Ring Opening Reactions with Diphenylcyclopropylcarbinol with Bromine

William B. Smith,* Gareth D. Barnard, Michael J. Shapiro, and Thomas W. Proulx

Department of Chemistry, Texas Christian University, Fort Worth, Texas 76129

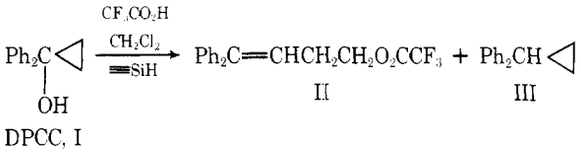
Received November 1, 1976

The reactions of diphenylcyclopropylcarbinol with 1 and 2 equiv of bromine in acetic acid have been carried out. In the first case the products are 1-acetoxy-2,4-dibromo-1,1-diphenyl-1-butanol and 2,4-dibromo-1,1-diphenyl-1-butene. In the latter case no dibromo acetate is formed, and it has been demonstrated that this product in the presence of excess bromine is converted to the latter two products. The dibromo acetate is not formed upon treatment of 4-bromo-1,1-diphenyl-1-butene with bromine in acetic acid. The mechanistic implications of these observations are considered.

With regard to their possible reactions with bromine the cyclopropylcarbinols may be considered to be difunctional compounds capable of undergoing the ring opening reactions of cyclopropanes or the elimination of water by the bromine acting in its capacity as a Lewis acid. This capability has been demonstrated in several studies of the bromination of 3,5-cyclocholestan-6β-ol as well as its methyl ether and acetate derivatives; the product in each case being an essentially quantitative yield of 3β,5α,6β-tribromocholestane.[1] When treated with a deficiency of bromine in ether at 0 °C cholesteryl bromide was isolated, and it was proposed that this material served as an intermediate in the formation of the tribromide. The formation of cholesteryl bromide was proposed as a consequence of first an S_Ni replacement of the 6β-hydroxyl group by bromine followed by an *i*-steroid rearrangement. The possible simultaneous loss of hydroxyl and ring opening nucleophilic attack of bromine at the 3 position was not considered, though it will be shown subsequently that this possibly exists.

In searching for a model system in which to examine the bifunctional character of the cyclopropylcarbinols, diphenylcyclopropylcarbinol (DPCC, I) was chosen because the products could be expected to be readily identified and analyzed by proton and carbon NMR spectroscopy and the expected benzhydryl-like carbocation formed by loss of hydroxyl would be relatively stable and unlikely to undergo extensive rearrangement.

The treatment of DPCC with trifluoroacetic acid in the presence of triethyl- or triphenylsilane has been reported to yield both the olefin ester II and diphenylcyclopropylmethane (III).[2] The latter arises from the trapping of the diphenylcyclopropylcarbinyl cation by the hydride, while II may arise from a nucleophilic attack of the acid on the cyclopropyl ring of the cation or by a concerted process of such a ring opening with the loss of water. The latter explanation was preferred as no 1,1-diphenyl-1-butene was found among the products—a fact attributed to a lack of electrophilic character in the cyclopropyl methylenes of the cation.

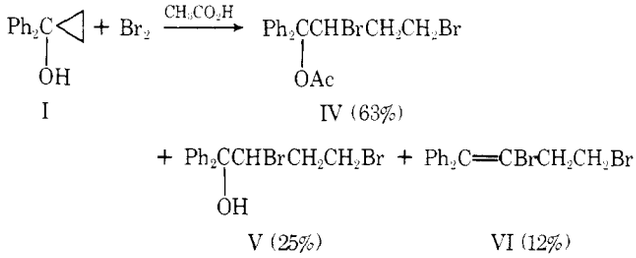


DPCC, I II III

During the course of the study described here, Skell, Day, and Shea[3] reviewed, corrected, and extended the understanding of the reactions of bromine with cyclopropane and several alkylcyclopropanes. In order to avoid the free-radical chain process, the reaction must be conducted in the dark. The ionic reaction is often sluggish, leading to a complex mixture of isomeric mono-, di-, and tribromoalkanes which require a sequence of bromination, dehydrobromination, and rearrangement steps which are initiated by electrophilic attack of bromine on the cyclopropyl ring system.

Results

The reaction of diphenylcyclopropylcarbinol in the dark with 1 equiv of bromine in acetic acid is over in about 3 h at room temperature. Conventional workup of the reaction mixture by drowning in water, extraction, and a wash with bicarbonate to remove excess acetic acid gave the products shown below.



