tion of Id. The crude product was recrystallized from ligroin $(60-70^{\circ})$ to give 1.42 g. (36%) of IIf, m.p. $121-122.5^{\circ}$, $[\alpha] D + 4.5^{\circ}$ (chloroform). A 1% solution of active IIf, $[\alpha] D + 4.5^{\circ}$ in chloroform, racemized after 2.5 hr. at 95-100°, and a sample having $[\alpha] D + 2.5^{\circ}$ racemized in a 1% ethanol solution in 30 minutes at 100°. In both solvents some decomposition to iodine took place.

To 6.0 g. of 2-chloro-4-iodo-3-phenyl-2-cyclobutenone (IIe) in 10 ml. of acetone there was added 3.0 g. of brucine in 35 ml. of acetone. After a few seconds a precipitate formed. The mixture was poured into 250 ml. of water and extracted with 200 ml. of ether. The ether extract was shaken with three 100-ml. portions of 3 N hydrochloric acid and once with 150 ml. of water, dried, and evaporated *in vacuo*. The residue was recrystallized at room temperature from a mixture of chlorcform and ligroin (60-70°) and there was obtained 4.5 g. (75%) of IIe having m.p. 90-91.5°, $[\alpha]_D$ +2.0° (acetone). Some activity is lost on recrystallization from hot solvents due to thermal racemization.

Resolution of 2-chloro-4-bromo-3-phenyl-2-cyclobutenone (IIb) was carried out as described for IIe. From 6.3 g. of inactive IIb and 3.0 g. of brucine there was recovered 4.0 g. (63%) of IIb having m.p. $90.5-91.5^{\circ}$, $[\alpha]_{\rm D} + 2.24^{\circ}$ (acetone). Brucine could not be used to resolve 2-chloro-2-bromo-3-

Brucine could not be used to resolve 2-chloro-2-bromo-3phenylcyclo-butenone (Ib) since rearrangement took place to give IIb. Partially active Ib was obtained with optical rotations as high as $[\alpha] D - 3.16^{\circ}$ (acetone) from the reaction of bromine with optically active 2-chloro-4-iodo-3-phenyl-2cyclobutenone (IIe).

Kinetic Procedures.—Reaction between sodium iodide and 2,4-dichloro-3-phenylcyclobutenone (IIa) was carried out in sealed vials. A weighed sample (42 mg.) of IIa in a small test-tube was placed within a larger tube containing 5 ml. of standardized 0.1 M sodium iodide solution. The outer tube was then sealed under nitrogen. The tubes were immersed in a water-bath maintained at 39.7°; reaction was started by inverting the tubes to allow the contents to mix thoroughly, and the rate was followed by titrating the contents for iodide ion with 0.025 M potassium iodate according to the procedure of Tamele, et al.¹³

Cording to the procedure of Tamele, *et al.*¹³ The faster reaction of 2,2-dichloro-3-phenylcyclobutenone (Ia) with iodide enabled reaction to be carried out in a glassstoppered bottle since solvent evaporation was negligible. A weighed sample (0.8 g.) was dissolved in 100 ml. of 0.1 *M* sodium iodide and 5-ml. aliquots of this solution were withdrawn at suitable intervals and titrated with potassium iodate.

The rearrangement of 2-chloro-2-bromo-3-phenylcyclobutenone (Ib) with bromide ion was followed polarimetrically. The sample of Ib used had m.p. $90-93^{\circ}$, $[\alpha]^{2_{3D}} - 1.93^{\circ}$, and was shown by infrared to contain up to 2% of the 2,4-isomer IIb. The rate of change in optical rotation of an acetone solution 0.348 *M* in Ib and 0.00991 *M* in lithium bromide was followed in a water-jacketed 2-dm. polarimeter tube maintained at 25°. When racemization was complete, the recovered material was shown by its infrared spectrum to be pure IIb having m.p. $90.5-91.3^{\circ}$. The rate of racemization of 0.4 *M* acetone solutions of active IIb, 0.01–0.02 *M* in lithium bromide, was similarly determined.

(13) M. Tamele, C. J. Ott, K. E. Marple and G. Hearne, Ind. Eng. Chem., 33, 115 (1941).

