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Unprecedented Synthesis of 3-Alkenyl-3-ethoxy-2-iminoketones via 1,3-Dipolar Cycloadditions of Nitrones with Alkynyl Fisher Carbene Complexes

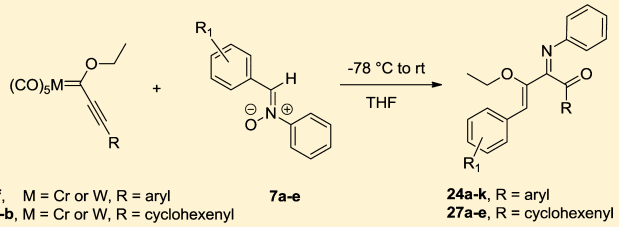
María Inés Flores-Conde,[†] Miguel Angel Vázquez,[‡] Leonor Reyes,[†] Joaquín Tamariz,[†] and Francisco Delgado*[,†]

[†]Departamento de Química Orgánica, Escuela Nacional de Ciencias Biológicas, Instituto Politecnico Nacional, Prol. Carpio y Plan de Ayala, 11340 Mexico, D. F., Mexico

[‡]Departamento de Química, Universidad de Guanajuato, Noria Alta S/N, 36050 Guanajuato, Gto., Mexico

Supporting Information

ABSTRACT: The synthesis of novel and highly substituted (2*Z*,3*Z*)-3-ethoxy-1-(aryl/cyclohexenyl)-4-aryl-2-(phenylimino)but-3-en-1-one derivatives **24a−k** and **27a−e** by an unexpected and previously unreported [3 + 2] cycloaddition/rearrangement and ring-opening cascade process of the Fischer carbene complexes $(CO)_5M{=}C(C{\equiv}C{-}Ar)OCH_2CH_3$ **1a−c** (M = Cr) and **1d−f** (M = W) and $(CO)_5M{=}C(C{\equiv}C\text{-cyclohexenyl})OCH_2CH_3$ **23a** (M = Cr) and **23b** (M = W) with *C*,*N*-diaryl nitrones (**7a−f**) is described. It is likely that the unstable 2,3-dihydroisoxazole carbene complexes produced in the [3 + 2] cycloaddition undergo a rapid and new rearrangement, followed by a stereoselective electrocyclic ring-opening process at a low temperature, to give only the (*Z*,*Z*) diastereoisomers **24a−k** and **27a−e** as the isolated products. The stereochemical assignment of the products was supported by NOE measurements and by single-crystal X-ray diffraction.



INTRODUCTION

Since the discovery of metal−carbene complexes by E. O. Fischer in 1964,[1] these have been demonstrated to be excellent partners for different reactions and have been repeatedly used in the synthesis of new organic and organometallic compounds.[2] Alkenyl and alkynyl Fischer carbene complexes of group 6 are of particular interest, because they can be involved in diverse cycloaddition reactions that offer access to heterocyclic and carbocyclic rings. Moreover, they can readily undergo novel cascade processes or unique rearrangement reactions,[3] making them fascinating substrates from both synthetic and mechanistic points of view.

For example, these carbene complexes can lead to the synthesis of *cis*-1,3,5-metallahexatrienes, which are potentially amenable to a number of synthetic transformations.[4] Recently, we reported an unusual behavior of alkynyl Fischer carbene complexes **1** toward pentamethylcyclopentadiene **2** under thermal conditions.[5] The *cis*-1,3,5-metallahexatrienes **3a−c**, formed from this initial Diels−Alder reaction, were involved in the formation of the benzannulation product as well as its subsequent rearrangement to yield the 1,2- and 1,4-naphthofurandiones **4** and **5** (Scheme 1).

On the other hand, 2,3-dihydroisoxazoles are a class of compounds endowed with a broad range of interesting reactivity patterns. They are accessible by 1,3-dipolar cycloaddition of nitrones (as dipoles) with acetylenecarboxylates (as dipolarophiles).[6] One of the important transformations of 2,3-dihydroisoxazoles is carried out by their rearrangement reaction.[7] Several experimental[8−10] and theoretical[11] studies have been performed on the application of nitrones in 1,3-dipolar cycloadditions with the highly electrophilic C−C triple bond of alkynyl Fischer carbene complexes. In one of these reports, Kalinin et al.[8] have shown that the 1,3-dipolar cycloaddition reaction of trimethylsilylethynyl carbene complexes of Cr(0) and W(0) **6a,b** with *C*,*N*-diphenyl nitrone **7** gave the 2,3-dihydrooxazole carbene complexes **9a,b**, resulting from the rearrangement of the unstable 2,3-dihydroisoxazole carbene complexes **8a,b**. These interesting findings were however limited to these substrates (Scheme 2).

In another study, Chan et al.[9b] reported the generation of 2,3-dihydroisoxazole carbene complexes **13−19** through highly regioselective 1,3-dipolar reactions of phenylethynyl carbene complexes **1** with the *C*-aryl-*N*-alkyl nitrones **10−12** (Scheme 3). However, all attempts to perform the 2,3-dihydroisoxazole-dihydrooxazole carbene complex rearrangement were unsuccessful, obtaining only the oxidation product of the corresponding [3 + 2] cycloadduct **13−19**.

Barluenga et al.[10a] extended this study to alkylethynyl carbenes, reporting that the reaction of *tert*-butylethynyl carbene complex **20** with *C*-aryl-*N*-methyl nitrones **10** yielded similar results to those reported by Chan.[9b] However, they

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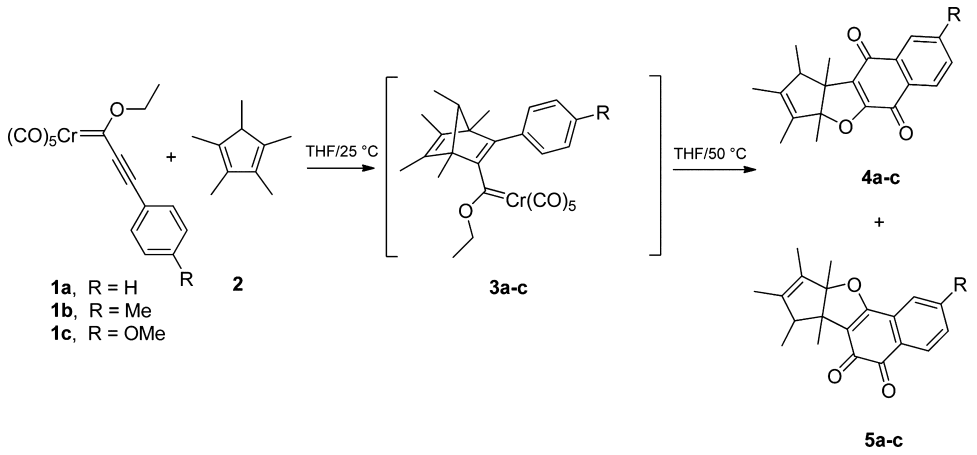
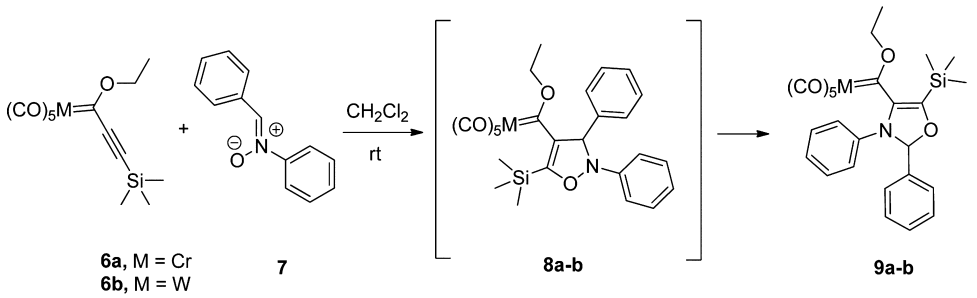
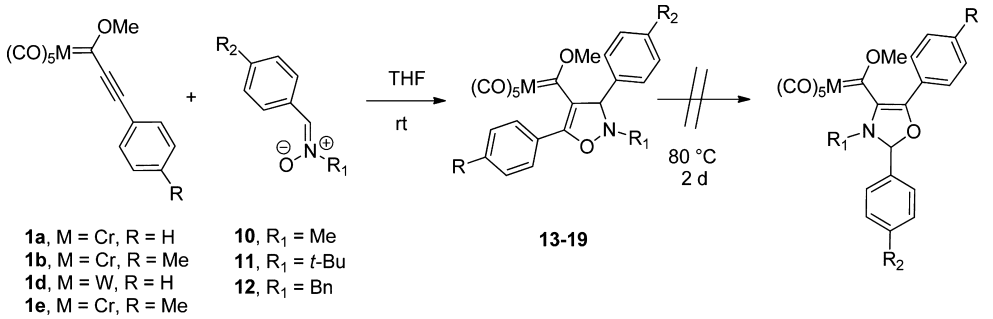
Scheme 1



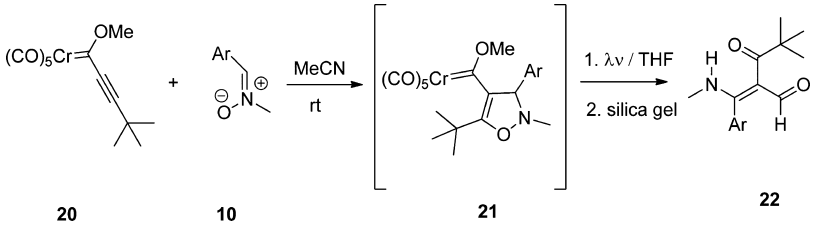
Scheme 2



Scheme 3



Scheme 4



noted that the resulting adducts **21** decomposed to the respective *β*-enaminoketoaldehydes **22** after several days and that exposure to sunlight accelerated this rearrangement (Scheme 4).

