4-Bromo-5,5-dimethylbicyclo[2.1.1]hexane-1-carboxaldehyde (10).—The amino alcohol (1.21 g) was dissolved in 29 ml of a 50% acetic acid solution. The deamination was done under nitrogen at a temperature of 0–5°. A magnetic stirrer provided efficient stirring. Sodium nitrite (2.76 g, 0.04 mol) was dissolved in 10 g of water, and the solution was added in a period of 10 min. The cold mixture was stirred for an additional 20 min, and the acid was neutralized with a saturated solution of sodium carbonate. The solid product was isolated by filtration and washed with cold water. After the product was dried in a vacuum desiccator, sublimation [60–70° (1 mm)] furnished 0.75 g (66%) of aldehyde. Recrystallization from low-boiling petroleum ether (30–60°) afforded the aldehyde **10**: mp 125–127° (bath preheated to 120°); λ_{max} 3.57, 3.69, 5.87 (CHO group), 7.22, and 7.28 μ (*gem*-dimethyl group); nmr spectrum ($CDCl_3$) δ 0.96 (singlet, 3 H, C-5 *endo*-CH_3), 1.32 (singlet, 3 H, C-5 *exo*-CH_3), 1.73 (doublet, 1 H, J = 7.5 cps, C-6 *endo*-H), 2.06 (multiplet, 4 H, C-2 and C-3 H_2), 2.72 (double multiplets, 1 H, J = 7.5 cps, C-6 *exo*-H), and 9.58 (singlet, 1 H, C-1 CHO).

Anal. Calcd for $C_9H_{13}OBr$: C, 49.79; H, 6.04; Br, 36.81. Found: C, 49.67; H, 6.00; Br, 36.91.

The 4-toluenesulfonylhydrazone of aldehyde **10** was prepared. The aldehyde was transferred from the Hirsh funnel in the above procedure to a solution of 4-toluenesulfonylhydrazine (0.96 g) in the minimum amount of hot methanol. The derivative was prepared and isolated in the usual way. After recrystallization from methanol the hydrazone amounted to 1.44 g (72%), mp 133–134°.

Anal. Calcd for $C_{16}H_{21}BrN_2O_2S$: C, 49.87; H, 5.49; Br, 20.73. Found: C, 50.07; H, 5.49; Br, 20.99.

The semicarbazone was prepared from the aldehyde in the above procedure with the theoretical amount of semicarbazide hydrochloride and sodium acetate in aqueous ethanol. Recrystallization from ethanol furnished the derivative (45% yield) with mp 147–148° (bath preheated to 140°).

Anal. Calcd for $C_{10}H_{16}BrN_3O$: C, 43.79; H, 5.78; N, 15.32. Found: C, 43.80; H, 5.79; N, 15.50.

4-Bromo-5,5-dimethylbicyclo[2.1.1]hexane-1-carboxylic Acid (12).—The aldehyde from the above preparation was dissolved in 50 ml of acetone and 4 ml of water. Powdered potassium permanganate (0.82 g) was added to the warm solution. Excess permanganate was destroyed with glycerol, and the solvent was removed. The residue was triturated several times with dilute base. After filtration, the alkaline solution was acidified. The solid product was isolated and sublimed at 60–80° (1 mm). The acid amounted to 0.51 g (42% based on **9**): mp 136–139°; nmr spectrum ($CDCl_3$) δ 0.95 (singlet, 3 H, C-5 *endo*-CH_3), 1.28 (singlet, 3 H, C-5 *exo*-CH_3), 1.80 (doublet, 1 H, J = 7.5 cps, C-6 *endo*-H), 2.07 (multiplet, 4 H, C-2 and C-3 H_2), 2.65 (double multiplets, 1 H, J = 7.5 cps, C-6 *exo*-H), 11.28 (singlet, 1 H, C-1 COOH).

In one oxidation the product was an acid that did not contain bromine on analysis. After crystallization from aqueous ethanol the impure acid melted at 158–159°, and unsaturation was evident in the ultraviolet (uv) spectrum.

4-Bromo-2-hydroxy-7,7-dimethyl-1-norbornylcarbamyl Azide (13).—The semicarbazide **5** (1.51 g) was dissolved in 20 ml of 90% acetic acid. Sodium nitrite (5.52 g) was dissolved in 20 ml of water, and the solution was added dropwise to the semicarbazide. The solution was stirred for 1 hr at room temperature. The product precipitated on the addition of water. The solid was recrystallized from ethanol to furnish the azide (70%): mp 151–152° dec; λ_{max} 4.66 (azide) and 5.95 μ (C=O).

Anal. Calcd for $C_{10}H_{15}BrN_4O_2$: C, 39.61; H, 4.98; N, 18.47. Found: C, 39.76; H, 4.84; N, 18.49.

4-Bromo-7,7-dimethyl-2-oxo-1-norbornylcarbamyl Azide (14).—The azide **13** (2.89 g) was added to glacial acetic acid (150 ml) that contained 0.95 g of chromium trioxide. The solution was stirred for 2 hr at room temperature. The solvent was neutralized with sodium carbonate, and the product was extracted with ether. The ethanol solution was dried with anhydrous magnesium sulfate, and the solvent was removed with a vacuum evaporator. Crystallization of the residue from aqueous ethanol gave the azide **14** (56% yield): mp 150–151°; λ_{max} 3.00 (NH), 4.67 (N_3), 5.72 (C=O), and 5.83 μ (C=O).

Anal. Calcd for $C_{10}H_{13}N_4O_2$: C, 39.87; H, 4.35; N, 18.59. Found: C, 40.23; H, 4.25; N, 18.10.

1,3-Di-4-bromo-7,7-dimethyl-2-oxo-1-norbornylurea (15).—The azide **14** (2.0 g) was dissolved in 30 ml of tetrahydrofuran. Dilute hydrochloric acid (10 ml) was added, and the solution was maintained at reflux for 1 hr. The acid was neutralized with dilute sodium hydroxide and the volatile solvent was removed with a vacuum evaporator. The residue was extracted with ether. The ethereal solution was dried and the solvent was removed. The residue was crystallized from ethyl acetate to provide the product **15** (25% yield): mp 228–230° dec; λ_{max} 3.0 (NH), 5.70 (C=O), and 5.93 μ (C=O).

Anal. Calcd for $C_{19}H_{26}BrN_2O_3$: C, 46.53; H, 5.34; N, 5.71. Found: C, 46.58; H, 5.61; N, 5.75.

Registry No.—**3**, 19029-14-2; **3** (N-nitroso derivative), 39029-15-3; **5**, 19029-16-4; **6**, 19029-17-5; **7**, 19029-18-6; **9**, 19029-19-7; **10**, 19029-51-7; **10** (4-toluenesulfonylhydrazone), 19039-29-3; **10** (semicarbazone), 19039-30-6; **12**, 19039-31-7; **13**, 19029-20-0; **14**, 19029-21-1; **15**, 19029-22-2; 1-bromo-2,2-dimethylbicyclo[2.2.1]heptan-3-one, 13743-41-4.