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Small-Ring Compounds. XXVII. Nucleophilic Displacement Reactions of Some Halogen-substituted Phenylcyclobutenes¹

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Nucleophilic substitution reactions of 1,1-difluoro-2,2-dichloro-3-phenylcyclobutene and 1,1-difluoro-2,4-dichloro-3-phenylcyclobutene with potassiun hydroxide in ethanol and with phenyllithium have been found to proceed with rearrangement, and have led to preparations of some new cyclobutene and cyclobutenone derivatives.

Cycloaddition reactions between fluoroalkenes and substituted acetylenes and ethylenes have proved to be of considerable value in the synthesis of many cyclobutene and cyclobutane derivatives.^{2–5} For example, the addition of 1,1-difluoro-2,2-dichloroethylene and phenylacetylene gives 1,1-difluoro-2,2-dichloro-3-phenylcyclobutene (I), and if the reaction is carried out in the presence of triethylamine, the adduct is the allylic isomer of I, namely 1,1-difluoro-2,4-dichloro-3-phenylcyclobutene (II).²



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Compounds I and II and other adducts of related structure have been found to undergo some interesting nucleophilic displacement reactions which frequently are accompanied by allylic rearrangement.⁶ The present paper describes much of this work—specifically the displacement reactions of I and II with ethanolic potassium hydroxide and with phenyllithium.

Reaction with Ethanolic Potassium Hydroxide.— The reactivity of the allylic chlorine atoms of both adducts I and II is apparent in their respective reactions with potassium hydroxide in ethanol. An exothermic reaction took place between I and an equimolar amount of the basic reagent with immediate precipitation of potassium chloride. The organic product isolated was a colorless oil to which is assigned the structure 1,1-difluoro-2-chloro-4-ethoxy-3-phenyl-2-cyclobutene (III). This structure is indicated from the proton nuclear magnetic resonance spectrum (n.m.r.) of III, shown in Fig. 1A, from which can be identified an ethyl group, a phenyl group and an allylic ring-hydrogen. An alternative formulation of III as a vinyl ether rather

(6) See also the contribution by E. F. Jenny and J. Druey, THIS JOURNAL, 82, 3111 (1960).

⁽²⁾ J. D. Roberts, G. B. Kline and H. E. Simmons, Jr., THIS JOURNAL, 75, 4765 (1953).

⁽³⁾ E. J. Smutny and J. D. Roberts, *ibid.*, **77**, 3420 (1955); E. J. Smutny, M. C. Caserio and J. D. Roberts, *ibid.*, **82**, 1793 (1960).

⁽⁴⁾ E. F. Silversmith, Y. Kitahara, M. C. Caserio and J. D. Roberts, *ibid.*, **80**, 5840 (1958).

⁽⁵⁾ C. M. Sharts, Ph.D. Thesis, California Institute of Technology, 1959.

than an allylic ether is ruled out since the infrared spectrum of III does not possess a strong doublebond absorption at 5.70–5.77 μ which is characteristic of vinyl ether derivatives of fluorinated cyclobutenes.⁷ Moreover, the similarity between the ultraviolet spectra of III and 1,1-difluoro-2-chloro-3phenylcyclobutene⁴ (cf. Table I suggests they have closely similar structures.



The reaction of II with potassium hydroxide in refluxing absolute ethanol could not be arrested at the point corresponding to the displacement of one chlorine atom. Instead, both chlorine atoms were lost and 1,1-difluoro-2,2-diethoxy-3-phenylcyclobutene (IV) was formed. The structure of IV was unequivocally established from its n.m.r. spectrum which gave proton resonances corresponding to a phenyl group, a vinyl ring hydrogen and two equivalently situated ethyl groups (Fig. IB).

 TABLE I

 Ultraviolet Spectra of Substituted Cyclobutenes and

 Related Compounds^a



Compound	Rı	R_2	Rı	m_{μ}	€max
III	Н	$\mathrm{OC}_2\mathrm{H}_{5}$	Cl	262	21,400
Х	Н	C_6H_5	C1	260	20,300
				266	20 , 500
1,1-Difluoro-2-	Н	н	Cl	260	20,700
chloro- 3- phenylcyclo- butene				265	20,400
IV	$\mathrm{OC}_{2}\mathrm{H}_{5}$	$\mathrm{OC}_{2}\mathrm{H}_{\mathfrak{b}}$	Н	254	17,000
V	Н	$\mathrm{OC}_{2}\mathrm{H}_{5}$	$\mathrm{OC}_2\mathrm{H}_{\mathfrak{d}}$	265	23,400

^{*a*} Cary recording spectrophotometer, model 11M, with 1cm. quartz cells, using cyclohexane as solvent.



