Expeditious Synthesis of 2,3,6-Trisubstituted 2*H*-1,3-Oxazin-4(3*H*)-ones via the Tertiary Amine-Induced Reaction of 2-Diazo-3-oxoalkanals and Imines Under Mild Conditions

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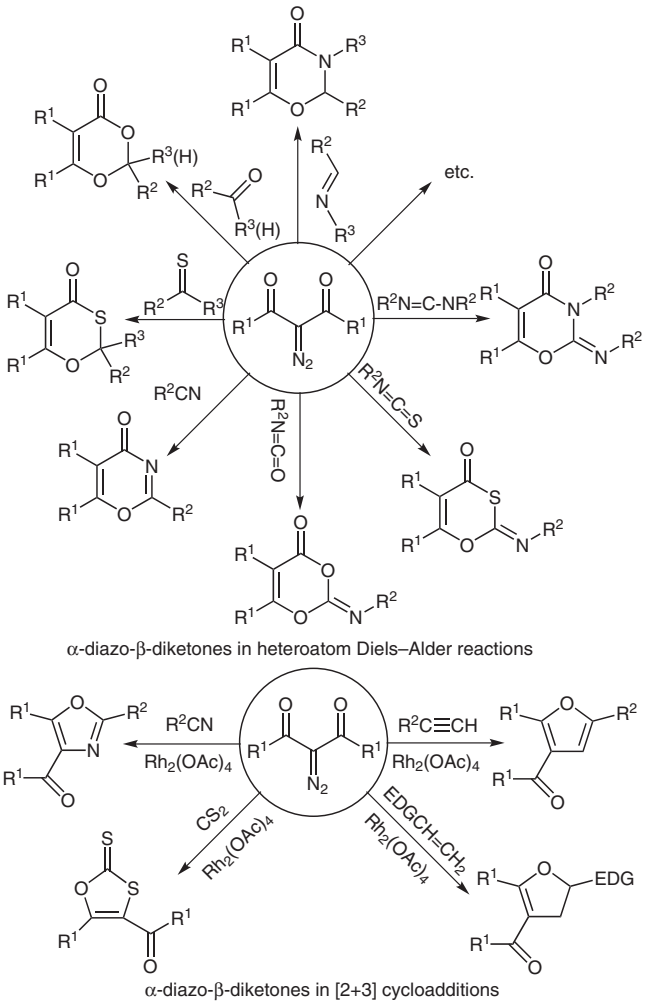
Abstract: A series of 2,3,6-trisubstituted 2*H*-1,3-oxazin-4(3*H*)-one derivatives were conveniently synthesized in satisfactory to good yields by the reaction of imines with 2-diazo-3-oxoalkanals in the presence of a catalytic amount of a tertiary amine during several seconds under mild condition. Different bases and α-diazo-β-dicarbonyl compounds were also evaluated and a reaction mechanism is proposed. Compared with the corresponding thermal- and photo-induced reactions, the current method is a metal-free, mild, highly regioselective, and more efficient approach for the synthesis of 2*H*-1,3-oxazin-4(3*H*)-one derivatives.

Key words: acylketene, amine-induced reaction, cycloaddition, 2-diazo-3-oxoalkanal, Diels–Alder reaction, imine, oxazinone

α-Diazo-β-dicarbonyl compounds (α-diazo-β-diketones and α-diazo-β-oxoalkanals) are important synthetic intermediates in organic chemistry.[1] They have been widely used in the synthesis of heterocyclic compounds via cycloadditions.[1] α-Diazo-β-diketones undergo heteroatom Diels–Alder reactions with unsaturated compounds, such as imines,[2] aldehydes and ketones,[3] thiones,[4] nitriles,[5] isocyanates,[2a] isothiocyanates,[2a,6] carbodiimides,[2a] etc., respectively, to afford 2*H*-1,3-oxazin-4-ones, 4*H*-1,3-dioxin-4-ones, 4*H*-1,3-oxathiin-4-ones, 1,3-oxazin-4-ones, 2*H*-1,3-oxazine-2,4(3*H*)-diones, 2-thioxo-2*H*-1,3-oxazin-4(3*H*)-ones, 2-alkylimino-2*H*-1,3-oxazin-4(3*H*)-ones, and so on (Scheme 1). They undergo [2+3] cycloadditions in the presence of transition-metal catalysts, generally dirhodium tetraacetate, with nitriles,[7] carbon disulfide,[8] electron-rich olefins,[5,9] and alkynes[10] to produce 4-acyloxazoles, 1,3-oxathiole-2-thiones, 3-acyl-4,5-dihydrofurans, and 3-acylfuran derivatives, respectively (Scheme 1). However, α-diazo-β-oxoalkanals have been seldom applied in organic synthesis. They were condensed with primary amines, ammonium, hydroxylamine, and semicarbazide to yield the corresponding 1-substituted 4-acyl-1*H*-1,2,3-triazoles in moderate to good yields under acidic conditions.[11] Decomposition of diazomalonaldehyde under catalysis of dirhodium tetraacetate with alkyl vinyl ether leads to 2-alkoxy-2,3-dihydro-4-pyrones, which on exposure to an acid give 4-pyrones;[12] and affords 2-substituted 1,3-oxazole-4-carboxaldehydes via 1,3-dipolar cycloaddition with nitriles.[13] Diazomalonaldehyde reacts with trimethylsilyl vinyl ethers under the catalysis of copper sulfate to give 4-pyrones as well.[14]

