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Dual reactivity of imidic carbonyl ylides in Rh(II)-catalyzed reactions of α-diazocarbonyl compounds with succinimide

Vsevolod Nikolaev,[a] Lothar Hennig,[b] Heinz Heimgartner,[c] Barbel Schulze[b] and Valerij Nikolaev[a,*]

[a]*Saint-Petersburg State University, University Prosp. 26, St.-Petersburg 198504, Russia*
[b]*Universität Leipzig, Institut für Organische Chemie, Johannisallee 29, D-04103 Leipzig, Germany*
[c]*Institute of Organic Chemistry, University of Zurich, Winterthurerstrasse 190, CH-8057 Zurich, Switzerland*

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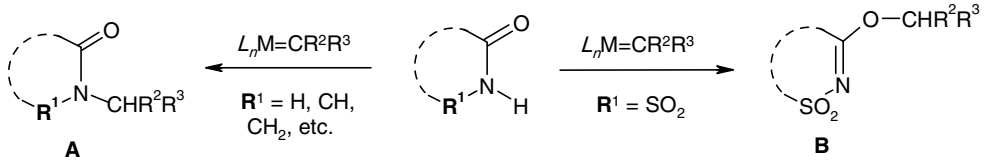
Abstract—Stabilization of imidic carbonyl ylides derived from α-diazocarbonyl compounds and succinimide occurs in two different ways: ylides from diazoesters experience a [1,4]-hydrogen shift to produce the corresponding *O*-alkylimidates while their analogues with at least one acyl group undergo [1,5]-electrocyclization yielding 1,3-dioxoles.

Catalytic decomposition of α-diazocarbonyl compounds in the presence of amides, lactams, and other compounds with an unsubstituted CO–NH group in their structure usually gives rise to the N-alkylation products **A** (Scheme 1).[1,2] However, we have shown that similar Rh(II)-catalyzed reactions of diazo compounds with oxoisothiazole 1,1-dioxides (saccharins) and their acyclic analogues containing a CO–NH–SO_2 group, results in exclusive O-alkylation of the sulfonimidic carbonyl group and formation of compounds **B**, which are formally the insertion products of the oxocarbenes into the O–H bond of the enol form of the sulfonimides[3] (Scheme 1).

The reaction proceeds chemoselectively on the imidic carbonyl group in good preparative yields and, according to the ^{1}H NMR data, no *N*-alkyl-saccharins or any other 'side' products were produced in these reactions.

The reason for such a significant difference in the reactivity of the CO–NH group in saccharin and analogues, by comparison with amides and lactams, remains unclear as yet. With the aim of examining this question we have carried out a detailed study of the catalytic reactions of diazocarbonyl compounds with 'carbocyclic' analogues of oxoisothiazole 1,1-dioxides, that is, phthalimide, maleimide, and other imides of carboxylic acids.[4] In this letter, the results of the Rh(II)-catalyzed reactions of diazocarbonyl compounds with succinimide **1** are presented.

Four acyclic diazocarbonyl compounds **2** were selected as the precursors of Rh(II)-oxocarbenoids **2′** in catalytic



Scheme 1. N-Alkylation of amides, lactams versus O-alkylation of sulfonimides in Rh(II)-catalyzed reactions of α-diazocarbonyl compounds.

Keywords: Diazo compounds; Rhodium catalysis; Carbonyl ylides; Imides; *O*-Alkylimidates; 1,3-Dioxoles.
* Corresponding author at present address: 8 Linija 35, Apt. 5, St.-Petersburg 199004, Russia. Tel.: +7 812 323 10 68; fax: +7 812 428 69 39; e-mail: vnikola@VN6646.spb.edu

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reactions with succinimide **1**: diazomalonic **2a** and diazoacetic **2b** esters, diazoacetoacetic ester **2d**, and diazoacetylacetone **2c**, being distinct types of aliphatic diazo compounds with rather different chemical reactivities.[1,5]

The experiments[6] showed that the catalytic decomposition of diazo compounds **2** in the presence of imide **1** proceeded in two different directions: *diazoesters* **2a**,**b** yielded only *O*-alkylimidates **3a**,**b**, whereas with *diazodicarbonyl compounds* **2c**,**d**, possessing at least one α-keto group, 1,3-dioxoles **4a**,**b** were isolated as the single reaction products (Scheme 2).

