

Rh^{II}-Catalyzed Thermal Cyclopropanations of a Phenyliodonium Bis(carbomethoxy)methylide with Alkenes and Dienes

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Received 23 July 2001

Abstract: Iodonium ylide **2**, derived from dimethyl malonate, undergoes facile thermal cycloaddition with alkenes and dienes catalyzed with Rh₂(OAc)₄ to form the corresponding cyclopropanedicarboxylates and vinylcyclopropanedicarboxylates, respectively, in excellent yields.

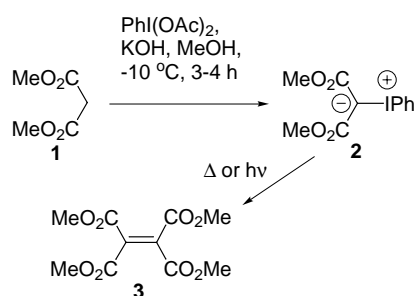
Key words: hypervalent iodine, ylide, Rh-catalysis, alkene, 1,3-diene, cyclopropane

Iodonium ylides,³ a class of hypervalent iodine-compounds,⁴ have been used quite often as rather reactive alternatives to diazo compounds without major drawbacks such as explosive and health hazards. Quite generally speaking, an iodonium ylide can be easily prepared⁵ from the corresponding active methylene compound and a hypervalent iodine precursor, i.e. PhI(OAc)₂. Its reactivity pattern³ consists of its decomposition in various solvents, C-H insertion reactions, oxidation reactions, and/or cycloaddition reactions leading to a variety of products, usually new heterocyclic compounds. A major question arising from the literature⁶ is whether or not a carbene (or a carbenoid) is involved in this rich reactivity pattern. A singlet or triplet carbene (or a carbenoid) could easily explain the observed results but this could not be always the case.

We were more fascinated with the synthetic applications than the mechanistic aspects of the reactivity of iodonium ylides. Within our studies, we had seen rich reactivity of a β-dicarbonyl^{7a,b} iodonium ylide with various substrates, improvement⁷ of the reaction yield by shifting from the cheap Cu-catalyst into the expensive Rh-catalyst, while we were observing the loss of stereochemistry.^{7c,d} This fact had been explained as the result of a two step polar reaction although there is no strong evidence that an initially-formed cyclopropane rearranged into dihydrofuran. On the other hand, recently it was reported⁸ that a phenyliodonium ylide is a precursor for dicarboethoxycarbene. So, with the aim to develop and define the scope and limitation of this synthetic methodology, we extended our study to the reactivity of phenyliodonium bis(carbomethoxy)methylide towards alkenes and dienes.

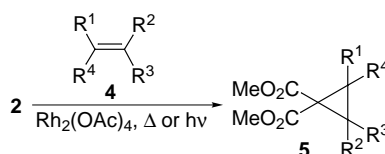
The reaction of methyl malonate (**1**) with diacetoxyiodobenzene in basic methanol at -10 °C leads to the

isolation^{6b} of iodonium ylide **2** in moderate yields (Scheme 1). Heating or irradiating a suspension of iodonium ylide **2** in an appropriate solvent yields tetracarboxymethoxyethylene (**3**) quantitatively. This alkene is a side product of all attempted cycloadditions of iodonium ylide **2**, possibly produced by attack of a „carbene intermediate“ on **2**.




Scheme 1

Nevertheless, this formal carbene dimer was produced in minor amounts, when an excess of an alkene is present. The reaction⁹ with styrene **4a** and indene **4h** were used as a probe to examine the overall yield of the desired reaction. Heating a mixture of **2** and styrene **4a** in the presence of catalytic amounts of Rh₂(OAc)₄ or Cu(acac)₂ led to the isolation of cyclopropanedicarboxylate **5a** (Scheme 2) in 80% and 57% yield, respectively. On the other hand, irradiating a suspension of **2** and **4a** in CH₃CN led to the isolation of **5a** in 51% yield. Although the photochemical reaction yields cyclopropane **5a** in moderate yield, the Rh-catalyzed process is superior. Similarly, heating a mixture of **2** and indene **4h**, with no catalyst or with catalytic amounts of Rh₂(OAc)₄ or Cu(acac)₂ led to the isolation of the corresponding cyclopropanedicarboxylate **5h** in 58%, 88%, and 80% yield, respectively. Albeit, the non-catalyzed reaction yields cyclopropane **5h** in moderate yields, again the thermal-catalyzed (Rh^{II} or Cu^{II}) conditions are superior. Other catalysts, such as RhCl₃, PdCl₂, etc., failed to accelerate this cycloaddition.