1,3-Oxazinone derivatives are important biologically active compounds, showing antibacterial,[15] anti-inflammatory,[16] antinociceptive activities,[17] etc. 2*H*-1,3-Oxazin-4(3*H*)-one derivatives have been generally prepared by thermal heteroatom Diels–Alder reaction of imines with acylketenes,[1] which can be generated mainly from α-diazo-β-dicarbonyl compounds, including α-diazo-β-diketones and α-diazo-β-oxoalkanals, 1,3-dioxinones, furan-



Scheme 1 Application of α-diazo-β-diketones in synthesis of heterocycles via cycloadditions

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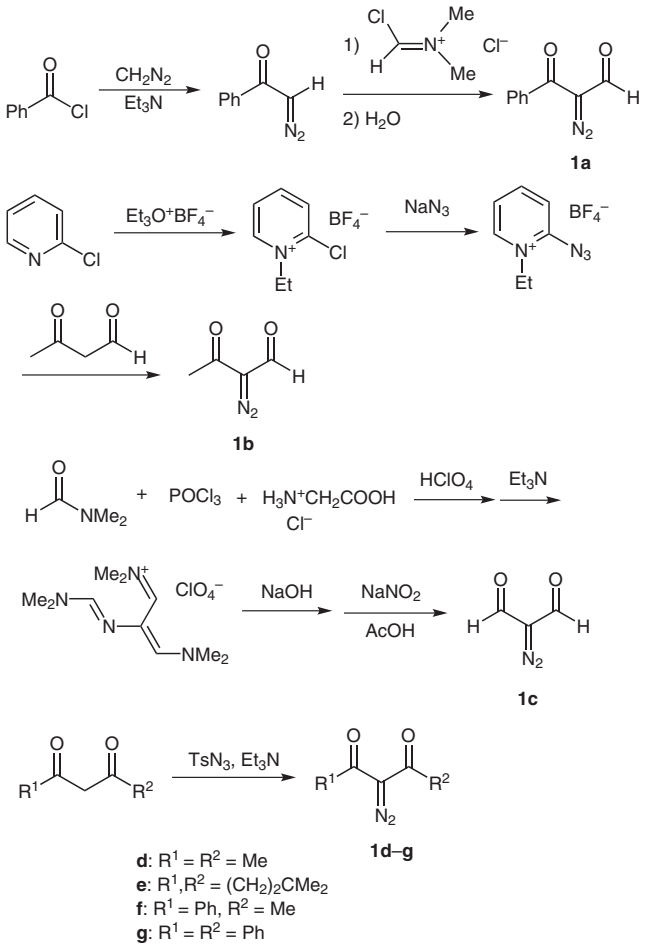
2,3-diones, as well from carboxylic acid derivatives and alkynol derivatives.[1] Recently, we found that 2-diazo-3-oxoalkanals undergo Wolff rearrangement to generate acylketenes, which react with imines to afford 2*H*-1,3-oxazin-4(3*H*)-ones in satisfactory yields under photoirradiation conditions.[18] The cycloaddition of α-diazo-β-diketones and/or 2-diazo-3-oxoalkanals with imines occurs at high temperature under thermal conditions[1,2] or in low yields and slow reaction rates under photoirradiation.[18] It is desired to develop an efficient approach to conduct the reaction. To improve the synthetic efficiency, a search for catalysts was done to increase the reaction rates under mild reaction conditions. It was reported that a mere trace of amine can cause diazomalonaldehyde to liberate nitrogen to generate a polymer composed of formylketene.[19] Thus, it was assumed that organic bases would attack the positive part of the diazo group to promote the release of nitrogen and further Wolff rearrangement. Therefore, the efficiency of organic bases as catalysts was evaluated in reactions of representative α-diazo-β-diketones and 2-diazo-3-oxoalkanals with imines. Herein, we present our results on the tertiary amine-catalyzed reaction of 2-diazo-3-oxoalkanals and imines to synthesize 2*H*-1,3-oxazin-4(3*H*)-ones expeditiously.

Representative 2-diazo-3-oxoalkanals and α-diazo-β-diketones can be prepared conveniently from the corresponding 3-oxoalkanals and β-diketones, or from α-diazo ketones. 2-Diazo-3-oxo-3-phenylpropanal (**1a**) was prepared from 2-diazoacetophenone and the Vilsmeier–Haack reagent,[11a] which was synthesized from DMF and oxalyl chloride.[20] 2-Diazo-3-oxobutanal (**1b**) was prepared from 3-oxobutanal via the diazo transformation with 2-azido-1-ethylpyridinium tetrafluoroborate.[21] Diazomalonaldehyde (**1c**) was obtained via hydrolysis and diazotization of *N*,*N*-dimethyl-*N*-[2-(dimethylaminomethylene)amino-3-dimethylamino]prop-2-enylideneammonium perchlorate,[11a] which was prepared from DMF, phosphorus oxychloride, and glycine hydrochloride in the presence of perchloric acid[22] (Scheme 2). α-Diazo-β-diketones **1d–f** were prepared from the corresponding β-diketones via the diazo transformation with tosyl azide[2f] (Scheme 2).

