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MARKOVNIKOV HYDRATION OF VINYLCYCLOPROPANES BY OXYMERCURATION-DEMERCURATION *

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Summary

Representative vinylcyclopropanes (Ia—Ic) were hydrated in a Markovnikov fashion by oxymercuration-demercuration. Isolated yields of α-cyclopropyl-substituted alcohols were more than 80%. 2,2-Diphenyl-1-vinylcyclopropane (Id) was the only olefin that produced a mixture of the expected alcohol, IId, and a rearranged product III. At 0° C, However, the amount of III was minimal (ca. 6%), and hence the Markovnikov hydration of Id was accomplished. The consumption of two molar equivalents of mercuric acetate in the formation of III was demonstrated by demercuration with sodium borodeuteride.

Introduction

Hydroboration-oxidation [1] and oxymercuration-demercuration [2] are two important reactions, both developed as useful synthetic methods by Brown and his coworkers, to hydrate carbon-carbon double bonds. The former is especially valuable for the anti-Markovnikov hydration of olefins and the latter is a useful, mild method of hydrating olefins in Markovnikov fashion.

Although anti-Markovnikov hydration of vinylcyclopropanes has been accomplished by hydroboration-oxidation [3], Markovnikov hydration of such olefins by acid-catalyzed hydration has caused troubles [4]. Thus the treatment of 1,1-dicyclopropylethylene (Ia) with dilute perchloric acid in dioxane/water has been reported to give a mixture composed of 1,1-dicyclopropylethanol (IIa) and 2-cyclopropyl-2-methyltetrahydrofuran (in 8/2 ratio after 2.5 min and 1/10 after 8 min) [4] Similar observations were made with 1-cyclopropylstyrene (Ib), but vinylcyclopropane and 2-cyclopropylpropene could be hydrated without complication [4]. Apparently, the kinetically controlled product is the expected alcohol, but the alcohols substituted by an additional group capable of

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* Dedicated to Professor Herbert Charles Brown on the occasion of his 66th birthday.

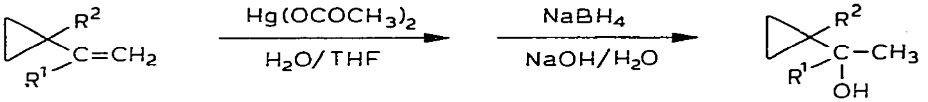
stabilizing cations ionize easily under the reaction conditions and rearrangement occurs to produce the thermodynamically controlled products. From a synthetic standpoint, therefore, it may be desirable to develop an alternate method to effect clean hydration of such vinylcyclopropanes.

Accordingly, we examined the oxymercuration-demercuration of these olefins. Although we were not certain about the survival of the cyclopropane ring in this reaction, because three-membered rings are known to be cleaved by mercuric salts [5], we found that the hydration was accomplished successfully. Recently, Brown and his coworkers [6] have also reported the hydration of 2,2-dichloro-1-vinylcyclopropane by oxymercuration-demercuration.

Results and discussion

Hydration of representative vinylcyclopropanes

Oxymercuration-demercuration reactions of vinylcyclopropanes Ia—Ic were carried out by the standard method [2a,d,e,g,h]. The time required for the disappearance of the yellow suspensions (T_1) was as short as those observed for many alkenes [2]. The isolated alcohols IIa—IIc were essentially pure (GLC) and their yields were greater than 80%. The structures of the alcohols were established by comparison with authentic compounds prepared from the corresponding ketones by the Grignard procedure. Thus, oxymercuration-demercuration is shown to be a useful alternative to the acid-catalyzed hydration in the Markovnikov hydration of these vinylcyclopropanes.



(Ia) R^1 = cyclo-C_3H_5, R^2 = H
(Ib) R^1 = C_6H_5, R^2 = H
(Ic) R^1 = H, R^2 = CH_3

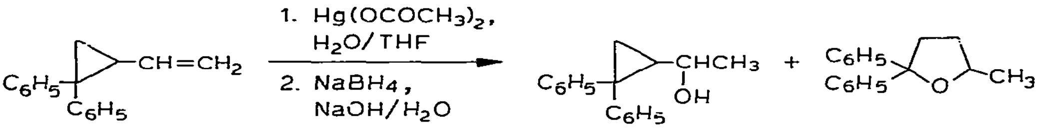
(IIa) R^1 = cyclo-C_3H_5, R^2 = H
(IIb) R^1 = C_6H_5, R^2 = H
(IIc) R^1 = H, R^2 = CH_3

Hydroboration-oxidation of Ia—Ic also proceeded without trouble and pure alcohols, the anti-Markovnikov hydration products were obtained in high yield.