The aforementioned results prompted us to study the [3 + 2] cycloaddition reaction between the *C*,*N*-diaryl nitrones **7a**–**f** and several activated aryl- and cyclohexenylethynyl carbene complexes, **1a**–**f** and **23a**,**b**, to better understand the factors controlling these pathways. To the best of our knowledge, no systematic study has been carried out in relation to the influence of the *N*-aryl substituent in the nitrones on the course of these reactions.

We herein report an unprecedented [3 + 2] cycloaddition/rearrangement and ring-opening cascade process of alkynylcarbene complexes with substituted *C*,*N*-diaryl nitrones, providing an efficient and stereoselective approach to highly substituted (2*Z*,3*Z*)-3-ethoxy-1-(aryl/cyclohexenyl)-4-aryl-2-(phenylimino)but-3-en-1-one derivatives **24** and **27**. In

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addition, we evaluated the substituent effect of the aromatic rings, in both 1,3-dipoles and carbene complexes, on the reactivity as well as the regio- and stereoselectivity of this cascade process. Finally, derivatization of compound **24b** was carried out by reacting with 2,4-dinitrophenylhydrazine (**33**) to produce a mixture of chemoisomeric hydrazones **34** and **35**.

RESULTS AND DISCUSSION

[3 + 2] Cycloaddition. The starting compounds (pentacarbonyl)(alkynyl)(ethoxy)carbene chromium(0) and tungsten(0) complexes **1a−f** and **23a,b** and *C,N*-diaryl nitrones **7a−f** were prepared by the standard methods previously reported[12,13] (Figure 1).

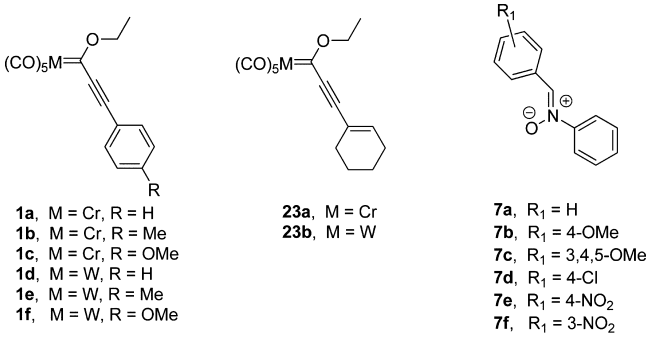

Figure 1.

The (arylethynyl)(ethoxy)carbene complexes **1a−f** were evaluated in terms of reactivity and selectivity toward *C,N*-diphenyl nitrones **7a−e** in [3 + 2] cycloaddition reactions. Initially, a mixture of the phenylethynyl carbene **1a** (1.0 molar equiv) and *C,N*-diaryl nitrone **7a** (1.0 molar equiv) was reacted in dry THF at room temperature, until a color change (from red to green in ∼30 min) took place in the solution. After workup, an unexpected and new (2*Z*,3*Z*)-3-ethoxy-1-(phenyl)-4-phenyl-2-(phenylimino)but-3-en-1-one (**24a**) was obtained in moderate yield (30%). *β*-Phenylamino carbene **25** and benzaldehyde **26** were also detected in the reaction mixture (Scheme 5), which probably stemmed from the descomposition of nitrone **7a**. Thus, through the latter process a molecule of the respective aniline was generated, followed by a conjugated addition to the carbene **1a** to afford **25**. The structural characterization of product **24a** was made on the basis of spectroscopic analysis.

In contrast to the previously reported approach,[8,9b,10a] it was interesting and surprising that the reaction did not afford either the expected [3 + 2] cycloadducts **13−19** or the rearranged cycloadduct **9**. Rather, novel compound **24a** was obtained in a moderate yield.

In an attempt to further improve the adduct yield, the reaction was started at a low temperature (−78 °C), and then the mixture was allowed to slowly warm to room temperature for ∼4 h. Under these reaction conditions, not only was adduct **24a** obtained in a better yield (57%) (Table 1, entry 1) but the decomposition of nitrone and formation of *β*-phenylamino carbene **25** was inhibited.

To validate this new process and to evaluate the substituent effect of R and R_1 in 1,3-dipoles and dipolarophiles, as well as to assess the possible effect of the metal on the reactivity and stereoselectivity of the reaction, a series of reactions were carried out under the same conditions using diverse substituted starting materials (Table 1).

When *C,N*-diaryl nitrones **7b,c**, bearing an electron-releasing group (R_1 = 4-OMe, R_1 = 3,4,5-OMe), were reacted with carbene complex **1a**, the conversion rate slightly increased (Table 1, entries 2 and 3), obtaining **24b** and **24c**, respectively, in higher yields. However, when reacting nitrones **7d,e** (substituted with an electron-withdrawing group) with carbene complex **1a**, a lower conversion to the corresponding product took place (Table 1, entries 4, 5).

We decided to evaluate the effect of the substituent in the aromatic ring of the carbene complexes. Thus, carbenes **1b** and **1c** were reacted with nitrone **7b** (Table 1, entries 6 and 10) with the result that **1c** reacted slower and produced a lower yield of **24j** than **1b**. At first, we considered that this behavior was due to a decreased reactivity caused by the strong electron-releasing effect of the methoxy group in **1c**.[14] However, this apparent cause was later found not to be the most significant, as evidenced by the fact that the reaction with **7b** was slower for carbene **1a** than **1b** and occurred at a similar rate for **1b** and **1c** (Table 1, entries 2, 6, and 10). Actually, these three carbenes reacted with nitrone **7e** in identical reaction times and in similar yields (Table 1, entries 5, 8, and 11).

Finally, with the aim of exploring the scope and limitations of the process, as well as of detecting the effect on the substituent in the carbene complexes, the cyclohexenylethynyl carbene complexes **23a** (M = Cr) and **23b** (M = W) were reacted with various dipoles **7**, under conditions identical to those used for reacting **1a−f**. The cycloaddition reactions employing **23a,b** yielded products **27a−e** as a single *Z,Z*-isomer, respectively (Table 2, entries 1−8).

Since cycloadducts **24a−k** and **27a−e** were obtained as a single *Z,Z*-isomer with comparable reaction times and yields (Tables 1 and 2), the reactivity and selectivity of carbene complexes of W(0) **1d−f** and **23b** are similar to those found for the carbenes of Cr(0) **1a−c** and **23a**, suggesting a negligible effect between chromium and tungsten metal atoms during the process.

The structural characterization of the isolated products **24** and **27** was made by spectroscopic data. For instance, high-

Scheme 5

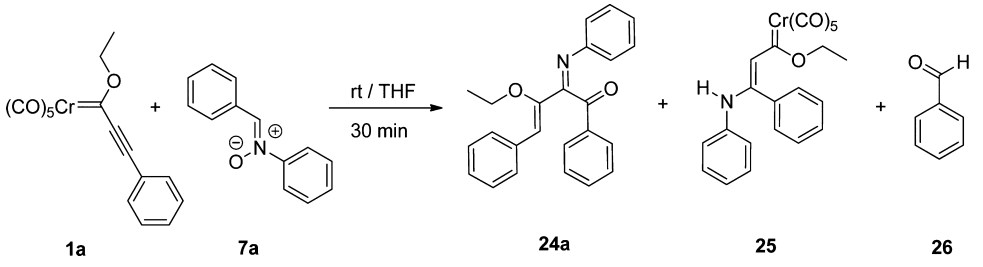

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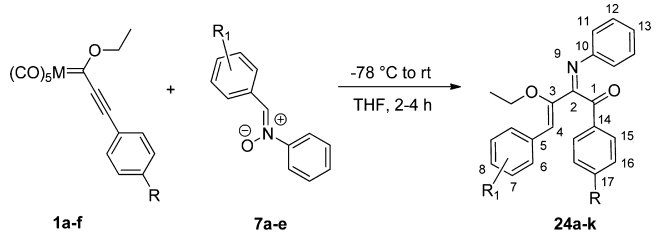
Table 1. Reaction Conditions and Yields in the Cascade Process of Phenylethynyl Carbenes 1a−f with *C,N*-Diphenyl Nitrones 7a−e[a]

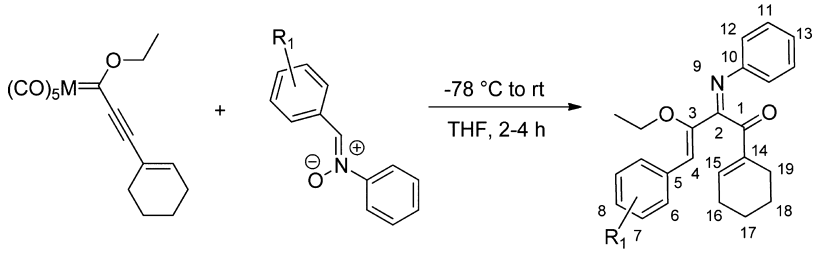


1a-f 7a-e 24a-k

entry	carbene	M	nitrone	R	R_1	reaction time (h)	adduct	yield (%)[b]
1	**1a**	Cr	**7a**	H	H	3.5	**24a**	57
2	**1a**	Cr	**7b**	H	4-OMe	3.0	**24b**	70
3	**1a**	Cr	**7c**	H	3,4,5-OMe	2.0	**24c**	75
4	**1a**	Cr	**7d**	H	4-Cl	2.5	**24d**	55
5	**1a**	Cr	**7e**	H	4-NO_2	4.0	**24e**	44
6	**1b**	Cr	**7b**	4-Me	4-OMe	2.0	**24f**	60
7	**1b**	Cr	**7d**	4-Me	4-Cl	3.5	**24g**	47
8	**1b**	Cr	**7e**	4-Me	4-NO_2	4.0	**24h**	40
9	**1c**	Cr	**7a**	4-OMe	H	3.5	**24i**	55
10	**1c**	Cr	**7b**	4-OMe	4-OMe	3.0	**24j**	45
11	**1c**	Cr	**7e**	4-OMe	4-NO_2	4.0	**24k**	40
12	**1d**	W	**7a**	H	H	3.5	**24a**	50
13	**1d**	W	**7e**	H	4-NO_2	4.0	**24e**	42
14	**1e**	W	**7b**	4-Me	4-OMe	3.5	**24f**	53
15	**1e**	W	**7d**	4-Me	4-Cl	4.0	**24g**	45
16	**1f**	W	**7a**	4-OMe	H	2.0	**24i**	55
17	**1f**	W	**7b**	4-OMe	4-OMe	3.0	**24j**	40

[a]All entries were carried out with a 1 molar equiv of **1** and **7** in dry THF, beginning at −78 °C and slowly warming to rt. [b]After column chromatography.