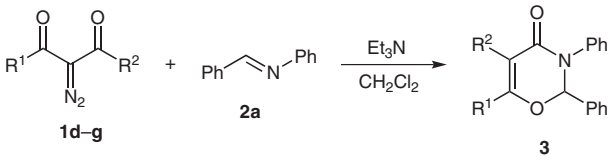
The reactivity of different α-diazo-β-dicarbonyl compounds **1** with benzylideneaniline (**2a**) was initially evaluated under the catalysis of triethylamine (Table 1). The results indicate that 2-diazo-3-oxoalkanals **1a**,**b** and diazomalonaldehyde (**1c**) are exceptionally reactive. After a drop of triethylamine was added to a mixture of an α-diazo-β-keto aldehyde and an imine, the α-diazo-β-keto aldehyde released nitrogen rapidly. The Wolff rearrangement and cycloaddition with the imine, for 2-diazo-3-oxo-3-phenylpropanal (**1a**), took place during 1–2 second(s), giving rise to the desired product 2,3,6-triphenyl-2*H*-1,3-oxazin-4(3*H*)-one (**3a**) in a satisfactory yield. Although the reaction can be conducted under solvent-free conditions, to mix two reactants completely and to perform the reaction smoothly, an α-diazo-β-keto aldehyde and an imine were dissolved in a small amount of dichloromethane before addition of a tertiary amine. 2-Diazo-3-oxobutanal (**1b**) and diazomalonaldehyde (**1c**) produced complex products possibly due to their high reactivity. However, α-diazo-β-diketones **1d–g** are inert and do not participate in any reaction under the same reaction conditions.



Scheme 2 Preparation of α-diazo-β-dicarbonyl compounds **1**

Secondly, the reaction of 2-diazo-3-oxo-3-phenylpropanal (**1a**) and *N*-benzylideneaniline (**2a**) was selected as a model reaction to evaluate the catalytic efficiency of different bases (Table 2, entries 1–8). The results indicate that all aliphatic tertiary amines can catalyze the reaction, but the yield of the desired product decreases obviously with increasing steric hindrance of bases. Under the catalysis of secondary amine piperidine, only trace of the product was obtained. However, aromatic tertiary amine *N*,*N*-dimethylaniline and pyridine, as well triphenylphosphine, cannot catalyze the reaction. In the case of inorganic bases, both weak base potassium carbonate and strong base sodium hydride are not efficient catalysts for the reaction. To further verify the effect of organic bases on the reaction, the reaction of 2-diazo-3-oxo-3-phenylpropanal (**1a**) and *N*-benzylidenebenzylamine (**2b**) was conducted with different tertiary amines as catalysts (Table 2, entries 9–12). The results show that the yield decreases with increasing steric hindrance from triethylamine to tributyl-

Table 1 Evaluation of Different α-Diazo-β-dicarbonyl Compounds **1** in the Reaction with *N*-Benzylideneaniline (**2a**) under the Catalysis of Triethylamine



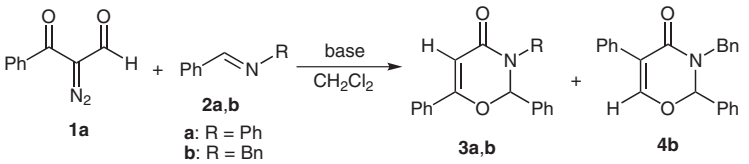
Entry	Diazo compound **1**			Time	Yield (%)
	1	R^1	R^2		
1	**1a**	Ph	H	2 s	54
2	**1b**	Me	H	2 s	complex products
3	**1c**	H	H	2 s	complex products
4	**1d**	Me	Me	24 h	no reaction
5	**1e**	$CH_2CMe_2CH_2$		24 h	no reaction
6	**1f**	Ph	Me	24 h	no reaction
7	**1g**	Ph	Ph	24 h	no reaction

amine to ethyldiisopropylamine (DIPEA) although the yield is higher than that in the reaction with *N*-benzylideneaniline (**2a**). Triphenylphosphine cannot catalyze the reaction either. However, besides the 2,3,6-trisubstituted 2*H*-1,3-oxazin-4(3*H*)-one (**3b**), its regioisomer, the 2,3,5-trisubstituted 2*H*-1,3-oxazin-4(3*H*)-one (**4b**), was also obtained in a low yield under the catalysis of triethyl- and tributylamines.

