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MERCURATION OF PHENYL CYCLOPROPANES: SPATIAL FACTORS

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Summary

Mercuration of *trans*-1-phenyl-2-cyclohexylcyclopropane and stereoisomeric 1,2-di- and 1,2,3-triphenylcyclopropanes has been studied. An increase in the number of substituents in the cyclopropane ring leads to an increase in the stability of the ring towards mercury acetate, and substitution in the aromatic ring is the main process with 1,2,3-triphenylcyclopropane.

Introduction

The action of mercuric acetate in hydroxyl-containing solvents on alkyl cyclopropanes [1-5] or monoaryl cyclopropanes [6] is known to result in the opening of the smaller ring and the formation of γ-mercurated alcohols or their derivatives. Predominantly the bond between the least and the most substituted carbon atoms is broken. That the initial attack is electrophilic agrees with the fact that electron-donor substituents directly bonded to the cycle accelerate its reaction with mercury acetate whereas electron-acceptor substituents decelerate it [7,8]. With substituted phenylcyclopropanes, it was found that the mechanism involved donor—acceptor complexation at the smaller cycle and the ring opening rate in the complex depended essentially on the aromatic substituent [9,10]. Stereoisomeric 1,2-diphenylcyclopropanes are stable towards mercuric acetate [11,12] at room temperature regardless of the solvent employed. No mercuration is observed under more drastic conditions (64°C) either, in methanol. In acetic acid at 75-80°C the difference in reactivity is felt and the *cis*-isomer undergoes opening of the smaller ring to an extent of 20% while the *trans*-isomer remains unaffected [11]. 1,1-Diphenylcyclopropane reacts even at room temperature in methanol [11].

Thus, the data suggest that the presence and arrangement of substituents

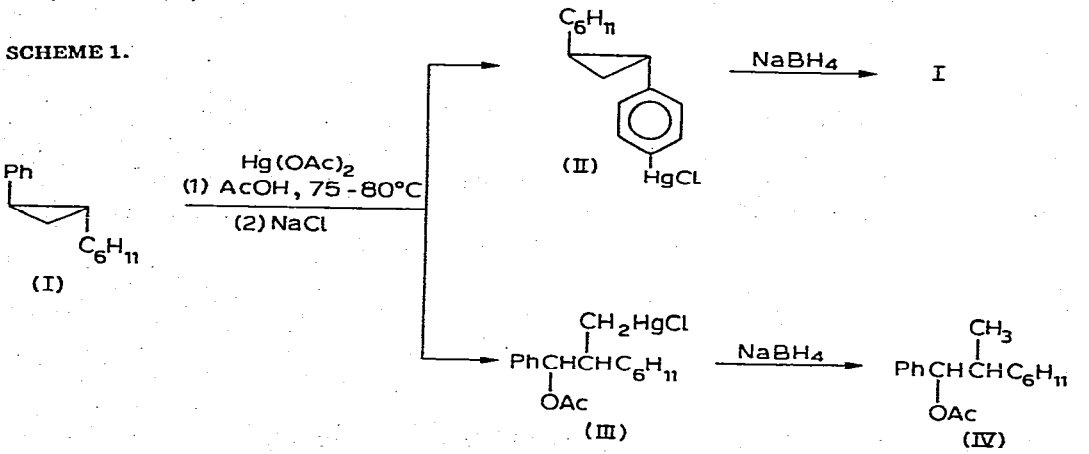
in the three-membered ring significantly influence the reactivity toward mercuric acetate*.

Discussion

To study the spatial and electron factors in more detail, we have investigated the action of mercuric acetate on *trans*-1-phenyl-2-cyclohexylcyclopropane and stereoisomeric 1,2-di- and 1,2,3-triphenylcyclopropanes.

trans-1-Phenyl-2-cyclohexylcyclopropane (I) does not react with mercuric acetate in glacial acetic acid at room temperature (under these conditions the cyclopropane ring in phenylcyclopropane is opened completely) but at 75-80° it undergoes substitution in the benzene ring to an extent of 7% (the product is *trans*-1-(*p*-chloromercuryphenyl)-2-cyclohexylpropane (II))** and opening of the smaller ring to an extent of 50% (the product is 1-phenyl-2-cyclohexyl-1-acetoxy-3-chloromercurypropane (III)). The ring opening occurs at the bond of the unsubstituted carbon with the carbon to which the phenyl radical is attached (Scheme 1).