Hydration of 2,2-diphenyl-1-vinylcyclopropane (Id)

2,2-Diphenyl-1-vinylcyclopropane (Id) is an olefin possessing a high tendency to rearrange [7], and its oxymercuration-demercuration was somewhat complex. When Id was treated with an equimolar amount of mercuric acetate, the reaction proceeded only to an extent of 65% after 16 h, although T_1 was ca. 50 sec. GLC analyses of the organic product fraction showed that it contained at least three components, in a ratio of 17/24/59. The latter two were characterized as the expected alcohols, IId-1 and IId-2. They are diastereoisomeric of each other; IId-1 may be assigned as the (*R*,*R*)-(*S*,*S*) isomer and IId-2 as the (*R*,*S*)-(*S*,*R*) isomer * (see p. 39). Jones oxidation of the crude reaction mixture gave a single ketone and its lithium aluminium hydride reduction regenerated IId-1 and IId-2 in 9/1 ratio.

The third component obtained in the oxymercuration-demercuration was characterized as 2-methyl-5,5-diphenyltetrahydrofuran (III). Control experiments proved that both IId-1 and IId-2 were stable under the reaction conditions. Moreover, the ratio of III/IId-1/IId-2 remained constant at various reaction times

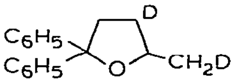


(Id) (IId) (III)

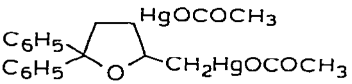
(T_2). Accordingly, it may be concluded that the substituted tetrahydrofuran compound III is a primary product of the oxymercuration. This conclusion is supported further by the following experiments.

Since considerable amounts of the starting olefin were recovered in the reaction, it was presumed that 2 mol of mercuric acetate per mol of Id were consumed in the formation of III. In fact, demercuration with sodium borodeuteride gave 2-(methyl-d_1)-5,5-diphenyltetrahydrofuran-3-d_1 (IV). The positions of deuterium substitution were unambiguously determined by NMR spectroscopy. Thus, the organomercurial leading to III must be the bis-mercurated V.

After these experiments, the amount of mercuric acetate was doubled to achieve higher conversions of Id. In addition, the reactions were examined at various temperatures to maximize the amount of the desired alcohols IId. The results are summarized in Table 1. Although it has been reported [2j] that oxymercurated species can isomerize on standing in the presence of an excess of mercuric acetate, the ratio III/IId was not influenced by the increased amount of mercuric acetate at 25° C. At 0° C, the amount of III decreased considerably and the preparation of IId became practical.



(IV)



(V)

Reaction scheme for the oxymercuration of Id

We should like to propose the following scheme for the production of IId and III. Since the bis-mercurated species should have the structure V, the initial attack of mercuric acetate must occur at the double bond, not at the cyclopropane ring of Id. If the latter were the case, the tetrahydrofuran derivative produced should be 3-methyl-2,2-diphenyltetrahydrofuran, because cyclopropane ring cleavage is known to occur by attack of mercuric acetate at the least sub-

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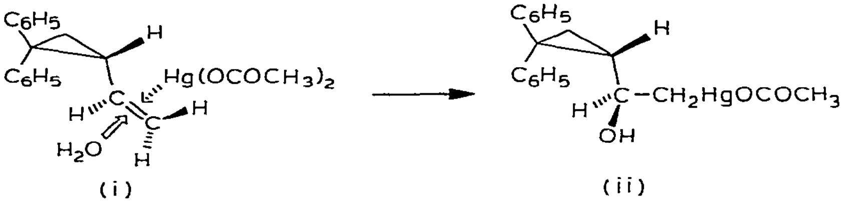
[*] The configurations are deduced from mechanistic considerations. If one assumes that attack of mercuric acetate takes place from the less hindered side of an extended bisected conformation of Id (i), the (R,S)-(S,R) isomer may result. Since such a conformation will be the most preferable one for Id, the isomer produced in larger amount, namely IId-2, may have this configuration. The assumption is further supported by an observation that, at higher temperatures, the amount of III increased mainly at the expense of IId-2. The conformation and the attacking mode (i) are suitable for the rearrangement. Instability of IId-1 and IId-2 did not allow us to separate them by column chromatography.