After evaluation of different α-diazo-β-dicarbonyl compounds and bases, it was found that 2-diazo-3-oxo-3-phenylpropanal (**1a**) is a suitable precursor of heteroatom-containing diene and triethylamine is the more efficient catalyst for the reaction. The reaction was further extended to various linear and cyclic imines **2a–i** (Table 3). For each of imines, the desired products were obtained in satisfactory to good yields. For imine **2g** with a chiral carbon atom, a pair of diastereomeric products were generated in a ratio of 6:1 of *anti*-isomer/*syn*-isomer on the basis of ^{1}H NMR analysis (Table 3, entry 7). In the reaction with imine **2i**, the desired Diels–Alder product **3i** was obtained, accompanied with benzoyl *trans*-β-lactam product **5i**, which was generated from imine **2i** and benzoylketene, produced from diazo compound **1a**, via the Staudinger reaction through the imine attack to the ketene from its *exo*-side and subsequent conrotatory ring closure.[23] Although diazomalonaldehyde did not produce the desired product with linear imine **2a**, it did with cyclic imine **2i** in a low yield of 26% (Table 3, entry 10).

To compare the current method with the thermal and photo reactions, we carried out the reaction of 2-diazo-3-oxo-3-phenylpropanal (**1a**) and imine **2b** under thermal and photo conditions, respectively (Scheme 3). The results indicate that the triethylamine-catalyzed reaction shows advantages not only in the reaction rate, but also in yield and regioselectivity, revealing that benzoyl formyl carbene generated from 2-diazo-3-oxo-3-phenylpropanal (**1a**) prefers a hydrogen shift to give rise to benzoylketene under triethylamine-catalyzed and thermal conditions, whereas

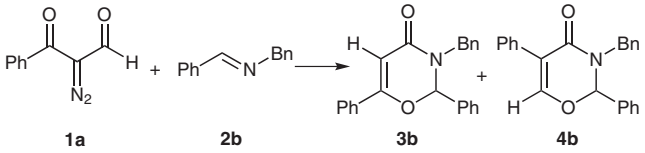
Table 2 Evaluation of the Catalytic Efficiency of Different Bases in the Reaction of 2-Diazo-3-oxo-3-phenylpropanal (**1a**) with Imines **2a** and **2b**



Entry	Imine **2**	Base	Time	Yield (%)
1	**2a**	Et_3N	2 s	54
2	**2a**	Bu_3N	10 s	36
3	**2a**	piperidine	2 s	trace
4	**2a**	$PhNMe_2$	24 h	no reaction
5	**2a**	pyridine	24 h	no reaction
6	**2a**	Ph_3P	24 h	no reaction
7	**2a**	K_2CO_3	24 h	no reaction
8	**2a**	NaH	24 h	no reaction
9	**2b**	Et_3N	2 s	92 (**3/4** = 93:7)
10	**2b**	Bu_3N	10 s	83 (**3/4** = 88:12)
11	**2b**	DIPEA	15 s	54 (**3/4** = 100:0)
12	**2b**	Ph_3P	24 h	no reaction

it does not show any selectivity under photoirradiation conditions.

As for the reaction mechanism, it is proposed that a tertiary amine attacks the middle nitrogen atom of the diazo group of 2-diazo-3-oxo-3-phenylpropanal (**1a**) or diazomalonaldehyde (**1c**) to generate a zwitterionic intermediate, which further undergoes an electron transfer to form a diacylcarbene through loss of nitrogen and the amine. The diacylcarbene undergoes the Wolff rearrangement to produce the acylketene, which undergoes a heteroatom Diels–Alder cycloaddition to yield the desired 2,3,6-trisubstituted 2*H*-1,3-oxazin-4(3*H*)-one **3** (Scheme 4).



thermal reaction: in refluxing toluene, 1 h, 76% yield, **3b**/**4b** = 86:14
photo reaction: UV light, in CH_2Cl_2, 2 h, 78% yield, **3b**/**4b** = 50:50
Et_3N-catalyzed reaction: in CH_2Cl_2, 2 s, 92% yield, **3b**/**4b** = 93:17

Scheme 3 Comparison of thermal, photo, and Et_3N-catalyzed reactions of diazo compound **1a** and imine **2b**

Table 3 Reaction of 2-Diazo-3-oxo-3-phenylpropanal (**1a**) and Diazomalonaldehyde (**1c**) with Various Imines **2**