Free-Radical α Bromination of Cyclopropyl Compounds by N-Bromosuccinimide

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Attempts to carry out free-radical bromination of norcarane using N-bromosuccinimide (NBS) resulted solely in rearrangement of the NBS to β-bromopropionyl isocyanate. However, with the model systems cycloprop[2,3]indene, benzylcyclopropane, *trans*-1-benzyl-2-methylcyclopropane, and bicyclo[4.1.0]hept-3-ene, in which the carbons α to the cyclopropane rings are activated toward radical formation by adjacent phenyl or vinyl substituents, azobisisobutyronitrile-initiated NBS bromination in carbon tetrachloride solution proceeds smoothly and rapidly. Product formation in each case is derived predominantly *via* initial hydrogen atom abstraction from a carbon α to a cyclopropane ring. Bromide products derived both from cyclopropylcarbinyl and rearranged allylcarbinyl radical intermediates were observed. In certain cases, products resulting from ion-pair rearrangements and eliminations from initially formed, highly reactive cyclopropylcarbinyl bromides were also found.

During the past several years, considerable interest has been shown[1] in the chemistry of systems which can react *via* formation of cyclopropylcarbinyl or allylcarbinyl radical intermediates. Much of this work was done with the objective of finding evidence for rate accelerations caused by cyclopropyl or homoallyl participation at the transition states in radical-forming reactions. Also, information was sought regarding whether two discrete classical radical intermediates or a

(1) For articles which summarize much of the research which has been done in this area, see: (a) C. Walling in "Molecular Rearrangements," Vol. I, P. DeMayo, Ed., Interscience Publishers, Inc., New York, N. Y., 1963, pp 407–455; (b) R. Breslow, ref 1a, pp 289–294; (c) L. K. Montgomery, J. W. Matt, and J. R. Webster, *J. Amer. Chem. Soc.*, **89**, 923 (1967); (d) S. J. Cristol and R. V. Barbour, *ibid.*, **90**, 2832 (1968).

single nonclassical radical intermediate is involved in those reactions in which both cyclopropylcarbinyl and allylcarbinyl products are obtained.

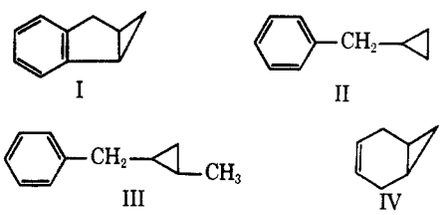
In connection with our solvolytic studies concerning the chemistry and mechanisms of reaction of cyclopropylcarbinyl cation systems, we became interested in the possibility of carrying out free-radical α brominations of cyclopropyl compounds by N-bromosuccinimide (NBS). It was anticipated that this process might provide a valuable mechanistic tool for learning more about the structures and behavior of cyclopropylcarbinyl radical as well as cation intermediates. Also, we hoped that the NBS bromination of hydrocarbons containing cyclopropane rings might prove to be useful for the synthesis of a variety of structurally complex cyclopropylcarbinyl and allylcarbinyl bromides which were needed for our solvolysis studies.

The behavior of NBS as a source of bromine for free-radical brominations has been studied in detail by numerous workers.[2] The process has been shown to involve the highly selective bromine radical as the hydrogen atom abstracting species.[3] At the transition state, polar structures involving partial charge separation make substantial contributions.[3a,4] Thus, it would be expected that the structure at the transition state for hydrogen atom abstraction by a bromine atom from a carbon α to a cyclopropane ring should reflect partially the stabilization which has been observed[5] for cyclopropylcarbinyl cations, and that the α-hydrogen abstraction should be a favored process.

Although there are a large number of examples[6] in the literature of free-radical α chlorinations of cyclopropyl compounds, only a few cases have been reported[7] of attempted free-radical α brominations. All of these were done using NBS as the brominating agent. However, with only one of the systems,[7b] benzylcyclopropane, was direct evidence found for bromination α to a cyclopropane ring. In the other cases only dibromides resulting from bromine addition to the cyclopropane rings, or products resulting probably *via* HBr eliminations from intermediate dibromides, were obtained.

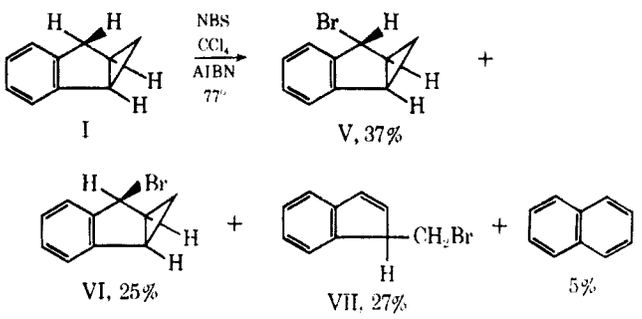
Results and Discussion

In our initial studies which attempted to effect an α bromination by NBS on the simple cyclopropyl compound norcarane, using either light or benzoyl peroxide initiation, we immediately encountered a serious difficulty. The only reaction which took place, after a considerable induction period, was rearrangement of the NBS to β-bromopropionyl isocyanate.[8] This product was observed in a 70% yield based on starting NBS. Thus, we shifted our attention to a study of the NBS brominations of cyclopropyl compounds in which the α carbons are activated toward hydrogen abstraction by adjacent phenyl or vinyl substituents. With these systems, it was hoped that their reactivities with regard to α-hydrogen abstraction would be sufficiently enhanced such that complications due to the NBS–β-bromopropionyl isocyanate rearrangement or to bromine atom attack upon the cyclopropane rings to give ring-opened dibromides would be minimized. We chose compounds I–IV to use as our model systems because of their ready availability and because of their structural variety.



Cycloprop[2,3]indene (I).[9]—The reaction of cycloprop[2,3]indene with NBS in a 1:1 mole ratio under reflux in carbon tetrachloride solution using azobisisobutyronitrile (AIBN) as the initiator proceeded smoothly and rapidly to give *ca.* 65% conversion of the cycloprop[2,3]indene. The products formed and their yields, based on reacted cycloprop[2,3]indene, are shown in Scheme I. Control experiments were run

SCHEME I



which showed that these products are all stable under the reaction conditions and thus, except for naphthalene, must be direct products of the radical reactions and not of subsequent thermal ion-pair reactions. The structures of the products were elucidated by spectroscopic methods and the yields were determined by a combination of nmr and glpc analytical procedures, as shown in the Experimental Section.

The *exo*- and *endo*-1-bromocycloprop[2,3]indenes (V and VI), which possess unrearranged structures, comprise a major portion of the NBS bromination

(2) For a general review on NBS bromination, see: L. Horner and E. H. Winkelmann, "Newer Methods of Preparative Organic Chemistry," Vol. III, W. Foerst, Ed., Academic Press, New York, N. Y., 1964, pp 151–198.

(3) (a) C. Walling, A. L. Rieger, and D. D. Tanner, *J. Amer. Chem. Soc.*, **85**, 3129 (1963); (b) R. E. Pearson and J. C. Martin, *ibid.*, **85**, 354 (1963); (c) G. A. Russell, C. DeBoer, and K. M. Desmond, *ibid.*, **85**, 365 (1963).