I IV (63%) V (25%) VI (12%)

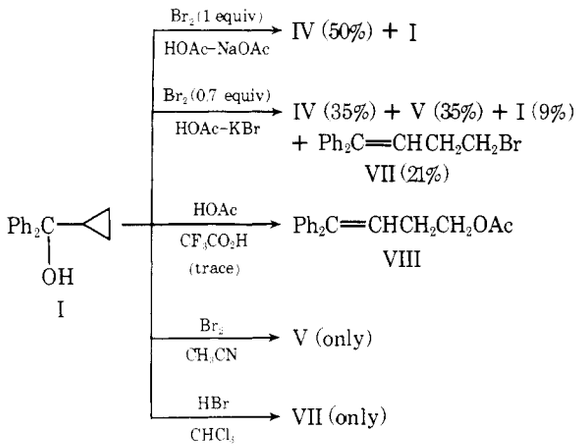
The structures of each were determined by proton and carbon NMR spectroscopy, elemental and/or high-resolution mass spectrometry, and synthesis or comparison with known compounds from the literature. When the reaction was conducted directly in the NMR probe using perdeuterioacetic acid or worked up by removing the solvent at reduced pressure no dibromo olefin VI was noted, and the products were IV and V only in essentially equal amounts. Thus, VI appears not to be a direct reaction product (see also below).

When I is reacted in the same fashion with 2 equiv of bromine the color is not discharged after several days. However, the reaction was found to be over essentially after 3 h or less as above. The products were the dibromo alcohol V (43%) and the dibromo olefin VI (57%) only. Indeed, if one followed the course of the reaction in the NMR probe in perdeuterioacetic acid it became apparent that as the dibromo acetate IV was created it was destroyed by the excess bromine forming the mixture of V and VI. In an independent experiment pure IV in acetic acid was treated with bromine to also give V and VI. In fact, in a similar experiment the dibromo alcohol V was rapidly dehydrated by bromine in acetic acid to form VI. Such dehydrations of tertiary alcohols with bromine have been observed before.[4]

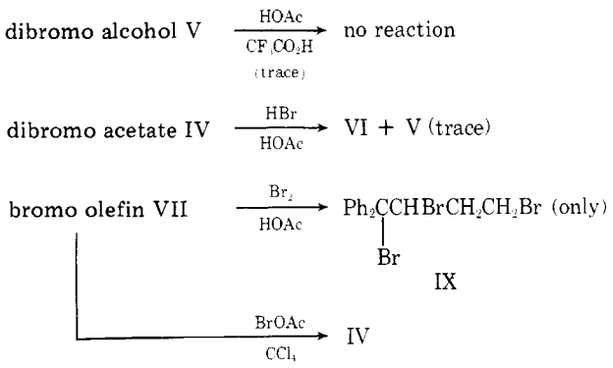
A variety of reactions of DPCC and related compounds have been carried out in an attempt to explicate the mechanism of the reaction. These are summarized in Schemes I and II and will be mentioned as pertinent to the subsequent discussion. Of particular interest, however, is the observation that when the reaction medium is buffered with sodium acetate the reaction with bromine is greatly slowed and only the dibromo acetate IV is formed. In contrast, when the medium contains added potassium bromide the bromine color is discharged quite rapidly. While this might be due only to a normal salt effect, the appearance of the bromo olefin VII as a new product suggests the possible presence of hydrogen bromide or an altered mode of reaction.

Finally, the bromo olefin VII (Scheme II) when treated with

Scheme I



Scheme II



bromine in acetic acid yields a quantitative conversion to the tribromide IX. No evidence for the formation of the dibromo acetate IV could be found. In contrast, when V is treated with acetyl hypobromite high yields of IV result plus smaller amounts of IX presumably formed by the incomplete conversion of the bromine to hypobromite.

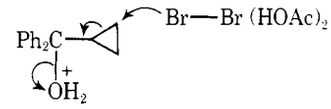
Discussion

The formation of the dibromo alcohol V when DPCC (I) is brominated in acetic acid or in an aprotic solvent such as acetonitrile is reasonably the result of a conventional electrophilic attack of bromine on the cyclopropane ring just as pictured by Skell, Day, and Shea.[3] Subsequent dehydration of V by bromine or some other acid accounts for the formation of the dibromo olefin VI.

Of greater interest in this study is the dibromo acetate IV. This product is not formed by the prior esterification of DPCC and then electrophilic ring bromination, for DPCC fails to esterify under any usual experimental conditions. Indeed, treatment of DPCC in acetic acid with acid yields the ring-opened acetate VIII, and no derivatives of VIII are found in the bromination. Furthermore, attempts to acetylate the dibromo alcohol V also under a variety of conditions failed in each case.