Table 2. Conditions and Yields in the Cascade Reaction of Cyclohexenylethynyl Carbenes 23a,b with *C,N*-Diphenyl Nitrones 7a,b and 7d−f[a]



23a-b 7a-f, 7e-f 27a-e

entry	carbene	M	nitrone	R_1	reaction time (h)	adduct	yield (%)[b]
1	**23a**	Cr	**7a**	H	2.5	**27a**	45
2	**23a**	Cr	**7b**	4-OMe	2.0	**27b**	53
3	**23a**	Cr	**7e**	4-NO_2	4.0	**27d**	40
4	**23a**	Cr	**7f**	3-NO_2	4.0	**27e**	36
5	**23b**	W	**7a**	H	3.0	**27a**	35
6	**23b**	W	**7b**	4-OMe	3.0	**27b**	45
7	**23b**	W	**7d**	4-Cl	3.0	**27c**	37
8	**23b**	W	**7e**	4-NO_2	3.5	**27d**	40

[a]All entries were carried out with a 1 molar equiv of **23** and **7** in dry THF, beginning at −78 °C and slowly warming to rt. [b]After column chromatography.

resolution mass spectrometry (HRMS) of **24i** showed the expected mass (*m*/*z* 385.1695), while the infrared spectrum displayed characteristic absorptions at 1600 (C═N), 1565 (C═O), and 1262 cm^{-1} (C═C-OEt). The ^1H NMR spectrum showed the presence of 14 aromatic protons at 7.78−6.78 ppm, two singlets at 6.33 and 3.77 ppm identified as the methine (H-4) and methoxy (OMe) groups, respectively, and a quartet and a triplet at 4.22 and 1.40 ppm integrating for two and three protons of the ethoxycarbonyl group, respectively. The ^{13}C NMR spectrum displayed signals at 194.8 and 164.9 ppm due to the carbonyl and imino groups, respectively, as well as two signals at 151.6 and 126.4 ppm for the vinyl carbons of the enol

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moiety, 12 signals at 164.3−114.0 ppm for aromatic carbons, and three signals at 67.9, 55.4, and 15.6 ppm for sp^3 carbon atoms. In the ^{13}C NMR spectra, it is interesting to note the low-field chemical shifts of the vinylic carbon (C-4) in all adducts (∼149.0−154.0 ppm). This indicates that the electron-donating effect of the ethoxy group does not shield the vinyl *β*-carbon or its associated proton. This may be due to the presence of the aryl group *cis* to the ethoxy group, which prevents coplanarity between the oxygen lone pairs and the double bond (see Figure 3). Assignment of all signals in the ^1H

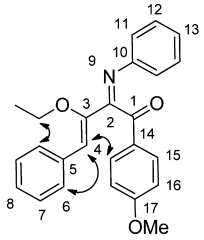

Figure 2. NOEs observed upon irradiation of protons H-4, H-6, H-15, and OCH_2CH_3 for derivative compound **24i**.

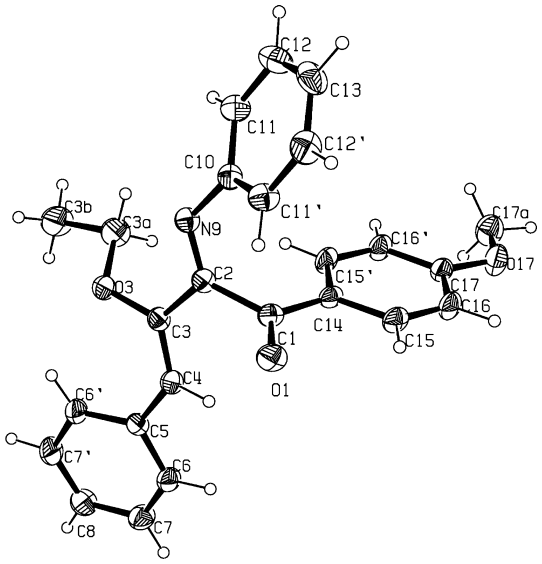

Figure 3. ORTEP diagram of **24i**. Thermal ellipsoids are shown at the 30% probability level. Selected bond distances (Å) and angles (deg): N(9)−C(2) = 1.275(2), C(2)−C(3) = 1.477(2), C(3)−C(4) = 1.341(2), O(3)−C(3) = 1.3670(18).

and ^{13}C NMR spectra was performed based on the results of 2D experiments (gHSQC and gHMBC). For instance, the gHMBC spectrum of all products showed long-range two- or three-bond C−H correlations between the proton H-4 at ∼6.33 ppm and the carbon atoms at ∼129.9 (C-4b), ∼151.6 (C-3), and ∼164.9 (C-2) ppm, in agreement with the presence of a 4-phenyl-2-(phenylimino)but-3-en-1-one core.

The (2*Z*,3*Z*) configuration of **24i** was supported by NOE experiments, which showed an enhancement of the signals of protons H-6 and H-15 when H-4 was irradiated and the same effect in the signal of the latter when protons H-6 and H-15 were irradiated (Figure 2). In addition, there was an observable enhancement of the signal attributed to proton H-6 upon irradiation of the methylene in the ethoxy group (Figure 2). This indicates that the aryl group at C-4 and the ethoxy group at C-3 are attached to the double carbon−carbon bond in a *Z* configuration, and consequently the imino carbon (C-2)−nitrogen double bond has a *Z* configuration.

Single-crystal X-ray diffraction crystallography of compound **24i** allowed us to confirm its structure (Figure 3). It exhibits the 2*Z*,3*Z* configuration of the backbone N(9)−C(2)−C(3)−C(4) in an *s-trans* conformation [C(3)−C(4)−C(5)−C(6) = 165.28(18)°] and the near planarity of the same [torsion angle = −178.52(14)°] including the C-4 phenyl ring. As suggested by the NMR spectral data, the ethoxy group is not coplanar to the carbon−carbon double bond, C(3a)−O(3)−C(3)−C(4) = −118.11(18)°. The torsion angle N(9)−C(2)−C(1)−O(1) = 99.91(19)° also reveals that the benzoyl moiety adopts a conformation out of the plane formed by the conjugated phenylvinyl *N*-phenylimino system.

Under the same conditions, equimolecular amounts of **1c** and **7a** were reacted in 15 mL of $CDCl_3$ as the solvent and monitored by ^1H NMR in order to detect the presence of any transient species during the course of the cascade reaction. Aliquots were taken from the reaction mixture every 15 min for 2.0 h. After the first 15 min, it was possible to observe three groups of signals: a singlet at 6.33 ppm, a quartet at 4.21 ppm, and a triplet at 1.40 ppm. These signals were attributed to the H-4 protons, the methylene (CH_2), and the methyl (CH_3) of the ethoxy group, respectively, of compound **24i**. Additionally, a quartet at 4.78 ppm and a triplet at 1.60 ppm were assigned to the ethoxy group of the carbene **1c**. As the reaction progressed, the former signals were found to increase and the latter signals to decrease. This result suggests that, once formed, the 2,3-dihydroisoxazole of **1c**, as the 1,3-dipolar cycloaddition adduct of **7a**, rapidly reacts to produce the final product **24i**.

Therefore, it is likely that the stability of the 2,3-dihydroisoxazole adduct is strongly altered by the electronic effect of the carbene group and the *N*-phenyl substituent introduced by the *C*,*N*-diaryl nitrone **7**, promoting conversion into the rearranged and open-ringed final product **24**. This outcome is partially in agreement with the report by Kalin and co-workers. They also used a *C*,*N*-diaryl nitrone, finding that the 1,3-dipolar adduct was not isolated, but instead only products **9a**,**b**, resulting from the rearrangement of the 2,3-dihydroisoxazole carbenes **8a**,**b** (Scheme 2).[8] However, our results are in contrast to those reported by Chan and co-workers,[9b] who were able to isolate the corresponding adducts **13**−**19** (Scheme 3). Furthermore, derivatives **24** do not have the structure of enaminones **22** reported by Barluenga and co-workers, which were produced by oxidation and heterocyclic ring-opening of the 1,3-dipolar cycloaddition adduct **21** (Scheme 4).[10a] Indeed, we found no examples in the literature of the ability to attain this type of compounds (**24** and **27**) from a cascade process, starting from the reaction between an *N*-phenyl nitrone and an aryl- or a cyclohexenylethynyl carbene complex. From the structural point of view, the cycloaddends used in the previous reports[8,9b,10a] seem to be similar to those employed in this study. However, the substituents in the cycloaddends used herein apparently had a significant effect on the stability of the 1,3-dipolar adducts, promoting the N−O bond cleavage as the first step in the process of rearrangement. The lone electron pair of the nitrogen atom in the initially formed 1,3-dipolar adducts perturbs (raising the energy) the oxygen lone electron pair, polarizing the N−O bond and promoting its cleavage, as anticipated by Baldwin.[7a] The *alpha effect*[14] could be the origin of this polarization, as a consequence of the repulsion between the lone electron pairs of the heteroatoms.[7a,15] This polarization can produce an

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electron deficiency at the nitrogen atom, which is largely stabilized by the presence of the aryl ring, favoring the N−O bond cleavage.[7a,b] The stability of this bond could also be related to the stability of the enolate produced by this cleavage. In this sense, the strong electron-withdrawing effect of the carbene moiety could play a significant role in stabilizing the electron density released by the N−O cleavage (Figure 4).

