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Rh^{II}-catalyzed cycloadditions of carbomethoxy iodonium ylides[†]

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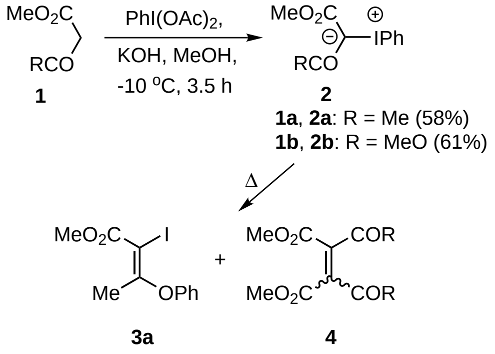
Abstract—Carbomethoxy iodonium ylides, generated from methyl acetoacetate and methyl malonate, respectively, are exploited in synthesis of cyclopropanes, cyclopropenes as well as various heterocycles. © 2002 Elsevier Science Ltd. All rights reserved.

Despite the fact that a significant number of iodonium ylides,[1] a class of hypervalent iodine compounds, are known in the literature, their chemistry still remains unexplored, especially when compared to the corresponding diazo compounds.[2] Generally speaking, the easily isolable[3] phenyliodonium ylides, formed quantitatively from the reaction of an active methylene compound and a hypervalent iodine precursor, have often been used as alternatives to diazo precursors in metal-catalyzed or photochemical cycloadditions and CH insertion reactions.[4] These reactions occur sometimes in the absence of catalysts, albeit in much lower yields. Quite generally speaking, phenyliodonium ylides usually decompose at lower temperatures than the corresponding diazo compounds, thus leading to better yields of the desired products.

The major drawback of iodonium ylide chemistry, is the requirement for two similar strong electron-withdrawing substituents at the carbanionic center. Generally, such ylides are isolable in pure form, while ylides with different carbanionic substituents are rather labile entities with unknown behavior.

Ylides **2**, bearing at least one carbomethoxy substituent were easily prepared from methyl acetoacetate **1a** and methyl malonate **1b**, respectively, in moderate yields (Scheme 1), employing the well-known procedure.[3,4b] There are two I–C bonds which could, in principle, be cleaved. Cleavage of the I–C$_{\text{aromatic}}$ bond could yield an iodo ether **3**, resembling the decomposition product of a β-dicarbonyl iodonium ylide, while the cleavage of the I–C$_{\text{carbanionic}}$ bond could yield initially a carbene (or carbenoid) leading finally to alkene **4**, a product resembling the decomposition of a bis(carbo-methoxy) iodonium ylide. Upon heating ylide **2a** in various solvents, iodo ether **3a** and alkene **4a** (*cis*/*trans* mixture) were isolated in varying amounts (Scheme 1). The formation of iodo ether **3a** was suppressed when a catalyst, e.g. $Rh_2(OAc)_4$, $Cu(acac)_2$, or photochemical conditions were used and alkene **4a** was isolated instead. The structure of iodo ether **3a** was elucidated from the fact that the methyl group of the carbomethoxy substituent appears at δ 3.79, indicating that it is *anti* to the phenoxy group. In contrast, alkene **4b** was the only isolable product when ylide **2b** was heated or irradiated under various conditions.

As was anticipated, ylide **2a** reacts[5] easily with styrene **5a** leading to the corresponding cyclopropane **6a**[6] in moderate yields (Scheme 2). Although the reaction works thermally without any catalyst, it was found that $Rh_2(OAc)_4$ gives rise to the best yield (85% yield, *cis*/*trans* 8.1:1.9).



Scheme 1.

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[†] Dedicated to Professor Dr. Waldemar Adam, University of Würzburg, on the occasion of his 65th birthday.

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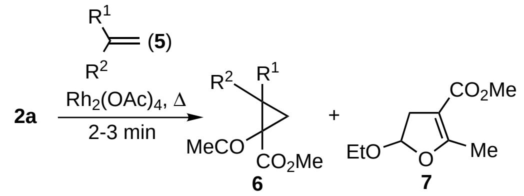
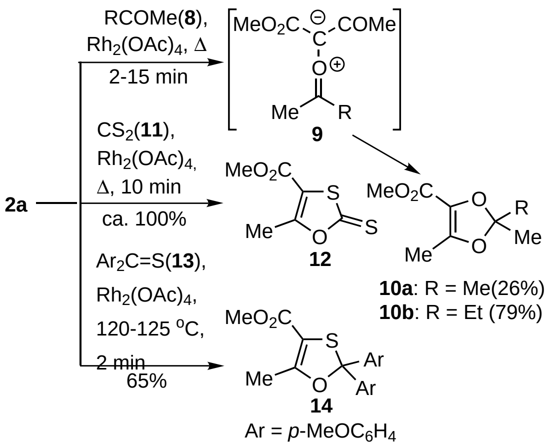


Scheme 2.