(4) S. S. Friedrich, E. C. Friedrich, L. J. Andrews, and R. M. Keefer, unpublished work.

(5) (a) Reference 1b, pp 254–276; (b) M. Hanack and H. J. Schneider, *Angew. Chem. Intern. Ed. Engl.*, **6**, 666 (1967).

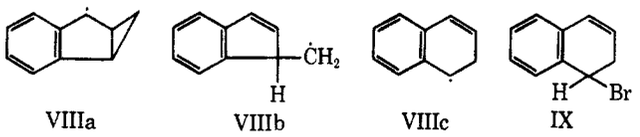
(6) (a) H. C. Brown and M. Barkowski, *J. Amer. Chem. Soc.*, **74**, 1894 (1952); (b) H. Hart and D. P. Wyman, *ibid.*, **81**, 4891 (1959), (c) D. E. Applequist, G. F. Fanta, and B. W. Henrikson, *ibid.*, **82**, 2368 (1960); (d) D. E. Applequist and J. A. Landgrebe, *ibid.*, **86**, 1543 (1964); (e) P. K. Freeman, F. A. Raymond, J. C. Sutton, and W. R. Kindley, *J. Org. Chem.*, **33**, 1448 (1968); (f) C. Walling and P. S. Fredricks, *J. Amer. Chem. Soc.*, **84**, 3326 (1962); (g) E. Renk, P. R. Shafer, W. H. Graham, R. H. Mazur, and J. D. Roberts, *ibid.*, **83**, 1987 (1961).

(7) (a) H. G. Kuivila, S. C. Caywood, W. F. Boyce, and F. L. Langevin, *ibid.*, **77**, 5175 (1955); (b) J. G. Bennett and S. C. Bunce, *J. Org. Chem.*, **25**, 73 (1960); (c) M. Gaitonde, P. A. Vatakencherry, and S. Dev, *Tetrahedron Lett.*, 2007 (1964).

(8) (a) J. C. Martin and P. D. Bartlett, *J. Amer. Chem. Soc.*, **79**, 2533, (1957); (b) H. W. Johnson and D. E. Bublitz, *ibid.*, **79**, 753 (1957); **80**, 3150 (1958).

(9) Compound I and its derivatives will be named and numbered hereafter, for simplicity, as derivatives of the indene system rather than using the 1,1a,6,6a-tetrahydrocycloprop[*a*]indene nomenclature.

products from cycloprop[2,3]indene. These can be explained as being formed *via* the cyclopropylcarbinyl radical intermediate VIIIa resulting from initial abstraction of a hydrogen atom from the 1 position of



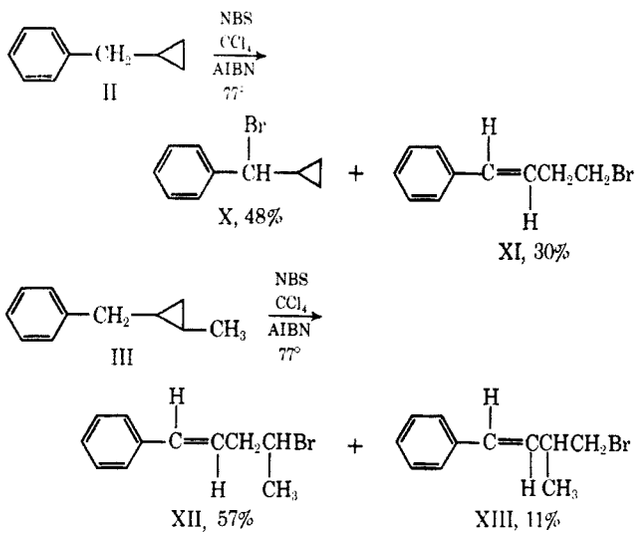
VIIIa VIIIb VIIIc IX

cycloprop[2,3]indene. A moderate yield of 1-bromomethylindene (VII) is also observed which can arise *via* bromine attack on the ring-opened allylcarbinyl radical VIIIb. A probable pathway for the formation of naphthalene is *via* reaction of the allylcarbinyl radical VIIIc with bromine to give 1-bromo-1,2-dihydronaphthalene (IX). This material would be expected to immediately eliminate HBr by an ionic mechanism to give naphthalene.

The incomplete conversion of cycloprop[2,3]indene in its reaction with NBS, which is also observed with the other cyclopropyl compounds studied, may be a result of several processes. One of these is the rearrangement of NBS to β-bromopropionyl isocyanate. Although β-bromopropionyl isocyanate could not be directly observed as a product of the cycloprop[2,3]indene reaction, small amounts must have been formed. Also, the 6% of undetermined products, which on the basis of our experiments must be di- or higher brominated materials, could account for a large portion of the NBS utilized.

Benzylcyclopropane (II) and *trans*-1-Benzyl-2-methylcyclopropane (III).—The reactions of benzylcyclopropane and *trans*-1-benzyl-2-methylcyclopropane with equimolar ratios of NBS in carbon tetrachloride solution under reflux using AIBN as the initiator both proceeded smoothly and rapidly, but resulted in only approximately 50% conversions of the cyclopropyl compounds. The products formed and their yields, after a reaction time of about 7 min following the induction period, are shown in Scheme II.

SCHEME II



The bromination mixture composition from the *trans*-1-benzyl-2-methylcyclopropane reaction is unchanged on further refluxing of the reaction mixture for 30 min. However, when the initial benzylcyclopropane reaction mixture is refluxed for the same period, a large change in the X to XI ratio takes place. After a total additional reflux time of 1 hr, the observed yields of α-bromobenzylcyclopropane (X) and *trans*-1-phenyl-4-bromo-1-butene (XI) are changed to 12 and 68%, respectively. Thus, it is apparent that on heating, α-bromobenzylcyclopropane undergoes an essentially quantitative rearrangement, presumably *via* an ion-pair mechanism, to afford the thermodynamically more stable *trans*-1-phenyl-4-bromo-1-butene.

In connection with these results, it should be noted that Bennett and Bunce[7b] have reported that when benzylcyclopropane is refluxed with NBS for 4 hr in carbon tetrachloride solution using a benzoyl peroxide initiator, a 41% yield of α-bromobenzylcyclopropane is obtained. They also reported that α-bromobenzylcyclopropane is obtained in 88% yield by treatment of phenylcyclopropylcarbinol with phosphorus tribromide at −15°. However, there is now some question as to whether their bromide is not actually rearranged *trans*-1-phenyl-4-bromo-1-butene. The properties of their product are almost identical with those of the *trans*-1-phenyl-4-bromo-1-butene reported by Hanack and coworkers[10] as the exclusive product from the reaction of phosphorus tribromide at −15° with phenylcyclopropylcarbinol. Moreover, Close[11] has reported that the reaction of phosphorus trichloride with phenylcyclopropylcarbinol gives 1-phenyl-4-chloro-1-butene as the only product.