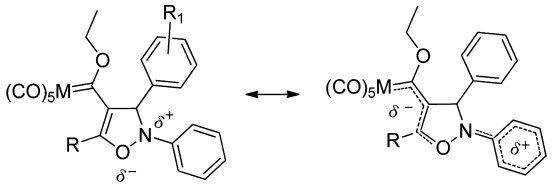


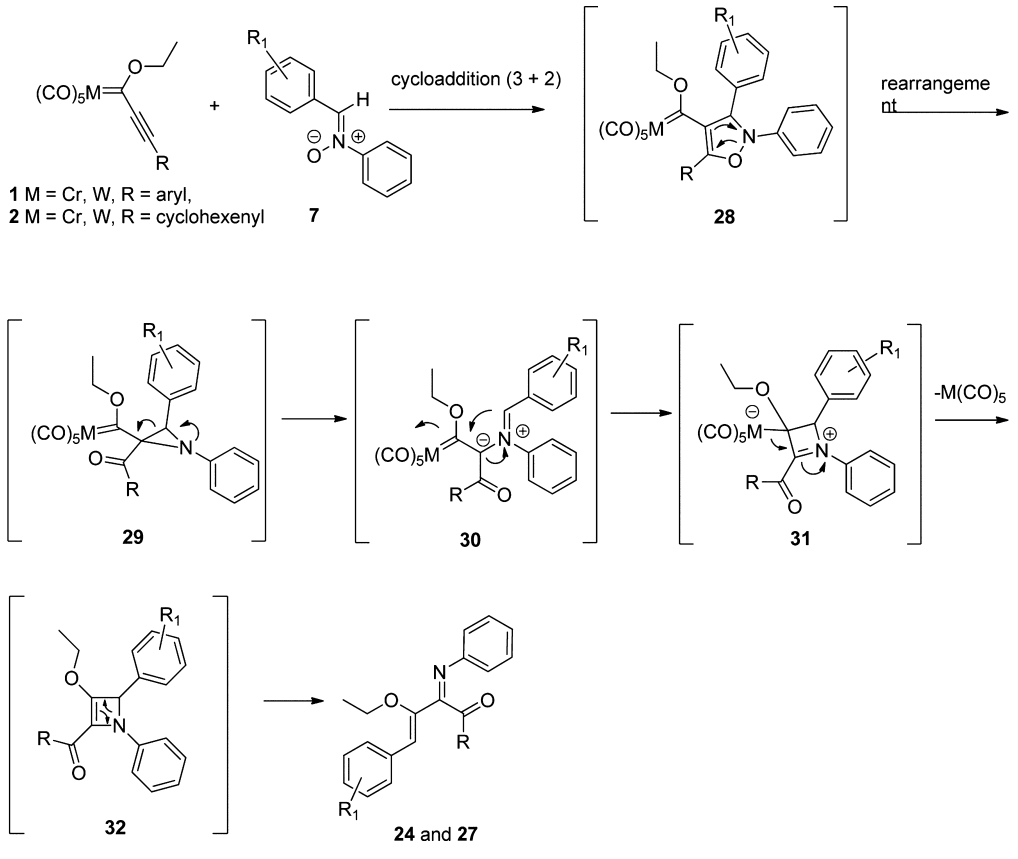
Figure 4. Polarization proposed for the N−O bond in the 2,3-dihydroisoxazole adducts.

Thus, the resulting negative charge borne by the oxygen atom would be stabilized by delocalization onto the carbene complex conjugated double bond. As a result, the yielded 1,3-adducts from the *N*-phenyl nitrones should be more susceptible to a N−O bond cleavage, leading to the observed rearranged products.

Although it was not possible to isolate or even obtain spectroscopic evidence of the 2,3-dihydroisoxazole carbene complex **28** or the azomethine ylide complex **30**, their plausible ephemeral existence as intermediates could account for the reaction pathway. A mechanism for this cascade process is proposed in Scheme 6.

The reaction sequence seems to be triggered by ring-opening of the initial and unstable 2,3-dihydroisoxazole carbene complex **28**. This is probably promoted by the strong electron demand of the carbene moiety conjugated to the endocyclic double bond, together with the polarization of the N−O bond,[7a] which can be explained, as aforementioned, by the *alpha effect*.[14,16] Although this effect is manifested particularly in nucleophiles, such as hydrogen peroxide, oximes, and hydrazines,[16e−n] it seems likely that the destabilization of the heteroatom lone pair interaction may also be involved in the N−O bond polarization of the 4-isoxazoline ring of **28**.[16n] In addition, according to Baldwin et al.,[7a] the N−O bond cleavage is accelerated by the presence of the *N*-phenyl group that stabilizes the resulting zwitterionic species,[7b] which leads to the formation of the corresponding 2-acylaziridine complex intermediate **29**. As is well known, the aziridine ring moiety can open to the azomethine ylide complex **30**,[6a,b,7] in which the reorganization of the dipole charges is promoted by the reactivity of the carbon−metal complex to give rise to the zwitterionic dihydroazete iminocyclobutene pentacarbonylchromium complex intermediate **31**.[3i,j] Decomposition of the latter yields (3-ethoxy-1,4-dihydroazet-2-yl)(phenyl)methanone (**32**), which in turn undergoes a conrotatory ring-opening that leads to the observed series of stable derivatives **24** and **27** (Scheme 6). It is noteworthy that, in accordance with the proposed mechanism, the latter compounds would not be produced if the first 1,3-dipolar cycloaddition were not a highly regioselective process, with both cycloaddends exclusively oriented to form the 2,3-dihydroisoxazole carbene complexes **28**.[17]

Scheme 6



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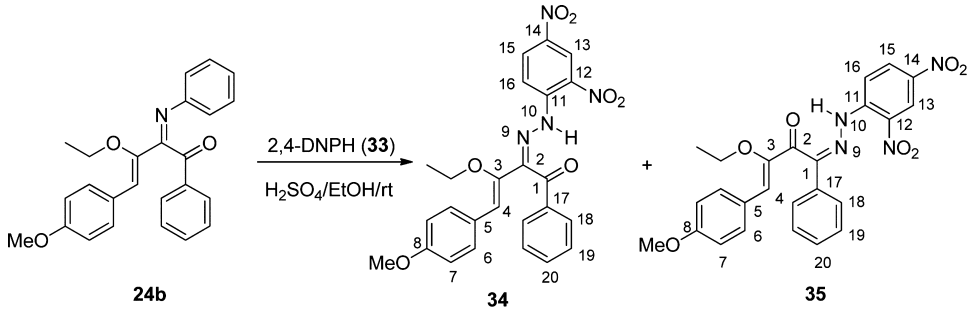
Scheme 7



A preliminary reactivity evaluation of these compounds consisted of treating the isolated 2-(phenylimino)but-3-en-1-one **24b** with 2,4-dinitrophenylhydrazine (2,4-DNPH). Formation of a mixture of hydrazones **34**/**35** was found in good yield (90%) (Scheme 7). Hydrazone **34** was isolated as orange-red crystals, and its structure was established by X-ray diffraction analysis (Figure 5), revealing that the addition of the 2,4-DNPH took place at the *N*-phenylimino group, maintaining the same (2*Z*,3*Z*) configuration of the double bonds. Moreover, the conjugated phenylvinyl *N*-phenylimino system adopts a planar *s-trans* conformation, leaving the benzoyl moiety in a nonplanar conformation as well, which is similar to that found with precursors **24**.

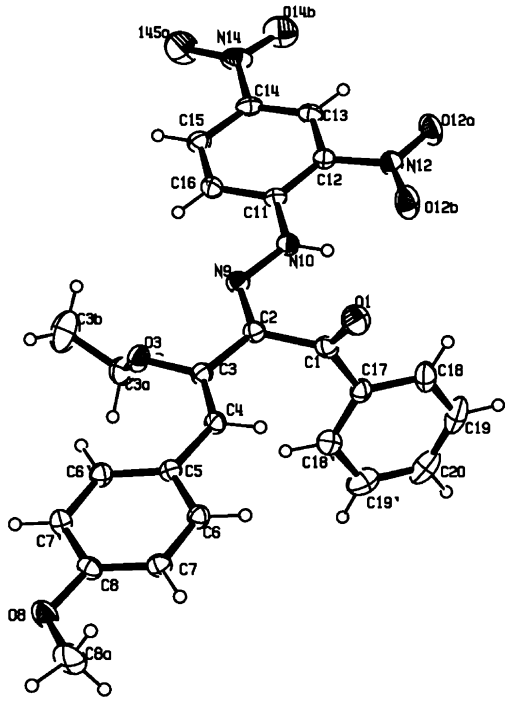


Figure 5. ORTEP diagram of **34**. Thermal ellipsoids are shown at the 30% probability level. Selected torsion angles (deg): N(9)−C(2)−C(3)-C(4) = −172.37(11), C(3)−C(4)−C(5)−C(6) = −177.61(12), C(3a)−O(3)−C(3)−C(4) = −114.65(14), N(9)−C(2)−C(1)−O(1) = 85.38(16).