An unexpected result was obtained when either I or III was heated at reflux with excess ethanolic potassium hydroxide. A diethyl ether was formed, isomeric with IV, and the n.m.r. spectrum shown in Fig. 1C clearly illustrates that its two ethyl groups are not in equivalent chemical environments. Accordingly, this compound must be 1,1-difluoro-2,4-diethoxy-3-phenylcyclobutene (V). Further, the

(7) J. D. Park, M. L. Sharrah and J. R. Lacher, THIS JOURNAL, 71, 2337 (1949).



Fig. 1.—N.m.r. spectra at 60 mc.; chemical shift is given in c.p.s. with water as the zero of reference: A, 1,1-difluoro-2-chloro-4-ethoxy-3-phenyl-2-cyclobutene (III); B, 1,1-difluoro-2,2-diethoxy-3-phenylcyclobutene (IV); C, 1,1-difluoro-2,4-diethoxy-3-phenylcyclobutene (V); D, 1,1-difluoro-2,4-diethoxy-3-phenylcyclobutene (V); D, 1,1-difluoro-2-chloro-3,4-diphenyl-2-cyclobutene (X) in acetone solution (solvent not shown).

infrared spectrum of V has an intense band at $5.75 \ u$ which corresponds to the position of double bond absorption of a vinyl ether derivative of a fluorinated cyclobutene.⁷

Formation of the monoether III from I undoubtedly proceeds by an SN2' mechanism. Such a reaction path is not unexpected since allylic α -dihalides are known to be susceptible to this type of displace-



ment mechanism.8 However, the 2,4-dichlorocyclobutene II must necessarily lose the first chlorine in a similar SN2' process since the alternative SN2 formulation would give the monoether III. The reaction is unusual in that γ -substituted allylic halides, $>C_{\gamma}=C_{\beta}-C_{\alpha}$, rarely undergo SN2' dis-

placements, particularly when the substituent is a chlorine atom.⁹ The proposed α -chloroether intermediate VI would, in all probability, rapidly undergo further substitution since such compounds are known to be highly reactive toward nucleophilic reagents.¹⁰

Clearly, formation of the diether V from III must involve substitution of the vinyl chlorine by ethoxide ion. This is remarkable in view of the notoriously inert character of vinyl halides, although instances of vinyl fluorine substitutions are known.^{7,11,12} Indeed, the same diether V was obtained when 1,1,2-trifluoro-2-chloro-3-phenylcyclobutene³ was refluxed with excess potassium hydroxide in ethanol which implies by analogy with the behavior of I that vinyl fluorine is substituted by ethoxide.



Treatment of III, IV and V with hot concentrated sulfuric acid led to the formation of phenylcyclobutadienoquinone3 (VII) in each case. However, when IV was heated with dilute hydrochloric acid in aqueous dioxane, only the diether grouping was hydrolyzed and 4,4-difluoro-2-phenylcyclobu-

(8) P. B. D. de la Mare and C. A. Vernon, J. Chem. Soc., 3325, 3331, 3628 (1952).

(9) (a) R. H. DeWolfe and W. G. Young, Chem. Revs., 56, 753, (1956); (b) M. Gazith and W. T. Miller, Jr., 130th Meeting of the American Chemical Society, Atlantic City, N. J., September, 1956, p. 17M; (c) W. T. Miller, Jr., and A. H. Fainberg, THIS JOURNAL, 79. 4164 (1957).

(10) (a) C. T. Mason, C. W. R. Wade and H. W. Pouncy, Jr., ibid., **76**, 2255 (1954); (b) P. Ballinger, P. B. D. de la Mare, G. Kohnstam and B. M. Prestt, J. Chem. Soc., 3641 (1955). (11) E. F. Silversmith and J. D. Roberts, THIS JOURNAL, 80, 4083

(1958).