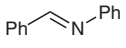
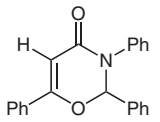
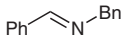
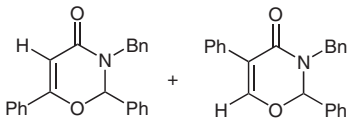
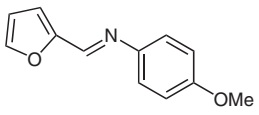
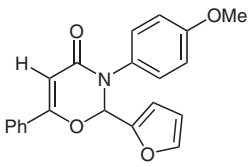
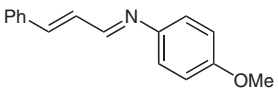
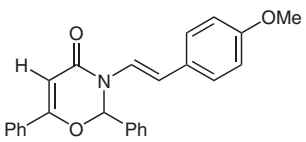
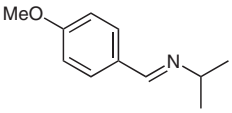
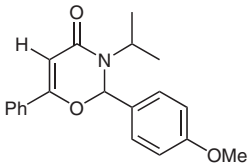
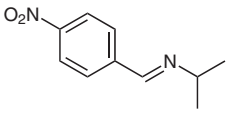
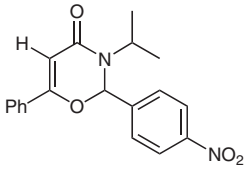
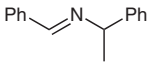
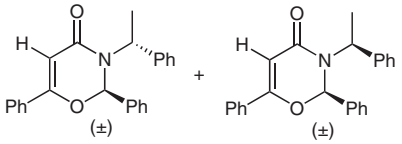
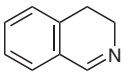
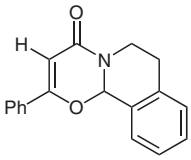
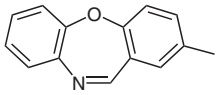
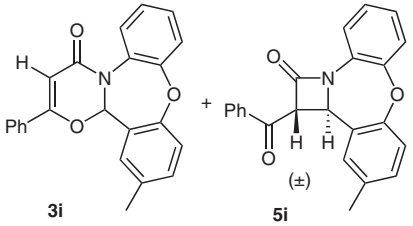
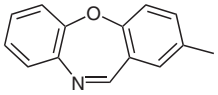
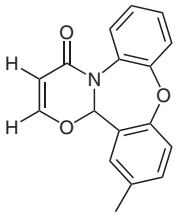
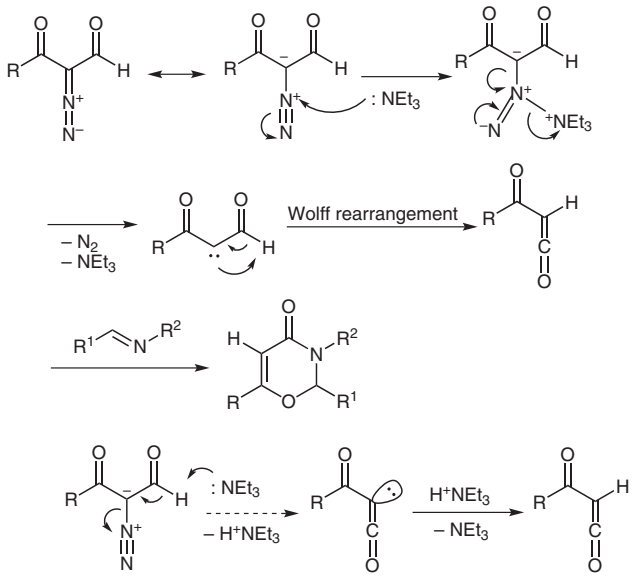
Entry	Diazoacetate **1**	Imine **2**	β-Lactam **3**	Yield (%)[a]
1	**1a**	 **2a**	 **3a**	54
2	**1a**	 **2b**	 **3b** + **4b**	86 (**4b**: 6%)
3	**1a**	 **2c**	 **3c**	68
4	**1a**	 **2d**	 **3d**	47
5	**1a**	 **2e**	 **3e**	78
6	**1a**	 **2f**	 **3f**	85

Table 3 Reaction of 2-Diazo-3-oxo-3-phenylpropanal (**1a**) and Diazomalonaldehyde (**1c**) with Various Imines **2** (continued)

Entry	Diazoacetate **1**	Imine **2**	β-Lactam **3**	Yield (%)[a]
7	**1a**	 **2g**	 *anti*-**3g** + *syn*-**3g**	90 (*anti*/*syn* = 6:1)[b]
8	**1a**	 **2h**	 **3h**	42
9	**1a**	 **2i**	 **3i** + **5i**	35 (**5i**: 6%)
10	**1c**	 **2i**	 **3j**	26

[a] Yields of isolated products (sum of *cis*- and *trans*-product yields).
[b] Ratio was determined via ^{1}H NMR analysis of the reaction mixture.



Scheme 4 Proposed mechanism for reaction of diazo compounds **1** and imines **2** under the catalysis of triethylamine

Despite α-diazo-β-keto aldehydes are active and α-diazo-β-diketones are inert in the presence of tertiary amines, it seems that the hydrogen atom in the formyl group plays an important role in the reaction. We initially assumed that the amine first abstracts the hydrogen atom to generate a 2-diazo-3-oxoacyl anion intermediate, which induces the Wolff rearrangement to produce an acylketene anion. The anion abstracts a proton from the generated ammonium in the reaction system to form the acylketene, which undergoes Diels–Alder reaction to produce the desired product. However, α-diazo-β-keto aldehydes are inert to the strong base sodium hydride with weak nucleophilicity, revealing that bases, especially tertiary amines, cannot abstract the hydrogen atom of the formyl group. On the other hand, less steric tertiary amines (favorable nucleophiles) show higher activity than more steric ones (unfavorable nucleophiles), supporting the proposed mechanism through the amine attack to the diazo group.