CONCLUSIONS

We report an unexpected and new [3 + 2] cycloaddition/rearrangement and ring-opening cascade reaction of the (aryl/cyclohexenyl)(ethoxy) carbene complexes of Cr(0) and W(0) **1a−f** with *C*,*N*-diaryl nitrones **7a−f**, leading to novel and highly substituted (2*Z*,3*Z*)-3-ethoxy-1-(aryl/cyclohexenyl)-4-aryl-2-(phenylimino)but-3-en-1-one derivatives **24a−k** in high regio- and stereoselectivity. Furthermore, the cascade reactions between carbene complexes **23a,b** and *C*,*N*-diaryl nitrones **7a,b** and **7d−f** successfully proceeded to afford the (2*Z*,3*Z*)-3-ethoxy-1-(cyclohexenyl)-4-aryl-2-(phenylimino)but-3-en-1-ones **27a−e**, corroborating the high regioselectivity found in the [3 + 2] cycloadditions. This unprecedented transformation is presumably carried out by a mechanism in which the 2,3-dihydroisoxazole carbene complexes **28** are formed and undergo consecutive reactions of rearrangement and ring-opening, being strongly affected by the electron-withdrawing effect of the metal−carbene moiety conjugated to the endocyclic double bond and by the congestion generated by the vicinal hindered substituted centers in the heterocycle. The reactivity and synthetic applications of this series of novel polyfunctionalized molecules **24** and **27** are currently under study, and the results will be reported in due course.

EXPERIMENTAL SECTION

General Procedures and Instrumentation. All reactions were carried out under nitrogen in anhydrous solvents. Glassware was dried in an oven prior to use. Commercially available compounds were used without further purification. Tetrahydrofuran was distilled from sodium benzophenone ketyl under an N_2 atmosphere prior to use. *n*-Hexane and ethyl acetate were distilled before use. Melting points (uncorrected) were determined with a Fisher-Johns melting point apparatus. ^{1}H NMR and ^{13}C NMR spectra were recorded on a Varian Mercury (300 MHz) and Varian VNMR System (500 MHz) instruments, in $CDCl_3$ as solvent and with TMS as internal reference. High-resolution mass spectra (HRMS) were obtained with a JSM-GCMate II mass spectrometer, and electron impact techniques (70 eV) were employed. X-ray data were collected on an Oxford Diffraction Xcalibur S single-crystal X-ray difractometer. Thin-layer chromatography (TLC) analyses were performed using silica plates and were visualized using UV (254 nm) or iodine. Flash column chromatography was performed over Natland International Co. silica gel (230−400 mesh). *C*,*N*-Diaryl nitrones **7a−f** and carbene complexes **1a−f** and **23a,b** were prepared by the standard methods previously reported.[12,13]

General Method for the Tandem [3 + 2] Cycloaddition/Rearrangement and Ring-Opening Process of the Adducts 24a−k, 27a,b, and 27d,e. Method A. A solution of the corresponding *C*,*N*-diaryl nitrones **7a−e** (1.0 molar equiv) in freshly dried THF (15 mL) was slowly added dropwise via cannula to carbene complexes of Cr(0) **1a−c** and **23a** (1.0 molar equiv) at −78 °C under a nitrogen atmosphere, and then the mixture was allowed to slowly reach room temperature (~2−4 h), until the color of the solution changed from red to green. At this point, the solvent was removed under vacuum and the residue was dissolved in EtOAc (10 mL) and filtered over Celite. The solvent was removed under vacuum, and the crude product was purified by flash column chromatography over silica

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gel using *n*-hexane/EtOAc (98:2), to afford the corresponding adducts **24a−k**, **27a,b**, and **27d,e**.

General Method for the Tandem [3 + 2] Cycloaddition/Rearrangement and Ring-Opening Process of the Adducts 24a, 24e−j, and 27a−d. Method B. A solution of the corresponding *C,N*-diaryl nitrones **7a−f** (1.0 molar equiv) in freshly dried THF (15 mL) was slowly added dropwise via cannula to carbene complexes of W(0) **1d−f** and **23b** (1.0 molar equiv) at −78 °C under a nitrogen atmosphere, and then the mixture was allowed to slowly reach room temperature (∼2−4 h), until the color of the solution changed from red to brown. At this point, the solvent was removed under vacuum and the residue was dissolved in EtOAc (10 mL) and filtered over Celite. The solvent was removed under vacuum, and the crude product was purified by flash column chromatography over silica gel using *n*-hexane/EtOAc (98:2) to afford the corresponding adducts **24a**, **24e−j**, and **27a−d**.

(2*Z*,3*Z*)-3-Ethoxy-1,4-diphenyl-2-(phenylimino)but-3-en-1-one (24a). According to general method A, the reaction between **7a** (0.562 g, 2.85 mmol) and carbene **1a** (1 g, 2.85 mmol) afforded **24a** (0.579 g, 57%) as a yellow solid: mp 53−54 °C. According to general method B, the reaction between **7a** (0.203 g, 1.03 mmol) and carbene **1d** (0.500 g, 1.03 mmol) afforded **24e** (0.184 g, 50%): FT-IR (KBr) ν_{max} 1671, 1590, 1271 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.41 (t, J = 7.0 Hz, 3H, OCH_2CH_3), 4.21 (q, J = 7.2 Hz, 2H, OCH_2CH_3), 6.34 (s, 1H, H-4), 6.81−6.85 (m, 2H, H-11), 6.88−6.92 (m, 1H, H-13), 7.10−7.20 (m, 2H, H-12), 7.28−7.30 (m, 1H, H-8), 7.31−7.37 (m, 4H, H-16 and H-7), 7.45−7.50 (m, 1H, H-17), 7.72−7.75 (m, 2H, H-6), 7.76−7.8 (m, 2H, H-15); ^{13}C NMR (125 MHz, $CDCl_3$) δ 15.6 (OCH_2CH_3), 67.9 (OCH_2CH_3), 120.3 (C-11), 124.6 (C-13), 126.4 (C-4), 128.4 (C-8), 128.5 (C-12), 128.7 (C-16 and C-7), 129.1 (C-15), 129.9 (C-6), 134.0 (C-5), 134.2 (C-17), 134.6 (C-14), 148.9 (C-10), 151.5 (C-3), 164.8 (C-2), 196.7 (C-1); HRMS (EI+) calcd for $C_{24}H_{21}NO_2$ 355.1572, found (M+) 355.1527.

(2*Z*,3*Z*)-3-Ethoxy-4-(4-methoxyphenyl)-1-phenyl-2-(phenylimino)but-3-en-1-one (24b). According to general method A, the reaction between **7b** (0.322 g, 1.41 mmol) and carbene **1a** (0.500 g, 1.42 mmol) afforded **24b** (0.385 g, 70%) as a yellow solid: mp 97−98 °C; FT-IR (KBr) ν_{max} 1671, 1583, 1254 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.42 (t, J = 7.0 Hz, 3H, OCH_2CH_3), 3.81 (s, 3H, OCH_3), 4.21 (q, J = 7.0 Hz, 2H, OCH_2CH_3), 6.28 (s, 1H, H-4), 6.80−6.83 (m, 2H, H-11), 6.84−6.88 (m, 2H, H-7), 6.89−6.90 (m, 1H, H-13), 7.00−7.10 (m, 2H, H-12), 7.32−7.36 (m, 2H, H-16), 7.44−7.49 (m, 1H, H-17), 7.60−7.73 (m, 2H, H-6), 7.77−7.79 (m, 2H, H-15); ^{13}C NMR (125 MHz, $CDCl_3$) δ 15.6 (OCH_2CH_3), 55.2 (OCH_3), 67.6 (OCH_2CH_3), 113.9 (C-7), 120.4 (C-11), 124.4 (C-13), 126.7 (C-4), 126.8 (C-14), 128.4 (C-12), 128.7 (C-16), 129.2 (C-15), 131.6 (C-6), 134.1 (C-17), 134.7 (C-5), 149.0 (C-10), 149.9 (C-3), 159.9 (C-8), 164.8 (C-2), 196.9 (C-1); HRMS (EI+) calcd for $C_{25}H_{23}O_3N$ 385.1678, found (M+) 385.1678.

(2*Z*,3*Z*)-3-Ethoxy-1-phenyl-2-(phenylimino)4-(3,4,5-trimethoxyphenyl)but-3-en-1-one (24c). According to general method A, the reaction between **7c** (0.818 g, 2.85 mmol) and carbene **1a** (1.0 g, 2.85 mmol) afforded **24c** (0.957 g, 75%) as a bright yellow, viscous oil: FT-IR (KBr) ν_{max} 1663, 1597, 1258 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.45 (t, J = 7.2 Hz, 3H, OCH_2CH_3), 3.84 (s, 6H, $2OCH_3$), 3.86 (s, 3H, OCH_3), 4.24 (q, J = 7.2 Hz, 2H, OCH_2CH_3), 6.24 (s, 1H, H-4), 6.82−6.84 (m, 2H, H-11), 6.88−6.91 (m, 1H, H-13), 7.00−7.12 (m, 4H, H-6 and H-12), 7.32−7.36 (m, 2H, H-16), 7.45−7.50 (m, 1H, H-17), 7.76−7.80 (m, 2H, H-15); ^{13}C NMR (125 MHz, $CDCl_3$) δ 15.8 (OCH_2CH_3), 56.0 ($2OCH_3$), 60.8 (OCH_3), 67.9 (OCH_2CH_3), 107.2 (C-6), 120.3 (C-11), 124.6 (C-13), 126.6 (C-4), 128.5 (C-12), 128.7 (C-16), 129.2 (C-15), 129.4 (C-8), 134.3 (C-17), 134.6 (C-14), 138.7 (C-5), 148.8 (C-10), 151.0 (C-3), 152.9 (C-7), 164.5 (C-2), 196.8 (C-1); HRMS (EI+) calcd for $C_{27}H_{27}O_5N$ 445.1889, found (M+) 445.1871.

