Isoxazolium N-ylides and 1-oxa-5-azahexa-1,3,5-trienes on the way from isoxazoles to 2H-1,3-oxazines


Abstract
Theoretical and experimental studies of the reaction of isoxazoles with diazo compounds show that the formation of 2H-1,3-oxazines proceeds via the formation of (3Z)-1-oxa-5-azahexa-1,3,5-trienes which undergo a 6π-cyclization. The stationary points corresponding to the probable reaction intermediates, isoxazolium N-ylides, were located by DFT calculations at the B3LYP/6-31G(d) level only for derivatives without a substituent in position 3 of the isoxazole ring. These isoxazolium N-ylides are thermodynamically and kinetically very unstable. According to the calculations and experimental results 2H-1,3-oxazines are usually more thermodynamically stable than the corresponding open-chain isomers, (3Z)-1-oxa-5-azahexa-1,3,5-trienes. The exception are oxaazahexatrienes derived from 5-alkoxyisoxazoles, which are thermodynamically more stable than the corresponding 2H-1,3-oxazines. Therefore, the reaction of diazo esters with 5-alkoxyisoxazoles is a good approach to 1,4-di(alkoxycarbonyl)-2-azabuta-1,3-dienes. The reaction conditions for the preparation of aryl- and halogen-substituted 2H-1,3-oxazines and 1,4-di(alkoxycarbonyl)-2-azabuta-1,3-dienes from isoxazoles were investigated.

Introduction
Isoxazoles are versatile building blocks, which have found extensive use in organic synthesis [1-3]. However, reactions of isoxazoles with diazo compounds have scarcely been studied [1-5]. In 2008 Davies and Manning [4,5] discovered the Rh-catalyzed reaction of diazo esters with 3,5-dialkylisoxazoles, benzo[d]isoxazole and 3-chlorobenzo[d]isothiazole leading to the corresponding 2H-1,3-oxazines, 2H-benzo[e][1,3]oxazine and 2H-benzo[e][1,3]thiazine. The authors assumed that the reaction of isoxazoles A with diazo esters B involved an isoxazolium N-ylide intermediate C formed by an attack of the rhodium carbenoid onto the isoxa-
Scheme 1: Mechanistic scheme of the formation of 2H-1,3-oxazine by the reaction of isoxazoles with a diazo compound.

Scheme 2: Mechanistic scheme of the formation of 2H-1,3-oxazine by the reaction of azirine with a diazo compound.

The reaction of a carbenoid with isoxazoles is the only known one-step intermolecular reaction which can in principle produce isoxazolium N-yldes from N-unsubstituted isoxazole derivatives. The formation of such ylides as reactive intermediates in the reactions of bases on isoxazolium salts was earlier supposed [6-9]. However, the detection of isoxazolium N-ylides has never been reported.

Recently, we found an alternative synthetic approach to derivatives of 2H-1,3-oxazines via a Rh₂(OAc)₄-catalyzed reaction of diazo esters with 2-acyl-2H-azirines F. This reaction involves the intermediate formation of azirinium ylides G, their transformation into 1-oxa-5-azahexa-1,3,5-triene D, and finally the 6π-electrocyclization of the latter to give oxazine E (Scheme 2) [10,11].
Results and Discussion

The theoretical study of the reaction mechanism was started with an evaluation of the thermodynamic and kinetic stabilities of isoxazolium N-ylides, probable intermediates in a carbenoid- or carbene-mediated one-atom isoxazole ring expansion. Preliminary calculations at the DFT B3LYP/6-31G(d) level with the PCM solvation model for dichloromethane were performed for the model reaction of isoxazoles A with methoxycarbonylcarbene (Figure 1). The stationary points corresponding to isoxazolium N-ylides C formed by an attack from the methoxycarbonylcarbene on the nitrogen of isoxazole A were found only for isoxazoles without substituent R\textsubscript{1} in position 3.

