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Catalytic and enantioselective aza-ene and hetero-Diels–Alder reactions of alkenes and dienes with azodicarboxylates

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Lewis acids such as $Cu(OTf)_2$, $Zn(OTf)_2$, $Yb(OTf)_3$ and $Nd(OTf)_3$ catalyze the aza-ene reaction of alkenes with azodicarboxylates, giving the allylic amination adducts. The use of bis(2,2,2-trichloroethyl)azodicarboxylate as the amination reagent and $Cu(OTf)_2$ and $Yb(OTf)_3$ as the catalysts gave the aza-ene reaction of different alkenes, leading to the corresponding allyl amines in high yields. Chiral copper complexes prepared from $Cu(OTf)_2$ and chiral bisoxazoline ligands were found to catalyze the enantioselective aza-ene reaction of azodicarboxylates with alkenes and the hetero-Diels–Alder reaction with cyclopentadiene, giving the corresponding aza-ene- and hetero-Diels–Alder adducts, respectively, in good yields and moderate enantioselectivities.

Introduction

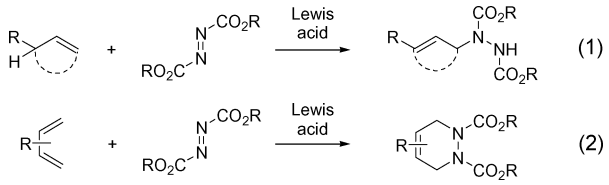
The ene reaction provides a powerful method for C–C bond formation with concomitant activation of an allylic C–H bond. The ene reaction converts alkenes into more functionalized allylic compounds; *e.g.* the use of aldehydes as enophiles leads to homoallylic alcohols (carbonyl-ene reaction)[1] and aldimines afford homoallylic amines (imine-ene reaction).[1a,2] Allylic amines are important functional groups in organic chemistry[3] and few options are offered to synthetic chemists for their preparation from alkenes.[2b] The existing methods mainly involve *e.g.* sulfur[4,5] or selenium diimido compounds,[6] *N*-sulfinylben-zenesulfonamide,[3] *N*-phenyl-1,2,4-triazoline,[7a] *N*-methyl- and *N*-phenyl-1,2,4-triazoline-3,5-diones[7b,c] or acylnitroso compounds[8] as aminating species for alkenes.

An interesting alternative for the synthesis of allylic amines, which would also be complementary to the previous methods, is the use of azo compounds as aminating agents. Thus, the amination of an alkene could take place *via* an aza-ene reaction to afford the aminated product with transposition of the double bond using *e.g.* diethyl azodicarboxylate (DEAD)[9] and bis(2,2,2,-trichloroethyl)azodicarboxylate (BTCEAD)[10] as the nitrogen source.

It is well known that Lewis acids can catalyze carbonyl-ene and imine-ene reactions.[1a,c] In contrast, Lewis-acid catalysis of the analog aza-ene reactions has received little attention. Initial attempts to mediate the ene-reaction of 1-pentene with DEAD using Et_2AlCl or Me_2AlCl, in toluene, at −78 °C led to a transfer of the alkyl group from the Lewis acid to the azo compound.[9a] The use of $BF_3{\cdot}Et_2O$, Et_2BBr and $ZnBr_2$ showed no reaction at rt, while $Ti(O^iPr)_4$ resulted in reduction of the azo compound to the corresponding hydrazine. Finally, it was discovered that a stoichiometric amount of $SnCl_4$ successfully mediated the desired aza-ene reaction of various alkenes with DEAD at −60 °C.[9a]

To the best of our knowledge, no catalytic aza-ene reaction has been reported. In this paper we disclose the development of the Lewis-acid catalyzed reactions of azodicarboxylates with different alkenes (eqn. 1, Scheme 1). Furthermore, we will also present that this Lewis-acid catalyzed approach can be used for the hetero-Diels–Alder reaction of conjugated dienes with azodicarboxylates (eqn. 2, Scheme 1).

The field of asymmetric catalysis has produced remarkable results in the area of Diels–Alder and hetero-Diels–Alder reactions, where a high degree of development has been achieved.[11]

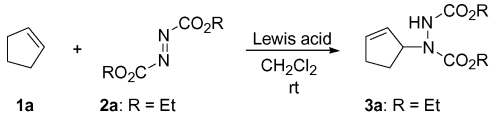


Scheme 1 Catalytic aza-ene- (eqn. 1) and hetero-Diels–Alder (eqn. 2) reaction of azadicarboxylates.