In the NBS bromination of *trans*-1-benzyl-2-methylcyclopropane, only allylcarbinyl products are observed. This is in contrast to the benzylcyclopropane case where the major product of the radical reaction is α-bromobenzylcyclopropane. The lack of cyclopropylcarbinyl product from the *trans*-1-benzyl-2-methylcyclopropane bromination must result because of the electron-releasing effect of the methyl group which should accelerate both the cyclopropylcarbinylallylcarbinyl radical and ion-pair bromide rearrangements. However, the available data do not allow one to distinguish which of these is responsible for the exclusive formation of the allylcarbinyl bromide products XII and XIII.

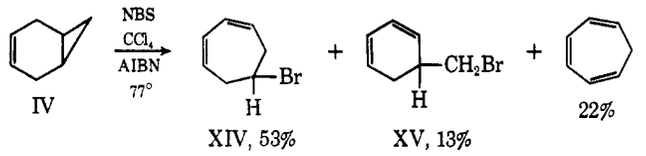
With regard to the 50% conversions of the benzyl- and *trans*-1-benzyl-2-methylcyclopropanes on reaction with 1:1 molar quantities of NBS, this again must be due in part to the formation of di- or higher brominated products. We observed that 20 and 30%, respectively, of undetermined, low volatility materials are formed in the reactions. However, a major portion of the NBS utilization can be accounted for by the observed formation of a 25–30% yield of β-bromopropionyl isocyanate, based on starting NBS, from the benzylcyclopropane reaction and a 20–25% yield from the *trans*-1-benzyl-2-methylcyclopropane reaction.

Bicyclo[4.1.0]hept-3-ene (IV).—The final model compound studied was bicyclo[4.1.0]hept-3-ene, and is of special interest since it is the only example in which activation of an α position to a cyclopropane ring is provided by a vinyl substituent. As with the other cyclopropyl compounds, the reaction of bicyclo[4.1.0]-hept-3-ene with NBS in a 1:1 mole ratio started quickly and proceeded smoothly and rapidly. Examination of the reaction mixture by nmr and glpc techniques indicated that 70% of the bicyclo[4.1.0]hept-3-ene had

(10) M. Hanack, S. Kang, J. Häffner, and K. Görler, *Ann.*, **690**, 98 (1965).
(11) W. J. Close, *J. Amer. Chem. Soc.*, **79**, 1455 (1957).

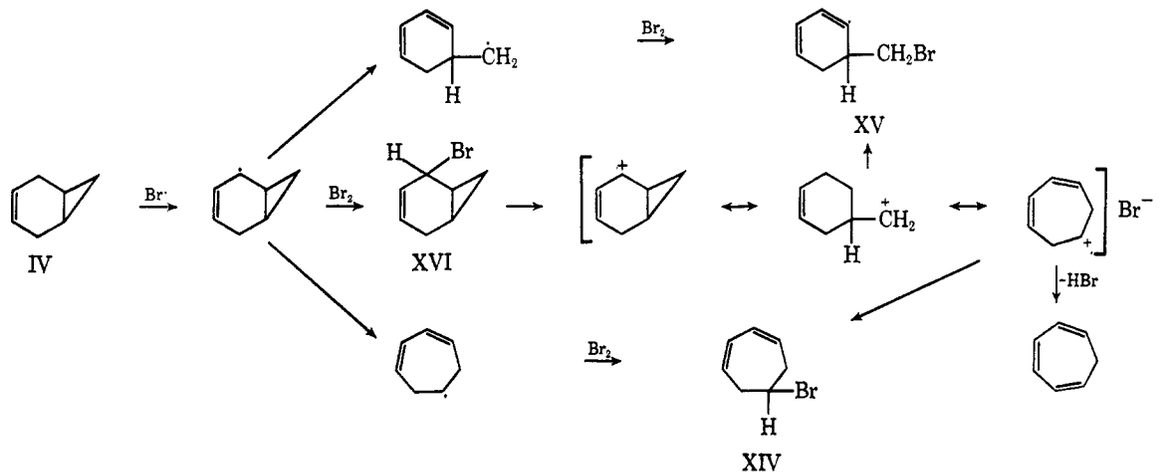
reacted. The products formed and their yields, based on reacted starting material, are shown in Scheme III.

SCHEME III



propylcarbinyl radical intermediates in this study, it is also apparent that NBS bromination studies on cyclopropyl systems can yield valuable information regarding the reactivities and products expected for the same systems in carbonium ion reactions. For several of the model compounds which we have investigated the observed products must be in part, or entirely, derived from ion-pair reactions of initially formed cyclopropylcarbinyl bromides. It is anticipated that continued investigation of free-radical α-hydrogen abstraction reactions on selected cyclopropyl compounds will provide considerable insight into the relationships between free-radical and cationic cyclopropylcarbinyl systems.

SCHEME IV



Control experiments showed that these materials are stable under the reaction conditions, and that complete reaction of the NBS had occurred.

It is possible that 1-bromocyclohepta-3,5-diene (XIV) and 1-bromomethylcyclohexa-2,4-diene (XV) may be formed directly from the radical reaction. However, it is highly unlikely that tropilidine is a direct product of the radical reaction. A more likely pathway is *via* the thermal ion-pair decomposition of 2-bromobicyclo-[4.1.0]hept-3-ene (XVI), as shown in Scheme IV. 2-Bromobicyclo[4.1.0]hept-3-ene is an expected initial product from the radical bromination process and should possess the high reactivity which is necessary for the facile tropilidine formation. Ion-pair rearrangement of XVI may also provide a major pathway for formation of 1-bromocyclohepta-3,5-diene and 1-bromomethylcyclohexa-2,4-diene.

Conclusions

For the activated cyclopropyl compounds which we have examined, at least 68% and as much as 94% of the NBS reaction proceeds *via* initial abstraction of a hydrogen atom from a carbon α to a cyclopropane ring. Bromides formally derived from both cyclopropylcarbinyl and allylcarbinyl radical intermediates have been observed directly from two of the systems investigated. In the other two cases, any initially formed cyclopropylcarbinyl bromides apparently rearranged immediately to allylcarbinyl bromides or elimination products by ion-pair mechanisms, and thus are not observed. The products in each case can be explained as arising through initial formation of cyclopropylcarbinyl radicals which subsequently rearrange partly to allylcarbinyl radical species before attack upon bromine occurs to yield the bromide products.

Besides the information gained concerning cyclo-

Finally, it is obvious that NBS bromination of cyclopropyl compounds should be a valuable tool for synthesis of highly reactive, or structurally interesting cyclopropylcarbinyl and allylcarbinyl bromides. Many substituted cyclopropanes which can be employed as starting materials are now readily available *via* the Simmons–Smith[12] cyclopropane synthesis or its modifications.[13] In the case of allylcarbinyl bromide products, these can be readily separated from the product mixtures because of their high thermal stabilities as compared to the corresponding cyclopropylcarbinyl bromides. For the synthesis of highly reactive cyclopropylcarbinyl bromides, perhaps photoinitiated brominations with NBS or with low concentrations of bromine at low temperatures may be useful. Studies will be continued on both the synthetic and mechanistic aspects of free-radical α bromination of cyclopropyl hydrocarbons.