Further, these ylides undergo a ring opening via very low activation barriers (0.2–1.5 kcal/mol) to give (3Z)-1-oxa-5-azahexa-1,3,5-trienes. This is expected, because the oxazole N–O bond is very weak and the reaction is pseudopericyclic [21,22]. The calculated low thermodynamic and kinetic stabilities of the isoxazolium ylides (Figure 1) give only a small chance of detecting their formation even in cases where they can theoretically be formed. If the starting isoxazole contains substituent R\textsubscript{3}, an attack of a carbene on the isoxazole nitrogen leads to (3Z)-1-oxa-5-azahexa-1,3,5-triene without an activation barrier. The latter derived from isoxazoles without a methoxy substituent in position 5 can cyclize via a low activation barrier (<12.5 kcal/mol) to the corresponding 2H-1,3-oxazines. All calculated 1-oxa-5-azahexa-1,3,5-trienes, excluding the ones derived from 5-methoxy-substituted isoxazoles, are thermodynamically less stable than 2H-1,3-oxazines. In contrast, 1,4-di(methoxy carbonyl)-2-azabuta-1,3-dienes are much more stable than the corresponding 1,3-oxazines. We also evaluated the possibility of an attack of methoxycarbonylcarbene on the isoxazole oxygen. According to calculations (see Supporting Information File 1) a carbene attack on the isoxazole oxygen is significantly less favorable than an attack on the nitrogen.

The results of the calculations do not fundamentally change if methoxycarbonylcarbene is substituted with (methoxycarbonyl)phenylcarbene or di(methoxycarbonyl)carbene (Figure 2). Again, only oxaaazahexatrienes D derived from 5-methoxy-
substituted isoxazoles are much more stable than the corresponding oxazines E. Therefore, one can expect the formation of only 1-oxa-5-azahexa-1,3,5-trienes when reacting diazo compounds with 5-methoxyisoxazoles.

To start with, we reacted 4-phenyl-substituted isoxazole 1a and phenyl diazoacetate 2a under the reaction conditions used in [4] (catalyst: 1–3 mol % of Rh₂(OAc)₄, solvent: CH₂Cl₂ or CICH₂CH₂Cl, 40 or 84 °C) (Scheme 3). Unexpectedly, attempts to prepare oxazine 3a under these conditions were unsuccessful (Scheme 3) and isoxazole 1a was completely recovered.

**Scheme 3: Reaction of isoxazole 1a and diazo ester 2a.**

Oxazine 3a was obtained in 14% yield when heated under reflux in CH₂Cl₂ and with the use of dirhodium tetraoctanoate instead of Rh₂(OAc)₄ as a catalyst. This unsatisfactory result prompted us to test a carbene instead of a Rh(II) carbenoid, since it has been found [23] that carbenes can be successfully generated by thermolysis of diazo compounds without a catalyst in inert solvents with high boiling points, such as trifluoromethylbenzene. These conditions were attempted for the preparation of oxazines from isoxazole 1a and diazo compounds 2a–c (Table 1, entries 1–5). The use of a higher boiling-point solvent may also be a means to overcome the low solubility of arylisoxazoles. The formation of an oxazine occurred only with phenyl diazoacetate 2a under these conditions.

To overcome the inactivity of diazo compounds 2b,c the use of higher temperature and microwave irradiation were investigated, but only traces of oxazines 3b,c were then detected by ¹H NMR spectroscopy (Table 1, entries 6–8).

The conditions of choice for the synthesis of ary1-substituted 2H-1,3-oxazines proved to be heating under reflux in PhCF₃ and 1.5–3 mol % of Rh₂(OAc)₂ as a catalyst. Under these conditions oxazines 3a–m were synthesized (Table 2). The yields of oxazines can be improved by using a higher excess of...
**Table 1:** Reaction of azirines 1a with diazo compounds 2a–c without a catalyst.