(i) (ii)

TABLE 1

EFFECT OF TEMPERATURE ON THE RATIO OF THE PRODUCTS IN OXYMERCURATION-DEMERCURATION OF 2,2-DIPHENYL-1-VINYLCYCLOPROPANE (Id)

Id/Hg(OCOCH$_3$)$_2$	Temperature (°C)	Conversion (%)	Products [a]	
			III	IId (Ratio) [b]
1/1	room temp.	65	17	83 (1/2.5)
1/2	0	87	6	94 (1/4)
1/2	25	91	12	88 (1/2.2)
1/2	65	95	63	37 (1/0.5) [c]

[a] Determined by GLC and normalized. [b] The ratio of diastereomers, IId-1/IId-2. [c] Several other minor components were detected.

stituted carbon atom of the cyclopropane to generate the most stable carbonium ion [5]. The intermediate VI * thus formed then will be attacked by water either at the internal carbon of the original double bond or the phenyl-substituted carbon to give the normal product or rearranged oxymercurated intermediate VII. This rearrangement is not important in the reactions of other vinylcyclopropanes such as Ia—Ic, because they lack the phenyl groups which apparently provide extra-stabilization in the rearrangement. Internal alkoxymercuration will then take place to afford the ether V.

Since Id was recovered from the reaction in considerable extent whereas the bis-oxymercuration proceeded effectively, the intermediate oxymercurial such as VII must suffer attack of mercuric acetate in preference to Id. It appears likely that this is primarily the result of the relative solubilities of Id and VII in the reaction medium **.

Contrary to these observations, Id produces cleanly the anti-Markovnikov hydrated alcohol in the hydroboration-oxidation reaction [7], which is consistent with the concerted nature of such reactions [1]. In its reaction with tetracyanoethylene, on the other hand, Id produces totally rearranged adducts [7]. The exclusive formation of the rearranged adducts in this reaction is explained by the assumptions that the reaction proceeds via a zwitterionic intermediate and that the two phenyl groups on the cyclopropane ring greatly increase the rate of the ring cleavage. Comparisons of the results of these three reactions of Id suggest that oxymercuration is a stepwise process but that the development of positive charge at the carbon atom next to the cyclopropane ring should be minimal. The observations that Wagner—Meerwein rearrangements seldom take place in the oxymercuration reaction [2a,c] also may suggest this. Thus the

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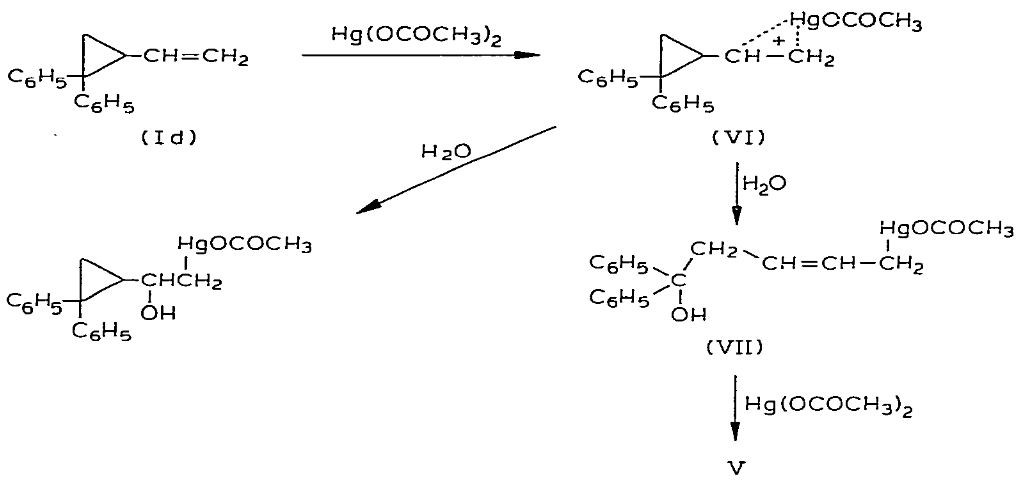
* In Scheme 1, the intermediate is depicted as a mercurinium ion for convenience; see references 2f and 2 j for the discussion of such intermediate.

** There may be an alternate explanation, which assumes allylic rearrangement for VII to produce the terminal olefin substituted by mercury at the carbon next to the double bond. The rearrangement provides an equally reactive site for the oxymercurated intermediate (an internal olefin, such as VII, is less reactive than the terminal olefin [2g]). The carbon—mercury bond is known to stabilize the adjacent cation [8], and hence such olefin will be more reactive than simple alkenes. The formation of the five-membered ring ether is well known to occur in such species as those possessing 4-penten-1-ol structure [2e,k], but unknown for 3-buten-1-ol.



first-formed species in the reaction may be most economically described as a mercurinium ion.