(12) A. T. Blomquist and E. A. La Lancette, 135th Meeting of the American Chemical Society, Boston, Mass., April, 1959, p. 54-O.



tenone (VIII) resulted. This ketone is isomeric with 4,4-diffuoro-3-phenylcyclobutenone (IX) prepared previously.³ The n.m.r. spectra of both ke-



tones are shown in Figs. 2A and 2B. The vinyl ring proton of VIII appears as a triplet owing to spinspin coupling with two equivalent fluorine nuclei, and the coupling constant, A_{ij} , has a value of 1–2 c.p.s. (Fig. 2B). In the proton spectrum of the isomeric ketone IX, the chemical shifts of the vinyl and phenyl hydrogens at 60 Mc. are very nearly equal and hence are not resolved separately (Fig. 2Å). However, the H-F coupling constant was measured from the fluorine spectrum of IX which is a simple doublet of A_{ij} equal to 12 c.p.s.¹³ The smaller magnitude of A_{ij} for VIII relative to IX is consistent with the structure assigned to VIII since cross-ring H–F splitting in cyclobutenes is substantially greater than adjacent H-F splitting.18 It is worth noting that the position of resonance for the vinyl hydrogen of VIII occurs at a remarkably low field strength relative to that of IX and not too far from the customary place for aldehyde protons. Displacements with Phenyllithium.—A vigorous

reaction took place between phenyllithium and an equivalent of 1,1-difluoro-2,2-dichloro-3-phenylcyclobutene (I) in ether solution. One chlorine atom was displaced by a phenyl group and a new solid compound X was formed. The inertness of the residual chlorine atom of X toward alcoholic silver nitrate, and the similarity between the ultraviolet spectra of X, III and 1,1-difluoro-2-chloro-3phenyl-2-cyclobutene⁴ (Table I), suggests that X is 1,1-difluoro-2-chloro-3,4-diphenyl-2-cyclobutene. This was confirmed from its n.m.r. spectrum (Fig. 1D) which possesses a strong proton resonance due to the phenyl hydrogens and a relatively weak doublet at higher field strengths due to the allylic ring hydrogen. Phenyllithium therefore attacks I at the vinyl carbon of the allylic system to effect an SN2' displacement. In all respects, this result is analogous to the reaction of I with ethanolic potassium hydroxide.



Hydrolysis of X with sulfuric acid gave a monoketone XI, the structure of which was established as

(13) C. M. Sharts and J. D. Roberts, THIS JOURNAL, 79, 1008 (1957).



2-chloro-3,4-diphenyl-2-cyclobutenone from its infrared, ultraviolet and n.m.r. spectra.

In contrast, the reaction between phenyllithium and 1,1-difluoro-2,4-dichloro-3-phenylcyclobutene (II) proved to be complex. Both lithium chloride and lithium fluoride were identified as inorganic products, and a crude organic product was isolated as a yellow solid in poor yield. This compound, XII, after repeated crystallizations from chloroform-ethanol mixtures, was obtained eventually as beautifully formed colorless crystals which discolored on heating near 180° and melted with decomposition at 204-206°. Elementary analysis indicated an empirical formula of C₂₂H₁₅F which corresponds to the displacement of both chlorine atoms of II with phenyl groups, and loss of the elements of hydrogen fluoride. A molecular weight determination by the Rast method proved unreliable since the compound was found to decompose in the camphor melt; instead, an isothermal distillation method¹⁴ was used and the observed molecular weight established the formula of XII as $(C_{22}H_{15}F)_2$. This result suggests the interesting possibility that XII is formed by the dimerization of fluorotriphenylcyclobutadiene which may well be an intermediate in the reaction of phenyllithium with II.



The structure of the dimer XII is not yet established; further details of its chemistry will be published at a later date.

Displacements with Piperidine.—It is convenient here to report on the reactions of piperidine with some halogen-substituted phenylcyclobutanes. In particular, an exothermic reaction was observed to take place between 1,1,2-trifluoro-2-chloro-3phenylcyclobutane⁴ (XIII) and excess piperidine, and the product isolated when the reaction mixture was allowed to stand overnight is thought to be 1,1-difluoro-2-piperidino-3-phenyl-2-cyclobutene (XV) on the basis of its infrared, ultraviolet and n.m.r. spectra (the latter having no vinyl hydrogen). When the reaction time was shortened to two hours, a different product was obtained which was identified the 1,1,2-trifluoro-3-phenyl-2-cycloas butene⁴ (XIV). This result implies that the piperidino compound XV is formed in two steps from XIII, the first being the elimination of hydrogen chloride to give XIV and the second step involving displacement of the vinyl fluorine of XIV with piperidine. As already mentioned, such displacements are not uncommon in fluorinated cyclobutenes.^{7,11,12} However, the reaction of 1,1difluoro-2,2-dichloro-3-phenylcyclobutane4 with ex-

(14) C. B. Childs, Anal. Chem., 26, 1963 (1954).