(2*Z*,3*Z*)-4-(4-Chlorophenyl)-3-ethoxy-1-phenyl-2-(phenylimino)but-3-en-1-one (24d). According to general method A, the reaction between **7d** (0.165 g, 0.714 mmol) and carbene **1a** (0.250 g, 0.714 mmol) afforded **24d** (0.152 g, 55%) as an orange, viscous oil: FT-IR (KBr) ν_{max} 1671, 1584, 1089 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.39 (t, J = 7.0 Hz, 3H, OCH_2CH_3), 4.22 (q, J = 7.0 Hz, 2H, OCH_2CH_3), 6.28 (s, 1H, H-4), 6.81−6.85 (m, 2H, H-11), 6.88−6.92 (m, 1H, H-13), 7.00−7.12 (m, 2H, H-12), 7.27−7.32 (m, 2H, H-7), 7.31−7.37 (m, 2H, H-16), 7.45−7.50 (m, 1H, H-17), 7.66−7.70 (m, 2H, H-6), 7.75−7.79 (m, 2H, H-15); ^{13}C NMR (125 MHz, $CDCl_3$) δ 15.6 (OCH_2CH_3), 68.1 (OCH_2CH_3), 120.3 (C-11), 124.8 (C-13), 124.9 (C-4), 128.5 (C-7), 128.6 (C-12), 128.8 (C-16), 129.2 (C-15), 131.1 (C-6), 132.5 (C-8), 134.3 (C-17 and C-5), 134.5 (C-14), 148.7 (C-10), 151.8 (C-3), 164.4 (C-2), 196.6 (C-1); HRMS (EI+) calcd for $C_{24}H_{20}ClNO_2$ 389.1183, found (M+) 389.1190.

(2*Z*,3*Z*)-3-Ethoxy-4-(4-nitrophenyl)-1-phenyl-2-(phenylimino)but-3-en-1-one (24e). According to general method A, the reaction between **7e** (0.690 g, 2.85 mmol) and carbene **1a** (1.0 g, 2.85 mmol) afforded **24e** (0.503 g, 44%) as a pale orange, viscous oil. According to general method B, the reaction between **7e** (0.10 g, 0.14 mmol) and carbene **1d** (0.20 g, 0.414 mmol) afforded **24e** (0.069 g, 42%): FT-IR (KBr) ν_{max} 1670, 1594, 1341 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.41 (t, J = 7.2 Hz, 3H, OCH_2CH_3), 4.30 (q, J = 7.2 Hz, 2H, OCH_2CH_3), 6.35 (s, 1H, H-4), 6.83−6.87 (m, 2H, H-11), 6.91−6.96 (m, 1H, H-13), 7.10−7.15 (m, 2H, H-12), 7.34−7.39 (m, 2H, H-16), 7.48−7.53 (m, 1H, H-17), 7.75−7.79 (m, 2H, H-15), 7.86−7.90 (m, 2H, H-6), 8.17−8.20 (m, 2H, H-7); ^{13}C NMR (125 MHz, $CDCl_3$) δ 15.6 (OCH_2CH_3), 68.6 (OCH_2CH_3), 120.3 (C-11), 122.4 (C-4), 123.6 (C-7), 125.3 (C-13), 127.9 (C-12), 128.6 (C-16), 128.7 (C-15), 130.2 (C-6), 134.2 (C-14), 134.5 (C-17), 140.6 (C-5), 146.9 (C-8), 148.3 (C-10), 154.3 (C-3), 163.8 (C-2), 196.3 (C-1); HRMS (EI+) calcd for $C_{24}H_{20}N_2O_4$ 400.1423, found (M+) 400.1475.

(2*Z*,3*Z*)-3-Ethoxy-4-(4-methoxyphenyl)-1-(4-methylphenyl)-2-(phenylimino)but-3-en-1-one (24f). According to general method A, the reaction between **7b** (0.270 g, 1.37 mmol) and carbene **1b** (0.500 g, 1.37 mmol) afforded **24f** (0.304 g, 60%) as a bright yellow solid: mp 90−91 °C. According to general method B, the reaction between **7b** (0.091 g, 0.403 mmol) and carbene **1e** (0.20 g, 0.403 mmol) afforded **24f** (0.085 g, 53%): FT-IR (KBr) ν_{max} 1668, 1603, 1254 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.42 (t, J = 7.2 Hz, 3H, OCH_2CH_3), 2.31 (s, 3H, CH_3), 3.79 (s, 3H, OCH_3), 4.21 (q, J = 7.2 Hz, 2H, OCH_2CH_3), 6.26 (s, 1H, H-4), 6.83−6.88 (m, 4H, H-7 and H-11), 6.90−6.91 (m, 1H, H-13), 7.07−7.14 (m, 4H, H-12 and H-16), 7.68−7.72 (m, 4H, H-6 and H-15); ^{13}C NMR (125 MHz, $CDCl_3$) δ 15.6 (OCH_2CH_3), 21.7 (CH_3), 55.2 (OCH_3), 67.6 (OCH_2CH_3), 113.8 (C-7), 120.4 (C-11), 124.4 (C-13), 126.8 (C-4), 126.8 (C-5), 128.4 (C-12), 129.4 (C-16), 129.5 (C-15), 131.6 (C-6), 132.2 (C-14), 145.4 (C-17), 149.1 (C-10), 150.0 (C-3), 159.9 (C-8), 164.9 (C-2), 196.4 (C-1); HRMS (EI+) calcd for $C_{26}H_{25}O_3N$ 399.1834, found (M+) 399.1833.

(2*Z*,3*Z*)-4-(4-Chlorophenyl)-3-ethoxy-1-(4-methylphenyl)-2-(phenylimino)but-3-en-1-one (24g). According to general method A, the reaction between **7d** (0.092 g, 0.39 mmol) and carbene **1b** (0.14 g, 0.39 mmol) afforded **24g** (0.075 g, 47%) as a bright yellow, viscous oil. According to general method B, the reaction between **7d** (0.231 g, 1.0 mmol) and carbene **1e** (0.50 g, 1.0 mmol) afforded **24g** (0.182 g, 45%): FT-IR (KBr) ν_{max} 1667, 1604, 1281 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.39 (t, J = 7.0 Hz, 3H, OCH_2CH_3), 2.31 (s, 3H, CH_3), 4.22 (q, J = 7.0 Hz, 2H, OCH_2CH_3), 6.26 (s, 1H, H-4), 6.83−6.87 (m, 2H, H-11), 6.88−6.93 (m, 1H, H-13), 7.00−7.11 (m, 2H, H-12), 7.12−7.15 (m, 2H, H-7), 7.26−7.30 (m, 2H, H-16), 7.65−7.70 (m, 4H, H-6 and H-15); ^{13}C NMR (125 MHz, $CDCl_3$) δ 15.5 (OCH_2CH_3), 21.7 (CH_3), 68.0 (OCH_2CH_3), 120.3 (C-11), 124.6 (C-4), 124.7 (C-13), 128.5 (C-7), 128.6 (C-16), 129.3 (C-12), 129.5 (C-15), 131.0 (C-6), 132.0 (C-14), 132.5 (C-5), 134.2 (C-8), 145.5 (C-17), 148.8 (C-10), 151.9 (C-3), 164.5 (C-2), 196.0 (C-1); HRMS (EI+) calcd for $C_{25}H_{22}ClO_2N$ 403.1339, found (M+) 403.1345.

(2*Z*,3*Z*)-3-Ethoxy-4-(4-nitrophenyl)-1-(4-methylphenyl)-2-(phenylimino)but-3-en-1-one (24h). According to general method A, the reaction between **7e** (0.198 g, 0.82 mol) and carbene **1b** (0.30 g, 0.82 mmol) afforded **24h** (0.136 g, 40%) as an orange solid: mp 100−101 °C; FT-IR (KBr) ν_{max} 1665, 1515, 1340 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.41 (t, J = 7.0 Hz, 3H, OCH_2CH_3), 2.33 (s, 3H, CH_3), 4.30 (q, J = 7.0 Hz, 2H, OCH_2CH_3), 6.33 (s, 1H, H-4), 6.86−6.88 (m, 2H, H-11), 6.94−6.96 (m, 1H, H-13), 7.12−7.17 (m, 4H, H-

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12 and H-16), 7.67−769 (m, 2H, H-15), 7.86−7.89 (m, 2H, H-6), 8.10−8.20 (m, 2H, H-7); ^{13}C NMR (125 MHz, $CDCl_3$) δ 15.5 (OCH_2CH_3), 21.8 (CH_3), 68.6 (OCH_2CH_3), 120.3 (C-11), 122.3 (C-4), 123.6 (C-7), 125.2 (C-13), 128.6 (C-16), 129.4 (C-15), 129.7 (C-12), 130.2 (C-6), 131.8 (C-14), 140.6 (C-5), 145.9 (C-17), 146.9 (C-8), 148.4 (C-10), 154.4 (C-3), 163.9 (C-2), 195.7 (C-1); HRMS (EI+) calcd for $C_{25}H_{22}N_2O_4$ 414.1580, found (M+) 414.1555.

(2*Z*,3*Z*)-3-Ethoxy-1-(4-methoxyphenyl)-4-phenyl-2-(phenylimino)but-3-en-1-one (24i). According to general method A, the reaction between **7a** (0.155 g, 0.78 mmol) and carbene **1c** (0.300 g, 0.78 mmol) afforded **24i** (0.167 g, 55%) as a bright yellow solid: mp 98−99 °C. According to general method B, the reaction between **7a** (0.192 g, 0.97 mmol) and carbene **1f** (0.500 g, 0.97 mmol) afforded **24i** (0.207 g, 55%): FT-IR (KBr) ν_{max} 1660, 1595, 1262 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.41 (t, J = 7.2 Hz, 3H, OCH_2CH_3), 3.79 (s, 3H, OCH_3), 4.21 (q, J = 7.2 Hz, 2H, OCH_2CH_3), 6.33 (s, 1H, H-4), 6.70−683 (m, 2H, H-16), 6.84−6.87 (m, 2H, H-11), 6.89−6.92 (m, 1H, H-13), 7.10−7.13 (m, 2H, H-12), 7.25−7.29 (m, 1H, H-8), 7.31−7.34 (m, 2H, H-7), 7.73−7.74 (m, 2H, H-6), 7.75−7.78 (m, 2H, H-15); ^{13}C NMR (125 MHz, $CDCl_3$) δ 15.5 (OCH_2CH_3), 55.4 (OCH_3), 67.9 (OCH_2CH_3), 114.0 (C-16), 120.3 (C-11), 124.5 (C-13), 126.4 (C-4), 127.7 (C-5), 128.3 (C-12), 128.4 (C-7), 128.6 (C-8), 129.9 (C-6), 131.7 (C-15), 134.1 (C-14), 149.0 (C-10), 151.6 (C-3), 164.3 (C-17), 164.9 (C-2), 194.8 (C-1); HRMS (EI+) calcd for $C_{25}H_{23}NO_3$ 385.1678, found (M+) 385.1695.