Experimental Section

Boiling points are uncorrected. Ultraviolet spectra were recorded on a Beckman DB instrument and infrared spectra were taken with a Perkin-Elmer Model 237B instrument. Mass spectra were run on a Varian Associates Model M-66 spectrometer by Mr. Kei Miyano. Microanalyses were performed by Galbraith Laboratories, Inc., Knoxville, Tenn.

Nuclear Magnetic Resonance Spectra.—All nmr spectra were obtained using a Varian Associates Model A-60A instrument.

(12) (a) H. E. Simmons and R. D. Smith, *J. Amer. Chem. Soc.*, **81**, 4256 (1959); (b) E. P. Blanchard and H. E. Simmons, *ibid.*, **86**, 1337 (1964); (c) H. E. Simmons, E. P. Blanchard, and R. D. Smith, *ibid.*, **86**, 1347 (1964).

(13) (a) E. LeGoff, *J. Org. Chem.*, **29**, 2048 (1964); (b) J. Furukawa, N. Kawabata, and J. Nishimura, *Tetrahedron*, **24**, 53 (1968); *Tetrahedron Letters*, 3495 (1968).

They were run either directly on the carbon tetrachloride solutions of the NBS bromination product mixtures, or in the case of pure compounds, as 5–10% solutions in carbon tetrachloride. Tetramethylsilane (TMS) was used as an internal standard, and chemical shift values are reported in parts per million (δ) downfield from the TMS. For quantitative nmr analyses of the NBS bromination product mixtures, at least four integrations were obtained for the peak areas of each different proton absorption. Integral amplitudes were maximized so as to obtain the highest possible accuracy. Average values of the integrations were used for calculation of the product compositions.

Gas–Liquid Partition Chromatography.—Both analytical and preparative-scale gas–liquid partition chromatography were carried out on an Aerograph A90-P3 instrument equipped with a Pyrex injector insert. A 5 ft × 0.25-in. stainless steel column with a 20% SE-30 on 60–80 mesh Chromosorb W packing was used for the separations. Helium (100 ml/min) was employed as the carrier gas. The retention times (in minutes) of certain of the compounds which were encountered in this work are as follows: (50°) tropilidine, 3.8; bicyclo[4.1.0]hept-3-ene, 4.6; (100°) 1-bromocyclohepta-3,5-diene and 1-bromomethylcyclohexa-2,4-diene, 8.3; (150°) benzylcyclopropane, 1.7; *trans*-1-benzyl-2-methylcyclopropane, 2.0; cycloprop[2,3]indene, 2.3; naphthalene, 2.8; 1-bromomethylindene, 7.4; *trans*-1-phenyl-4-bromo-1-butene, 9.5; diphenylmethane, 10.0; 1-bromonaphthalene, 10.5; *trans*-1-phenyl-4-methyl-4-bromo-1-butene and *trans*-1-phenyl-3-methyl-4-bromo-1-butene, 12.0. The numbers in parentheses are column operating temperatures.

Materials.—Commercial samples of cyclohexene, zinc dust (Mallinckrodt, AR), methylene iodide, azobisisobutyronitrile (Eastman White Label), 30-mesh zinc granules, carbon tetrachloride (J. T. Baker, AR), benzoyl peroxide (Matheson Coleman and Bell), N-bromosuccinimide (Arapahoe), 1,4-cyclohexadiene, allylbenzene (Chemical Samples Co.), and *trans*-1-phenyl-2-butene [Aldrich; pure *trans* by glpc; ir (neat) 965 cm^{-1}] were used without further purification. Indene (Eastman Yellow Label) was purified before use by careful fractional distillation.

Norcarane.—This material was prepared by the procedure of Simmons and Smith[12a] from cyclohexene, methylene iodide, and the Shank and Shechter[14] zinc–copper couple: bp 115–117°; $n^{25}D$ 1.4557 (lit.[12a] bp 116.5°, $n^{25}D$ 1.4546); nmr (CCl_4), δ 0.00 (q, 1 H), 0.75 (m, 3 H), 1.20 (m, 4 H), and 1.67 ppm (m, 4 H).

Cycloprop[2,3]indene (I).—Using the method of Goodman and Eastman,[15] this material was prepared from indene, methylene iodide, and a zinc–copper couple in ether and purified by distillation through a 60-cm tantalum spiral column: bp 83–85° (18 mm); $n^{25}D$ 1.5570 [lit.[15] bp 104° (40 mm), $n^{26}D$ 1.5545]; nmr (CCl_4) δ 0.00 (q, 1 H), 1.00 (sextet, 1 H), 1.70 (m, 1 H), 2.25 (m, 1 H), 2.84 (d, 1 H), 2.97 (q, 1 H), and 6.80 ppm (m, 4 H).

Benzylcyclopropane (II).—A zinc–copper couple (30 g, 0.46 mol) was prepared from 30-mesh zinc granules by the procedure of LeGoff.[13a] The couple was covered with 100 ml of anhydrous ethyl ether and treated, while heating and stirring, over a period of 0.5 hr by dropwise addition of a mixture of 80 g (0.30 mol) of methylene iodide and 24 g (0.20 mol) of allylbenzene. The mixture was then stirred and refluxed for an additional 40 hr. After the usual work-up by the careful dropwise addition of saturated ammonium chloride solution, followed by washing with saturated sodium carbonate and water and drying ($MgSO_4$), the product was distilled under vacuum through a 60-cm tantalum spiral column. A 10-g quantity of allylbenzene was recovered and 10.0 g (64%) of pure benzylcyclopropane was obtained: bp 81° (20 mm); $n^{25}D$ 1.5130 [lit.[12a] bp 122–124° (102 mm), $n^{25}D$ 1.5132]; nmr (CCl_4), δ 0.15 (m, 2 H), 0.50 (m, 2 H), 0.95 (m, 1 H), 2.52 (d, 2 H, J = 6.5 Hz), and 7.16 ppm (s, 5 H).

***trans*-1-Benzyl-2-methylcyclopropane (III).**—A zinc–copper couple (40 g, 0.61 mol) was prepared from 30-mesh zinc granules by the procedure of LeGoff.[13a] The couple was covered with 100 ml of anhydrous ethyl ether and treated, while stirring and heating over a period of 0.5 hr, by dropwise addition of a mixture of 107 g (0.40 mol) of methylene iodide and 26 g (0.20 mol) of *trans*-1-phenyl-2-butene. The mixture was then stirred and refluxed for an additional 20 hr before working up by the usual procedure. Distillation of the product mixture through a 60-cm tantalum spiral column gave 14.4 g (50%) of *trans*-1-benzyl-2-methylcyclopropane: bp 84–84.5° (15 mm); $n^{25}D$ 1.5026; nmr (CCl_4), δ 0.33 (m, 4 H), 0.92 (d, 3 H, J = 5 Hz), 2.42 (d, 2 H, J = 6 Hz), and 7.16 ppm (s, 5 H). *Anal.* Calcd for $C_{11}H_{14}$: C, 90.35; H, 9.65. Found: C, 90.24; H, 9.66.