The structures of compounds **3** were established by an X-ray crystal-structure determination of one of the adducts **3a** (Fig. 1) and on the basis of the similarity in the location of the most characteristic signals for the methine and methylene groups in the NMR spectra of compounds **3a**,**b**[7] with the appropriate spectral data of *O*-alkylimidates derived from saccharins and their acyclic counterparts.[3] The chemical shifts of these diagnostic signals for the O–*CH* and O–CH_2 groups in the ^{1}H and ^{13}C NMR spectra are, for compounds **3a**,**b**: 5.89, 4.93 and 76.3, 66.7 ppm while the relevant derivatives of saccharin are 6.10, 5.18 and 75.9, 66.5 ppm and the acyclic sulfonamides are 5.96, 5.10 and 76.0, 66.1 ppm.[3] Comparison of these data along with crystallographic analysis of the adduct **3a** clearly demonstrated that the isolated derivatives **3a**,**b** from succinimide have the structure of *O*-alkylimidates.

The composition and structure of another set of compounds, **4a**,**b**, isolated from catalytic reactions of diazoketoester **2c** and diazodiketone **2d** with succinimide **1**, were ascertained first of all from their spectral characteristics.[8] For example, from mass spectrometry and elemental analysis, the molecular formula of compound **4b** ($C_9H_{11}N$, *m*/*z* 197 [$M^{+\cdot}$]) corresponds to the adduct of **1** and diacetylcarbene in the ratio 1:1. In the ^{13}C NMR spectrum of compound **4b**, nine signals were observed. In the case of N- or O-alkylation products of imide **1**, one might expect only five or seven carbon signals. Additionally, in the spectra of compound **4b**, diagnostic signals of the O–*CH* group, typical for *O*-alkylimidates and the products of N-alkylation (in the diketo form[9]), were absent.[3,7]

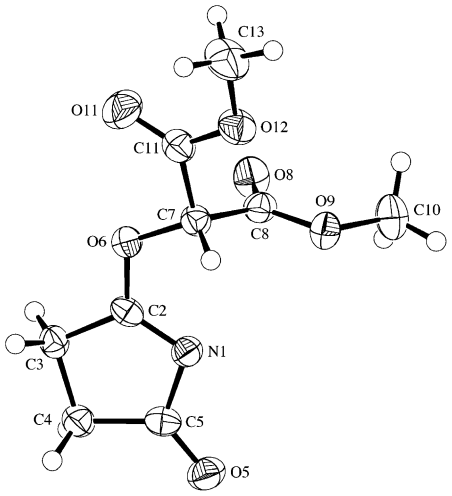
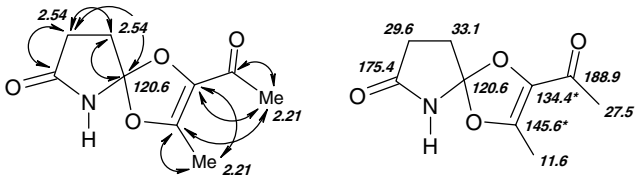


Figure 1. ORTEP plot[10] of the crystal structure of *O*-alkylimidate **3a**.[11]