Scheme 2

Table 1 Reaction^a of Iodonium Ylide **2** with Alkenes **4**

Entry	Alkene	Substituents				Reaction conditions			Product	Yield (%) ^b
		R ¹	R ²	R ³	R ⁴	Catalyst	Temp (°C)	Time (min)		
1	4a	Ph	H	H	H	Rh ₂ (OAc) ₄	120	1	5a	80
						Cu(acac) ₂	80	10		57
						hν ^c , CH ₃ CN		100		51
2	4b	PhCH ₂	H	H	H	Rh ₂ (OAc) ₄	120	1	5b	99
3	4c	Ph	H	H	Me	Rh ₂ (OAc) ₄	120	5	5c	81
4	4d	Ph	H	H	Ph	Rh ₂ (OAc) ₄	120	1	5d	67
5	4e	Me	<i>i</i> -Pr	H	H	Rh ₂ (OAc) ₄	reflux	30	5e	81
6	4f	Me	H	<i>i</i> -Pr	H	Rh ₂ (OAc) ₄	reflux	20	5f	12
7	4g	(CH ₂) ₃		H	H	Rh ₂ (OAc) ₄	reflux	20	5g	91
8	4h		H	H	H	Rh ₂ (OAc) ₄	120	20	5h	88
						Cu(acac) ₂	100	30		80
							100	40		58
9	4i	(CH ₂) ₄		H	H	Rh ₂ (OAc) ₄	reflux	3	5i	63

^a All reactions were performed by heating a mixture of iodonium ylide (**1.50** mmol), alkene (excess) and catalytic amount of Rh₂(OAc)₄ at the given temperature (°C) for the required time (min).

^b Isolated yield after column chromatography.

^c Hg street lamp 400W, medium pressure.

The reaction was extended to a variety of alkenes **4b–g,4i**, which underwent facile cycloadditions, affording the corresponding cyclopropanedicarboxylates **5** in excellent yields (Table 1). It is noteworthy that the reaction proceeds without the use of an inert atmosphere. Acyclic **4a–f**, with various degrees of substitution, as well as cyclic alkenes **4g–i** were found to undergo cycloaddition. The reactions with 2-methyl-3-pentene (entries 5, 6 Table 1) were used to examine the spin state of a possible intermediate carbene (or carbenoid); *cis*-alkene **4e** led to the formation of *cis*-cyclopropane **5e** in 81% yield, while *trans*-alkene **4f** led to a complex reaction mixture, from which *trans*-cyclopropane **5f** was isolated in only 12% yield. The very high degree of stereospecificity indicates cyclopropanation⁸ of the double bond by a singlet carbene, but the data presented in Table 1 indicate also that the addition of iodonium ylide **2** into alkenes is rather more sensitive to steric effects than electronic, a similar observation to that of dimethyl diazomalonate.¹⁰ The addition seems to be electrophilic in nature, but steric factors are dominant.

Having this in mind, we turned our attention into cycloadditions with dienes **6** (Scheme 3). Reaction with a diene

could lead eventually to cyclopentenenes, or with minor alterations to cycloheptadienes.¹¹ Indeed, heating a suspension of iodonium ylide **2** with the appropriate diene **6** in the presence of catalytic amounts of Rh₂(OAc)₄ led to the isolation of vinylcyclopropanes **7** in excellent yields. Acyclic **6a,b**, as well as cyclic dienes **6c–j** were found to undergo cycloadditions (Table 2) while non-conjugated dienes **6e–h** or conjugated dienes **6a–c,i,j** led to the corresponding cyclopropanes **7**. Again, the data presented in Table 2 indicate that the addition of iodonium ylide **2** to dienes is rather more sensitive to steric effects than electronic (cf. entries 4, 7, 8 of Table 2).