SCHEME 1.



The lower reactivity of I compared with phenylcyclopropane may be assigned to spatial hindrance created by the two bulky substituents. Consequently, along with electron factors mentioned earlier [9,10], spatial factors significantly affect the cyclopropane reactivity.

We wanted to reinvestigate mercuration of *cis*- (V) and *trans*- (VI) -1,2-diphenylcyclopropanes. In these compounds stereochemical factors resemble those operating in I whereas the three-membered ring may conjugate with two phenyls.

Mercuration of V and VI in glacial acetic acid at 75-80°C shows that the

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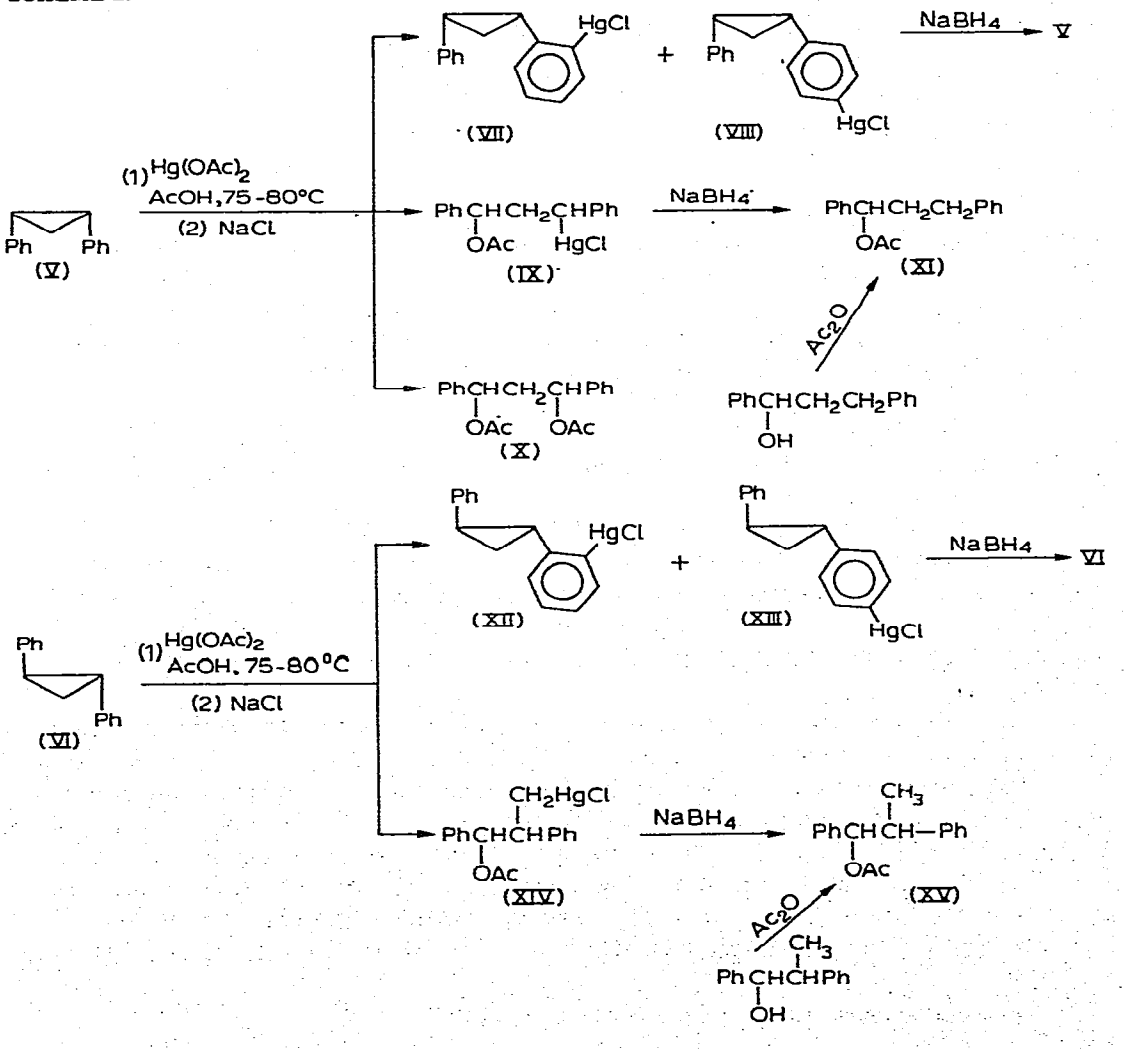
* We found [13] simultaneously with De Puy and McGirk [14] that an increase in the number of substituents in the cyclopropane ring leads to an increase in the stability of the ring towards mercury acetate. Their PMR spectra revealed a benzene ring substitution product in the reaction mixture resulting from mercuration of *anti*-1-phenyl-*cis*-2,3-dimethylcyclopropane with mercury trifluoroacetate. No individual product, however, was isolated.

