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CHEMISTRY

# Reaction of Methyl Diazoacetate with Unsaturated Heterocyclic Derivatives of Carbonyl Compounds Catalyzed by $Rh_2(OAc)_4$

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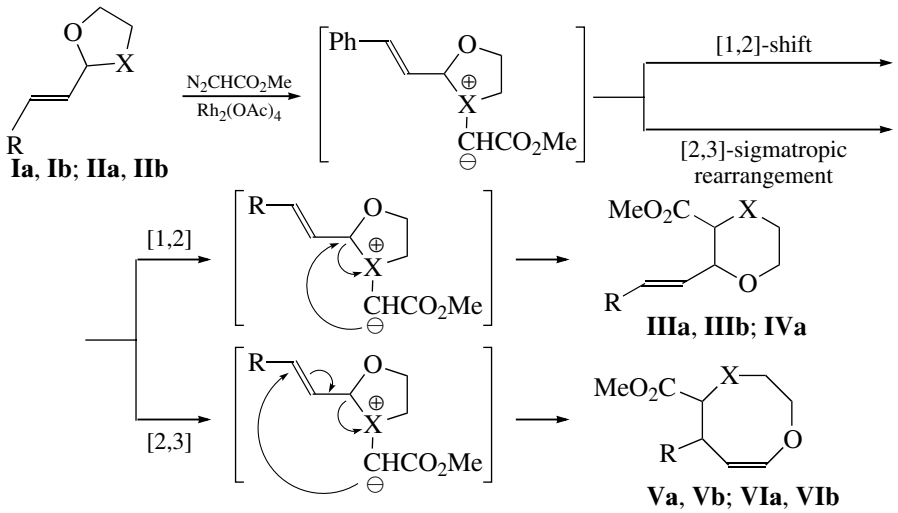
Heterocyclic compounds containing morpholine and oxathiane fragments show a wide spectrum of physiological activity [1–3]. Among different methods for the synthesis of these compounds, the intramolecular rearrangement of oxonium, ammonium, and sulfonium ylides resulting from the catalytic reaction of diazo compounds with 1,3-diheterocycloalkanes is the most convenient route [4–8]. For example, the reaction of methyl diazoacetate with 1,3-dioxanes in the presence of $Rh_2(OAc)_4$ leads to 1,4-dioxepanes, the *cis* isomer predominating when the initial 1,3-dioxane contains a substituent in the second position [9].

Therefore, it seemed useful to study the catalytic reaction of methyl diazoacetate with heterocyclic derivatives of unsaturated carbonyl compounds (cyclic acetals (ketals), 1,3-oxazolidines, and 1,3-oxathiolanes).

The study showed that the reaction of $N_2CHCO_2Me$ with 1,3-diheterocycloalkanes (**I**, **IIa**, **IIb**) in the presence of $Rh_2(OAc)_4$ occurred preferably via the ylide mechanism to give the products of formal insertion of methoxycarbonylcarbene into the C–X bond. The formation of ylides takes place by the electrophilic addition of carbenoid species generated from methyl diazoacetate to the heteroatom under the action of the catalyst.

Thus, the cyclic acetals (**Ia**, **Ib**) and 1,3-oxathiolanes (**IIa**, **IIb**) under the above conditions react with methyl diazoacetate to yield the products of C–X insertion (**III**, **IVa**, **IVb**) and [2,3]-sigmatropic rearrangement (**V**, **VIa**, **VIb**). It should be noted that no products of cycloaddition of methoxycarbonylcarbene to the C=C bond were detected in the reaction mixture.




R = Me, X = O (**Ia**, **IIIa**, **Va**); X = S (**IIa**, **IVa**, **VIa**)
R = Ph, X = O (**Ib**, **IIIb**, **Vb**); X = S (**IIb**, **VIb**)

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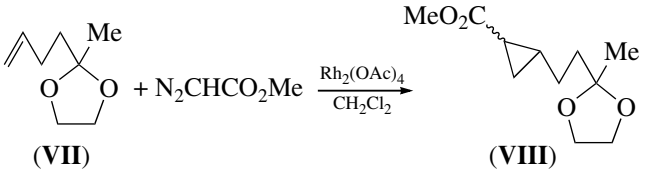
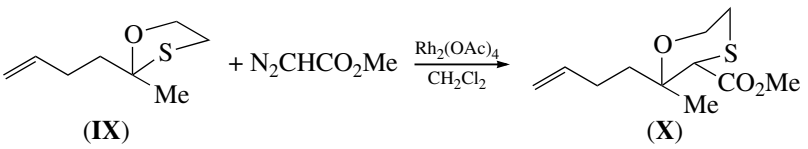
The reaction of 2-(3-butenyl)-2-methyl-1,3-dioxolane (**VII**) with $N_2CHCO_2Me$ in the presence of $Rh_2(OAc)_4$ leads to the formation of a mixture of dimethyl esters of *trans*- and *cis*-2-[2-(2-methyl-1,3-dioxolan-2-yl)ethyl]cyclopropanecarboxylic acids (**VIII**) in a 3 : 2 ratio and 40% total yield.