Fig. 2.—N.m.r. spectra at 60 mc.; in acetone solution (solvent not shown); chemical shift is given in c.p.s. with water as the zero of reference: A, 4,4-difluoro-3-phenyl-cyclobutenone (IX); B, 4,4-difluoro-2-phenylcyclobutenone (VIII).

cess piperidine gave only 1,1-difluoro-2-chloro-3phenyl-2-cyclobutene.⁴ Therefore, under conditions in which the vinyl fluorine of XIV is displaced to give the piperidino compound XV, vinyl chlorine remains inert.



When XV was heated with 96% sulfuric acid, the *gem*-diffuoro group was hydrolyzed to a carbonyl group, and the product isolated was assigned the structure 2-piperidino-3-phenyl-2-cyclobutenone on the basis of its infrared, ultraviolet and n.m.r. spectra and its reduction with zinc amalgam and hydrochloric acid to phenylcyclobutane. The stability of the enamine group of XV to acidic hydrolysis seems particularly noteworthy.

Experimental

1,1-Difluoro-2-chloro-4-ethoxy-3-phenyl-2-cyclobutene (III).--1,1-Difluoro-2,2-dichloro-3-phenylcyclobutene² (20.0 g., 0.0851 mole) in 20 ml. of absolute ethancl was added with stirring to a solution of 6.4 g. (0.10 mole) of 85% potassium hydroxide in 120 ml. of absolute ethanol. A precipitate of potassium chloride appeared immediately. The mixture was refluxed for 30 min., cooled, filtered and evaporated to about 80 ml. at reduced pressure. The residual solution was diluted with 220 ml. of water and extracted with three 100-ml. portions of ether. The combined ether extracts were washed with water and dried over magnesium sulfate. The ether was removed and the residue distilled to give 16.4 g. (79%) of III as an almost colorless oil of b.p. $105-106^{\circ}$ (2 mm.), n^{25} D 1.5182.

Anal. Calcd. for $C_{12}H_{11}OF_2Cl$: C, 58.91; H, 4.53. Found: C, 59.29; H, 4.63.

1,1-Difluoro-2,2-diethoxy-3-phenylcyclobutene (IV).--,1,1-Difluoro-2,4-dichloro-3-phenylcyclobutene² (13.0 g., 0.0553 mole) in 15 ml. of absolute ethanol was added with stirring to a solution of 8.9 g. (0.13 mole) of 85% potassium hydroxide in 160 ml. of absolute ethanol. The mixture slowly became turbid. After refluxing for 1.5 hr., the mixture was cooled, filtered and evaporated at reduced pressure to remove most of the solvent. The product IV was extracted as described above for compound III. Distillation in vacuo gave 10.4 g. (74%) of IV as a colorless oil of b.p. $80-82^{\circ}$ (1 mm.); the major fraction had b.p. $81.5-82^{\circ}$ (1 mm.), n^{25} D 1.4982.

Anal. Calcd. for $C_{14}H_{16}O_2F_2$: C, 66.13; H, 6.34. Found: C, 66.10; H, 6.45.

1,1-Diffuoro-2,4-diethoxy-3-phenylcyclobutene (V).—To a solution of 14 g. (0.21 mole) of 85% potassium hydroxide in 80 ml. of absolute ethanol was added 10.0 g. (0.0425 mole) of 1,1-diffuoro-2,2-dichloro-3-phenylcyclobutene.² The mixture was refluxed for 4 hr., cooled and filtered, and the filtrate was evaporated to half-volume at reduced pressure. The product V was extracted with ether as described above for compound III. After evaporation of the ether, the residual oil was distilled *in vacuo* to give 8.1 g. (75%) of V, b.p. 95-98° (1 mm.). Redistillation gave V as a colorless oil, n^{25} p 1.5073.

Anal. Caled. for $C_{14}H_{16}O_{2}F_{2};\,$ C, 66.13; H, 6.34. Found: C, 65.93; H, 6.03.

By the same procedure V was obtained from 1,1-difluoro-2-chloro-4-ethoxy-3-phenyl-2-cyclobutene (III) and 1,1,2-trifluoro-2-chloro-3-phenylcyclobutene.³

Reactions with Sulfuric Acid.—One-gram samples of III and IV were heated with 1.2 ml. of concentrated sulfuric acid and 0.3 ml. of water at 100° for 15 min. On pouring the mixture into ice-water, a yellow solid precipitated, which, after purification by sublimation and recrystallization from acetone, was obtained as bright yellow crystals of m.p. 152-153°, identical in all respects with an authentic sample of phenylcyclobutadienoquinone.³ Similarly, 3.9 g. of V in 30 cc. of concentrated sulfuric acid and 5 cc. of water gave after 3 min. at 100° followed by quenching with ice-water, a yellow precipitate which was identified as phenylcyclobutenedienoquinone after purification by chromatographing on alumina.