Bicyclo[4.1.0]hept-3-ene (IV).—A zinc–copper couple (60 g, 0.92 mol) was prepared from 30-mesh zinc granules by the procedure of LeGoff.[13a] The couple was covered with 200 ml of anhydrous ethyl and over a period of 1 hr, while stirring and heating, was treated by dropwise addition with a mixture of 170 g (0.63 mol) of methylene iodide and 25 g (0.31 mol) of 1,4-cyclohexadiene. After the addition was completed, the mixture was stirred and refluxed for 22 hr. The mixture was worked up in the usual manner by addition of saturated ammonium chloride solution, followed by washing with saturated aqueous sodium carbonate solution and water, and dried over anhydrous magnesium sulfate. Distillation at atmospheric pressure through a 60-cm tantalum spiral column gave 9.0 g (30%) of pure bicyclo[4.1.0]hept-3-ene: bp 114–114.5°; $n^{25}D$ 1.4750 [lit.[12c] bp 57° (100 mm), $n^{25}D$ 1.4739]; nmr (CCl_4), δ 0.40 (m, 2 H), 0.92 (m, 2 H), 2.25 (s, 4 H), and 5.33 ppm (s, 2 H). Along with VIII was also obtained 5.5 g (16%) of a mixture of isomeric tricyclo[5.1.0^{1,7}0^{3,5}]octanes: bp 137–143°; $n^{25}D$ 1.4776 [lit.[12c] bp 73–80° (100 mm)]; nmr (CCl_4), δ 0.00 (m, 1.5 H), 0.55 (m, 6.5 H), 1.71 (m, 3.5 H), and 2.30 ppm (m, 0.5 H). Simmons and coworkers[12c] have reported that in this mixture, the *endo* and *exo* isomers are present in the ratio of 3.3:1.

Attempted NBS Bromination of Norcarane.—To a solution of 1.0 g (10.5 mmol) of norcarane in 25 ml of carbon tetrachloride was added 1.8 g (10.1 mmol) of NBS and 0.1 g of benzoyl peroxide initiator. The mixture, which was protected from atmospheric moisture by a drying tube, was then stirred and refluxed for 2 hr. At the end of this period the NBS had disappeared from the bottom of the flask, but no bromine or hydrogen bromide had been evolved and no succinimide was present at the surface of the solution. An nmr spectrum of the crude reaction mixture showed that the norcarane was unchanged, but did indicate the formation of a 70% yield, based on starting NBS, of β-bromopropionyl isocyanate. This was identified by the presence in the spectrum of two mirror-image triplets at δ 2.90 (2 H, $BrCH_2CH_2$) and 3.38 ppm (2 H, $BrCH_2$).

Bromination of Cycloprop[2,3]indene (I) by NBS.—A mixture of 0.95 g (7.30 mmol) of cycloprop[2,3]indene and 1.36 g (7.65 mmol) of NBS in 20 ml of carbon tetrachloride was treated with 0.1 g of azobisisobutyronitrile initiator and heated quickly to reflux while stirring in a apparatus which was protected by a drying tube. The radical reaction started quickly, and the reaction mixture turned only slightly yellow by the end of the run. No HBr was evolved. After the reaction was completed (*ca.* 10 min), as indicated by the absence of NBS at the bottom of the reaction vessel, the reaction mixture was cooled and an nmr spectrum and gas–liquid partition chromatogram were taken directly on the liquid portion of the mixture. Continued refluxing for 30 min longer did not cause any changes in the nmr spectrum. The mixture was then filtered to remove succinimide and concentrated by atmospheric pressure distillation through a short Vigreux column. The pale yellow oil which remained was separated into several fractions by vacuum distillation through a micro (1-ml capacity) distillation apparatus. The first fraction [bath 80° (5 mm)] was found by glpc analysis and by examination of its nmr spectrum to consist mainly of unreacted cycloprop[2,3]indene (I) along with a little naphthalene product. The second fraction [bath 130° (0.2 mm)] was found by nmr examination to consist of a mixture of 45% 1-bromomethylindene (VII), 34% *exo*-1-bromocycloprop[2,3]indene (V), and 21% *endo*-1-bromocycloprop[2,3]indene (VI). Some dark tarry residue remained in the distillation pot. The naphthalene was identified by its glpc retention time, infrared spectrum, and characteristic odor. The isomeric 1-bromocycloprop[2,3]indenes could not be separated from each other or from the 1-bromomethylindene by distillation or by preparative glpc methods owing to their thermal instability. Only a single bromide peak was observed in the gas–liquid partition chromatogram of a mixture of the three bromides, and collection of this peak showed that it consisted entirely of 1-bromomethylindene (VII). The 1-bromocycloprop[2,3]indenes, however, were readily identified by certain characteristic proton absorptions in the nmr spectrum of the distilled mixture of the three bromide products. For the *exo*-bromide V, absorptions were observed at δ 0.17 (m, 1 H, cyclopropyl) and 5.35 ppm (d, 1 H, J = 2 Hz, >CHBr) which

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were well separated from all other absorptions. For the *endo*-bromide VI, absorptions were observed at δ 0.72 (m, 1 H, cyclopropyl) and 5.75 ppm (d, 1 H, J = 6.5 Hz, >CHBr). Other cyclopropyl proton absorptions which could not be differentiated for the two isomers were at δ 0.88–1.40 (m, 1 H) and at 2.00–2.90 ppm (m, 2 H). The aromatic multiplet for the mixture of the three bromides was centered at δ 7.27 ppm. Characterization of the 1-bromomethylindene (VII) was straightforward since it could be isolated in a pure state by preparative glpc: n^{25}D 1.6003; uv max (absolute $(C_2H_5)_2O$), 256 mμ (ε 7370), 288 (453), and 294 (170); nmr (CCl_4), δ 3.26 (m, 1 H, >CHCH$_2$), 3.76 (m, 2 H, CH$_2$Br), 6.63 (q, 1 H, J = 6 and 1.5 Hz, vinyl), 6.86 (q, 1 H, J = 6 and 1 Hz, vinyl), and 7.30 ppm (m, 4 H, aromatic); mass spectrum (70 eV), m/e 210 and 208 (molecule ion), 129 and 128. *Anal.* Calcd for $C_{10}H_9Br$: C, 57.46; H, 4.35; Br, 38.19. Found: C, 57.59; H, 4.23; Br, 38.31.

Using this product information, it was then possible to determine the composition of the original reaction mixture from its gas–liquid partition chromatogram and by consideration of the corrected per hydrogen integrated peak areas for selected nmr proton absorptions of the unreacted starting material and each product. The area under the aromatic proton multiplet, corrected for the presence of naphthalene and the fact that it contains four protons, was used as the standard for the total cycloprop[2,3]indene used in the reaction. It was found that 60% of the cycloprop[2,3]indene (I) had reacted to give 35% *exo*-1-bromocycloprop[2,3]indene (V), 24% *endo*-1-bromocycloprop[2,3]indene (VI), 28% 1-bromomethylindene (VII), and 7% naphthalene. In a similar run in 10 ml of carbon tetrachloride solvent with 0.485 g (3.73 mmol) of cycloprop[2,3]indene and 0.717 g (4.03 mmol) of NBS, 70% of the cycloprop[2,3]indene reacted to give 37% V, 25% VI, 27% VII, and 5% naphthalene.