(**VII**) (**VIII**)

At the same time, the reaction of 2-(3-butenyl)-2-methyl-1,3-oxathiolane (**IX**) with $N_2CHCO_2Me$ catalyzed by $Rh_2(OAc)_4$ is accompanied by the insertion of a methoxycarbonylmethylene fragment into a five-membered ring resulting from the Stevens rearrangement of the initially formed *S*-ylide to give selectively methyl 2-(3-butenyl)-2-methyl-1,4-oxathiane-3-carboxylate (**X**) in 50% yield.




(**IX**) (**X**)

We obtained unexpected results for the reaction of 2-(*trans*-2-phenylethenyl)-3-ethyl-1,3-oxazolidine (**XI**) and 2-(3-butenyl)-2-methyl-3-ethyl-1,3-oxazolidine (**XII**) with $N_2CHCO_2Me$ in the presence of $Rh_2(OAc)_4$. It was found that $Rh_2(OAc)_4$ catalyzes the cleavage of initial oxazolidines (**XI**, **XII**) to form cinnamaldehyde and hexen-2-one, respectively.

Thus, our study showed that the direction of the reaction of the unsaturated compounds with $N_2CHCO_2Me$ in the presence of $Rh_2(OAc)_4$ is deter-

**Table 1.** Yields and $^1H$ NMR spectra for compounds **IIIa**, **IIIb**, **IVa**, **Va**, **Vb**, **VIa**, **VIb**, **VIII**, and **X**