The rate of bromination of DPCC is greatest in acetic acid containing potassium bromide where some small amounts of hydrogen bromide may be present. In buffered acetic acid the reaction is slowest, while the reaction in acetic acid is intermediate in rate. Thus, it appears likely that the reaction is acid catalyzed. Since the esterification results discussed above rule out the likely formation of the diphenylcyclopropylcarbinyl cation during the bromination, a more unusual pathway for the formation of IV is called for.

Nucleophilic attack of bromine on DPCC with a concomitant loss of water can be pictured as



The acetic acid is included because it is known that complexes of the acid with bromine exist.[5] The result of a process such as that pictured would be the formation of the bromo olefin VII and a positive bromine stabilized by the acetic acid or more likely present as acetyl hypobromite. The formation of VII in appreciable amounts when excess bromide ion is present results from trapping of the positive bromine entity by bromide. Finally, it was demonstrated that the acetyl hypobromite will add to VII in acetic acid to yield IV. The evidence of Carey and Tremper[2] that the ring opening of DPCC to form II may involve a nucleophilic attack on the cyclopropane ring may be taken as supporting evidence for the mechanism proposed here. Thus, bromine may attack cyclopropane rings in either an electrophilic or nucleophilic sense.

The evidence concerning the bromination of 3,5-cyclocholestan-6β-ol can now be reassessed. In an aprotic solvent the formation of cholesteryl bromide occurs by nucleophilic attack of the bromine on the cyclopropane ring at C-3 with loss of the hydroxyl. When there is a deficiency of bromine the reaction terminates, but with adequate bromine the observed tribromide is formed. Unfortunately, the bromination of the cycloalcohol in acetic acid has not been reported.

Experimental Section

General. Diphenylcycloproplycarbinol was obtained from Aldrich and used directly. Proton and carbon-13 NMR spectra were obtained on JEOL MH-100 and FX-60 FT instruments, respectively. All chemical shifts are referenced to tetramethylsilane. Combustion analyses were obtained from Galbraith Laboratories, Knoxville, Tenn., and high-resolution mass spectral analyses were performed by Mr. G. Gabel on the Consolidated Electronics Corp. Model 21-110B mass spectrometer in the Biochemistry Department, Texas A and M University.

Cyclopropyldiphenylcarbinol. Reactions with Acetic Acid. A. A solution of 1.12 g (5.0 mmol) of diphenylcyclopropylcarbinol was prepared in 40 ml of glacial acetic acid and 0.80 g (5.0 mmol) of bromine was added. The mixture was allowed to stand overnight at room temperature in the dark. The reaction mixture was then poured into 100 ml of water and extracted with 3 × 50 ml of chloroform, the combined chloroform extracts were washed with 6% sodium bicarbonate, and the chloroform was removed on a rotary evaporator. The whole crude reaction product was analyzed by proton NMR as consisting of 63% 1-acetoxy-2,4-dibromo-1,1-diphenylbutane, 25% 2,4-dibromo-1,1-diphenyl-1-butanol, and 12% 2,4-dibromo-1,1-diphenyl-1-butene.

The crude product was dissolved in boiling hexane and, upon cooling, deposited 1-acetoxy-2,4-dibromo-1,1-diphenylbutane: mp 112–113 °C; NMR ($CDCl_3$) δ 1.65 (m, 1 H), 2.04 (s, 3 H), 2.50 (m, 1 H), 3.60 (m, 2 H), 6.24 (dd, 1 H, J = 12 and 3 Hz); ^{13}C NMR ($CDCl_3$) δ 22.1 (q), 31.2 (t), 37.7 (t), 56.6 (d), 86.3 (s), 127.0 (d), 127.5 (d), 128.1 (d), 129.1 (d), 139.6 (s), 169.0 (s).[6]

Anal. Calcd for $C_{18}H_{18}O_2Br_2$: C, 50.6; H, 4.5; Br, 37.4. Found: C, 50.87; H, 4.39; Br, 37.4.

The other products are described below.

B. A solution of 1.12 g (5 mmol) of diphenylcyclopropylcarbinol in 40 ml of glacial acetic acid was treated with 1.60 g (10 mmol) of bromine. The reaction mixture was treated in all respects as before. After standing overnight a reddish color still persisted; however, no starting material remained at this time. The workup was as before. The NMR analysis of the whole product gave 43% 2,4-dibromo-1,1-diphenyl-1-butanol and 57% 2,4-dibromo-1,1-diphenyl-1-butene.