4,4-Diffuoro-2-phenylcyclobutenone (VIII).—A mixture of 2.0 g. (7.9 mmoles) of IV, 4 ml. of water, 15 ml. of dioxane and 1 ml. of concentrated hydrochloric acid was refluxed gently for 2.5 hr. The mixture was poured over crushed ice and the resulting white solid collected and sub-limed at $70-80^{\circ}$ (2 mm.). Recrystallization from cyclohexane gave 0.89 g. (63%) of colorless crystals of VIII having m.p. 90.0–90.6°.

Anal. Caled. for C₁₀H₆OF₂: C, 66.67; H, 3.36. Found: C, 66.53; H, 3.29.

The 2,4-dinitrophenylhydrazone of VIII had m.p. 245.2–246° after recrystallization from ethyl acetate.

Anal. Calcd. for $C_{16}H_{10}O_4N_4F_2$: C, 53.34; H, 2.80. Found: C, 53.26; H, 2.94.

1,1-Difluoro-2-chloro-3,4-diphenyl-2-cyclobutene (X).— To a solution of 5.9 g. (0.025 mole) of 1,1-difluoro-2,2-dichloro-3-phenylcyclobutene² (I) in 50 ml. of ether there was added slowly with stirring a solution of 0.031 mole of phenyllithium in 70 ml. of ether. A vigorous reaction took place and external cooling was necessary. After the addition was complete, the mixture was stirred for a further 40 min., then poured over a mixture of ice and 10 ml. of dilute hydrochloric acid. The ether layer was washed with water and the aqueous layer was extracted with ether. The combined ether extracts were dried over magnesium sulfate and evaporated. The solid residue was recrystallized from pentane to give 3.60 g. of X, m.p. 59-60°. Evaporation of the mother liquor followed by sublimation of the residue gave a further 2.4 g. of X, m.p. $59-60^{\circ}$. The over-all yield was 87%. Further recrystallization from pentane gave white crystals of m.p. $60.0-60.5^{\circ}$. Compound X gave no precipitate with alcoholic silver nitrate.

Anal. Caled. for $C_{16}H_{11}F_2C1$: C, 69.45; H, 4.01. Found: C, 69.68; H, 3.94.

1,1-Difluoro-3,4-diphenyl-2-cyclobutenone (XI).—A mixture of X (1.0 g.) and 3 ml. of concentrated sulfurie acid was stirred and heated at $70-75^{\circ}$ for 10 minutes. Reaction was quenched with crushed ice and the product was extracted with ether. After drying over magnesium sulfate, the ether was evaporated and the residue recrystallized from a mixture of pentane and cyclohexane to give 0.60 g. of XI as nearwhite crystals of m.p. 78-79°. A further 0.13 g. was obtained after concentration of the mother liquors bringing the over-all yield to 65%. After a further recrystallization, XI had m.p. 79.3–80.0°.

Anal. Caled. for C₁₆H₁₁OCl: C, 75.45; H, 4.35. Found: C, 75.58; H, 4.40.

The 2,4-dinitrophenylhydrazone of XI had m.p. 223-224° after recrystallization from ethyl acetate.

Anal. Calcd. for $C_{22}H_{15}O_4N_4Cl$: C, 60.77; H, 3.48. Found: C, 61.02; H, 3.69.

Reaction of 1,1-Difluoro-2,4-dichloro-3-phenylcyclobutene with Phenyllithium.—In an atmosphere of nitrogen, 11.6 g. (0.0495 mole) of II in 75 ml. of ether was added slowly with stirring to a solution of 0.15 mole of phenyllithium in 235 ml. of ether which was cooled in an ice-salt-bath. The mixture immediately darkened and became deep reddishbrown as reaction progressed. Copious precipitation of inorganic salts became evident toward the end of the addition which required about 75 min. When the addition was complete, a test for excess phenyllithium was negative. The mixture was poured into water and extracted with ether. The aqueous extract gave positive tests for fluoride and chloride ions. The ether extracts were dried and evaporated. The residual dark brown oil was dissolved in 20 ml. of hot chloroform and about 3 ml. of 95% ethanol was then added. On standing, yellow crystals separated slowly. The yield of crude material was 2.55 g. (17%). Recrystallization was effected by dissolving the crude product in the minimum volume of refluxing chloroform and adding hot ethanol until the first crystals appeared. By repetition of this procedure, colorless crystals of compound XII were obtained which, on heating, turned yellow at about 180° and melted with decomposition at 204-206°.