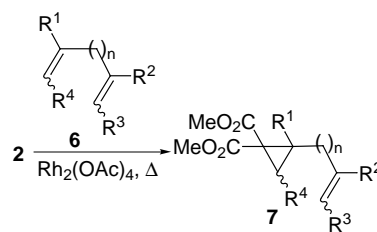

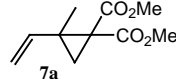

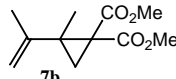

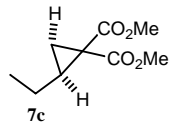
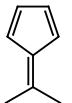
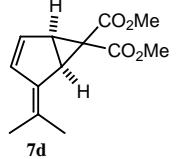

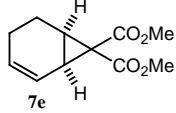

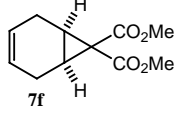
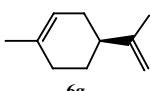
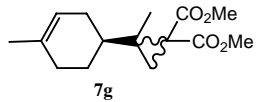
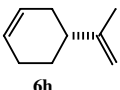
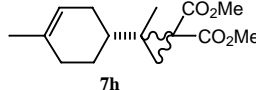

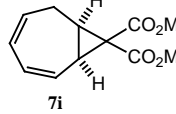
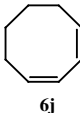
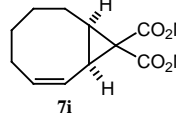
**Scheme 3**

Table 2 Reaction^a of Iodonium Ylide **2** with Dienes **6**

Entry	Diene	Reaction conditions		Product	Yield (%) ^b
		Temp (°C)	Time (min)		
1		reflux	30		95
2		reflux	5		88
3		120	1		ca 100
4		80–85	5		71
5		120	1		ca 100
6		120	1		44
7		95–97	5		61 (dr 52:48)
8		125	2		55 (dr 50:50)
9		reflux	5		81
10		120	2		58

^a A suspension of iodonium ylide (1.5 mmol), diene (excess), and catalytic amount of Rh₂(OAc)₄ was heated at the above mentioned temperature for the given time.

^b Isolated yield after column chromatography.

In summary, Rh₂(OAc)₄ is an effective catalyst for the syntheses of cyclopropane derivatives of predictable stereochemistry, from the reaction of iodonium ylide of dimethyl malonate with alkenes and dienes. The examples

that are reported here demonstrate the synthetic potential of the iodonium ylide strategy for the construction of cyclopropanes. We are currently examining the optimization and applications of this useful synthetic sequence.

References and Notes

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- (9) **Representative Experimental Procedure. Synthesis of 5a:** A mixture of iodonium ylide **2** (0.5 g, 1.50 mmol), styrene **4a** (1.0 g, 9.62 mmol) and catalytic amounts (0.1 mol%) of $\text{Rh}_2(\text{OAc})_4$ was heated at 120 °C for 1 min. The reaction mixture was subjected to column chromatography (silica gel, CH_2Cl_2) to afford **5a**^{6b} (0.28 g, 80%) as colorless oil. IR (neat): $\nu = 3010, 2940, 1720, 1430, 1328, 1270, 1210, 1190, 1175, 1125 \text{ cm}^{-1}$; ^1H NMR (250 MHz, CDCl_3): $\delta = 1.68\text{--}1.75$ (m, 1 H), 2.15–2.20 (m, 1 H), 3.18–3.23 (m, 1 H), 3.34 (s, 3 H), 3.77 (s, 3 H), 7.16–7.25 (m, 5 H); ^{13}C NMR (63 MHz, CDCl_3): $\delta = 19.0, 32.4, 37.2, 52.0, 52.7, 127.3, 127.5, 128.4, 134.6, 166.9, 170.1$. **Synthesis of 7a:** A mixture of iodonium ylide **2** (0.5 g, 1.50 mmol), 6,6-dimethylfulvene **6d** (1.0 g, 9.43 mmol) and catalytic amounts (0.1 mol%) of $\text{Rh}_2(\text{OAc})_4$ was heated at 80–85 °C for 5 min. The reaction mixture was subjected to column chromatography (silica gel, CH_2Cl_2) to afford **7d** (0.25 g, 71%) as yellow oil. ^1H NMR (250 MHz, CDCl_3): $\delta = 1.80$ (s, 3 H), 1.89 (s, 3 H), 2.94 (dd, $J = 2.2, 6.1$ Hz, 1 H), 3.02 (d, $J = 6.1$ Hz, 1 H), 3.56 (s, 3 H), 3.70 (s, 3 H), 5.90–5.94 (m, 1 H), 6.13 (d, $J = 5.4$ Hz, 1 H); ^{13}C NMR (63 MHz, CDCl_3): $\delta = 21.2, 22.0, 34.4, 38.6, 43.3, 52.0, 52.6, 130.2, 130.5, 132.7, 135.9, 166.0$.
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