

The Mechanism of 1,4 Alkyl Group Migration in Hypervalent Halonium Ylides: The Stereochemical Course

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Organohypervalent iodonium systems have been studied in far greater detail than their chloronium and bromonium counterparts.¹ An understanding of the reactivity of these systems is fundamental to the broader area of hypervalent organohalonium chemistry. Recently, reaction **1** to **3** was reported with intermediate **2** proposed as a precursor of **3** (Scheme 1).²

It was shown that the conversion of type **1** to **3** was a general reaction for the synthesis of 2-halo-3-alkoxyenones from benzyl chlorides and bromides and various 1,3-dicarbonyl phenyliodonium ylides. Acyl halides yielded the 2-halo-3-acyloxyenones.²

Structure **2** (Scheme 1) is provocative because it features a frontside intramolecular nucleophilic displacement at the benzylic carbon. Alternatively, taking the depicted flow of the electrons literally, it appears to be a process formally related to a 1,4 Stevens rearrangement.³ Process **1** to **2** to **3** is also related to the well-known thermally induced phenyl migration of 1,3-dicarbonylphenyliodonium ylides (**1** to **4**),⁴ with the difference that iodonium ylide **1** is a stable reactant whereas **2** is an unstable alkylchloronium ylide intermediate. Given the synthetic value of 2-halo-1,3-dicarbonyl systems,⁵ it appeared of interest to establish the mechanism of **1** to **3** especially with respect to stereochemical course of the reaction at the migrating group terminus, a point which obviously could not be determined for **1** to **4**.⁶

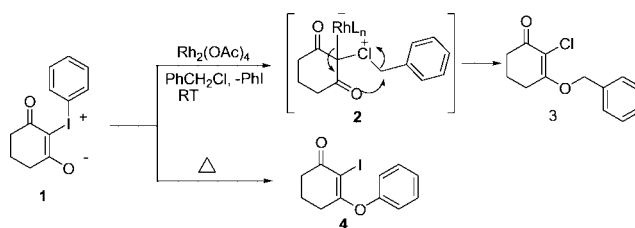
Examples in Table 1 confirm the benzyl migration (entries 1–6) and extend the prototypical reaction to novel allyl group migration (entries 7–9) as well as the novel arylation process⁷ (entries 10–13).

The first step in the elucidation of the mechanism of **1** to **3** was proof of intramolecularity. This was done using a classical crossover experiment. The reaction was intramolecular within the limits of HRMS detection.⁸ Next the stereochemical course with respect to displacement at the stereogenic benzylic center was determined using (*S*)- α -phenethyl chloride (entry 6).

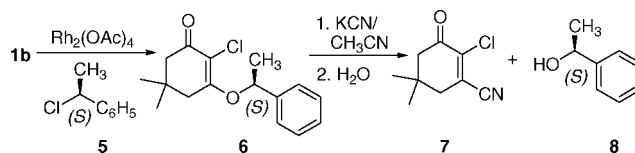
Under the standard reaction condition, it was found that **1** to **6** proceeded with 88.6% retention of configuration (Scheme 2).⁹

This result in itself does not define the mechanism, although a free planar carbocation or carbon radical can be excluded as a predominant intermediate in the rearrangement of **2** to **3**. Theoretical calculation provided further insight into the process on the basis of geometries optimized by Gaussian 98 at the B3LYP/6-31G level of theory, and we propose that the rearrangement of the benzyl chloronium ylide from **2** to **3** is a concerted process with an activation energy of 5.4 kcal/mol.¹⁰ Stationary points for the reactant **2**, the transition state, and product **3** are shown in the potential energy diagram (a) in Scheme 3. The process proceeds with a very low barrier and is highly exothermic, –37.50 kcal/mol. The activation energy calculated including the solvent benzyl chloride is 2.54 kcal/mol, indicating an essentially barrierless