Anal. Caled. for (C₂₂H₁₅F)₂: C, 88.56; H, 5.07; F, 6.37; mol. wt., 596. Found: C, 88.09; H, 5.12; F, 6.32, 6.46; mol. wt. (isothermal distillation¹⁴), 570, 594.

No success was obtained in attempts to improve significantly the yield of XII either by raising or lowering the temperature, altering the mole-ratio of phenyllithium to II or by inverting the order of addition.

1,1-Diffuoro-2-piperidino-3-phenyl-2-cyclobutene (XV).---1,1,2-Triffuoro-2-chloro-3-phenylcyclobutane⁴ (10.0 g., 0.045 mole) was added to 35 ml. of piperidine. An exothermic reaction took place and a precipitate separated. The mixture was left to stand overnight; it was then taken up in water and ether, the organic layer was washed with water, dried over magnesium sulfate and distilled. 1,1-Diffuoro-2-piperidino-3-phenyl-2-cyclobutene (10.6 g., 95%), b.p. 110-111° (1 mm.), was obtained.

Anal. Caled. for C₁₅H₁₇NF₂: C, 72.26; H, 6.87; N, 5.62. Found: C, 72.30; H, 7.00; N, 5.67.

A similar reaction using 1,1-difluoro-2,2-dichloro-3phenyl-2-cyclobutene⁴ (10.0 g., 0.043 mole) and 35 ml. of piperidine gave 6.75 g. (79%) of 1,1-difluoro-2-chloro-3phenyl-2-cyclobutene⁴ which was identified by comparison of its infrared spectrum with that of an authentic sample. 2-Piperidino-3-phenyl-2-cyclobutenone.—Compound XV

2-Piperidino-3-phenyl-2-cyclobutenone.—Compound XV (27.5 g., 0.11 mole) was heated with 50 ml. of 96% sulfuric acid at 50°. The reaction mixture became hot and hydrogen fluoride was evolved. After 12 min., the mixture was poured over crushed ice and the product (probably a sulfate salt) which precipitated was collected and repeatedly washed with water. The color of the product changed from white to yellow during the washing; when dry, it was recrystallized several times from pentane to give material of m.p. 47.5–48.5°.

Anal. Caled. for C₁₅H₁₇ON: C, 79.26; H, 7.54. Found: C, 79.00; H, 7.62.

Clemmensen Reduction of 2-Piperidino-3-phenyl-2cyclobutenone.—Zinc powder (250 g.) was treated with a solution of 25 g. of mercuric chloride in 250 ml. of water and 12.5 ml. of concentrated hydrochloric acid. The supernatant liquid was decanted and the solid washed with distilled water. A mixture of 250 ml. of water, 250 ml. of concentrated hydrochloric acid, 25 ml. of ethanol and 20 g. of 2-piperidino-3-phenyl-2-cyclobutenone was added to the amalgamated zinc. The reaction mixture was allowed to reflux for 75 min. and then was steam distilled. The distillate was extracted with ether; the organic layer was dried over magnesium sulfate and carefully distilled. Phenylcyclobutane (2.6 g., 22%) was obtained which was identified by comparison of its infrared spectrum with that of an authentic sample.

[CONTRIBUTION FROM THE LABORATORIES OF THE PHARMACEUTICAL RESEARCH DIVISION OF CIBA LTD.]

Nucleophilic Displacement Reactions of Some Halogen-substituted Phenylcyclobutenes and the Ring-opening Reaction of 2-Chloro-4-piperidino-3-phenyl-2-cyclobutenone

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Nucleophilic substitution reactions of 1,1-difluoro-2,2-dichloro-3-phenylcyclobutene, 1,1,2-trifluoro-2-chloro-3-phenylcyclobutene and 1,1-difluoro-2,4-dichloro-3-phenylcyclobutene with piperidine in benzene have been found to proceed with rearrangement. Hydrolysis of 1,1-difluoro-2-chloro-4-piperidino-3-phenyl-2-cyclobutene led to 2-chloro-4-piperidino-3-phenyl-2-cyclobutene, which underwent a fast ring-opening reaction at room temperature with a vinyl ketene as the intermediate. The ketene added water to produce 2-chloro-3-phenyl-4-piperidino-3-butenoic acid, which, on warming *in vacuo*, eliminated a molecule of HCl to yield 3-phenyl-4-piperidino-2-butenoic acid lactone. The ultraviolet and infrared spectra of β -aminostyrenes are discussed.