The enantioselectivity during Diels–Alder reactions is often effected by chiral ligand-bearing metal complexes. Catalysts producing the cycloadducts in high enantioselectivities include C_2-symmetric bisoxazoline-metal complexes,[12] which have proven to be successful when *N*-enoylimides and α-hydroxyenones are employed as dienophiles.[13]

Results and discussion

The allylic amination of cyclopentene **1a** by DEAD **2a** and BTCEAD **2b** catalyzed by Lewis acids (eqn. 3) are presented in Table 1.



1a **2a**: R = Et; **2b**: R = CH_2CCl_3 **3a**: R = Et; **3b**: R = CH_2CCl_3

Cyclopentene **1a** reacted with DEAD **2a** in the presence of $Yb(OTf)_3$ (10 mol%) and $Cu(OTf)_2$ (20 mol%) to give the aminated product **3a** in 10 and 33% yield, respectively, after long reaction times (entries 1, 2). The use of $Sn(OTf)_2$ as the catalyst afforded no reaction even when 1.0 eq. was used. The more reactive azodicarboxylate, BTCEAD **2b**, afforded the aza-ene reaction in up to 95% yield (entries 4–11) when Lewis acids such as $Yb(OTf)_3$, $Cu(OTf)_2$, $Nd(OTf)_3$ and $Zn(OTf)_2$ were used. Apart from the aza-ene reaction catalyzed by $Cu(OTf)_2$ (entries 6, 7), catalyst loading did not affect yields and reaction times significantly. A screening of solvents revealed that CH_2Cl_2 was the best for the aza-ene reaction.

With a series of catalytically active Lewis acids for the aza-ene reaction, various acyclic and cyclic alkenes were treated with BTCEAD **2b** to determine the scope of reaction (eqn. 4). The Lewis acids $Cu(OTf)_2$ (20 mol%) and $Yb(OTf)_3$ (10 mol%) were

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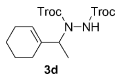
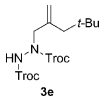
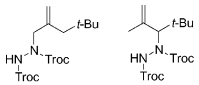
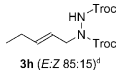
Table 1 Lewis-acid catalyzed aza-ene reaction of cyclopentene **1a** with azodicarboxylates **2a, b**

Entry	Azodicarboxylate	Lewis acid	Catalyst (%)	Time/h	Yield[a] (%)
1	**2a**	$Yb(OTf)_3$	10	144	**3a**–10
2	**2a**	$Cu(OTf)_2$	20	98	**3a**–33
3	**2a**	$Sn(OTf)_2$	100	20	**3a**–nr
4	**2b**	$Yb(OTf)_3$	10	60	**3b**–95
5	**2b**	$Yb(OTf)_3$	20	48	**3b**–92
6	**2b**	$Cu(OTf)_2$	10	44	**3b**–55
7	**2b**	$Cu(OTf)_2$	20	22	**3b**–76
8	**2b**	$Nd(OTf)_2$	10	45	**3b**–93
9	**2b**	$Nd(OTf)_2$	20	45	**3b**–95
10	**2b**	$Zn(OTf)_2$	10	48	**3b**–92
11	**2b**	$Zn(OTf)_2$	20	48	**3b**–90

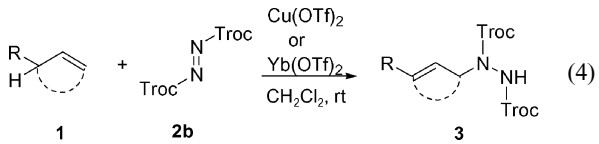
[a] Isolated yield.

Table 2 Aza-ene reactions of alkenes with BTCEBAD **2b** catalyzed by $Cu(OTf)_2$ and $Yb(OTf)_2$

Entry	Alkene	Lewis acid	Catalyst load (%)	Time/h	Product	Yield[a](%)
1	 **1a**	$Cu(OTf)_2$	20	22	 **3b**	76
		$Yb(OTf)_3$	10	60		95
2	 **1b**	$Cu(OTf)_2$	20	72	 **3c**	44
		$Yb(OTf)_3$	10	72		43
3	 **1c**	$Cu(OTf)_2$	20	1	 **3d**	98[b]
		$Yb(OTf)_3$	10	2		99
4	 **1d**	$Cu(OTf)_2$	20	1	 **3e**	96
		$Yb(OTf)_3$	10	144	 **3e** (4:1) **3f**	41[c]
5	 **1e**	$Cu(OTf)_2$	20	25	 **3g**	85
		$Yb(OTf)_3$	10	20		92
6	 **1f**	$Cu(OTf)_2$	20	20	 **3h** (*E*:*Z* 85:15)[d]	98
		$Yb(OTf)_3$	10	20		93