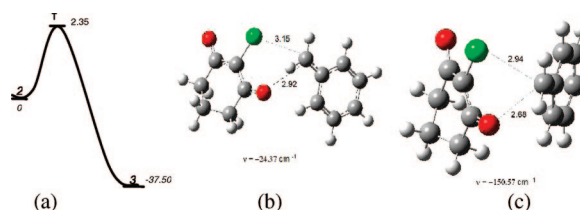
Scheme 1



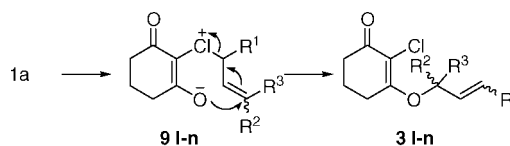
Scheme 2



Scheme 3. (a) The Relative Free Energy Profile Related to the Initial State **2** (kcal/mol); (b) Condensed Phase TS, and (c) Gas Phase TS



Scheme 4



I: R¹ = H, R² = R³ = CH₃, m: R¹ = CH₃, R² = R³ = H, n: R¹ = R² = H, R³ = CH₃

pathway, a consequence of dielectric solvent stabilization of the transition state. The two putative transition states in solvent (b) and in vacuum (c) are shown in Scheme 3. Analytical frequencies and structural parameters are given in the Supporting Information.

The activation energy for the concerted rearrangement of **1** to **4** is 17.7^{11a} or 22.6 kcal/mol,^{11b} a value much higher than that calculated for **2** to **3**, which may reflect the loss of aromaticity in the transition state separating **1** and **4** relative to the saturated alkyl group transfer **1** to **3**.

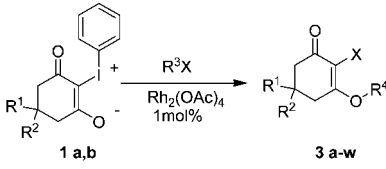
The analysis of stereochemical course of the rearrangement **1** to **3** and the computational study suggest that the intermediacy of **2** proposed by Lee and Jung² is indeed correct and, interestingly, was made absent any relevant experimental data. Having established the

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Table 1. Reactions of 1,3-Dicarbonyl Phenyl Iodonium Ylides **1a** and **1b** with Benzyl, Allyl, and Aryl Halides Using $\text{Rh}_2(\text{OAc})_4$ Catalysis^a

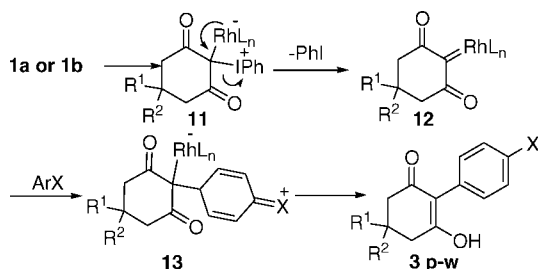


$\text{R}^1 = \text{R}^2 = \text{H} = \mathbf{1a}$, $\text{R}^1 = \text{R}^2 = \text{CH}_3 = \mathbf{1b}$, $\text{X} = \text{Cl}, \text{Br}$