<table>
<thead>
<tr>
<th>entry</th>
<th>2 (R¹, R²)</th>
<th>ratio 1a:2</th>
<th>time, h</th>
<th>T, °C</th>
<th>yield of 3, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>a (Ph, CO₂Me)</td>
<td>5:1</td>
<td>3.5</td>
<td>103</td>
<td>a, 34–42³</td>
</tr>
<tr>
<td>2ᵇ</td>
<td>a (Ph, CO₂Me)</td>
<td>5:1</td>
<td>3.5</td>
<td>103</td>
<td>a, traces</td>
</tr>
<tr>
<td>3</td>
<td>a (Ph, CO₂Me)</td>
<td>10:1</td>
<td>3.5</td>
<td>103</td>
<td>a, 88³</td>
</tr>
<tr>
<td>4</td>
<td>b (H, CO₂Et)</td>
<td>5:1</td>
<td>12</td>
<td>103</td>
<td>b, traces</td>
</tr>
<tr>
<td>5</td>
<td>c (CO₂Me, CO₂Me)</td>
<td>5:1</td>
<td>38</td>
<td>103</td>
<td>c, –</td>
</tr>
<tr>
<td>6</td>
<td>b (H, CO₂Et)</td>
<td>3:1</td>
<td>0.3</td>
<td>120, mw</td>
<td>b, traces</td>
</tr>
<tr>
<td>7</td>
<td>b (H, CO₂Et)</td>
<td>5:1</td>
<td>0.3</td>
<td>120, mw</td>
<td>b, traces</td>
</tr>
<tr>
<td>8ᵇ</td>
<td>c (CO₂Me, CO₂Me)</td>
<td>2:1</td>
<td>0.3</td>
<td>120, mw</td>
<td>c, traces</td>
</tr>
</tbody>
</table>

³Based on consumed 1a, the conversion of 1a was 12–15% (entry 1) and 9% (entry 3); b without solvent.

**Table 2:** Synthesis of oxazines 3a–m.

<table>
<thead>
<tr>
<th>1</th>
<th>2</th>
<th>R¹</th>
<th>R²</th>
<th>R³</th>
<th>R⁴</th>
<th>R⁵</th>
<th>ratio 1:2</th>
<th>3, yield, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>a</td>
<td>a</td>
<td>Me</td>
<td>Ph</td>
<td>Me</td>
<td>Ph</td>
<td>Me</td>
<td>1:1.7</td>
<td>a, 26</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1:3.3</td>
<td>a, 43</td>
</tr>
<tr>
<td>a</td>
<td>b</td>
<td>Me</td>
<td>Ph</td>
<td>Me</td>
<td>H</td>
<td>Et</td>
<td>1:1.9</td>
<td>b, 35</td>
</tr>
<tr>
<td>a</td>
<td>c</td>
<td>Me</td>
<td>Ph</td>
<td>Me</td>
<td>CO₂Me</td>
<td>Me</td>
<td>1:1.2</td>
<td>c, 67</td>
</tr>
<tr>
<td>b</td>
<td>a</td>
<td>Ph</td>
<td>H</td>
<td>Ph</td>
<td>Ph</td>
<td>Me</td>
<td>1:2.3</td>
<td>d, 66 (70)</td>
</tr>
<tr>
<td>b</td>
<td>b</td>
<td>Ph</td>
<td>H</td>
<td>Ph</td>
<td>H</td>
<td>Et</td>
<td>1:3.0</td>
<td>e, 34</td>
</tr>
<tr>
<td>b</td>
<td>c</td>
<td>Ph</td>
<td>H</td>
<td>Ph</td>
<td>CO₂Me</td>
<td>Me</td>
<td>1:3.4</td>
<td>f, 81</td>
</tr>
<tr>
<td>c</td>
<td>b</td>
<td>Ph</td>
<td>Cl</td>
<td>Ph</td>
<td>H</td>
<td>Et</td>
<td>1:3.7</td>
<td>g, 27 (73)</td>
</tr>
<tr>
<td>c</td>
<td>c</td>
<td>Ph</td>
<td>Cl</td>
<td>Ph</td>
<td>CO₂Me</td>
<td>Me</td>
<td>1:1.9</td>
<td>h, 48</td>
</tr>
<tr>
<td>d</td>
<td>b</td>
<td>Ph</td>
<td>Br</td>
<td>Ph</td>
<td>H</td>
<td>Et</td>
<td>1:3.0</td>
<td>i, 19 (75)</td>
</tr>
<tr>
<td>d</td>
<td>c</td>
<td>Ph</td>
<td>Br</td>
<td>Ph</td>
<td>CO₂Me</td>
<td>Me</td>
<td>1:1.5</td>
<td>k, 21</td>
</tr>
<tr>
<td>e</td>
<td>b</td>
<td>Ph</td>
<td>I</td>
<td>Ph</td>
<td>H</td>
<td>Et</td>
<td>1:3.3</td>
<td>l, 22 (63)</td>
</tr>
<tr>
<td>e</td>
<td>c</td>
<td>Ph</td>
<td>I</td>
<td>Ph</td>
<td>CO₂Me</td>
<td>Me</td>
<td>1:1.9</td>
<td>m, 21 (36)</td>
</tr>
</tbody>
</table>