(2*Z*,3*Z*)-3-Ethoxy-1,4-bis(4-methoxyphenyl)-2-(phenylimino)but-3-en-1-one (24j). According to general method A, the reaction between **7b** (0.417 g, 1.84 mmol) and carbene **1c** (0.70 g, 1.84 mmol) afforded **24j** (0.344 g, 45%) as a bright yellow solid: mp 70−71 °C. According to general method B, the reaction between **7b** (0.155 g, 0.68 mmol) and carbene **1f** (0.350 g, 0.68 mmol) afforded **24j** (0.113 g, 40%): FT-IR (KBr) ν_{max} 1663, 1597, 1258 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.42 (t, J = 7.0 Hz, 3H, OCH_2CH_3), 3.77 (s, 3H, OCH_3), 3.79 (s, 3H, OCH_3), 4.21 (q, J = 7.0 Hz, 2H, OCH_2CH_3), 6.28 (s, 1H, H-4), 6.77−6.80 (m, 2H, H-7), 6.84−6.87 (m, 4H, H-11 and H-16), 6.87−6.89 (m, 1H, H-13), 7.00−7.11 (m, 2H, H-12), 7.68−7.72 (m, 2H, H-6), 7.75−7.77 (m 2H, H-15); ^{13}C NMR (125 MHz, $CDCl_3$) δ 15.5 (OCH_2CH_3), 55.0 (OCH_3), 55.3 (OCH_3), 67.4 (OCH_2CH_3), 113.7 (C-16), 113.9 (C-7), 120.2 (C-11), 124.2 (C-13), 126.5 (C-4), 126.7 (C-5), 127.7 (C-14), 128.3 (C-12), 131.5 (C-6), 131.8 (C-15), 149.1 (C-10), 149.9 (C-3), 159.8 (C-8), 164.2 (C-17), 164.8 (C-2), 194.8 (C-1); HRMS (EI+) calcd for $C_{26}H_{25}NO_4$ 415.1784, found (M+) 415.1989.

(2*Z*,3*Z*)-3-Ethoxy-4-(4-nitrophenyl)-1-(4-methoxyphenyl)-2-(phenylimino)but-3-en-1-one (24k). According to general method A, the reaction between **7e** (0.317 g, 1.31 mmol) and carbene **1c** (0.500 g, 1.31 mmol) afforded **24k** (0.226 g, 40%) as an orange, viscous oil: FT-IR (KBr) ν_{max} 1660, 1595, 1263 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.42 (t, J = 7.0 Hz, 3H, OCH_2CH_3), 3.81 (s, 3H, OCH_3), 4.30 (q, J = 7.0 Hz, 2H, OCH_2CH_3), 6.33 (s, 1H, H-4), 6.82−6.85 (m, 2H, H-16), 6.86−6.90 (m, 2H, H-11), 6.93−6.97 (m, 1H, H-13), 7.12−7.17 (m, 2H, H-12), 7.74−7.77 (m, 2H, H-15), 7.86−7.89 (m, 2H, H-6), 8.15−8.19 (m, 2H, H-7); ^{13}C NMR (125 MHz, $CDCl_3$) δ 15.6 (OCH_2CH_3), 55.4 (OCH_3), 68.5 (OCH_2CH_3), 114.2 (C-16), 120.2 (C-11), 122.4 (C-4), 123.5 (C-7), 125.1 (C-13), 127.3 (C-14), 128.6 (C-12), 130.2 (C-6), 131.7 (C-15), 141.2 (C-5), 147.1 (C-8), 148.0 (C-10), 154.2 (C-3), 163.9 (C-2), 164.8 (C-17), 194.3 (C-1); HRMS (EI+) calcd for $C_{25}H_{22}N_2O_5$ 430.1529, found (M+) 430.1649.

(2*Z*,3*Z*)-1-Cyclohexenyl-3-ethoxy-4-phenyl-2-(phenylimino)-but-3-en-1-one (27a). According to general method A, the reaction between **7a** (0.220 g, 1.12 mmol) and carbene **23a** (0.400 g, 1.12 mmol) afforded **27a** (0.182 g, 45%) as a red, viscous oil. According to general method B, the reaction between **7a** (0.121 g, 0.617 mmol) and carbene **23b** (0.300 g, 0.617 mmol) afforded **27a** (0.077 g, 35%); FT-IR (KBr) ν_{max} 1656, 1596, 1224 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.37−1.42 (m, 7H, OCH_2CH_3, H-17 and H-18), 1.58−1.73 (m, 2H, H-19), 2.04−2.25 (m, 2H, H-16), 4.12−4.20 (m, 2H, OCH_2CH_3), 6.30 (s, 1H, H-4), 6.72−6.75 (m, 1H, H-15), 6.76−6.79 (m, 2H, H-11), 7.01−7.04 (m, 1H, H-13), 7.20−7.24 (m, 2H, H-12), 7.27−731 (m, 1H, H-8), 7.34−7.37 (m, 2H, H-7), 7.77−7.80 (m, 2H, H-6); ^{13}C NMR (125 MHz, $CDCl_3$) δ 15.6 (OCH_2CH_3), 21.3 (C-17), 21.3 (C-18), 21.8 (C-19), 26.2 (C-16), 67.8 (OCH_2CH_3), 120.1 (C-11), 124.3 (C-13), 126.0 (C-4), 128.4 (C-12), 128.5 (C-7), 128.6 (C-8), 129.9 (C-6), 134.2 (C-5), 138.5 (C-14), 147.6 (C-15), 149.9 (C-10), 151.8 (C-3), 165.5 (C-2), 197.7 (C-1); HRMS (EI+) calcd for $C_{24}H_{25}NO_2$ 359.1885, found (M+) 359.1913.

(2*Z*,3*Z*)-1-Cyclohexenyl-3-ethoxy-4-(4-methoxyphenyl)-2-(phenylimino)but-3-en-1-one (27b). According to general method A, the reaction between **7b** (0.320 g, 1.41 mmol) and carbene **23a** (0.500 g, 1.41 mmol) afforded **27b** (0.291 g, 53%) as a bright yellow, viscous oil. According to general method B, the reaction between **7b** (0.140 g, 0.617 mmol) and carbene **23b** (0.300 g, 0.617 mmol) afforded **27b** (0.108 g, 45%): FT-IR (KBr) ν_{max} 1655, 1584, 1253 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.36−1.41 (m, 7H, OCH_2CH_3, H-17 and H-18), 1.54−1.80 (m, 2H, H-19), 1.90−2.03 (m, 2H, H-16), 3.81 (s, 3H, OCH_3), 4.17−4.22 (m, 2H, OCH_2CH_3), 6.26 (s, 1H, H-4), 6.73−6.74 (m, 1H, H-15), 6.77−6.78 (m, 2H, H-11), 6.87−6.90 (m, 2H, H-7), 6.98−7.02 (m, 1H, H-13), 7.19−7.22 (m, 2H, H-12), 7.74−7.77 (m, 2H, H-6); ^{13}C NMR (125 MHz, $CDCl_3$) δ 15.5 (OCH_2CH_3), 21.2 (C-17), 21.3 (C-18), 21.7 (C-19), 26.0 (C-16), 55.1 (OCH_3), 67.3 (OCH_2CH_3), 113.7 (C-7), 120.0 (C-11), 124.0 (C-13), 126.1 (C-4), 126.9 (C-5), 128.3 (C-12), 131.4 (C-6), 138.4 (C-14), 147.3 (C-15), 149.9 (C-10), 150.1 (C-3), 159.7 (C-8), 165.5 (C-2), 197.7 (C-1); HRMS (EI+) calcd for $C_{25}H_{27}NO_3$ 389.1991, found (M+) 389.1988.

(2*Z*,3*Z*)-4-(4-Chlorophenyl)-1-cyclohexenyl-3-ethoxy-2-(phenylimino)but-3-en-1-one (27c). According to general method B, the reaction between **7d** (0.100 g, 0.43 mmol) and carbene **23b** (0.210 g, 0.43 mmol) afforded **27c** (0.063 g, 37%) as a red solid: mp 40−41 °C; FT-IR (KBr) ν_{max} 1656, 1586, 1382 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.36−1.41 (m, 7H, OCH_2CH_3, H-17 and H-18), 1.60−1.80 (m, 2H, H-19), 2.00−2.15 (m, 2H, H-16), 4.10−4.20 (m, 2H, OCH_2CH_3), 6.23 (s, 1H, H-4), 6.70−6.73 (m, 1H, H-15), 6.77−6.80 (m, 2H, H-11), 7.01−7.06 (m, 1H, H-13), 7.20−7.26 (m, 2H, H-12), 7.31−7.35 (m, 2H, H-7), 7.71−7.75 (m, 2H, H-6); ^{13}C NMR (75 MHz, $CDCl_3$) δ 15.6 (OCH_2CH_3), 21.2 (C-17), 21.3 (C-18), 21.7 (C-19), 26.2 (C-16), 67.9 (OCH_2CH_3), 120.0 (C-11), 124.5 (C-4), 124.5 (C-13), 128.5 (C-12), 128.6 (C-7), 130.0 (C-6), 132.6 (C-5), 134.1 (C-8), 138.4 (C-14), 147.9 (C-15), 149.7 (C-10), 152.1 (C-3), 165.1 (C-2), 197.6 (C-1); HRMS (EI+) calcd for $C_{24}H_{24}ClNO_2$ 393.1496, found (M+) 393.1491.