** In this and other cases, chloromercury derivatives were isolated by treating the reaction mixture with saturated aqueous sodium chloride.

cyclopropane ring in the hydrocarbons is more stable against mercuric acetate that it is in I; V undergoes 30% smaller ring opening, VI 21%. Also, the *trans*-isomer (VI) is markedly mercurated in the phenyl ring (see Table 1). Let us assume that spatial hindrance in I is close to that in VI, then the greater stability of the cyclopropane ring in the latter compound may be explained by conjugation of the ring with the two phenyls. Note that VI undergoes the benzene ring mercuration to no smaller extent than the cyclopropane ring opening, thus differring significantly from the related compound I in which the first reaction prevails (Table 1).

The reaction is affected strongly by the configuration of the reactants. (Scheme 2). For example, the *trans*-isomer (VI) undergoes mainly substitution in the aromatic ring whereas the smaller ring opening predominates in the *cis*-isomer (Table 1). The ring opening also proceeds in different ways. Firstly, the bond (C1—C2) between the most substituted atoms is broken in the *cis*-

SCHEME 2.

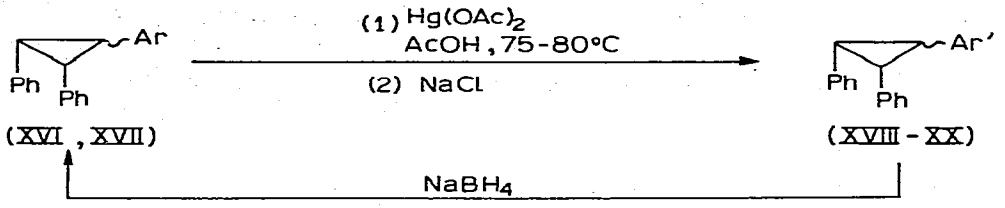


isomer (V) whereas the C1—C3 bond is broken in VI. Secondly, the bond decomposition in V is due not only to mercuration but also to oxidation, by mercuric acetate and the adduct IX is accompanied with 1,3-diphenyl-1,3-diacetoxypropane* (IX).

The spatial and substitution effects were further studied on *cis*- (XVI) and *trans*- (XVII)-1,2,3-triphenylcyclopropanes.

The smaller cycle in both compounds is stable against mercuric acetate (in acetic acid at 76-80°C) and mercuration of the phenyl ring is, to all intents and purposes, the only direction observed (Scheme 3).

SCHEME 3.



(a) Ar = *syn*-C_6H_5 (XVI); Ar' = *syn*-*o*-C_6H_4HgCl (XVIII), *syn*-*p*-C_6H_4HgCl (XIX)

(b) Ar = *anti*-C_6H_5 (XVII); Ar' = *anti*-*p*-C_6H_4HgCl (XX)

Mercuration of the *cis*-isomer (XVI) gives *syn*-1-(*o*-chloromercuryphenyl)-*cis*-2,3-diphenylcyclopropane (XVIII, yield 7%) and *syn*-1-(*p*-chloromercuryphenyl)-*cis*-2,3-diphenylcyclopropane (XIX, yield 14%); the initial hydrocarbon is recovered to an extent of 70%. The reaction mixture contains a compound revealing no cyclopropane protons (PMR) and exhibiting (IR) a band at 1735 cm^{-1} (C=O) and a band at 1235 cm^{-1} (C—O). These data prompt us that opening of the smaller ring, however insignificant, still has occurred.