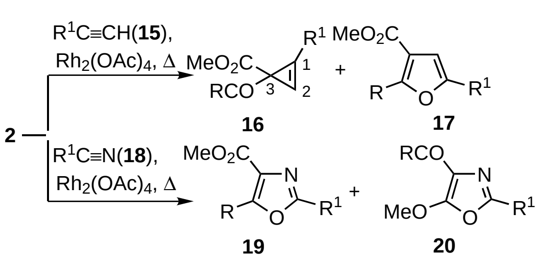
There is a pronounced preference for the formation of the cyclopropane bearing the phenyl and carbomethoxy substituents *cis* to one another. When the same reaction was repeated photochemically (400 W Hg lamp, medium pressure), the yields were somewhat lower (CH_3CN as solvent; 63% yield; *cis*/*trans* 5.5:4.5) while in the presence of benzophenone the yield was worse (51% yield; *cis*/*trans* 4.3:5.7). The reaction was extended to other mono- and disubstituted alkenes (Table 1) yielding the corresponding cyclopropanes **6** in moderate yields. Surprisingly, when ethyl vinyl ether **5e** was employed, dihydrofuran **7e** was isolated instead, quantitatively. Similar dihydrofurans were detected (<1%) in the reaction with styrenes **5a**,**b**, the most were probably formed during the column chromatography. There is extended literature concerning the question of the dihydrofuran formation, if it arises directly via 1,3-cycloaddition or via initially formed cyclopropyl ketones with or without partial loss of the stereochemical identity of the starting cyclopropane.[7]

Upon reaction of **2a** with methyl ketones **8**, dioxolanes **10** were isolated in good yields (Scheme 3). The formation of **10** implies the initial generation[8] of carbonyl ylides **9**, which further rearranged, intramolecularly, into dioxolanes **10**. Attempts to intermolecularly trap these carbonyl ylides with DMAP failed. Similarly, the reaction with carbon disulfide yields oxathiole **12** quantitatively, while reaction with *p*,*p*′-dimethoxythiobenzophenone results in the isolation of oxathiole **14** in 65% yield (Scheme 3).

Similar cycloadditions were observed upon reaction with terminal acetylenes. It is known, that copper(II) sulfate-catalyzed decomposition[9] of diethyl diazomalonate in the presence of phenylacetylene results in the formation of a mixture of a cyclopropene and a furan, while sensitized photolysis generates[10] furans as the primary products. The rhodium(II) acetate catalyzed decomposition[11] of diazo diketones in the presence of terminal alkynes, results in cyclopropenes or furans, the isolation of which depends on the nature of the electron withdrawing group of the carbenoid. However, the rhodium(II)-catalyzed reaction of iodonium ylides of β-diketones with terminal alkynes yields[12] furans in moderate yields, while photochemically,[13] a similar carboethoxy-iodonium ylide gives ethynylated compounds in 14% yield (ca. 1:1 mixture with the enolic form) upon reaction with phenylacetylene. Quite surprisingly, the thermal rhodium(II)-catalyzed decomposition of ylides



Scheme 3.



Scheme 4.

Table 1. Reactions of iodonium ylide **2a** with alkenes **5**

Alkene	Substituents		Conditions	Product	Yield (%)[a]
	R^1	R^2			
5a	C_6H_5	H	A	**6a**	58
			B		63
			C		51
5b	*p*-$MeOC_6H_4$	H	A	**6b**	65
5c	C_6H_5	Me	A	**6c**	31
5d	C_6H_5	C_6H_5	A	**6d**	33
5e	EtO	H	A	**7e**	ca. 100

[a] Yield of isolated product after column chromatography. **Method A**: ylide (0.5g; 1.57 mmol), alkene (1.0 g; 5.55–9.61 mmol), $Rh_2(OAc)_4$ (0.02 mol%), 95–100°C, 2–3 min. **Method B**: ylide (1.0 g; 3.14 mmol), alkene (1.0 g; 9.61 mmol), CH_3CN (10 mL), *hν* (400 W Hg street lamp), 35 min. **Method C**: ylide (1.0 g; 3.14 mmol), alkene (1.0 g; 9.61 mmol), Ph_2CO (0.57 g; 3.14 mmol), CH_3CN (10 mL), *hν* (400 W Hg street lamp), 45 min.