³Yields based on consumed isoxazole are listed in parentheses.

diazoc compounds. However, this also leads to an increase of the formation of side products, “carbenoid dimers”, which attribute to a more difficult isolation of the target products in some cases.

The structures of compounds 3 were verified by ¹H NMR, ¹³C NMR, IR spectroscopy, HRMS, and elemental analysis. The structures of compounds 3a,k were additionally confirmed by X-ray analysis (Figure 3).

The characteristic feature of the structure of compound 3a is the pseudo-axial position of the methoxycarbonyl group. The structure of compound 3a in the crystal corresponds to the most stable conformer according to calculations at DFT B3LYP/6-31G(d) level in vacuo (ΔΔG²⁹⁸ K (equatorial/axial = 1.2 kcal/mol). One of the possible reasons for the higher stability of conformer 3a with a pseudo-axial methoxycarbonyl group in comparison to conformer 3a’ with a pseudo-equatorial
The pseudo-axial position of the methoxycarbonyl group is assumed to be the anomeric effect [24]. The lengthening of the C–CO₂Me bond in conformer 3a compared to conformer 3a' (1.563/1.554 Å), corroborates this hypothesis. The pseudo-axial position of the methoxycarbonyl group is preferred for all calculated oxazines.

In the reactions of diazo esters with 5-alkoxy-substituted isoxazoles 1f, h, in contrast to isoxazoles 1a–e, no formation of 1,3-oxazines was detected. Instead, the corresponding 1-oxa-5-aza-hexa-1,3,5-trienes 4a–f were isolated in moderate to good yields (Table 3).

The structures of compounds 4a–f were verified by ¹H, ¹³C NMR, IR spectroscopy, and HRMS. Furthermore, the structures of compounds 4a, b were confirmed by X-ray analysis (Figure 4). According to ¹H NMR no corresponding 1,3-oxazines were formed.

**Table 3: Synthesis of 1-oxa-5-aza-hexa-1,3,5-trienes 4a–f.**

<table>
<thead>
<tr>
<th>Ph</th>
<th>N₂</th>
<th>CO₂R¹</th>
<th>R²</th>
<th>CO₂R</th>
<th>Ph</th>
<th>Yield, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>1f</td>
<td>a</td>
<td>Me</td>
<td>Me</td>
<td>Ph</td>
<td>4a</td>
<td>51 (69)</td>
</tr>
<tr>
<td>1f</td>
<td>c</td>
<td>Me</td>
<td>CO₂Me</td>
<td>Ph</td>
<td>4b</td>
<td>54 (61)</td>
</tr>
<tr>
<td>1f</td>
<td>d</td>
<td>Et</td>
<td>CO₂Et</td>
<td>Ph</td>
<td>4c</td>
<td>80 (89)</td>
</tr>
<tr>
<td>1f</td>
<td>e</td>
<td>Me</td>
<td>CF₃</td>
<td>Ph</td>
<td>4d</td>
<td>57</td>
</tr>
<tr>
<td>1f</td>
<td>f</td>
<td>-Bu</td>
<td>Me</td>
<td>CO₂Me</td>
<td>4e</td>
<td>29 (45)</td>
</tr>
<tr>
<td>1f</td>
<td>g</td>
<td>-Bu</td>
<td>Et</td>
<td>CO₂Et</td>
<td>4f</td>
<td>25 (38)</td>
</tr>
</tbody>
</table>

*Yields based on consumed isoxazole are listed in parentheses.