C. The reaction of 1.12 g (5 mmol) of diphenylcyclopropylcarbinol with 0.80 g (5 mmol) of bromine was carried out in a solvent prepared by reacting 3 g of anhydrous sodium carbonate with 40 ml of glacial acetic acid, then adding 4 ml of acetic anhydride. The reaction in the dark became colorless only after 5 days. Workup of the reaction as above showed over ca. 50% of the dibromo acetate above plus unreacted starting material.

Other Reactions of DPCC. A. Reaction with Bromine in Acetonitrile. A solution of 1.12 g (5 mmol) of diphenylcyclopropylcar-

binol in 40 ml of acetonitrile was reacted overnight at room temperature in the dark with 0.80 g (5 mmol) of bromine. The standard workup was used. Evaporation of the solvent gave a quantitative yield of a yellow oil which could not be distilled without decomposition. However, the NMR of the oil was that of a pure compound assigned the structure 2,4-dibromo-1,1-diphenyl-1-butanol (V): NMR (CCl_4) δ 2.00 (m, 1 H), 2.30 (m, 1 H), 2.82 (s, 1 H, OH), 3.58 (m, 2 H), 5.47 (dd, 1 H, J = 6 and 1 Hz), 7.2–7.7 (m, 10 H); IR (neat) 3560 cm^{-1}(OH).

Anal. Calcd for $C_{16}H_{16}OBr_2$: mol wt, 383.9543. Found: mol wt, 383.9548.

B. With Hydrobromic Acid. A solution of 2.0 g (0.9 mmol) of diphenylcyclopropylcarbinol in 20 ml of benzene was stirred with 25 ml of 48% hydrobromic acid for 1 h at room temperature. The reaction mixture was washed with water and dilute sodium bicarbonate. The solvent was evaporated, yielding 2.3 g (88%) of light yellow oil, 4-bromo-1,1-diphenyl-1-butene (VII). Purification by high-vacuum short-path distillation gave a product pure by NMR: NMR (CCl_4) δ 2.68 (q, 2 H), 3.40 (t, 2 H), 6.12 (t, 1 H), 7.25 (m, 10 H).

Anal. Calcd for $C_{16}H_{15}Br$: mol wt, 286.0357. Found: mol wt, 286.0364.

C. Reaction with Acetic Acid. A solution of 1.12 g (5 mmol) of diphenylcyclopropylcarbinol in 40 ml of glacial acetic acid was treated with one drop of trifluoroacetic acid at 80 °C for 3 h. The standard workup was used. The product was a slightly brown oil which gave the NMR spectrum expected for pure 4-acetoxy-1,1-diphenyl-1-butene:[2] NMR ($CDCl_3$) δ 2.02 (s, 3 H), 2.44 (t, 1 H, J = 6 Hz), 2.50 (t, 1 H, J = 6 Hz), 4.16 (t, 2 H, J = 6 Hz), 6.18 (t, 1 H, J = 6 Hz), 7.38 (m, 10 H).

Other Reactions. A. 1,2,4-Tribromo-1,1-diphenylbutane. A 5% solution of bromine in carbon tetrachloride was added slowly and dropwise to a solution of 500 mg of 4-bromo-1,1-diphenyl-1-butene (VII) in ca. 10 ml of carbon tetrachloride until the color persisted. The solution was washed with dilute sodium sulfite and the solvent evaporated. Attempted short-path distillation led to decomposition of the product. However, the whole crude product had the NMR of a single pure compound and gave the correct high-resolution MS for $C_{16}H_{15}Br_3$. The structure was assigned as 1,2,4-tribromo-1,1-diphenylbutane (IX) based on the NMR (CCl_4): δ 2.1 (m, 1 H), 2.95 (m, 1 H), 3.70 (m, 2 H), 5.52 (dd, 1 H, J = 7 and 2 Hz), 7.65 (m, 10 H).

Anal. Calcd for $C_{16}H_{15}Br_3$: mol wt, 447.9364. Found: mol wt, 447.9374.

B. Reaction of VII with Bromine in Acetic Acid. The following experiment was carried out in the MH-100 NMR in a standard 5-mm tube. A mixture of ca. 80 mg of VII in 0.6 ml of perdeuterioacetic acid was treated with slightly more than 1 equiv of bromine. The NMR spectrum changed quickly to that of the tribromide IX. No trace of the dibromo acetate IV was evidenced.