Table 2. Reactions of ylides **2** with alkynes **15** and nitriles **18**

Ylide	Alkyne/nitrile	Substituent		Reaction temp. (°C)	Conditions time (min)	Product [yield (%)][a]
		R^1	R^2			
2a	**15a**	Me	*n*Pr	Reflux	2	**16a** (66)
2b	**15a**	MeO	*n*Pr	Reflux	2	**16b** (36)
2a	**15b**	Me	Ph	100	1	**16c** (77)
2b	**15b**	MeO	Ph	110	2	**16d** (63), **17d** (29)
2a	**18a**	Me	Me	Reflux	5	**19a** (82)
2b	**18a**	Me	Me	Reflux	2	**19b** (65)
2a	**18b**	Me	$ClCH_2$	125	1	**19c** (39), **20c** (20)
2b	**18b**	MeO	$ClCH_2$	105	2	**19d** (61)
2a	**18c**	Me	$PhCH_2$	115	2	**19e** (61)
2a	**18d**	Me	Ph	120	1	**19f** (86)
2b	**18d**	MeO	Ph	120	2	**19g** (85)

[a] Yield of isolated product after column chromatography.

2 in the presence of terminal alkynes **15** leads to the isolation of cyclopropene **16** with good yields (Scheme 4). Only when ylide **2b** and phenylacetylene **15b** were employed was furan **17d** isolated as the by-product in 29% yield (Table 2) along with cyclopropene **16d** (63% yield). The structure of the cyclopropene was elucidated from the spectral data. For example, for **16c**, the absence of ^{13}C signals for enolic carbons at 160–170 ppm as well as signals at 205.6, and 171.5 for the ketone and ester groups, respectively, excluded furan structure **17**. The ^{13}C signals at 112.9, 96.2, and 40.3 ppm for the C-1, C-2, and C-3 cyclopropene carbon atoms, respectively, establish cyclo-propene structure **16**.

The rhodium(II)-catalyzed decomposition of ylides **2** in the presence of nitriles **18**, results in oxazoles **19**, **20** (Scheme 4) in good to excellent yields (Table 2). Although in general for ylide **2a**, the keto group participates in the formation of the oxazole ring, however there is an exception with chloroacetonitrile, where a separable mixture of oxazoles **19** and **20** in 39 and 20% yields, respectively, were isolated. On the other hand, ylide **2b** results in the isolation of oxazole **19** in good to excellent yields, similar to dimethyl diazomalonate.[14]

In summary, $Rh_2(OAc)_4$ is an effective catalyst for the syntheses of valuable cyclopropanes, cyclopropenes and heterocycles from the reaction of carbomethoxy-substituted iodonium ylides with alkenes, alkynes, methylketones, etc. The examples that are reported here, albeit with moderate to good yields, demonstrate the synthetic potential of the iodonium ylide strategy. We are currently examining the optimization and applications of this useful synthetic sequence.

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6. **Representative experimental procedure**. *Method A*: A suspension of the ylide (0.5 g; 1.57 mmol), styrene (1.0 g; 9.62 mmol), $Rh_2(OAc)_4$ (0.02 mol%) was heated at 95–100°C for 2 min. Purification by flash column chromatography on silica gel (eluent:methylene chloride) gave cyclopropane **6a** (290 mg; 85% yield; *cis*/*trans* 8.1:1.9). *Method B*: A suspension of ylide (1.0 g; 3.14 mmol),

