gln-L-Tyr-OEt (VIII), 75%, mp 206–209°, $[\alpha]D$ −10.4°, was obtained by condensation of the azide derived from III with VII. VIII was treated with hydrazine to afford *p*-MZ-L-Phe-D-Phe-L-Asn-L-Gln-L-Tyr-$NHNH_2$ (IX), 86%, mp 225–227°, $[\alpha]D$ −26.0°. BOC-L-Val-δ-Z-L-Orn-OEt[10] was similarly converted to BOC-L-Val-δ-Z-L-Orn-$NHNH_2$ (X), 83%, mp 175°, $[\alpha]D$ −14.1°. Oily Z-D-Phe-L-Pro-OEt, which was obtained, in a yield of 86%, by condensation of benzyloxycarbonyl-D-phenylalanine with L-proline ethyl ester *p*-toluenesulfonate[11] by the mixed anhydride method, was converted to the oily dipeptide ester hydrochloride (XI) by catalytic hydrogenation; 98%, R_f[12] 0.88. Oily Z-L-Leu-D-Phe-L-Pro-OEt, which was obtained, in a yield of 95%, from benzyloxycarbonyl-L-leucine and XI by the mixed anhydride method, was also converted to oily H-L-Leu-D-Phe-L-Pro-OEt·HCl (XII) by hydrogenation; 94%, R_f[12] 0.92. Condensation of the azide derived from X with XII gave BOC-L-Val-δ-Z-L-Orn-L-Leu-D-Phe-L-Pro-OEt (XIII), 69%, mp 167–170°, $[\alpha]D$ −32.1°. XIII was saponified with alkali to BOC-L-Val-δ-Z-L-Orn-L-Leu-D-Phe-L-Pro-OH (XIV), 86%, mp 122–125°, $[\alpha]D$ −39.0°. Removal of the *t*-butyloxycarbonyl group from XIV by treatment with hydrogen chloride in ethyl acetate yielded H-L-Val-δ-Z-L-Orn-L-Leu-D-Phe-L-Pro-OH·HCl (XV), 95%, mp 195–200° dec, $[\alpha]D$ −22.5°; an attempt to crystallize the HCl-free pentapeptide failed. Condensation of the azide derived from IX with XV gave *p*-MZ-L-Phe-D-Phe-L-Asn-L-Gln-L-Tyr-L-Val-δ-Z-L-Orn-L-Leu-D-Phe-L-Pro-OH (XVI), 75%, mp 233–236° dec, $[\alpha]D$ −31.6° (*Anal.* Calcd for $C_{83}H_{103}O_{10}N_{13}$: C, 62.82; H, 6.54; N, 11.48. Found: C, 62.58; H, 6.57; N, 11.63), after hydrogenation; R_f[13] 0.80. Treatment of XVI with 10 equiv of di-*p*-nitrophenyl sulfite[14] gave amorphous acyldecapeptide *p*-nitrophenyl ester (XVII). The *p*-methoxybenzyloxycarbonyl group of XVII was removed by the action of trifluoroacetic acid and the decapeptide *p*-nitrophenyl ester trifluoroacetate obtained was treated with a large amount of hot pyridine for the cyclization reaction.[15] Purification of the crude product by passing its aqueous dioxane solution through columns of Dowex 50 (H^+ form) and Amberlite IR-4B (OH^- form) gave cyclo-L-Phe-D-Phe-L-Asn-L-Gln-L-Tyr-L-Val-δ-Z-L-Orn-L-Leu-D-Phe-L-Pro (XVIII), 60% (from XVI), mp 263–265° dec, $[\alpha]D$ −111°, R_f[13] 0.94. *Anal.* Calcd for $C_{74}H_{93}O_{15}N_{13}$: C, 63.27; H, 6.67; N, 12.96. Found: C, 63.42; H, 6.86; N, 12.77. The molecular weight of XVIII was determined on a Model 301 A osmometer, Mechrolab Inc. (solvent, methanol) (calcd, 1405; found, 1422).[16] Removal of the benzyloxycarbonyl group from XVIII by catalytic hydrogenation in the presence of 1 equiv of hydrogen chloride in methanol provided cyclo-L-Phe-D-Phe-L-Asn-L-Gln-L-Tyr-L-Val-L-Orn-L-Leu-D-Phe-L-Pro·HCl·$7H_2O$ (I_s·HCl) as an air-dried product; 74%, mp 239–240° dec. *Anal.* (of a desiccator-dried sample). Calcd for $C_{68}H_{87}O_{13}N_{13}$·HCl·$5H_2O$: C, 56.75; H, 7.00; N, 13.03. Found: C, 57.12; H, 6.96; N, 12.79. Seven moles of water of crystallization was lost when the air-dried sample was heated at 110° under vacuum for 2 hr (calcd, 8.80%; found, 8.78%). Quantitative amino acid determination gave the following molar ratio: Phe, 3.0; Asp, 1.0; Glu, 1.0; Tyr, 0.8; Val, 1.0; Orn, 1.0; Leu, 1.0; Pro, 1.0; NH_3, 2.1.