**Figure 3:** Molecular structures of compounds 3a, k, displacement parameters are drawn at 50% probability level.

**Figure 4:** Molecular structures of compounds 4a, b, displacement parameters are drawn at 50% probability level.
Thus, only reactions of carbenoids with 5-alkoxy-substituted isoxazoles give the corresponding 1-oxa-5-azahexa-1,3,5-trienes instead of oxazines. To reveal the reason for this – either the destabilization of the oxazine or the stabilization of the 2-azabuta-1,3-diene when the phenyl group in 3d,e or 4g,h is exchanged for a methoxy group (compounds 4g,h were not isolated) – the corresponding changes in Gibbs free energy were evaluated from isodesmic reactions 1–4 (Scheme 4). These calculations were based on the Gibbs free energy of the compounds, which were obtained by DFT B3LYP/6-31G(d) calculations (ΔΔG\textsubscript{298} K, kcal/mol).

Although the substitution of the Ph group to a MeO group in compounds 3d,e results in a stabilization of the oxazines (Scheme 4, reactions 2 and 4), the formation of the corresponding 1-oxa-5-azahexa-1,3,5-trienes from 5-methoxy-substituted isoxazoles is mainly caused by the higher thermodynamic stability of 2-methoxy-substituted 1-oxa-5-azahexa-1,3,5-trienes 4a,b compared to 2-phenyl-substituted 1-oxa-5-azahexa-1,3,5-trienes 4g,h (Scheme 4, reactions 1 and 3). According to the X-ray analysis the R(MeO\textsubscript{2}C)C=N-group in compound 4 is not in conjugation with the remaining multiple bonds, that is, the methyl cinnamate conjugated system exerts a significantly greater influence on the stabilization than the corresponding chalcone system.

Thus, there is a good correspondence between the theoretical and experimental results, both of which support that Rh(II)-catalyzed reactions of diazo compounds with isoxazoles do not involve the formation of isoxazolium ylides but directly lead to the formation of azadienes, the latter can undergo a 6π-cyclization into the corresponding 1,3-oxazines. The position of the valence isomeric equilibrium depends on the relative thermodynamic stability of cyclic and acyclic isomers.

Additional evidence of a “one-step oxazahexatriene mechanism” of carbenoid-mediated isoxazole ring expansion originates from the results of the interaction of diazo compounds 2a–c with the complimentary isoxazole 1a and azirine 5 (Scheme 5). The reaction of isoxazoles with a carbenoid can only give a (3Z)-1-oxa-5-azahexa-1,3,5-diene due to geometrical restrictions. (3Z)-1-Oxa-5-azahexa-1,3,5-diene can then cyclize into the corresponding oxazine, so that the products of the reaction of 1a with diazo compounds 2a–c were only oxazines 3a–c (Table 2). In contrast, azirinium ylides 6a–c formed by the reaction of azirine 5 with diazo compounds 2a–c can transform into (3Z)- and (3E)-1-oxa-5-azahexa-1,3,5-triene 4i–k, but only the former can cyclize into 1,3-oxazines 3a–c (Scheme 5). In accordance with this, the reactions of azirine 5 with diazo compounds 2a–c (3E)-1-oxa-5-azahexa-1,3,5-trienes (E)-4i,k were isolated as well as oxazines 3a–c [10]. The corresponding ethyl 2-((E)-4-oxo-3-phenylpent-2-en-2-ylimino)acetate (E)-4j was not isolated from the reaction of azirine 5 with diazo compound 2b, probably due to its instability.