The *trans*-isomer (XVII) is substituted in the *para*-position of the *trans*-phenyl ring to an extent of 27% and gives *anti*-1-(*p*-chloromercuryphenyl)-*cis*-2,3-diphenylcyclopropane (XX).

In the triphenylcyclopropanes (XVI and XVII), where all the cyclopropane ring carbons are bonded with phenyls, the smaller cycle practically does not react with mercuric acetate. Consequently, the introduction of large substituents such as phenyl which conjugate with the smaller cycle and bar if from the reactants suppresses the mercuration and the accompanying opening of the smaller ring.

Table 1 shows that the amount of the products arising from the opening of the smaller ring decreases across the series phenylcyclopropane, *trans*-1-phenyl-2-cyclohexylcyclopropane, *cis*-1,2-diphenylcyclopropane, *trans*-1,2-diphenylcyclopropane, *cis*-1,2,3-triphenylcyclopropane and *trans*-1,2,3-triphenylcyclopropane. The amount of the substitution products rises in the same direction.

These results show that mercuration may effect both the smaller and the aryl cycles in arylcyclopropanes. The reaction course depends, of course, on both accessibility and reactivity of the sites mentioned. Introduction of phenyls

* Similar combinations were described in refs. 11 and 15-17.

TABLE 1

MERCURATION OF *trans*-1-PHENYL-2-CYCLOHEXYLCYCLOPROPANE, 1,2-DI-, AND 1,2,3-TRIPHENYLCYCLOPROPANES IN GLACIAL ACETIC ACID AT 75-80°C

Compound	Composition of reaction mixture (%)			
	Initial hydrocarbon	Ring opening products	Benzene ring substitution products	
			ortho	*para*
I	40	50		7
V	60	30	2	6
VI	51	21	3.5	20.5
XVI	70	traces	7	14
XVII	72			27

in the cyclopropane ring not only screens the ring but also stabilises it, owing to conjugation with the benzene ring. It is known that when alkylcyclopropanes are replaced by phenylcyclopropane the trimethylene ring stability toward electrophiles rises [18,19]; the rate of mercuration decelerates but the reaction course is still the same, viz., the smaller cycle is opened to give γ-mercurated alcohols or their derivatives.

With 1,2-diphenylcyclopropanes, mercuration goes in both possible directions; the smaller ring opens and the benzene ring is substituted. 1,2,3-Triphenylcyclopropanes undergo only the benzene ring substitution.

The contribution of conjugation in the stabilisation of the cyclopropane ring is also seen in comparing *trans*-1-phenyl-2-cyclohexyl- with *trans*-1,2-diphenylcyclopropanes and, on the other hand, *cis*- (V) with *trans*- (VI) -1,2-diphenylcyclopropanes, in their mercuration reactions.

Isolation and structural assignment

Hydrated silicic acid was used to separate all the chloromercury derivatives obtained, by column chromatography (eluent $CCl_4/CHCl_3$ 3/1).

Chloromercury derivatives II, VII, VIII, XII, XIII, XVIII, XIX and XX as benzene ring substitution products were assigned by reducing them with sodium borohydride to the starting I, V, VI, XVI and XVII, and by PMR spectroscopy (Table 2).

The *cis*-assignment in VII, VIII and XIX was made on the basis of ^{13}C NMR spectra; the cyclopropane carbon chemical shifts are greater in *trans*- than in *cis*-isomers [20] (Table 3).

The chloromercury group assignment in the phenyl rings of VII, VIII, XII and XIII was based on the number of equivalent carbons. The integral intensity ratio is 1/2/3/1 for the *para*-isomers VIII, XII and XIX, and it is 1/1/1/1/1/1 for the *ortho*-isomers VII and XII. The *ortho*-assignment for the chloromercury group agrees also with significant alteration of the cyclopropane C1 chemical shift in VII and XII (Table 3).

Structures of III, IX, X and XIV as cyclopropane ring opening products were proved spectrally and chemically. The IR spectral data given in Table 4, PMR spectral data in Table 2.