The synthetic product (I_s·HCl) was compared with the material (I_n·HCl)[17] of natural origin in chemical and biological properties. In addition to having the same R_f values on thin layer (R_f[13] 0.76) and paper chromatography (R_f[12] 0.92) and having indistinguishable paper electrophoretic patterns (solvent, formic acid–acetic acid–methanol–water, 1:3:6:10, v/v), I_s·HCl and I_n·HCl had completely superimposable infrared and ultraviolet spectra, identical behaviors on a carboxymethylcellulose column[18] (0.9 × 100 cm; solvent, 0.2 *M* pyridine–acetate buffer, pH 5.0), and the same optical rotation values ($[\alpha]D$ −108° for I_s·HCl and −108° for I_n·HCl (air-dried samples) (*c*, 0.14% in 50% ethanol); lit.[1] $[\alpha]^{25}D$ −111° for a sample dried at 110° (*c*, 1.37% in 50% ethanol). Furthermore, very close similarities were seen in the antibacterial activities of both compounds to microorganisms (Table I).[19]

Table I

	Amt of compd nec for complete inhbtn of growth, μg/ml				
	E. coli	*P. vulgaris*	*S. aureus*	*B. subtilis*	*M. avium*
(A) Stephenson-Whetham's Synthetic Medium (modified)					
I_s·HCl	>100	>100	20	10	>100
I_n·HCl	>100	50	20	20	>100
Gramicidin S·2HCl	>100	>100	5	5	>100
(B) Bouillon agar medium					
I_s·HCl	>100	>100	20	10	>100
I_n·HCl	>100	>100	20	10	>100
Gramicidin S·2HCl	>100	>100	2–5	2–5	>100

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(13) The R_f of the thin layer chromatography refers to the system 1-butanol–acetic acid–pyridine–water (4:1:1:2, v/v). Compounds possessing a free amino group were detected by spraying with ninhydrin and those with blocked amino groups by spraying with 47% hydrobromic acid, followed by ninhydrin.
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(18) We are indebted to Mr. H. Aoyagi in this laboratory, who has found the usefulness of the application of CM-cellulose column chromatography for the separation of a mixture of basic cyclic peptides.
(19) We are indebted to Dr. M. Shibata of Takeda Chemical Industries Ltd., Japan, for the biological assays.

The results obtained here confirm further the correctness of the structure of tyrocidine A given as I_n by Craig, *et al.*[20]

Work on syntheses of the cyclic decapeptides corresponding to the proposed structures for tyrocidine B[4] and C[5] is in progress in this laboratory.

(20) This work will be described in full in *Bull. Chem. Soc. Japan.*

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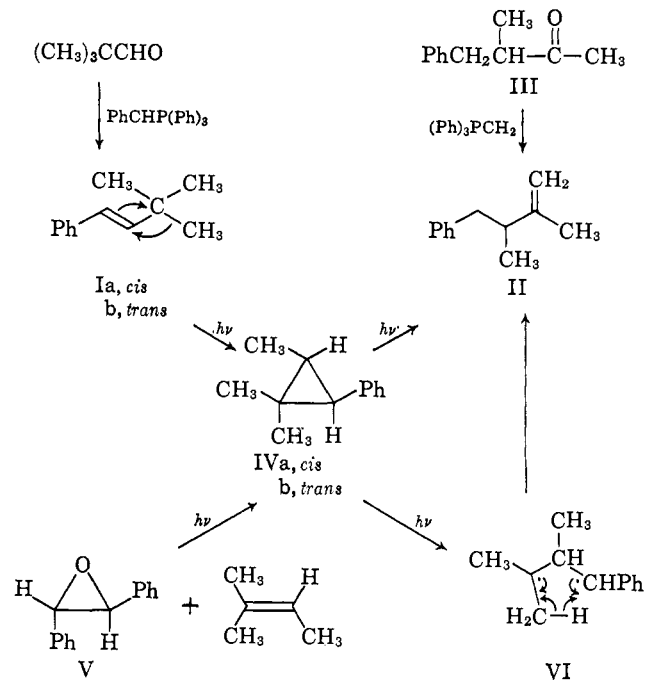
Photocyclization of 3,3-Dimethyl-1-phenylbutene-1. A Novel Photoinduced 1,2-Methyl Migration