Oxymercuration with mercuric nitrate was less promising. In the reaction of Id, more rearranged product was produced and the total yield of products was considerably lower.

Experimental

IR spectra were recorded on a Hitachi 215 grating infrared spectrophotometer and UV spectra on a Cary model 17 spectrometer. NMR spectra were recorded on a JEOL PS-100 high-resolution spectrometer using tetramethylsilane as an internal standard. Both preparative and analytical GLC were carried out on a Hitachi 063 gas chromatograph. All boiling and melting points are uncorrected.

General procedures for oxymercuration-demercuration

The oxymercuration-demercuration reactions were performed on a 10 mmol scale by following the standard method described by Brown [2a,d,e,g,h]. The conditions, T_1 (the time required for the disappearance of the yellow suspension), T_2 (the reaction time) and isolated yields of the resulting alcohols are summarized in Table 2.

1,1-Dicyclopropylethanol (IIa), b.p. 79—82°C/35 mmHg (lit. b.p. 56.6—58°C/

TABLE 2

OXYMERCURATION-DEMERCURATION OF VINYLCYCLOPROPANES AT ROOM TEMPERATURE

Vinylcyclopropane	THF/H_2O	T_1	T_2	Yield of alcohol (%) [a]
Ia	1/1	10 sec	10 min	83
Ib	2/1	3 min	60 min	88
Ic	1/1	1 sec	30 min	83

[a] Isolated yield.

10 mmHg [3c], 64°C/15 mmHg [9]), p-nitrobenzoate: m.p. 225—230°C, was identified by comparison with an authentic sample prepared from dicyclopropyl ketone and methylmagnesium bromide.

1-Cyclopropyl-1-phenylethanol (IIb), b.p. 99—103°C/3.5 mmHg (lit. 114.5—115.5°C/10 mmHg [3c]), was characterized by comparison with an authentic specimen prepared from cyclopropyl phenyl ketone and methylmagnesium bromide.

1-(1-Methylcyclopropyl)ethanol (IIc), b.p. 51—53°C/42 mmHg (lit. b.p. 133°C [10]), 3,5-dinitrobenzoate: m.p. 98—99°C (Anal. Found: C, 53.0; H, 4.7; N, 9.5. $C_{13}H_{14}N_2O_6$ calcd.: C, 53.1; H, 4.8; N, 9.5%.) was characterized by the following spectral data: IR (liquid film): 3400 (br), 3095, 1380 and 1020 cm^{-1}; NMR (CCl_4): δ 0.1—0.5 (m, 4), 1.01 (s, 3), 1.13 (d, 3, J 6.5 Hz), 2.46 ((br)s, 1, disappeared by the addition of D_2O) and 3.04 (q, 1, J 6.5 Hz).

Hydroboration-oxidation of some vinylcyclopropanes

1-Cyclopropylstyrene (Ib) and 1-methyl-1-vinylcyclopropane (Ic) were hydroborated and then oxidized according to standard procedures [1]. 2-Phenyl-2-cyclopropylethanol, b.p. 75—78°C/1 mmHg, IR (liquid film): 3400 (br), 3105, 3055, 3030, 1615, 1595, 1505, 1460, 1020 and 705 cm^{-1}; NMR (CCl_4): δ —0.1—0.7 (m, 4), 0.7—1.1 (m, 1), 1.86 (d of t, 1, J 9 and 6 Hz), 2.30((br)s, 1, disappeared by the addition of D_2O), 3.61 (d, 2, J 6 Hz) and 6.9—7.3 (m, 5), p-nitrobenzoate: m.p. 78.7—79.5°C (Anal. Found: C, 69.3; H, 5.4; N, 4.5. $C_{18}H_{17}O_4N$ calcd.: C, 69.4; H, 5.5; N, 4.5%) was isolated in 78% yield and 2-(1-methylcyclopropyl)ethanol, b.p. 79—80°C/46.5 mmHg, IR (liquid film): 3350 (br), 3095, 3015 and 1020 cm^{-1}; NMR (CCl_4): δ 0.1—0.4 (m, 4), 1.05 (s, 3), 1.46 (t, 2, J 7 Hz), 2.84 (s, 1, disappeared by the addition of D_2O) and 3.63 (t, 2, J 7 Hz), 3,5-dinitrobenzoate: m.p. 87—88°C (Anal. Found: C, 52.9; H, 4.6; N, 9.5. $C_{13}H_{14}N_2O_6$ calcd.: C, 53.1; H, 4.8; N, 9.5%) was obtained in 77% yield.