In summary, a series of 2,3,6-trisubstituted 2*H*-1,3-oxazin-4(3*H*)-one derivatives were expeditiously synthesized in satisfactory to good yields from the reaction of imines and 2-diazo-3-oxoalkanals under the catalysis of

tertiary amine during several seconds under mild condition. Different bases and α-diazo-β-dicarbonyl compounds were also evaluated, indicating that less steric tertiary amines are efficient catalysts and 2-diazo-3-oxoalkanals are suitable acylketene precursors. A reaction mechanism was proposed in which tertiary amines induce Wolff rearrangement of 2-diazo-3-oxoalkanals to generate acylketenes, which further undergo a heteroatom Diels–Alder reaction to yield 2,3,6-trisubstituted 2*H*-1,3-oxazin-3(4*H*)-ones. Compared with the corresponding thermal- and photo-induced reactions, the current method is a metal-free, mild, highly regioselective, and more efficient approach to synthesis of 2*H*-1,3-oxazin-4(3*H*)-one derivatives.

Melting points were measured on a Yanaco MP-500 melting point apparatus and are uncorrected. ^{1}H NMR and ^{13}C NMR spectra were recorded on a Varian Mercury Plus 300 (300 MHz) or Bruker AV 400 (400 MHz) spectrometer in $CDCl_3$ with TMS as an internal standard. HRMS data were carried out on a Bruker APEX IV Fourier transform ion cyclotron resonance mass spectrometer. IR spectra were determined on a Nicolet 5700 FT-IR spectrometer. All α-diazo-β-dicarbonyl compounds were prepared according to the reported methods,[2f,11a,20–22] and their analytical data are identical to those earlier reported in literatures.[2f,11a,20–22] Column chromatography was carried out on Haiyang silica gel (200–300 mesh) (Qingdao, China). CH_2Cl_2 was refluxed with CaH_2 and freshly distilled prior to use.

Caution: Diazomethane is toxic and potentially explosive. α-Diazo-β-diketones and α-diazo-β-oxoalkanals are also potentially explosive. All operations involving diazo compounds must be carried out in a well-ventilated hood with an adequate shield for safety, although no explosion had occurred in any of our experiments.

Reaction of 2-Diazo-3-oxoalkanals and Imines under the Catalysis of Tertiary Amine; General Procedure

To a solution of 2-diazo-3-oxoalkanal **1** (2 mmol) and an imine **2** (1 mmol) in CH_2Cl_2 (3 mL) was added a drop of a tertiary amine (0.3 mmol) under stirring in an ice-water bath or at r.t. N_2 was liberated immediately and TLC monitoring indicated that the reaction completed. After stirring for 2 s (with Et_3N) (10 s with Bu_3N and 15 s with DIPEA), the residue was separated on a silica gel column chromatographically [elution with EtOAc and petroleum ether (bp 60–90 °C) 1:10 to 1:20, v/v] to afford the product(s) **3** (Table 3).

2,3,6-Triphenyl-2*H*-1,3-oxazin-4(3*H*)-one (3a)

Yield: 177 mg (54%); colorless crystals; mp 161–162 °C (Lit.[24] mp 146–148 °C).

IR (KBr): 1663 cm^{-1} (C=O).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.08 (s, 1 H, CH), 6.87 (s, 1 H, CH), 7.22–7.74 (m, 15 H, ArH).

^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 90.1, 99.0, 125.0, 126.3, 126.4, 127.2, 128.65, 128.71, 129.1, 129.5, 131.4, 131.7, 136.5, 139.7, 161.4, 163.0.

3-Benzyl-2,6-diphenyl-2*H*-1,3-oxazin-4(3*H*)-one (3b)

Yield: 292 mg (86%); colorless crystals; mp 125–126 °C (Lit.[25] mp 123–124 °C).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.91 (d, *J* = 15.6 Hz, 1 H in CH_2), 5.41 (d, *J* = 15.6 Hz, 1 H in CH_2), 6.00 (s, 1 H, CH), 6.29 (s, 1 H, CH), 7.17–7.61 (m, 15 H, ArH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 46.5, 87.9, 97.7, 126.3, 127.4, 127.6, 127.8, 128.65, 128.66, 128.69, 129.8, 131.2, 131.8, 135.3, 136.9, 161.7, 164.0.

3-Benzyl-2,5-diphenyl-2*H*-1,3-oxazin-4(3*H*)-one (4b)

Yield: 22 mg (6%); colorless crystals; mp 142–143 °C.

IR (KBr): 1661 cm^{-1} (C=O).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.98 (d, *J* = 15.2 Hz, 1 H in CH_2), 5.47 (d, *J* = 15.2 Hz, 1 H in CH_2), 6.27 (s, 1 H, CH), 7.08 (s, 1 H, CH), 7.25–7.53 (m, 15 H, ArH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 46.9, 88.4, 116.8, 127.55, 127.59, 127.6, 128.0, 128.3, 128.7, 129.9, 132.6, 135.4, 136.8, 151.5, 162.6.

HRMS (ESI): *m*/*z* calcd for $C_{23}H_{20}NO_2$ [M + H]$^+$: 342.1489; found: 342.1503.

2-Fur-2-yl-3-(4-methoxyphenyl)-6-phenyl-2*H*-1,3-oxazin-4(3*H*)-one (3c)

Yield: 236 mg (68%); colorless crystals; mp 151–153 °C.