Sodium borohydride reduction of III, IX and XIV gave the respective

TABLE 2

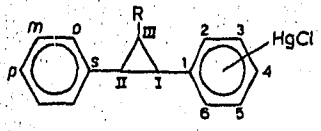
PMR SPECTRA

Compound	^{1}H chemical shift (δ, ppm)			Compound	^{1}H chemical shift (δ, ppm)			
	Aromatic protons				Aromatic protons	CH	CH_2	CH_3
I [a]	7.8 (5H, m)	*b*	*b*	III [a]	7.3 (5H, s)	5.9 (1H, d)	*b*	2.1 (3H, s)
II [a]	6.9-7.4 (4H, m)	*b*	*b*	IV [a]	7.1 (5H, s)	5.7 (1H, d)	*b*	1.9 (3H, s)
V [a]	6.8 (10H, s)	2.2 (2H, m)	1.2 (2H, m)	IX	7.2 (10H, m)	6.2 (1H, t)	3.2 (2H, m)	2.6 (3H, s)
VI [a]	6.9 (10H, m)	1.9 (2H, m)	1.2 (2H, m)			4.0 (1H, t)		
VII	7.8-7.9 (9H, m)	2.8 (2H, m)	1.7 (2H, m)	X	7.4 (10H, s)	5.7-6.2	2.3-2.7	1.15 (6H, s)
VIII	7.3-7.6 (9H, m)	2.4-2.9 (2H, m)	1.8 (2H, m)			(2H, m)	(2H, m)	
XII	7.6 (9H, m)	2.3 (2H, m)	1.5 (2H, m)	XI	7.2 (10H, d)	5.8 (1H, t)	2.3-2.4	2.1 (3H, s)
XIII	7.2 (9H, m)	2.2 (2H, m)	1.6 (2H, m)				(4H, m)	
XVI [a]	7.0 (15H, s)	2.8 (3H, s)		XV	7.3 (10H, m)	6.0 (1H, d)		2.2 (3H, s)
XVII [a]	7.5 (10H, s); 7.7 (5H, s)	3.2 (3H, s)				3.4 (1H, q)		1.6 (3H, d)
XVIII	7.2 (14H, m)	3.0 (3H, s)						
XIX	7.3 (14H, m)	2.9 (3H, s)						
XX	7.5-7.8 (14H, m)	3.4 (3H, s)						

[a] Against an HMDS internal reference. [b] Overlapped with cyclohexane ring protons.

TABLE 3

^{13}C NMR SPECTRA OF MERCURATED 1,2-DI- AND 1,2,3-TRIPHENYLCYCLOPROPANES



Compound	R	^{13}C Chemical shift (δ, ppm)												
		C_I	C_{II}	C_{III}	C_s	C_o	C_m	C_p	C_1	C_2	C_3	C_4	C_5	C_6
V	H	24.2	24.2	10.8	138.4	127.8	129.1	125.8						
VI	H	27.7	27.7	17.9	142.3	125.7	128.3	125.6						
VII	H	29.3	23.7	11.8	138.5	127.8	128.1	126.2	142.3	156.4	136.2	125.5	130.0	127.8
VIII	H	24.1	24.5	10.2	138.0	127.6	128.8	125.5	140.0	129.1	135.8	148.3	135.8	129.1
XII	H	31.4	28.7	18.1	142.2	125.8	128.3	125.6	146.3	154.1	136.6	125.6	128.3	126.0
XIII	H	27.7	28.0	18.8	142.2	125.5	128.4	125.5	142.3	125.5	136.7	148.3	136.7	125.5
XIX	C_6H_5	31.5	31.8	31.8	140.2	135.1	134.4	129.8	140.2	135.1	139.6	152.9	139.6	135.1

TABLE 4

IR SPECTRA OF CYCLOPROPANE RING OPENING PRODUCTS

Compound	ν (cm^{-1})	
	C = O	C—O
III	1740	1230
IV	1750	1240
IX	1735	1230
X	1725	1230
XI	1730	1235
XIV	1730	1230
XV	1730	1235

monoacetates IV, XI and XV; two of these were prepared by an independent synthesis.

Results of elemental analyses of I-XX are given in Table 5.