Oxymercuration-demercuration of 2,2-diphenyl-1-vinylcyclopropane (Id)

Treatment of 2,2-diphenyl-1-vinylcyclopropane (Id) with an equimolar amount of mercuric acetate in THF/water (1/1) resulted in recovery of the starting olefin in 35% yield even after 18 h (see Table 1). Accordingly, the reaction was performed with 1.1 g (5 mmol) of Id and 3.2 g (10 mmol) of mercuric acetate. The conversion now was nearly 90%. The product mixture obtained after demercuration was analyzed by GLC (PEG 20M, 5% on silane-treated Celite 545, at 200°C) *. A fraction boiling at 117—120°C/0.01 mmHg (1.9 g) was collected and the three components were collected separately by GLC. Each component was examined by IR and NMR. The first component possessing the shortest retention time was characterized as 2-methyl-5,5-diphenyltetrahydrofuran (III): m.p. 60.2—60.8°C (Anal. Found: C, 85.7; H, 7.6. $C_{17}H_{18}O$ calcd.: C, 85.7; H, 7.6%); IR: no OH band; NMR (CCl_4): δ 1.14 (d, 3, J 6 Hz), 1.54 (d of q, 1, J 12 and 7 Hz), 1.98 (d of q, 1, J 12 and 7 Hz), 2.3—2.8 (m, 2), 4.19 (sextet, 1, J ca. 6 Hz) and 6.9—7.5 (m, 10). The last two components were characterized as a pair of diastereomers, IId-1 (shorter reten-

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* Satisfactory results were obtained only with a column pretreated by hexamethyldisilazane.

tion time) and IId-2 (longer retention time) (Anal. (as a mixture) Found: C, 85.1; H, 7.5. $C_{17}H_{18}O$ calcd.: C, 85.7; H, 7.6%); IId-1; NMR (CCl_4): δ 1.0—1.5 (m, 3), 1.25 (d, 3, *J* 6 Hz), 1.5—1.9 (m, 1), 2.7—3.1 (m, 1) and 6.9—7.4 (m, 10); IId-2: NMR (CCl_4): δ 1.0—1.4 (m, 1), 1.23 (d, 3, *J* 6 Hz), 1.4—1.9 (m, 3), 2.95 (pentuplet with further small splittings, 1, *J* 6 Hz) and 6.9—7.4 (m, 10). Overlapping of the OH proton in both spectra with those of the cyclopropane ring protons was proved by the addition of D_2O. The deuterated products IId-1-d_1 and IId-2-d_1 exhibited a different pattern for the signals at 1.4—1.9 and 2.8—3.9. IId-1-d_1 gave a doublet of triplets at 2.9 whereas IId-2-d_1 gave a broad quartet there.

Since purification of IId-1 and IId-2 was troublesome due to the instability of the carbinols, the structures were confirmed further by their oxidation. Jones oxidation of the crude product gave (2,2-diphenylcyclopropyl) methyl ketone in ca. 45% yield; m.p. 58—59°C (Anal. Found: C, 86.2; H, 6.8. $C_{17}H_{16}O$ calcd.: C, 86.4; H, 6.8%); IR (Nujol): 1705 cm^{-1}; NMR (CCl_4): δ 1.44 (d of d, 1, *J* 8 and 4.5 Hz), 2.02 (s, 3), 2.11 (d of d, 1, *J* 6 and 4.5 Hz), 2.70 (d of d, 1, *J* 8 and 6 Hz) and 7.0—7.3 (m, 10). Lithium aluminum hydride reduction (ether) of the ketone regenerated IId-1 and IId-2 (9/1) in 95% yield.

The oxymercuration-demercuration reactions of Id were also performed at temperatures other than 25°C. IId-2 was the major isomer at or below 25°C, but IId-1 became major at 65°C. The results are summarized in Table 1.

NMR analyses of IV

The deuterated tetrahydrofuran derivative IV, obtained in the demercuration with sodium borodeuteride, exhibited a reasonable NMR spectrum. Intensities of the methyl protons and C-3 protons were 2 and 1, respectively, and the C-2 proton appeared as a quartet, which was a sextet in III.

Acknowledgement

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