| Compound | Yield, % | $^1H$ NMR spectrum (δ, ppm, *J*, Hz) |
|---|---|---|
| **IIIa** (X = O, R = Me) | 32 | 1.72 (d, 3 H, Me, $^3J$ = 6.3); 3.86 (m, 2 H, $H_2C(5)$); 3.95 (m, 2 H, $H_2C(6)$); 3.83 (dd, 1 H, HC(3), $^3J$ = 5.8, $^3J$ = 8.8); 3.92 (s, 3 H, OMe); 4.15 (d, 1 H, HC(2), $^3J$ = 5.8); 5.41 (dd, 1 H, HC(1'), $^3J$ = 8.8, $^3J$ = 15.7); 5.82 (dq, 1 H, HC(2'), $^3J$ = 6.3, $^3J$ = 15.7) |
| **IIIb** (X = O, R = Ph) | 47 | 3.73 (s, 3 H, OMe); 3.88–3.96 (m, 4 H, $H_2C(5)$ and $H_2C(6)$); 4.04 (d, 1 H, HC(2), $^3J$ = 8.8); 4.25 (dd, 1 H, HC(3), $^3J$ = 7.1, $^3J$ = 8.8); 6.15 (dd, 1 H, HC(1'), $^3J$ = 16.0, $^3J$ = 7.1); 6.72 (d, 1 H, HC(2'), $^3J$ = 16.0); 7.27–7.35 (m, 5 H, Ar) |
| **IVa** (X = S, R = Me) | 8 | 1.68 (d, 3 H, Me, $^3J$ = 6.1); 2.39 (m, 2 H, $H_2C(6)$); 3.95 (m, 2 H, $H_2C(5)$); 3.45 (d, 1 H, HC(2), $^3J$ = 12.5); 3.71 (s, 3 H, OMe); 4.78 (dd, 1 H, HC(3), $^3J$ = 12.5, $^3J$ = 6.7); 5.51 (dk, 1 H, HC(2'), $^3J$ = 6.1, $^3J$ = 15.5); 5.72 (dd, 1 H, HC(1'), $^3J$ = 6.7, $^3J$ = 15.5) |
| **Va** (X = O, R = Me) | 55 | 1.02 (d, 3 H, Me, $^3J$ = 7.2); 2.76–2.89 (ddq, 1 H, HC(6), $^3J$ = 5.1, $^3J$ = 7.2, $^3J$ = 10.1); 3.70 (t, 2 H, $H_2C(3)$, $^3J$ = 7.1); 3.71 (s, 3 H, OMe); 4.36 (t, 2 H, $H_2C(2)$, $^3J$ = 7.1); 4.54 (d, 1 H, HC(5), $^3J$ = 10.1); 4.82 (dd, 1 H, HC(7), $^3J$ = 5.1, $^3J$ = 6.3); 5.79 (d, 1 H, HC(8), $^3J$ = 6.3) |
| **Vb** (X = O, R = Ph) | 23 | 3.52 (t, 2 H, $H_2C(3)$, $^3J$ = 7.2); 3.73 (s, 3 H, OMe); 4.04 (d, 1 H, HC(5), $^3J$ = 8.8); 4.25 (dd, 1 H, HC(6), $^3J$ = 6.3, $^3J$ = 8.8); 4.47 (t, 2 H, $H_2C(2)$, $^3J$ = 7.2); 6.15 (dd, 1 H, HC(7), $^3J$ = 6.3, $^3J$ = 16.0); 6.72 (d, 1 H, HC(8), $^3J$ = 16.0); 7.27–7.35 (m, 5 H, Ar) |
| **VIa** (X = S, R = Me) | 8 | 1.00 (d, 3 H, Me, $^3J$ = 6.8); 2.66 (ddq, 1 H, HC(6), $^3J$ = 5.0, $^3J$ = 7.0, $^3J$ = 6.8); 3.08 (t, 2 H, $H_2C(3)$, $^3J$ = 7.1); 3.67 (s, 3 H, OMe); 3.71 (d, 1 H, HC(5), $^3J$ = 7.0); 4.16 (t, 2 H, $H_2C(2)$, $^3J$ = 7.1); 5.52 (dd, 1 H, HC(7), $^3J$ = 5.0, $^3J$ = 6.2); 5.87 (d, 1 H, HC(8), $^3J$ = 6.2) |
| **VIb** (X = S, R = Ph) | 10 | 2.72 (t, 2 H, $H_2C(3)$, $^3J$ = 7.1); 3.71 (s, 3 H, OMe); 3.96 (dd, 1 H, HC(6), $^3J$ = 5.0, $^3J$ = 7.8); 4.28 (t, 2 H, $H_2C(2)$, $^3J$ = 7.1); 4.42 (d, 1 H, HC(5), $^3J$ = 7.8); 5.48 (dd, 1 H, HC(7), $^3J$ = 7.7, $^3J$ = 5.0); 6.04 (d, 1 H, HC(8), $^3J$ = 7.7); 7.27–7.35 (m, 5 H, Ar) |
| **VIII** | 40 | 0.89 (m, 2 H, $CH_2$ in cyclopropane ring); 0.96 and 1.26 (both m, 1 H each, 2 CH in cyclopropane ring); 1.27 (s, 3 H, Me); 1.33 and 1.74 (both m, 1 H each, $C\underline{H}_2CH$); 1.47 (m, 2 H, $CH_2C$); 3.63 (s, 3 H, OMe); 3.71–3.91 (m, 4 H, $H_2C(4)$ and $H_2C(5)$) |
| **X** | 50 | 1.48 (s, 3 H, Me); 1.87 (t, 4 H, $H_2C(1')$, $^3J$ = 6.7); 2.08 (m, 2 H, $H_2C(2r')$); 2.88 (q, 2 H, $H_2C(5)$, $^3J$ = 6.3); 3.69 (m, 1 H, HC(3)); 3.71 (s, 3 H, OMe); 3.78 (dt, 2 H, $H_2C$ (6), $^3J$ = 6.3, $^3J$ = 7.8); 5.00 (br d, 2 H, $H_2C$=, $^3J$ = 17.2); 5.82 (ddt, 1 H, =CH, $^3J$ = 6.5, $^3J$ = 10.2, $^3J$ = 17.2) |