Roberts and co-workers¹ have reported a simple way of synthesizing halogen-substituted phenylcyclobutenes and phenylcyclobutenones. The structural features and simplicity of the preparations prompted us to produce a wide variety of this type of compound for pharmacological and microbiological screening. The present paper will stress those of our findings that are of more immediate interest from a chemical point of view. In the few areas where our efforts overlapped with the work of Roberts and his group,^{1c,1d} the results are in good agreement; mainly, however, our separate efforts proved to be complementary.

Nucleophilic Displacement Reaction of 1,1-Difluoro-2,2-dichloro-3-phenylcyclobutene (I) with Piperidine in Benzene.-1,1-Difluoro-2,2-dichloro-3-phenylcyclobutene (I) reacts very smoothly with piperidine in benzene to yield a new monopiperidino compound which was assigned structure II. It is completely inert in its reactivity both toward excess base and dilute mineral acid, a behavior which would hardly be expected of the two possible isomeric substitution products III and IV.² Compound III is most likely the highly reactive intermediate of a nucleophilic displacement described in the following section. The amino-styrene IV would supposedly hydrolyze under the influence of dilute hydrochloric acid. However, a hydrochloride $(\lambda_{max} 260 \text{ m}\mu, \epsilon 19,600, 95\% \text{ ethanol})$ could be prepared of product II which hydrolyzed in water to give back unchanged the free base ($\lambda_{max} 262 \text{ m}\mu$, ϵ 19,900, 95% ethanol; 264 mµ, ϵ 19,700, CH₂Cl₂). Also, prolonged warming in an acid medium did not affect the substitution product. On the basis of these observations, combined with further evidence

 (a) J. D. Roberts, G. B. Kline and H. E. Simmons, Jr., THIS JOURNAL, **75**, 4765 (1953).
 (b) E. J. Smutny and J. D. Roberts, *ibid.*, **77**, 3420 (1955)
 (c) Y. Kitahara, M. C. Caserio, F. Scardiglia and J. D. Roberts, *ibid.*, **82**, 3106 (1960)
 (d) M. C. Caserio, H. E. Simmons, Jr., A. E. Johnson and J. D. Roberts, *ibid.*, **82**, 3102 (1960).

(2) (a) C. T. Mason, C. W. R. Wade and H. W. Pouncy, Jr., *ibid.*, **76**, 2255 (1954);
 (b) P. Ballinger, P. B. D. de la Mare, G. Kohnstam and B. M. Prestt, J. Chem. Soc., 3641 (1955).

mentioned in the last section of this paper, the monopiperidino compound was assigned structure II.



The nucleophilic displacement reaction on the allylic gem-dichloride I obviously proceeded with rearrangement. Very probably we are dealing here with an SN2' mechanism, a mode of substitution which had to be reckoned with, since it has been demonstrated by de la Mare and co-workers³ that this type of substitution reaction is quite common with a number of open chain allylic gem-dihalides. With the stereochemical relationship between the entering and leaving group in SN2' displacements having been established as cis,⁴ it is possible to propose a conceivable mechanism for the nucleophilic attack of piperidine on compound I involving the cyclic transition state V.⁵

In this connection the fact may also be of interest that in 1,1,2-trifluoro-2-chloro-3-phenylcyclo-

(3) P. B. D. de la Mare and C. A. Vernon, *ibid.*, 3325, 3331, 3628 (1952); P. B. D. de la Mare, E. D. Hughes, P. C. Merriman, L. Pichat and C. A. Vernon, *ibid.*, 2563 (1958); for further references on SN2' see footnotes lc and ld.

(4) W. G. Young, I. D. Webb and H. L. Goering, THIS JOURNAL,
73, 1076 (1951); G. Stork and W. N. White, *ibid.*, 75, 4119 (1953);
78, 4609 (1956).

(5) A. G. Catchpole, E. D. Hughes and C. K. Ingold, J. Chem. Soc., 8 (1948).