Bromination of Benzylcyclopropane (II) by NBS.—To a mixture of 1.02 g (7.73 mmol) of benzylcyclopropane and 1.37 g (7.69 mmol) of NBS in 20 ml of carbon tetrachloride was added 0.1 g of azobisisobutyronitrile initiator. This mixture was then heated at reflux until all of the NBS appeared to have reacted (*ca.* 15 min). The reaction mixture was worked up and the product composition was determined using nmr, distillation, and glpc techniques similar to those employed for analysis of the cycloprop[2,3]indene product mixture. It was found that 50% of the benzylcyclopropane had reacted to give 37% α-bromobenzylcyclopropane (X) and 44% *trans*-1-phenyl-4-bromo-1-butene (XI).[10] A 30% yield of β-bromopropionyl isocyanate, based on starting NBS, was also observed.

In a similar run with 0.543 g (4.11 mmol) of benzylcyclopropane and 0.710 g (3.99 mmol) of NBS in 10 ml of carbon tetrachloride solvent, the reaction mixture was refluxed for 7 min. Nmr analysis showed that 53% of the benzylcyclopropane had reacted to give 48% X and 30% XI. A 26% yield of β-bromopropionyl isocyanate, based on starting NBS, was also observed. On further refluxing of the product mixture for 30 min, the percentage of unreacted benzylcyclopropane in the mixture was unchanged. However, the yields of X and XI had changed to 26 and 53%, respectively, and on continued refluxing for 30 min longer changed further to 12 and 68%, respectively. On the basis of these thermal decomposition studies, it can be roughly estimated that at zero reflux time the yields of α-bromobenzylcyclopropane and *trans*-1-phenyl-4-bromo-1-butene must have been approximately 60 and 20%, respectively.

The structures of the benzylcyclopropane bromination products were determined as follows. α-Bromobenzylcyclopropane (X) could not be separated from the reaction mixture either by distillation or by glpc techniques owing to its thermal instability. However it was readily identified on the basis of its nmr proton absorption at δ 4.25 ppm (d, 1 H, J = 9.5 Hz, –CHBr) which decreased on heating the bromination reaction mixture. *trans*-1-Phenyl-4-bromo-1-butene (XI)[10] was separated from the reaction mixture by distillation [bath 130° (0.2 mm)] and was purified by preparative glpc: n^{25}D 1.5870; uv max (absolute $(C_2H_5)_2O$), 250 mμ (ε 19,600), 283 (2120), and 292 (1610); ir (neat), 965 cm^{-1} (*trans*-CH=CH); nmr (CCl_4), δ 2.77 (m, 2 H, C=CCH$_2$), 3.39 (t, 2 H, CH$_2$Br), 6.30 (m, 2 H, –HC=CH–), and 7.25 ppm (s, 5 H, arom); mass spectrum (70 eV), m/e 212 and 210 (molecule ion), 131, 117, 115, and 91. The assignment of a *trans* structure for XI is supported by the observation that its nmr vinyl proton multiplet is identical in appearance with that for the vinyl proton multiplet of a known sample of *trans*-cinnamyl alcohol.

Bromination of *trans*-1-Benzyl-2-methylcyclopropane (III) by NBS.—To a mixture of 1.010 g (6.92 mmol) of *trans*-1-benzyl-2-methylcyclopropane and 1.250 g (7.04 mmol) of NBS in 20 ml of carbon tetrachloride was added 0.1 g of azobisisobutyronitrile initiator. This mixture was then heated at reflux for *ca.* 10 min before cooling and taking an nmr spectrum of the liquid portion of the product mixture. Continued refluxing of the reaction mixture for 30 min did not cause any significant changes in the nmr spectrum.

The reaction mixture was then worked up using distillation and glpc procedures, and the product composition was determined using quantitative nmr techniques. This was done by consideration of the per hydrogen peak areas in the nmr spectrum of the bromination product mixture for selected proton absorptions of the unreacted starting material and each product. The five-proton aromatic absorption was used as the standard for the total *trans*-1-benzyl-2-methylcyclopropane used in the reaction. By this procedure it was found that 50% of the *trans*-1-benzyl-2-methylcyclopropane had reacted to give 56% *trans*-1-phenyl-4-methyl-4-bromo-1-butene (XII) and 12% *trans*-1-phenyl-3-methyl-4-bromo-1-butene (XIII). A 22% yield of β-bromopropionyl isocyanate, based on starting NBS, was also observed. In a similar run using 0.510 g (3.49 mmol) of III and 0.674 g (3.78 mmol) of NBS in 10 ml of carbon tetrachloride solvent, 54% of the initial III reacted to give 57% XII and 11% XIII. A 25% yield of β-bromopropionyl isocyanate, based on starting NBS, was also observed.

The *trans*-1-benzyl-2-methylcyclopropane bromination products were identified as follows. Distillation of the crude bromination product mixture gave a high-boiling fraction [bath 130° (0.3 mm)] which was found to consist entirely of an 82:18 mixture of *trans*-1-phenyl-4-methyl-4-bromo-1-butene (XII) and *trans*-1-phenyl-3-methyl-4-bromo-1-butene (XIII). Glpc analysis of the mixture of the two bromides showed only a single peak, and collection of this peak showed that it still contained a mixture of the two bromides in the same 82:18 ratio. Identification of the isomeric bromides was possible from their characteristic proton absorptions in the nmr spectrum of the mixture. For the major *trans*-1-phenyl-4-methyl-4-bromo-1-butene product (XII), absorptions were observed in CCl_4 at δ 1.65 (d, 3 H, J = 6.5 Hz, CH$_3$), 2.67 (q, 2 H, CH=CHCH$_2$), 4.08 (sextet, 1 H, CHCH$_3$Br), 6.33 (m, 2 H, >CH=CH<) and 7.25 ppm (s, 5 H, arom). For the minor *trans*-1-phenyl-3-methyl-4-bromo-1-butene product (XIII), absorptions were observed in CCl_4 at δ 1.25 (d, 3 H, J = 6.5 Hz, CH$_3$), *ca.* 2.65 (m, 1 H, CH=CHCHCH$_3$), 3.32 (d, 2 H, J = 6.5 Hz, CH$_2$Br), 6.33 (m, 2 H, >CH=CH<), and 7.25 ppm (s, 5 H, arom). The assignment of *trans* structures for XII and XIII is supported by the observation that the nmr vinyl proton multiplet for the mixture is almost identical in appearance with that for the vinyl proton multiplet of *trans*-1-phenyl-4-bromo-1-butene (XI). A sample of the bromide mixture was purified by preparative glpc: n^{25}D 1.5734; uv max [absolute $(C_2H_5)_2O$], 250 mμ (ε 20,100), 283 (2660), and 292 (1970); ir (neat), 965 cm^{-1} (*trans*-CH=CH–); mass spectrum (70 eV), m/e 226 and 224 (molecule ion), 145, 129, 117, 115, and 91. *Anal.* Calcd for $C_{11}H_{13}Br$: C, 58.69; H, 5.82; Br, 35.50. Found: C, 58.83; H, 5.65; Br, 35.76.