**Table 2.** $^{13}C$ NMR spectral data for compounds **IIIa**, **IIIb**, **IVa**, **Va**, **Vb**, **VIa**, **VIb**, **VIII**, and **X**

| Compound | $^{13}C$ NMR spectrum (δ, ppm) |
|---|---|
| **IIIa** | 17.4 (Me); 51.7 (OMe); 64.7 (C(5) and C(6)); 77.7 (C(3)); 79.4 (C(2)); 125.7 (C(1')); 129.6 (C(2')); 169.9 (CO) |
| **IIIb** | 52.4 (OMe); 63.7 (C(6)), 66.1 (C(5)); 73.4 (C(3)); 79.6 (C(2)); 123.9 (C(1')); 134.3 (C(2')); 127.8–128.9 (5 CH, Ar); 136.3 (C, Ar); 168.6 (CO) |
| **IVa** | 17.6 (Me); 28.3 (C(6)); 43.8 (C(2)); 53.3 (OMe); 69.4 (C(5)); 76.3 (C(3)); 126.4 (C(2')); 130.6 (C(1')); 172.9 (CO) |
| **Va** | 17.7 (Me); 33.4 (C(6)); 52.1 (OMe); 69.8 (C(3)); 70.7 (C(2)); 81.5 (C(5)); 120.0 (CH)); 145.6 (CH)); 168.7 (CO) |
| **Vb** | 46.7 (C(6)); 52.4 (OMe); 77.8 (C(5)); 79.6 (C(2) and C(3)); 118.3 (CH); 146.7 (CH); 127.8–128.9 (5 CH, Ar); 136.3 (C, Ar); 168.6 (CO) |
| **VIa** | 20.3 (Me); 28.4 (C(3)); 37.1 (CH(6)); 42.1 (CH (5)); 53.1 (OMe); 69.8 (C(2)); 117.1 (C(7)); 144.4 (C(8)); 178.7 (CO) |
| **VIb** | 28.4 (Me); 41.9 (C(5)); 47.0 (C(6)); 53.4 (OMe); 70.0 (C(2)); 115.7 (C(7)); 127.8–128.9 (5 H, Ar); 142.7 (C, Ar); 145.9 (C(8)); 178.4 (CO) |
| **VIII** | ***cis*-VIII.** 13.5 ($CH_2$ in cyclopropane ring); 18.2 (CH); 21.7 (CH); 23.6 (Me); 27.3 (C(2')); 38.2 (C(3')); 51.9 (OMe); 64.3 (C(4) and C(5)); 109.3 (C(2)); 173.0 (CO)<br>***trans*-VIII.** 15.3 ($CH_2$ in cyclopropane ring); 20.0 (CH); 22.4 (CH); 23.7 (Me); 27.5 (C(2')); 38.6 (C(3')); 52.0 (OMe); 64.3 (C(4) and C(5)); 109.5 (C(2)); 174.5 (CO) |
| **X** | 28.5 (Me); 30.7 (C(5)); 33.1 (C(1')); 34.5 (C(2')); 51.3 (C(3)); 51.4 (OMe); 69.7 (C(6)); 80.9 (C(2)); 114.1 ($CH_2$=); 137.3 (CH=); 170.0 (CO) |

mined by the nature of the substituent in the initial olefins.

## EXPERIMENTAL

$^1H$ and $^{13}C$ NMR spectra were recorded on a Bruker AM-300 spectrometer (300.13 and 75.47 MHz, respectively) in $CDCl_3$ with $SiMe_4$ as an internal reference. Qualitative and quantitative analysis of initial mixtures and reaction products was accomplished on a Chrom-5 chromatograph with a flame ionization detector (a $1200 \times 5$ mm column with 5% SE-30 on Inerton N-AW DMCS (0.125–0.160 mm); carrier gas, helium).

1,3-Dioxolanes (**Ia**, **Ib**) [10], 1,3-oxazolidines (**XI**, **XII**) [11], and 1,3-oxathiolanes (**IIa**, **IIb**) [12] were synthesized by known procedures. The purity of the unsaturated compounds used was at least 99%.

**Catalytic reaction of 2-alkenyl-1,3-diheterocyclopentanes with methyl diazoacetate (general procedure).** Methyl diazoacetate (0.7 g, 7.0 mmol) in 20 mL of $CH_2Cl_2$ was added to a solution of 7.0 mmol of an unsaturated compound (**Ia**, **Ib**, **IIa**, **IIb**, **VII**, **IX**, **XI**, or **XII**) and 0.07 mmol of $Rh_2(OAc)_4$ in 10 mL of the solvent over 1 h and the mixture was stirred additionally for 1–1.5 h with heating. The solvent was removed, the residue was dissolved in 10 mL of diethyl ether and passed through a thin layer of $Al_2O_3$, the solvent was removed under slightly reduced pressure, and the residue was distilled in vacuum or chromatographed on $SiO_2$.

The data on the compounds obtained are summarized in Tables 1 and 2.

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