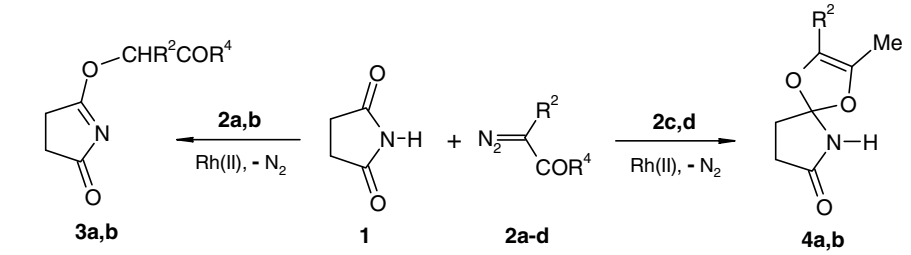
Furthermore, an analysis of cross-peaks in the HMBC and HMQC spectra of adduct **4b** (Scheme 3) showed that the H and C atoms of the two methyl groups of the former 'carbene' moiety (with chemical shifts at 11.6 and 27.5 ppm) interact with the double bond C-atoms at 134.4 and 145.6 ppm in the new molecule. Thus, one can conclude that the Me-groups are positioned at a distance not more than three covalent bonds from these C-atoms.

It is also evident from the HMBC spectra of adduct **4b** that the two CH_2 groups of the imidic fragment in the new compound (at 29.6 and 33.1 ppm) interact with



4b

Scheme 3. The structure of adduct **4b** as revealed by HMBC and HMQC experiments.



3a: R^2=CO_2Me, R^4=OMe; 70%
b: R^2=H, R^4=OEt; 53%

2a: R^2=CO_2Me; R^4=OMe;
b: R^2=H, R^4=OEt;
c: R^2=CO_2Et, R^4=Me;
d: R^2=COMe, R^4=Me

4a: R^2=CO_2Et; 58%
b: R^2=COMe; 87%

Scheme 2.

the C-atom at 120.6 ppm. Hence, in the course of the catalytic reaction, one of the succinimide carbonyl groups remained unchanged, whereas the other one was converted into an element of the new structure with the chemical shift of the C-atom now at 120.6 ppm.

Thus, the spectroscopic data of the adduct of succinimide **1** and diacetylcarbene most closely correlate with the structure of 2-acetyl-3-methyl-6-aza-1,4-dioxaspiro-[4.4]non-2-en-7-one **4b** (Scheme 3), which was confirmed by X-ray analysis (Fig. 2). The same reasonings were used for the interpretation of the spectra and elucidation of the structure of compound **4a**.

It appears then, that the reaction of imide **1** with Rh(II)-oxocarbenoids **2′** involves initial attack on the carbonyl O-atom by the electrophilic metal–carbene[1,12] and intermediate formation of highly reactive carbonyl ylides.[1,13,14] The subsequent *intramolecular* stabilization of the imidic carbonyl ylides **C** proceeds in two different ways, (a) and (b) (Scheme 4), and the direction of these transformations is evidently dictated by the nature of the substituents on the carbene moiety of intermediate **C**.

(a) Carbonyl ylides **C** *derived from diazoesters* **2a**,**b** and imide **1** are subject to an NH proton transfer and as such the final reaction products in these cases are solely *O*-alkylimidates **3a**,**b**.

The formation of *O*-alkylimidates **3a**,**b** from the ylides **C** can be explained by an intramolecular [1,4]-H-shift via a concerted mechanism,[1,12b,13c–f] or via a stepwise proton migration to the anionic center in the ylide **C**.[3] The 'oxonium' pathway for the formation of imidates **3a**,**b**, by a reaction of Rh(II)-oxocarbenoids **2′a**,**b** with the enol form of imide **1** and transient generation of the oxonium ylides,[1,12,15] is less likely. There is no spectral evidence for the existence of the enol form of succinimide **1** in solution or in the solid state.[16] According to the commonly accepted scheme for the insertion reaction with O–H-containing substrates,[1,12a,b,d,15b,c] the availability of the enol tautomer in the reaction mixture would be considered as a necessary requirement for the realization of the process through oxonium ylides.