(2*Z*,3*Z*)-1-Cyclohexenyl-3-ethoxy-4-(4-nitrophenyl)-2-(phenylimino)but-3-en-1-one (27d). According to general method A, the reaction between **7e** (0.341 g, 1.41 mmol) and carbene **23a** (0.50 g, 1.41 mmol) afforded **27d** (0.228 g, 40%) as a red solid: mp 41−42 °C. According to general method B, the reaction between **7e** (0.247 g, 1.02 mmol) and carbene **23b** (0.500 g, 0.1.02 mmol) afforded **27b** (0.166 g, 40%); FT-IR (KBr) ν_{max} 1598, 1520, 1343 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.39−1.42 (m, 7H, OCH_2CH_3, H-17 and H-18), 1.60−1.79 (m, 2H, H-19), 2.10−2.17 (m, 2H, H-16), 4.25 (q, J = 7.0 Hz, 2H, OCH_2CH_3), 6.31 (s, 1H, H-4), 6.70−6.73 (m, 1H, H-15), 6.77−6.80 (m, 2H, H-11), 7.05−7.09 (m, 1H, H-13), 7.22−7.28 (m, 2H, H-12), 7.91−7.95 (m, 2H, H-6), 8.18−8.22 (m, 2H, H-7); ^{13}C NMR (125 MHz, $CDCl_3$) δ 15.6 (OCH_2CH_3), 21.2 (C-17), 21.3 (C-18), 21.8 (C-19), 26.2 (C-16), 68.4 (OCH_2CH_3), 119.9 (C-11), 121.9 (C-4), 123.6 (C-7), 124.9 (C-13), 128.6 (C-12), 130.1 (C-6), 138.3 (C-14), 140.7 (C-5), 146.7 (C-8), 148.0 (C-15), 149.3 (C-10), 154.6 (C-3), 164.5 (C-2), 197.1 (C-1); HRMS (EI+) calcd for $C_{24}H_{24}N_2O_4$ 404.1736, found (M+) 404.2063.

(2*Z*,3*Z*)-1-Cyclohexenyl-3-ethoxy-4-(3-nitrophenyl)-2-(phenylimino)but-3-en-1-one (27e). According to general method A, the reaction between **7f** (0.34 g, 1.41 mmol) and carbene **23a** (0.50 g, 1.41 mmol) afforded **27e** (0.21 g, 36%) as an orange, viscous oil; FT-IR (KBr) ν_{max} 1575, 1529, 1350 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.42−1.46 (m, 7H, OCH_2CH_3, H-19 and H-20), 1.60−1.80 (m, 2H, H-21), 2.10−2.17 (m, 2H, H-18), 4.20−4.26 (m, 2H, OCH_2CH_3), 6.30 (s, 1H, H-4), 6.71−6.73 (m, 1H, H-17), 6.77−6.80 (m, 2H, H-13), 7.05−7.09 (m, 1H, H-15), 7.22−7.28 (m, 2H, H-14), 7.51−7.54 (m, 1H, H-9), 8.03−8.05 (m, 1H, H-10), 8.12−8.14 (m, 1H, H-8), 875−8.76 (m, 1H, H-6); ^{13}C NMR (125 MHz, $CDCl_3$) δ

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15.6 (OCH_2CH_3), 21.2 (C-19), 21.3 (C-20), 21.8 (C-21), 26.2 (C-18), 68.3 (OCH_2CH_3), 119.9 (C-13), 121.3 (C-4), 122.7 (C-8), 124.2 (C-6), 124.8 (C-15), 128.6 (C-14), 129.2 (C-9), 135.3 (C-10), 135.8 (C-16), 138.3 (C-5), 148.2 (C-7), 148.2 (C-17), 149.4 (C-12), 153.7 (C-3), 164.5 (C-2), 197.3 (C-1); HRMS (EI+) calcd for $C_{24}H_{24}N_2O_4$ 404.1736, found (M+) 404.1728.

Derivatization of Compound 24b. A solution of 2,4-dinitrophenylhydrazine (1.03 mmol, 0.203 g) in 5 mL of ethanol was cautiously added to **24b** (1.03 mmol, 0.40 g) at room temperature (4 h), until the formation of a red solid. At this point, the solvent was removed under vacuum, and the crude product was purified by column chromatography over silica gel using *n*-hexane/EtOAc (80:20), affording the derivative products as orange-red solids: **34** (30%, 8.34 mg, mp 155−156 °C) and **35** (38%, 0.142 mg, mp 152−153 °C).

(2*Z*,3*Z*)-3-Ethoxy-2-[2-(2,4-dinitrophenyl)hydrazono]-4-(4-methoxyphenyl)-1-phenylbut-3-en-1-one (34). FT-IR (KBr) ν_{max} 3263, 1665, 1595, 1335 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.48 (t, J = 7.0 Hz, 3H, OCH_2CH_3), 3.83 (s, 3H, OCH_3), 4.27 (q, J = 7.0 Hz, 2H, OCH_2CH_3), 6.82 (s, 1H, H-4), 6.87−6.89 (m, 2H, H-7), 726−748 (m, 3H, H-18 and H-20), 7.74−7.79 (m, 4H, H-6 and H-19), 8.18−8.20 (m, 1H, H-16), 8.39−8.42 (m, 1H, H-15), 9.12−9.13 (m, 1H, H-13), 11.76 (sa, 1H, N−H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 15.8 (OCH_2CH_3), 55.4 (OCH_3), 68.2 (OCH_2CH_3), 114.3 (C-7), 116.5 (C-16), 123.3 (C-13), 125.3 (C-5), 126.9 (C-19), 129.0 (C-18), 130.0 (C-15), 130.4 (C-12), 130.8 (C-20), 133.1 (C-6), 133.6 (C-17), 134.0 (C-4), 138.9 (C-14), 144.7 (C-11), 149.9 (C-3), 152.5 (C-2), 161.8 (C-8), 191.7 (C-1); EM HRMS (EI+) calcd for $C_{25}H_{22}N_4O_7$ 490.1488, found (M+) 490.1531.

(1*Z*,3*Z*)-3-Ethoxy-1-[2-(2,4-dinitrophenyl)hydrazono]-4-(4-methoxyphenyl)-1-phenylbut-3-en-1-one (35). FT-IR (KBr) ν_{max} 3444, 1613, 1506, 1315 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.45 (t, J = 7.0 Hz, 3H, OCH_2CH_3), 3.84 (s, 3H, OCH_3), 3 0.98 (q, J = 7.0 Hz, 2H, OCH_2CH_3), 6.25 (s, 1H, H-4), 6.90−6.92 (m, 2H, H-7), 752−755 (m, 2H, H-19), 7.65−7.67 (m, 1H, H-20), 7.73−7.74 (m, 2H, H-6), 7.74−7.79 (m, 1H, H-16), 8.01−8.03 (m, 2H, H-18), 8.27−8.29 (m, 1H, H-15), 9.15−9.16 (m, 1H, H-13), 12.9 (sa, 1H, N−H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.9 (OCH_2CH_3), 55.3 (OCH_3), 68.2 (OCH_2CH_3), 114.3 (C-7), 116.5 (C-16), 123.1 (C-13), 124.6, (C-4), 125.9 (C-5), 128.4 (C-19), 129.9 (C-15), 130.4 (C-18), 131.2 (C-12), 131.6 (C-6), 133.5 (C-20), 136.8 (C-17), 139.9 (C-14), 144.1 (C-11), 144.4 (C-3), 146.0 (C-1), 160.1 (C-8), 191.5 (C-2); HRMS (EI+) calcd for $C_{25}H_{22}N_4O_7$ 490.1488, found (M+) 490.1475.

Single-Crystal X-ray Crystallography. Single crystals were obtained by slow evaporation of concentrated solutions of **24i** (*n*-hexane, bright yellow solid) and **34** (*n*-hexane/AcOEt, orange-red crystals). These were mounted on glass fibers. Crystallographic measurements were performed on an Oxford Diffraction Xcalibur S single-crystal X-ray difractometer using Mo KR radiation (graphite crystal monochromator, λ = 71073 Å) at room temperature. Three standard reflections, which were monitored periodically, showed no change during data collection. Unit cell parameters were obtained from least-squares refinement of 26 reflections in the range $2° < 2\theta < 20°$. Intensities were corrected for Lorentz and polarization effects. No absorption correction was applied. Anisotropic temperature factors were introduced for all non-hydrogen atoms. Hydrogen atoms were placed in idealized positions, and their atomic coordinates refined. Structures were solved using the SHELXTL,[17] SHELX97,[18] or SIR92[19] program as implemented in the WinGX suite[20] and refined using SHELXTL or SHELX97 within WinGX, on a personal computer. In all cases ORTEP and packing diagrams were made with PLATON and ORTEP-3.[21]

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Figures giving ^1H and ^{13}C NMR data for **24a−k**, **27a−e**, **34**, and **35**, including images of HMQC, HMBC, and NOE experiments, and IR and mass spectra for most of the products. Tables of crystal data, atomic coordinates, bond lengths and angles, and anisotropic parameters for **24i** and **34**. Crystallographic information for **24i** and **34** in cif format, including X-ray diffraction data, atomic coordinates, thermal parameters, and complete bond distances and angles. This material is available free of charge via the Internet at http://pubs.acs.org and from the Cambridge Crystallographic Data Centre (fax: +44-1223-336-003; e-mail: deposit@ccdc.cam.ac.uk; or http://www.ccdc.cam.ac.uk) as supplementary publication nos. CCDC 936758 (**24i**) and CCDC 936889 (**34**).

■ AUTHOR INFORMATION

Notes

The authors declare no competing financial interest.

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