Experimental

IR spectra were run as liquid films or Vaseline oil mulls on a Zeiss UR-20 machine. PMR spectra were recorded on a Varian T-60 in CH_2Cl_2, $CHCl_3$, and CCl_4 against an HMDS external reference. Proton noise-decoupled ^{13}C NMR spectra were obtained on a Varian XL-100-15 intrument under deuterium (D_2O) lock conditions. The samples were in 8 mm diameter ampoules inside larger (12 mm diameter) ampoules filled with D_2O. The signal accumulation and analysis were made on a 620 computer. Chemical shifts were measured against a DMSO internal reference and converted to the TMS scale [$(^{13}CH_3)_2SO$ = 40.48 ± 0.05 ppm].

TABLE 5

CONSTANTS AND ANALYSES

Compound	R_f [b]	M.p. (°C)	Analysis found (calcd.) (%)		
			C	H	Hg
II	0.65	179	41.46 (41.74)	4.75 (4.37)	45.99 (46.08)
III	0.40	140	41.05 (41.37)	4.62 (4.46)	45.10 (45.34)
IV	0.60	72	78.36 (78.46)	9.62 (9.60)	
VII	0.60	136	42.07 (42.24)	3.14 (3.03)	46.20 (46.71)
VIII	0.56	175	42.22 (42.24)	3.09 (3.03)	46.26 (46.71)
IX	0.33	134	41.50 (41.80)	3.55 (3.49)	41.30 (41.00)
X	0.30	[a]	72.31 (72.50)	6.35 (6.35)	
XI	0.40	b.p. 163/2	80.46 (80.31)	7.02 (7.08)	
XII	0.57	107	42.00 (42.24)	3.27 (3.03)	46.20 (46.71)
XIII	0.52	170	42.18 (42.24)	3.01 (3.03)	46.54 (46.71)
XIV	0.30	126	41.70 (41.80)	3.44 (3.49)	41.43 (41.00)
XV	0.40	[b]	80.18 (80.31)	7.05 (7.08)	
XVIII	0.55	211	50.15 (50.00)	3.54 (3.37)	39.20 (39.69)
XIX	0.50	194	49.70 (50.00)	3.47 (3.37)	39.10 (39.69)
XX	0.50	175	50.22 (50.00)	3.46 (3.37)	39.40 (39.69)

[a] Viscous oil. [b] Mixture of stereoisomers. [c] For chromatography conditions, see the experimental section.

GLC analyses (except for organomercury compounds) were made on a Tsvet machine. Column length 3 m, column diameter 4 mm, 5% SE-30 on Chromosorb N-AW-DMCS, helium carrier gas 60 ml/min, column temperature 180 or 220°C.

The starting hydrocarbons were obtained by known methods: I [21], V [22], VI [22], XVI [23], XVII [24].

Mercuration of I, V, VI, XVI und XVII in glacial acetic acid

A mixture of a hydrocarbon (0.01 mol) and mercuric acetate (0.01 mol) in 100 ml glacial acetic acid was heated at 75-80°C for 24 h, cooled down, poured into water, and extracted with $CHCl_3$. The extracts were treated with NaCl several times, dried over $MgSO_4$, and the solvent was removed. Fractional chromatography on a $SiO_2 \cdot nH_2O$ column gave the starting hydrocarbon (eluted with CCl_4) and the organomercurial (eluted with $CCl_4/CHCl_3$ 3/1). The compounds are described in Tables 1 and 5.

Reduction of organomercury compounds with sodium borohydride

Sodium borohydride (0.012 mol) was added by small portions to a solution of an organomercury compound (0.01 mol) in 50 ml anhydrous ethanol and the mixture was stirred at 20°C for 48 h. It was diluted with water, acidified with 2 *N* HCl, extracted with $CHCl_3$, the extracts were dried over $CaCl_2$, the solvent was removed, and the residue was chromatographed on an Al_2O_3 column with CCl_4 eluent to give the respective organomercurials. The results are summarised in Table 5.

1,3- and 1,2-Diphenyl-1-acetoxypropanes (XI and XII)

These were obtained from the respective α- and β-phenylethylmagnesium bromides acted upon by benzaldehyde, followed by acetic anhydride acetylation of the resulting alcohols. Compound XI, b.p. 162°C/2 Torr, lit. [25] 164°C/2 Torr; XV, b.p. 127°C/0.2 Torr, lit. [26] 128°C/0.25 Torr.

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