In the series of oxoisothiazole 1,1-dioxides, a similar sulfonimidic [1,4]-H-shift was observed previously with all carbonyl ylides, independently of the structure of the initial diazo compounds, that is both diazoesters and diazoketones.[3] This is presumably due to an easier intramolecular [1,4]-H-shift in the sulfonimidic carbonyl ylides caused by the presence of a highly electron-withdrawing α-sulfonyl group in their structure. This considerably increases the mobility of the H-atom in the sulfonimidic NH group, as compared with the imides of dicarboxylic acids, and for this reason, stabilization of the sulfonimidic carbonyl ylides occurs solely by the intramolecular hydrogen shift.[3]

(b) Carbonyl ylides **C** *derived from diazoketoester* **2c** *or diazodiketone* **2d**, bearing at least one acyl group (CH_3CO), undergo an intramolecular [1,5]-electrocyclization to give the corresponding spiro-1,3-dioxole derivatives **4a**,**b** (Scheme 4).

The presence of the acyl carbonyl group in the carbene fragment of the ylide is evidently a necessary requirement for the [1,5]-cyclization.[17] It seems likely that in this case a resonance structure of the carbonyl ylide with the negative charge on the O-atom of the acyl group and a positive charge on the imidic carbonyl C-atom (Scheme 4) contributes significantly to the resonance hybrid of the transient ylide **C**, favoring the dipolar [1,5]-electrocyclization.

The occurrence of 1,3-dioxoles during the decomposition of diazocarbonyl compounds in the presence of simple aldehydes and ketones has long been known,[1,18] but similar reactions with the imidic carbonyl group is revealed here for the first time. Originally it was suggested that the formation of 1,3-dioxoles **4** resulted from a 1,3-cycloaddition reaction of the carbene or metal–carbenoid as

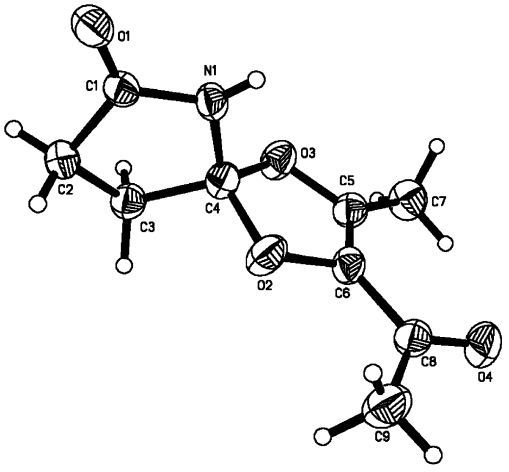
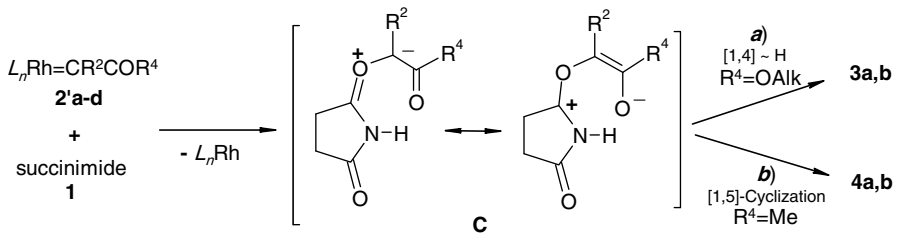


Figure 2. ORTEP plot[10] of the crystal structure of spiro-adduct **4b**.[11]



Scheme 4. Two different ways (a) and (b) for the stabilization of succinimidic carbonyl ylides **C**.

a 1,3-dipole with the C=O bond of a carbonyl substrate.[18a–d] However, currently the conventional mechanism of 1,3-dioxole formation in the decomposition of diazocarbonyl compounds in the presence of C=O-containing substrates, implies the intermediate occurrence of the relevant carbonyl ylides.[1,12,17,18e–g]

In summary, we have shown that the Rh(II)-catalyzed decomposition of acyclic diazocarbonyl compounds in the presence of succinimide proceeds chemoselectively at the imidic carbonyl group. Further stabilization of the resulting carbonyl ylides occurs in two different directions depending on the structure of the initial diazo compound: reactions with 2-diazoesters produce only *O*-alkylimidates, while with 2-diazo-1,3-ketoesters and 2-diazo-1,3-diketones, 1,3-dioxoles are formed exclusively.