IR (KBr): 1645 cm^{-1} (C=O).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.79 (s, 3 H, CH_3), 6.05 (s, 1 H, CH), 6.35 (dd, *J* = 1.6, 3.6 Hz, 1 H, ArH), 6.58 (d, *J* = 3.6 Hz, 1 H, ArH), 6.70 (s, 1 H, CH), 6.90 (d, *J* = 8.8 Hz, 2 H, ArH), 7.27 (d, *J* = 8.8 Hz, 2 H, ArH), 9.35–7.48 (m, 4 H, ArH), 7.71 (d, *J* = 7.2 Hz, 2 H, ArH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 55.5, 85.0, 98.6, 110.6, 111.4, 114.5, 126.6, 127.2, 128.7, 131.4, 131.7, 131.8, 143.9, 149.0, 158.3, 161.2, 162.6.

HRMS (ESI): *m*/*z* calcd for $C_{21}H_{18}NO_4$ [M + H]$^+$: 348.1230; found: 348.1228.

3-(4-Methoxystyryl)-2,6-diphenyl-2*H*-1,3-oxazin-4(3*H*)-one (3d)

Yield: 180 mg (47%); colorless crystals; mp 115–116 °C.

IR (KBr): 1662 cm^{-1} (C=O).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.81 (s, 3 H, CH_3), 6.10 (s, 1 H, CH), 6.21 (d, *J* = 6.0 Hz, 1 H, CH), 6.52 (dd, *J* = 6.4, 15.6 Hz, 1 H, CH), 6.80 (d, *J* = 16 Hz, 1 H, CH), 6.91–7.76 (m, 14 H, ArH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 55.5, 90.7, 97.9, 114.6, 122.3, 126.4, 127.1, 128.1, 128.8, 128.9, 131.4, 131.6, 131.8, 135.1, 136.2, 158.5, 162.1, 163.3.

HRMS (ESI): *m*/*z* calcd for $C_{25}H_{22}NO_3$ [M + H]$^+$: 384.1594; found: 384.1598.

3-Isopropyl-2-(4-methoxyphenyl)-6-phenyl-2*H*-1,3-oxazin-4(3*H*)-one (3e)

Yield: 252 mg (78%); colorless crystals; mp 142–143 °C.

IR (KBr): 1650 cm^{-1} (C=O).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.09 (d, *J* = 6.4 Hz, 3 H, CH_3), 1.33 (d, *J* = 6.4 Hz, 3 H, CH_3), 3.74 (s, 3 H, CH_3), 4.88 (hept, *J* = 6.4 Hz, 1 H, CH), 5.89 (s, 1 H, CH), 6.51 (s, 1 H, CH), 6.85–7.58 (m, 9 H, ArH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 20.3, 21.3, 44.3, 55.2, 83.7, 99.0, 113.7, 126.2, 128.5, 128.6, 129.6, 130.9, 132.1, 159.8, 160.2, 163.1.

HRMS (ESI): *m*/*z* calcd for $C_{20}H_{22}NO_3$ [M + H]$^+$: 324.1594; found: 324.1600.

3-Isopropyl-2-(4-nitrophenyl)-6-phenyl-2*H*-1,3-oxazin-4(3*H*)-one (3f)

Yield: 288 mg (85%); colorless crystals; mp 152–153 °C.

IR (KBr): 1652 cm^{-1} (C=O).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.15 (d, *J* = 6.8 Hz, 3 H, CH_3), 1.38 (d, *J* = 6.8 Hz, 3 H, CH_3), 4.97 (hept, *J* = 6.8 Hz, 1 H, CH), 5.91 (s, 1 H, CH), 6.63 (s, 1 H, CH), 7.30–8.22 (m, 9 H, ArH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 20.4, 21.4, 44.6, 82.8, 99.3, 123.6, 126.1, 128.2, 128.7, 131.3, 131.4, 144.8, 148.4, 160.2, 162.6.

HRMS (ESI): *m*/*z* calcd for $C_{19}H_{19}N_2O_4$ [M + H]$^+$: 339.1339; found: 339.1355.

rel-(*R*)-2,6-Diphenyl-3-[(*R*)-1-phenylethyl]-2*H*-1,3-oxazin-4(3*H*)-one (*anti*-3g) and rel-(*R*)-2,6-Diphenyl-3-[(*S*)-1-phenylethyl]-2*H*-1,3-oxazin-4(3*H*)-one (*syn*-3g)
Yield: 324 mg (90%); colorless crystals; mp 167–168 C; *anti*/*syn* = 6:1, inseparable.

IR (KBr): 1642 cm^{-1} (C=O).

^{1}H NMR (400 MHz, $CDCl_3$): δ (*anti*-**3g**) = 1.45 (d, *J* = 7.2 Hz, 3 H, CH_3), 5.95 (s, 1 H, CH), 6.13 (q, *J* = 7.2 Hz, 1 H, CH), 6.28 (s, 1 H, CH), 7.10–7.58 (m, 15 H, ArH); δ (*syn*-**3g**) = 1.76 (d, *J* = 7.2 Hz, 3 H, CH_3), 5.91 (s, 1 H, CH), 5.95 (q, *J* = 7.2 Hz, 1 H, CH), 6.49 (s, 1 H, CH), 7.10–7.58 (m, 15 H, ArH).