styrene (1.0 g; 9.62 mmol) in CH$_3$CN (10 mL) was irradiated (400 W Hg lamp medium pressure) for 35 min. The solvent was evaporated under reduced pressure, purification by flash column chromatography on silica gel (eluent: methylene chloride) gave cyclopropane **6a** (431 mg; 63% yield; *cis*/*trans* 5.5:4.5). *Method C*: A suspension of ylide (1.0 g; 3.14 mmol), styrene (1.0 g; 9.62 mmol), benzophenone (0.57 g; 3.14 mmol) in CH$_3$CN (10 mL) was irradiated (400 W Hg lamp medium pressure) for 35 min. The solvent was evaporated under reduced pressure, purification by flash column chromatography on silica gel (eluent: methylene chloride) gave cyclopropane **6a** (350 mg; 51% yield; *cis*/*trans* 4.3:5.7). All products have been satisfactorily characterized by ^{1}H NMR, ^{13}C NMR and IR spectroscopy. Experimental data for **2**: colorless crystals; mp 112–114°C; IR (KBr) 3200, 1640, 1580, 1540, 1480, 1450, 1380, 1350, 1280, 1250, 1195, 1090, 1015, 900, 750, 700 cm^{-1}; ^{1}H NMR (250 MHz, DMSO-d_6) δ 2.39 (3H, s), 3.52 (3H, s), 7.38–7.50 (3H, m), 7.69–7.73 (2H, m); ^{13}C NMR (63.5 MHz, DMSO-d_6) δ 24.4, 49.6, 68.1, 113.1, 128.7, 129.5, 130.2, 164.2, 183.9. **3a**: white solid; mp 69–70°C; ^{1}H NMR (250 MHz, CDCl$_3$) 2.29 (3H, s), 3.79 (3H, s), 6.98 (2H, d, *J* 2.9 Hz), 7.14–7.20 (1H, m), 7.32–7.38 (2H, m); ^{13}C NMR (63.5 MHz, CDCl$_3$) 18.2, 52.9, 71.21 119.7, 124.8, 129.8,153.6, 165.3, 166.9. *cis*-**6a**: colorless oil; ^{1}H NMR (250 MHz, CDCl$_3$) δ 1.72 (1H, dd, *J* 4.6, 9.2 Hz), 2.22 (1H, dd, *J* 4.6, 8.1 Hz), 2.43 (3H, s), 3.28 (1H, t, *J* 8.6 Hz), 3.32 (3H, s), 7.09–7.29 (5H, m); ^{13}C NMR (63.5 MHz, CDCl$_3$) δ 21.3, 29.3, 35.4, 44.5, 51.7, 127.3, 128.0, 128.6, 134.8, 168.5, 202.0. *trans*-**6a**: colorless oil; ^{1}H NMR (250 MHz, CDCl$_3$) δ 1.67–1.73 (1H, m), 1.94 (3H, s), 2.28-2.33 (1H, m), 3.23–3.32 (1H, m), 3.80 (3H, s), 7.10–7.27 (5H, m); ^{13}C NMR (63.5 MHz, CDCl$_3$) δ 19.1, 27.3, 34.5, 44.1, 52.5, 127.3, 128.1, 128.6, 133.7, 170.9, 199.8. **10a**: colorless oil; ^{1}H NMR (250 MHz, CDCl$_3$) δ 1.56 (s, 6H), 2.15 (s, 3H), 3.78 (s, 3H); ^{13}C NMR (63.5 MHz, CDCl$_3$) δ 25.2, 25.5, 51.4, 53.5, 114.9, 161.5. **12**: colorless oil; ^{1}H NMR δ (250 MHz, CDCl$_3$) 2.50 (s, 3H), 3.75 (s, 3H); ^{13}C NMR (63.5 MHz, CDCl$_3$) δ 14.0, 52.5, 11.8, 159.0, 161.7, 200.2. **16c**: colorless oil; ^{1}H NMR (250 MHz, CDCl$_3$) δ 2.11 (s, 3H), 3.58 (s, 3H), 6.87 (s, 1H), 7.28–7.36 (m, 3H), 7.46–7.50 (m, 2H); ^{13}C NMR (63.5 MHz, CDCl$_3$) δ 27.7, 40.3, 51.9, 96.2, 112.9, 122.7, 128.1, 128.8, 130.0, 130.5, 171.5, 205.6; **17d**: colorless oil; ^{1}H NMR (250 MHz, CDCl$_3$) δ 3.82 (s, 3H), 4.19 (s, 3H), 6.85 (s, 1H), 7.23–7.27 (m, 1H), 7.33–7.40 (m, 2H), 7.52–7.55 (m, 2H); ^{13}C NMR (63.5 MHz, CDCl$_3$) δ 51.3, 58.1, 93.2, 106.3, 122.8, 127.2, 128.7, 129.7, 143.5, 161.6, 163.3. **20c**: colorless oil; ^{1}H NMR (250 MHz, CDCl$_3$) δ 2.40 (s, 3H), 4.20 (s, 3H), 4.49 (s, 2H); ^{13}C NMR (63.5 MHz, CDCl$_3$) δ 27.4, 35.8, 59.7, 147.3, 190.8.

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