entry	ylide	$\text{R}^3\text{-X}$	R^4	X	yield ^b (%)	
					3	3
1	1a 1b	$\text{C}_6\text{H}_5\text{CH}_2\text{Cl}$	$\text{C}_6\text{H}_5\text{CH}_2$	Cl	70(a)	73(b)
2	1a 1b	$3\text{-MeC}_6\text{H}_4\text{Cl}$	$3\text{-MeC}_6\text{H}_4$	Cl	62(c)	70(d)
3	1a 1b	$\text{C}_6\text{H}_5\text{CH}_2\text{Br}$	$\text{C}_6\text{H}_5\text{CH}_2$	Br	22(e)	35(f)
4	1a 1b	$3\text{-MeC}_6\text{H}_4\text{Br}$	$3\text{-MeC}_6\text{H}_4$	Br	30(g)	35(h)
5	1a 1b	$\text{C}_6\text{H}_5(\text{CH}_3)\text{CHCl}$	$\text{C}_6\text{H}_5(\text{CH}_3)\text{CH}$	Cl	53(i)	58(j)
6	1b	$(S)\text{-Ph}(\text{CH}_3)\text{CHCl}$	$(S)\text{-Ph}(\text{CH}_3)\text{CH}$	Cl		58(k)
7	1a	$\text{CH}_3\text{C}(\text{CH}_3)\text{CHCH}_2\text{Cl}$	$\text{CH}_3\text{CH}(\text{CH}_3)\text{C}$	Cl	56(l)	
8	1a	$\text{CH}_2\text{CHCH}(\text{Cl})\text{CH}_3$	$\text{CH}_3\text{CHCHCH}_2$	Cl	37(m)	
9	1a 1b	$\text{CH}_3\text{CHCHCH}_2\text{Cl}$	$\text{CH}_2\text{CH}(\text{CH}_3)\text{CH}$	Cl	60(n)	63(o)
10	1a 1b	$\text{C}_6\text{H}_5\text{F}$	H	$4\text{-FC}_6\text{H}_4$	22(p)	30(q)
11	1a 1b	$\text{C}_6\text{H}_5\text{Cl}$	H	$4\text{-ClC}_6\text{H}_4$	41(r)	38(s)
12	1a 1b	$\text{C}_6\text{H}_5\text{Br}$	H	$4\text{-BrC}_6\text{H}_4$	27(t)	37(u)
13	1a 1b	$\text{C}_6\text{H}_5\text{I}$	H	$4\text{-IC}_6\text{H}_4$	30(v)	38(w)

^a Conditions: Phenyliodonium ylide **1a** or **1b** (1 equiv)/alkyl, allyl, or aryl halide (10 equiv), $\text{Rh}_2(\text{OAc})_4$ (0.01 equiv)/Ar. ^b Isolated yields.

Scheme 5



sigmatropic nature of **1** to **3**, it was anticipated that allyl halides would behave similarly. Accordingly, we discovered the novel chloronio-Claisen rearrangement of the chloronium ylide (entries 7–9).¹²

The Claisen-type process can be described as shown in Scheme 4, which accounts for the observed regiochemistry.

Finally, we investigated the reaction of aryl halides with **1a** and **1b** under standard rhodium(II) conditions with the expectation of obtaining the corresponding aryl halonium ylides via a process analogous to **1** to **2**.^{13a,b}

In fact, only electrophilic aromatic substitution was observed, possibly via the intermediacy of **13** formed by electrophilic addition of the $\text{Rh}(\text{II})$ carbenoid to the electron-rich substituted aromatic ring (Scheme 5).¹⁴

In summary, this work advances our understanding of the unstable and elusive chloronium and bromonium ylides and suggests the application of this chemistry to obtain valuable synthetic building blocks.

Acknowledgment. We dedicate this work to Professor E. J. Corey on the occasion of his 80th birthday. Also we thank Professor Daesung Lee of this department for insightful discussions.

Supporting Information Available:

Additional experimental details. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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- (9) (*R*)- α -Phenethanol [α]_D = 44.0 (neat) was obtained from Alfa-Aesar and was converted to (*S*)- α -phenethyl chloride (**5**) [α]_D = 84.5 (*c* = 5.4 CHCl_3) using POCl_3/Pyr . Burwell, R. I.; Shields, A. D.; Hart, H. H. *J. Am. Chem. Soc.* **1954**, *76*, 908. The starting optical purity determined by chiral gas chromatography was 87% *S*, 13% *R*. The yield of **6** was 78.6% *S*, 21.4% *R* determined by chiral HPLC. Hydrolysis of **6** was nontrivial. Several standard acid-catalyzed ether cleavage reactions proceeded with benzylic oxygen cleavage. Method **6** to **7** to **8** (Scheme 2) is uniquely suited for the present case and to the best of our knowledge is a novel process.
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