Conclusion

According to DFT calculations at the B3LYP/6-31G(d) level and experimental data the formation of 2H-1,3-oxazines from the reaction of isoxazoles with diazo compounds proceeds...
H (300 MHz) and C (75 MHz) NMR spectra were determined in CDCl$_3$ with a Bruker DPX 300 and a Bruker AVANCE III 400 spectrometer. Chemical shifts (δ) are reported in parts per million downfield from tetramethylsilane. Mass spectra were recorded on a Bruker maXis HRMS-ESI-QTOF by using electrospray ionization in the positive mode. IR spectra were recorded on a Bruker FTIR spectrometer Tensor 27 by using KBr disks and only characteristic absorption bands are indicated. Single crystal X-ray data were collected by means of an Agilent Technologies Supernova Atlas and an Agilent Technologies Excalibur Eos diffractometer. The crystals were kept at 100 K during data collection. The structures have been solved by the direct methods and refined by means of the SHELXL-97 program [27] incorporated in the OLEX2 program package [28]. Crystallographic data for the structures 3a (CCDC 998319), 3k (CCDC 998318), 4a (CCDC 998317), 4b (CCDC 998316) have been deposited with the Cambridge Crystallographic Data Centre. Isoxazoles 1a [29], 1b [30], 1c-e [31], 1f,g [32] were prepared by the reported procedures.

General procedure of reacting isoxazoles with diazo compounds. A long Schlenk tube containing a mixture of isoxazole (0.3–1.2 mmol) and diazo compound (1 equiv) in PhCF$_3$ (1–2 mL) was put into an oil bath preheated to 110 °C. To the vigorously stirred mixture, Rh$_2$(OAc)$_4$ (1–5 mol %) was added in one portion and stirred until N$_2$ evolution has been stopped (10–15 min). An additional amount of diazo compound was added dropwise, and then the mixture was heated for an additional 15 min. The reaction mixture was cooled, concentrated in vacuo, and the residue was separated by column chromatography on silica with a mixture of hexane/ethyl acetate as eluent.

Methyl 4,6-dimethyl-2,5-diphenyl-2H-1,3-oxazine-2-carboxylate (3a)

Compound 3a (40 mg, 43%) was obtained from isoxazole 1a (50 mg, 0.289 mmol), diazo ester 2a (51 + 117 mg, 0.953 mmol) and Rh$_2$(OAc)$_4$ (3.8 mg, 3 mol %) in PhCF$_3$ (1 mL). Colourless solid; mp 72–74 °C (CF$_3$Ph); $^1$H NMR (400 MHz, CDCl$_3$) δ 1.89 (s, 3H, Me), 1.96 (s, 3H, Me), 7.02–7.05 (m, 2H, Ar-H), 7.29–7.44 (m, 6H, Ar-H), 7.78–7.82 (m, 2H, Ar-H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 23.6, 53.0, 91.2, 116.2, 126.4, 127.4, 127.5, 128.2, 128.5, 128.8, 130.3, 135.0, 138.9, 158.7, 165.5, 170.9; ESI-MS (m/z): calculated for C$_{20}$H$_{19}$NO$_3$ $^+$, 322.1438; found, 322.1444; Anal. calc’d for C$_{20}$H$_{19}$NO$_3$: C, 74.75; H, 5.96; N, 4.36; found: C, 75.04; H, 5.74; N, 4.64; IR (KBr, cm$^{-1}$): ν: 1743 (C=O); crystal data for 3a: C$_{20}$H$_{19}$NO$_3$, M = 321.36, monoclinic, space group $P2_1/n$, a = 10.2806(4), b = 10.5164(3), c = 15.3771(4) Å, β = 98.241(3)$^\circ$, V = 1645.32(9) Å$^3$, Z = 4, F(000) = 680, D$_\text{calc}$ = 1.297 mg m$^{-3}$, μ = 0.704 mm$^{-1}$, 8556 reflections were collected yielding 3164 unique ($R_{int}$ = 0.0191). The final wR$_2$ = 0.1000 (all data) and R$_1$ = 0.0354 for 2848 reflections with 1 ≥ 2σ, GOF = 1.030.