^{13}C NMR (100 MHz, $CDCl_3$): δ (*anti*-**3g**) = 17.7, 50.3, 84.7, 98.5, 126.4, 127.1, 127.4, 127.7, 128.4, 128.5, 128.8, 129.3, 131.1, 132.0, 137.5, 140.9, 160.3, 163.4; δ (*syn*-**3g**) = 17.8, 50.3, 84.9, 99.1, 126.4, 127.1, 127.4, 127.7, 128.1, 128.5, 128.8, 129.3, 131.1, 132.0, 137.5, 140.9, 160.3, 163.4.

HRMS (ESI): *m*/*z* calcd for $C_{24}H_{22}NO_2$ [M + H]$^+$: 356.1645; found: 356.1647.

2-Phenyl-6,7-dihydro[1,3]oxazino[2,3-*a*]isoquinolin-4(11b*H*)-one (3h)
Yield: 116 mg (42%); colorless crystals; mp 197–198 °C.

IR (KBr): 1660 cm^{-1} (C=O).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.85 (dt, *J* = 15.6, 4.0 Hz, 1 H, H in CH_2), 3.07 (ddd, *J* = 4.8, 10.8, 15.6 Hz, 1 H in CH_2), 3.36 (ddd, *J* = 3.6, 10.4, 12.8 Hz, 1 H), 4.42 (dt, *J* = 12.8, 4.8 Hz, 1 H), 6.24 (s, 1H), 7.25–7.56 (m, 10 H, ArH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 28.5, 37.8, 84.7, 117.4, 127.2, 127.6, 128.0, 128.3, 128.6, 128.7, 129.5, 130.1, 132.8, 136.3, 153.9, 163.6.

HRMS (ESI): *m*/*z* calcd for $C_{18}H_{16}NO_2$ [M + H]$^+$: 278.1176; found: 278.1177.

13-Methyl-2-phenyldibenzo[*b*,*f*][1,3]oxazino[3,2-*d*][1,4]oxazepin-4(14b*H*)-one (3i)
Yield: 124 mg (35%); colorless oil.

IR (KBr): 1672 cm^{-1} (C=O).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.33 (s, 3 H, CH_3), 6.18 (s, 1 H, CH), 6.72 (s, 1 H, CH), 7.17–7.83 (m, 12 H, ArH).

^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 20.8, 87.2, 97.9, 120.8, 121.0, 124.5, 125.3, 126.4, 127.8, 128.5, 128.8, 129.3, 131.2, 131.6, 131.7, 134.2, 153.8, 155.1, 163.5, 163.9.

HRMS (ESI): *m*/*z* calcd for $C_{23}H_{18}NO_3$ [M + H]$^+$: 356.12812; found: 356.12794.

rel-(1*R*,12b*R*)-1-Benzoyl-11-methyl-1*H*-azeto[1,2-*d*]dibenzo[*b*,*f*][1,4]oxazepin-2(12b*H*)-one (5i)
Yield: 21 mg (6%); colorless crystals; mp 167–168 °C.

IR (KBr): 1752, 1678 cm^{-1} (C=O).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.35 (s, 3 H, CH_3), 5.37 (d, *J* = 2.8 Hz, 1 H, CH), 6.38 (d, *J* = 2.8 Hz, 1 H, CH), 7.02–8.30 (m, 12 H, ArH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 20.9, 53.5, 63.2, 120.1, 121.5, 121.6, 124.9, 125.1, 126.5, 128.9, 129.3, 129.6, 129.7, 130.7, 134.1, 135.0, 135.7, 144.5, 156.3, 158.8, 190.4.

HRMS (ESI): *m*/*z* calcd for $C_{23}H_{17}NO_3$ + Na [M + Na]$^+$: 378.1101; found: 378.1111.

13-Methyldibenzo[*b*,*f*][1,3]oxazino[3,2-*d*][1,4]oxazepin-4(14b*H*)-one (3j)
Yield: 73 mg (26%); colorless crystals; mp 107–108 °C.

IR (KBr): 1680 cm^{-1} (C=O).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.34 (s, 3 H, CH_3), 5.62 (d, *J* = 6.0 Hz, 1 H, CH), 6.55 (s, 1 H, CH), 7.15–7.57 (m, 7 H, ArH), 7.56 (d, *J* = 6.0 Hz, 1 H, CH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 20.7, 87.4, 104.0, 120.8, 121.1, 124.6, 124.9, 128.2, 128.7, 129.0, 129.4, 131.8, 134.1, 154.0, 155.0, 156.2, 162.2.

HRMS (ESI): *m*/*z* calcd for $C_{17}H_{14}NO_3$ [M + H]$^+$: 280.0968; found: 280.0966.

Supporting Information for this article is available online at http://www.thieme-connect.com/ejournals/toc/synthesis.

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