Bromination of Bicyclo[4.1.0]hept-3-ene (IV) by NBS.—A mixture of 0.94 g (10.0 mmol) of bicyclo[4.1.0]hept-3-ene and 1.88 g (10.5 mmol) of NBS in 20 ml of carbon tetrachloride was treated with 0.1 g of azobisisobutyronitrile initiator and heated quickly to reflux. Near the end of the reaction (*ca.* 5 min), the surface of the succinimide turned bright yellow and a small amount of HBr was evolved. After the reaction was completed (*ca.* 10 min) the mixture was cooled and an nmr spectrum was taken. Refluxing for an additional 30 min caused no significant changes in the nmr spectrum.

The product mixture was then worked up in the usual manner and distilled. The first fraction [bath 75° (30 mm)] was found by nmr and glpc analyses to consist of a 70:30 mixture of bicyclo[4.1.0]hept-3-ene and tropilidine. The second fraction [bath 90° (0.4 mm)] appeared by nmr analysis to consist mainly of an 86:14 mixture of 1-bromocyclohepta-3,5-diene (XIV) and 1-bromomethylcyclohexa-2,4-diene (XV). Attempts to purify and separate the bromide mixture by preparative glpc methods resulted in extensive decomposition in the injector and gave only a single peak consisting of a 72:28 mixture of XIV and XV. The tropilidine was identified both by its glpc retention time and by its characteristic nmr spectrum (CCl_4): δ 2.19 (t, 2 H), 5.30

(m, 2 H), 6.10 (m, 2 H), and 6.50 ppm (t, 2 H). The structure of the 1-bromocyclohepta-3,5-diene (XIV) was assigned on the basis of its nmr proton absorptions in the mixture of the two bromide products (CCl_4): δ 2.94 (m, 4 H), 4.38 (m, 1 H, CHBr), and 5.80 ppm (m, 4 H, vinylic). Similarly, the structure of the 1-bromomethylcyclohexa-2,4-diene (XV) was assigned on the basis of its nmr proton absorptions (CCl_4): δ 2.38 (m, 3 H), 3.30 (d, 2 H, J = 6.5 Hz, CH_2Br), and 5.80 ppm (m, 4 H, vinylic). The distilled bromide mixture had uv max (absolute $(C_2H_5)_2O$), 245 mμ (ϵ 5500); mass spectrum (70 eV), *m/e* 172 and 174 (molecule ion), 93, 91, 79, and 77. *Anal.* Calcd for C_7H_9Br: C, 48.55; H, 5.20; Br, 46.24. Found: C, 48.42; H, 5.09; Br, 46.49.

Using the information from the above product separation procedures, it was then possible to determine, by nmr analysis, the composition of the original bromination mixture. It was found that 69% of the bicyclo[4.1.0]hept-3-ene had reacted to give 53% 1-bromocyclohepta-3,5-diene (XIV), 13% 1-bromomethylcyclohexa-2,4-diene (XV), and 22% tropilidine. In a similar run with 1.00 g (10.7 mmol) of bicyclo[4.1.0]hept-3-ene and 1.93 g (10.8 mmol) of NBS in 20 ml of carbon tetrachloride solvent, 70% of the bicyclo[4.1.0]hept-3-ene reacted to give 54% XIV, 13% XV, and 20% tropilidine.

Registry No.—N-Bromosuccinimide, 128-08-5; III, 18933-49-8; β-bromopropionyl isocyanate, 18926-24-4; V, 18944-78-0; VI, 18933-48-7; VII, 18926-25-5; X, 18926-26-6; XI, 7515-41-5; XII, 18944-79-1; XIII, 18933-51-2; tropilidene, 544-25-2; XIV, 18926-29-9; XV, 18926-28-8.

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New Reactions of Polyfluoroaromatic Compounds. Pentafluorophenylalanine and Tetrafluorotyrosine

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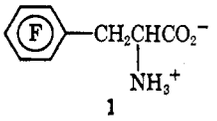
The reaction of α-bromo-β-pentafluorophenylpropionic acid (**4**) with ammonia gives *trans*-4-amino-2,3,5,6-tetrafluorocinnamic acid (**5**), rather than pentafluorophenylalanine (**1**). Compound **1** is prepared by hydrogenolysis of α-azido-β-pentafluorophenylpropionic acid, by reductive hydrolysis of the azlactone precursor, and by the acetamidomalonate procedure (the method of choice). Tetrafluorotyrosine (**2**) is prepared in 17% over-all yield from hexafluorobenzene by the latter method. The influence of polyfluoroaryl substitution on the acidity of the functional groups in these aromatic amino acids has been determined. The biological activity of **1** and **2** is discussed.

In two recent communications we reported the syntheses of *dl*-β-pentafluorophenylalanine[1] (**1**) and *dl*-tetrafluorotyrosine[2] (**2**). In the present paper we wish to discuss in detail the chemistry of these highly fluorinated α-amino acids and a number of related reactions of synthetic and mechanistic interest.



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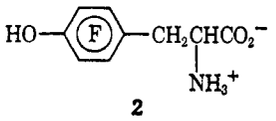

2

In our studies directed toward the synthesis of pentafluorophenylalanine, we approached this problem *via* the Meerwein arylation route. The application of this procedure to the preparation of amino acids has been reported by us[3] and others.[4]

The starting material for the synthesis was pentafluoroaniline (**3**), obtained in 86% yield by reaction of hexafluorobenzene with aqueous ammonia in a rocking-type autoclave at 170° for 24 hr. This was a substantial improvement over the yield reported previously.[5] A mixture of **3** and 48% hydrobromic acid, dissolved in acetone, was diazotized at 0–5° and added to acrylic acid in the presence of a catalytic amount of freshly purified copper(I) bromide to give 18% yield of α-bromo-β-pentafluorophenylpropionic acid (**4**). Attempted ammonolysis of **4**, by treating an ethanolic solution with liquid ammonia in a sealed tube for 4 days at room temperature, gave **5** in 91% yield. Compound **5** was soluble in aqueous alkali and did not form a hydrochloride. It absorbed bromine very slowly, but reacted rapidly with neutral potassium permanganate. A ninhydrin test was negative.

The infrared spectrum of **5** revealed two sharp bands at 3520 and 3415 cm^{-1}, broad weak absorption between 3100 and 2500 cm^{-1}, and a strong band at 1690 cm^{-1}. All of these observations suggested that **5** was an aminocinnamic acid. Comparison of its ultraviolet spectrum with those of related cinnamic acids[6,7] (Table I) provided strong evidence that this compound was *trans*-4-amino-2,3,5,6-tetrafluorocinnamic acid. Substitution of an amino group in the *para* position of *trans*-cinnamic acid causes a bathochromic shift of 67 mμ. Compound **5** shows a comparable shift of 68 mμ when compared with pentafluorocinnamic acid. The assignment is also consistent with previous observations that nucleophiles attack most substituted pentafluorophenyl compounds preferentially in the

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