**Scheme 5:** Reaction of complementary isoxazole 1a and azirine 5 with diazo esters.
Ethyl 4,6-dimethyl-5-phenyl-2H-1,3-oxazine-2-carboxylate (3b)

Compound 3b (52 mg, 35%) was obtained from isoxazole 1a (100 mg, 0.577 mmol), diazo ester 2b (66 + 58 mg, 1.09 mmol) and H\(_2\)(OAc)\(_4\) (7.6 mg, 3 mol %) in PhCF\(_3\) (1 mL). Colorless solid; mp ca. 25 °C; \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 1.37 (t, \(J = 7.1\) Hz, 3H, Me), 1.83 (d, \(J = 0.9\) Hz, 3H, Me), 1.85 (s, 3H, Me), 4.28–4.42 (m, 2H, CH\(_2\)), 5.60 (d, \(J = 0.9\) Hz, 1H, 2-H), 7.11–7.13 (m, 2H, Ar-H), 7.32–7.39 (m, 3H, Ar-H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 14.2, 17.0, 23.3, 62.0, 85.1, 116.0, 127.6, 128.6, 130.4, 135.1, 159.2, 166.2, 168.4; ESIMS (m/z): calcd for C\(_{15}\)H\(_{18}\)NO\(_{4}\)^+\(^+\), 260.1281; found, 260.1281; IR (KBr, cm\(^{-1}\)) v: 1737 (C=O).

Methyl 2,4,6-triphenyl-2H-1,3-oxazine-2-carboxylate (3d)

Compound 3d (245 mg, 66%); 70% based on consumed isoxazole) was obtained from isoxazole 1b (221 mg, 1.00 mmol), diazo ester 2a (176 + 224 mg, 2.27 mmol) and H\(_2\)(OAc)\(_4\) (6.6 mg, 0.15 mol %) in PhCF\(_3\) (2 mL). Colorless solid; mp 114–115 °C (hexane/ether); \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 3.72 (s, 3H, MeO), 6.69 (s, 1H, 5-H), 7.46–7.53 (m, 9H, Ar-H), 8.00–8.03 (m, 2H, Ar-H), 8.05–8.07 (m, 2H, Ar-H), 8.07–8.11 (m, 2H, Ar-H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\), 223 K) \(\delta\) 53.0, 93.2, 95.9, 126.7, 126.8, 127.2, 128.3, 128.5, 129.0, 130.9, 131.3, 132.2, 136.7, 139.0, 161.5, 161.3, 170.8; ESIMS (m/z): calcd for C\(_{24}\)H\(_{20}\)NO\(_{3}\)^+\(^+\), 370.1438; found, 370.1437; IR (KBr, cm\(^{-1}\)) v: 1735 (C=O).

Methyl 3-((Z)-(2-methoxy-2-oxo-1-phenylethylidene)amino)-3-phenylacrylate (4a)

Compound 4a (139 mg, 51%); 69% based on consumed isoxazole) was obtained from isoxazole 1f (175 mg, 1.00 mmol), diazo ester 2a (176 + 224 mg, 2.27 mmol) and H\(_2\)(OAc)\(_4\) (5 mg, 1.5 mol %) in PhCF\(_3\) (1 mL). Yellow solid; mp 141–143 °C, MeOH (lit. [33]: mp 142–143 °C, MeOH)) were isolated.

Supporting Information
Supporting Information File 1
Detailed experimental procedures including characterization data for all synthesized compounds, \(^1\)H and \(^{13}\)C NMR spectra for all new compounds, and computational details (energies of molecules, transition states, and the Cartesian coordinates of atoms). [http://www.beilstein-journals.org/bjoc/content/supplementary/1860-5397-10-197-S1.pdf]

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