Sir:

We wish to report the first example of a photoinduced 1,2-methyl migration in a simple hydrocarbon system.[1] Recent work on the photocyclization of propenes (which proceed with phenyl and/or hydrogen migration)[2] led us to believe that 1,2-alkyl migrations might be induced photochemically in such systems despite the absence of any confirmed reports of ground-state homolytic reactions of this type.[3] Comparatively little "ionic" character may be attributed to the π,π^* singlet and triplet states of alkyl- and aryl-substituted propenes. Presumably, then, the photochemistry of these hydrocarbons should approximate the unknown ground state homolytic processes more closely than the corresponding n,π^* reactions.[1]

A mixture (1.3:1) of *cis*- and *trans*-3,3-dimethyl-1-phenylbutene-1 (Ia and Ib, respectively) was synthesized by condensation of trimethylacetaldehyde[4] with the ylid prepared from benzyltriphenylphosphonium bromide and phenyllithium (63% yield); Ia: ν_{max} (cm^{-1}) 3060, 2960, 2870, 1600, 1475, 1360, 1230, 1200, 1070, 1028, 935, 918, 898, 828, 752, 698, and 660; λ_{max} 220 mμ (ϵ 6400); nmr τ 2.90 (5 H singlet), 3.54 and 3.75 (1 H doublet), 4.38 and 4.60 (1 H doublet), and 9.05 (9 H singlet); Ib: ν_{max} (cm^{-1}) 3030, 2960, 2900, 2870, 1360, 1266, 1203, 1070, 1026, 966, 744, and 690; λ_{max} 251 mμ (ϵ 18,100);[5] nmr τ 2.83 (5 H multiplet), 3.83 (2 H singlet), and 8.91 (9 H singlet). The assignment of *cis* stereochemistry to Ia and *trans* stereochemistry to Ib was made on the basis of the following spectroscopic evidence. The *trans* isomer Ib exhibits the characteristic out-of-plane deformation band for the vinyl hydrogens at 966 cm^{-1}. The ultraviolet spectra of Ia and Ib support this assignment. The λ_{max} of Ia is displaced approximately 20 mμ toward shorter wavelength than that of Ib, as might be anticipated. Furthermore, the *t*-butyl protons in the nmr spectrum of Ib are found at lower field than those of Ia, in agreement with prediction. A photoequilibrium between Ia and Ib is established rapidly under the irradiation conditions, and therefore separation was deemed unnecessary. Irradiation[6] of I in benzene (0.1 *M*) for 70 hr afforded almost exclusively 2,3-dimethyl-4-phenylbutene-1 (II).



Identification of the photoproduct II, ν_{max} (cm^{-1}) 3080, 3065, 3025, 2970, 2930, 1635, 1600, 1485, 1450, 1370, 1112, 1100, 1078, 1030, 890, 757, 736, 720, and 698; nmr τ 2.95 (5 H singlet), 5.37 (2 H singlet), 7.67–7.17 (3 H multiplet), 8.33 (3 H singlet), and 9.00 and 9.10 (3 H doublet), was achieved by comparison with an authentic sample prepared by condensation of triphenylmethylenephosphorane with 3-methyl-4-phenylbutanone-2 (III).[7]

The primary products in this photoreaction are presumably *cis*- and *trans*-2,2,3-trimethyl-1-phenylcyclopropane (IVa and b, respectively), whose presence in the irradiation mixtures is apparent from comparisons of gas chromatographic retention times. However, variation of the concentration and irradiation time did not permit maximization of the concentration of IVa and IVb to isolable levels.

Our conclusion that IVa and IVb are intermediates in the conversion of I to II is supported by the observation that the isomeric cyclopropanes (IVa and IVb) are *completely* converted to the olefin II after only 24-hr irradiation in benzene (0.1 *M*). It is clear in view of this result why the cyclopropanes do not accumulate upon photolysis of I. IVa and IVb were synthesized

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(5) Infrared spectra were determined as neat films on a Perkin-Elmer Model 337 infrared spectrophotometer while ultraviolet spectra were obtained in 95% ethanol on a Model 202 ultraviolet–visible spectrophotometer.

(6) An air-cooled (40°) Rayonet chamber reactor (Southern New England Ultraviolet Co., Middletown, Conn.) equipped with 16 8-w low-pressure mercury lamps was employed as a light source. All solutions were rigorously degassed. Gas chromatographic analyses and separations were conducted on a 210 × 0.6 cm i.d. glass column packed with 30% silicone gum (SE-30) on 60–80 mesh acid- and base-washed Chromosorb P. Satisfactory elemental analyses were obtained on all new compounds.

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