C. Reaction of VII with Acetyl Hypobromite. A solution of acetyl hypobromite in carbon tetrachloride was generated as described by Rolston and Yates[7] from 1.5 g of silver acetate. A solution of 1.0 g of VII in 10 ml of carbon tetrachloride was added at −20 °C. After warming to room temperature, the reaction mixture was filtered, washed, and concentrated to give 1.4 g of crude product which analyzed by NMR as 72% of dibromo acetate IV, and 28% of the tribromide IX.

D. Treatment of the Dibromo Acetate IV with Hydrogen Bromide in Acetic Acid. A solution of approximately 200 mg of the dibromo acetate IV in 1 ml of acetic acid was treated by bubbling in hydrogen bromide at room temperature for 2 min. After standing overnight the reaction mixture was worked up in the usual way. An NMR analysis of the product indicated that it was the dibromo olefin VI contaminated with a trace of the dibromo alcohol V.

E. Reactions Which Failed to Yield Product. The following reactions were attempted but only starting material was recovered: (1) Repeated attempts were made to acetylate the DPCC I and the dibromo alcohol V. Among these may be listed acetic anhydride and acetyl chloride both with and without pyridine. (2) The dibromo alcohol V did not react on standing with acetic acid. Catalysis by either small amounts of trifluoroacetic acid or 70% perchloric acid did not alter the starting material.

Acknowledgment. Grateful appreciation is extended to the Robert A. Welch Foundation for their support of this work.

Registry No.—I, 5785-66-0; IV, 61076-21-9; V, 61076-22-0; VI, 51752-40-0; VII, 6078-95-1; IX, 61076-23-1; bromine, 7726-95-6; 4-acetoxy-1,1-diphenyl-1-butene, 24104-21-0; acetyl hypobromite, 4254-22-2.

References and Notes

(1) C. W. Shoppee, R. W. Rees, G. H. R. Summers, and G. D. Phillips, *J. Chem. Soc.*, 2786 (1959), and references cited therein.
(2) F. A. Carey and H. S. Tremper, *J. Am. Chem. Soc.*, **91**, 2961 (1969).
(3) P. S. Skell, J. C. Day, and K. J. Shea, *J. Am. Chem. Soc.*, **98**, 1195 (1976).
(4) (a) V. I. Pansevich-Kolyada and N. A. Prilzhaev, *J. Gen. Chem. USSR (Engl. Transl.)*, **21**, 571 (1951); (b) D. W. Grant and R. Shilton, *J. Chem. Soc., Perkin Trans. 1*, 135 (1974).
(5) R. E. Buckles and J. F. Mills, *J. Am. Chem. Soc.*, **75**, 552 (1953).
(6) The structure has been confirmed by W. H. Watson of these laboratories by x-ray crystallography, and the data will be published elsewhwere.
(7) J. H. Rolston and K. Yates, *J. Am. Chem. Soc.*, **91**, 1469 (1969).

Structural Effects in Solvolytic Reactions. 19. The Relative Electron Releasing Capability of Methyl, Phenyl, and Cyclopropyl Groups as Measured by the Tool of Increasing Electron Demand

Herbert C. Brown,* M. Ravindranathan,[1] and Edward N. Peters[2]

Richard B. Wetherill Laboratory, Purdue University, West Lafayette, Indiana 47907

Received August 16, 1976

The rates of solvolysis of aryldimethylcarbinyl (*tert*-cumyl) and 1-aryl-1-phenyl-1-ethyl *p*-nitrobenzoates with representative substituents in the aryl ring were determined in 80% aqueous acetone in order to test, by the application of the tool of increasing electron demand, the relative capability of methyl, phenyl, and cyclopropyl groups to stabilize a carbonium ion center. The *tert*-cumyl system yields a ρ^+ of −4.72 and the 1-aryl-1-phenyl-1-ethyl system yields one of −3.23. These data, together with the earlier reported value of ρ^+ for 1-aryl-1-cyclopropyl-1-ethyl system, −2.78, reveal that the relative electron releasing abilities of these groups increase in the order methyl < phenyl < cyclopropyl, supporting the conclusions reached earlier based on both rate and equilibria studies, but in direct contradiction to conclusions based on ^{13}C NMR shifts.

The extent and the consequences of the stabilization of carbonium ion centers by attached groups have received considerable attention in recent years. For many years, the main tool in such studies has been the solvolytic behavior of appropriate derivatives. With the advent of ^{13}C NMR and the ability to prepare and observe carbonium ions under stable ion conditions, workers in the field have utilized ^{13}C shifts to estimate electron densities at the carbonium carbon and to