Acknowledgements

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6. Catalytic reactions were carried out using dirhodium tetraacetate by adding 1–2 mol % of the catalyst at 10–20 °C to a suspension of succinimide **1** and diazocarbonyl compound **2a–d** in dry dichloromethane. Upon completion of the reaction as indicated by TLC, the reaction mixture was separated on a column with neutral silica gel (eluant–CH_2Cl_2 or a mixture petroleum–CH_2Cl_2). The isolated compounds were analyzed using ^1H and ^{13}C NMR spectroscopy, mass spectrometry, and X-ray analysis. Since the catalytic reactions and isolated products were found to be very sensitive to traces of acids and moisture, the reagents were carefully purified by sublimation in vacuo (**1**) or by distillation under reduced pressure (diazocarbonyl compounds **2a–d**). The work-up procedure was performed, wherever possible, with exclusion of moisture in the system. *Caution*: *Diazocarbonyl compounds* **2** *should always be considered as potentially toxic and explosive substrates. They should be handled with care and without heating above 50–55 °C.*
7. *O-Alkylimidate* **3a**. Colorless crystals, mp 102–103 °C (benzene/Et_2O). ^1H NMR ($CDCl_3$, 300 MHz): δ, ppm: 2.79 (m, 2H, CH_2), 2.97 (m, 2H, CH_2), 3.87 (s, 6H, $2OCH_3$), 5.89 (s, 1H, OCH). Anal. Calcd for $C_9H_{11}NO_6$: C, 47.16; H, 4.85; N, 6.11. Found: C, 47.14; H, 4.91; N, 5.98. *O-Alkylimidate* **3b**. Colorless liquid, becomes yellow on standing in air. 1.24 (t, 3H, OCH_2CH_3, *J* 7.2 Hz), 2.71 (m, 2H, CH_2), 2.84 (m, 2H, CH_2), 4.19 (q, 2H, OCH_2CH_3, *J* 7.2 Hz), 4.93 (s, 2H, OCH_2). Anal. Calcd for $C_8H_{11}NO_4$: C, 51.90; H, 5.98; N, 7.56. Found: C, 51.95; H, 6.04; N, 7.59.
8. *Spiro-adduct* **4a**. Colorless crystals, mp 117–118 °C (Et_2O) (decomp.). ^{13}C NMR ($CDCl_3$): δ, ppm: 11.23 (C=C–CH_3), 14.3 (CH_2CH_3), 29.4 (C8), 33.1 (C9), 60.9 (CH_2CH_3), 120.7 (C5), 126.1 (C2), 146.5 (C3), 160.1 (CO_2), 175.3 (CONH). Anal. Calcd for $C_{10}H_{13}NO_5$: C, 52.87; H, 5.76; N, 6.16. Found: C, 52.91; H, 5.79; N, 6.21. *Spiro-adduct* **4b**. Colorless crystals, mp 155–156 °C (acetone) (decomp.). ^{13}C NMR ($CDCl_3$): δ, ppm: 11.6 (CH_3–C=C), 27.5 (CH_3–C=O), 29.6 (C8), 33.1 (C9), 120.6 (C5), 134.4 (C2), 145.6 (C3), 175.4 (CONH), 188.9 (C=O). Anal. Calcd for $C_9H_{11}NO_4$: C, 54.83; H, 5.62; N, 7.01. Found: C, 54.84; H, 5.65; N, 7.08.
9. The possibility of 100% enols in the case of the adduct **4b** (correspondingly seven and nine signals in the ^{13}C NMR spectra for N- and O-alkylated derivatives) can be ruled out since in the ^1H NMR spectra of compound **4b** there were no typical signals for enolic protons at 14.0–16.0 ppm. Changing the solvent (C_6D_6 instead of Me_2CO) did not shift the tautomeric equilibrium and did not lead to the appearance of a new set of signals in the NMR spectra.
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