[a] Isolated yield. [b] See reference 10. [c] Total yield. The isomers mixture could not be separated by FC. [d] Isomers ratio determined by ^{1}H NMR.

chosen as standard catalysts and the results are presented in Table 2.



(4)

Cyclohexene **1b** was less reactive than cyclopentene **1a** and after 72 h, 43–44% yield of product **3c** was isolated for both catalysts. In order to assess the regioselectivity of the reaction, alkenes with more than one allylic site were investigated. When ethylidenecyclohexane **1c** was used as the substrate, the reaction was complete in 1 or 2 h (entry 3) and the internal alkene **3d** was isolated as the main product in excellent yield.[10] With 2,4,4-trimethyl-pent-2-ene **1d** as the substrate (entry 4) the reaction course is dependent on the Lewis acid; $Cu(OTf)_2$ gave only adduct **3e** in very high yield (96%) after 1 h, while the reaction catalyzed by $Yb(OTf)_3$ gave a mixture of adducts **3e** and **3f** (ratio 4 : 1) in only 41% total yield after 144 h. The reason for this pronounced difference in reaction course using $Cu(OTf)_2$ and $Yb(OTf)_3$ is not known at present. Acyclic alkenes with internal and terminal double bonds also undergo the Lewis-acid catalyzed aza-ene reaction. Formation of the (*E*)-alkene was favored for both Lewis acids tested. Both (*E*)-hex-3-ene **1e** and 1-pentene **1f** gave the aminated products **3g** and **3h**, respectively, in high yields, using $Cu(OTf)_2$ and $Yb(OTf)_3$ as the catalysts (entries 5, 6).

By the use of literature methods the corresponding amines could be obtained in good yield from the aza-ene reaction products using Zn, HOAc–acetone[10,14] or Li–NH_3.[9a,15]

Based on the results of the Lewis-acid catalyzed aza-ene reactions, we next focused on trying to develop this reaction to be enantioselective using Lewis acids coordinated to a chiral ligand. So far, there have been no reports of catalytic enantioselective aza-ene reaction of alkenes with azodicarboxylates. Only a related procedure using chiral azo-enophile mediated by $SnCl_4$ has been disclosed by Brimble and Lee.[16]

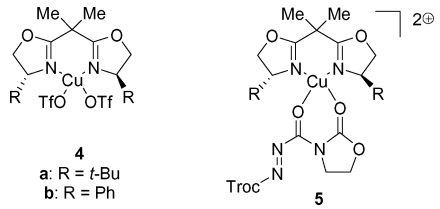
The first attempt of an enantioselective aza-ene reaction of BTCAD **2b** with cyclopentene **1a** catalyzed by chiral bisoxazoline(BOX)–Cu(II) complexes[12,17] gave a racemic product, probably due to mono-coordination between Cu(II) and one of the oxygen atoms in the azodicarboxylate. The aminated product **3b** was isolated as a racemate in 90% yield, in contrast to the 76% yield when the reaction was catalyzed by $Cu(OTf)_2$ alone. It was envisaged that an additional coordinative site in the azodicarboxylate could lead to a more stable catalyst–substrate

Table 3 Catalytic enantioselective aza-ene reaction of cyclopentene **1a** with TOCDF **2c** catalyzed by chiral BOX–$Cu(OTf)_2$ (20 mol%) complexes

Entry	Catalyst	Temp/°C	Time/h	Yield[a] (%) **6a – 7a**	Ee[b] (%) **6a – 7a**
1	$Cu(OTf)_2$	Rt	20	5 – 47	—
2	$Yb(OTf)_3$[c]	Rt	20	36 – 9	—
3	$Cu(OTf)_2$ (*R*)–Ph–BOX	Rt	16	60 –	40 – nd
4	$Cu(OTf)_2$ (*R*)–Ph–BOX	−24	48	45 –	40 – nd
5	$Cu(OTf)_2$ (*S*)-*t*-Bu–BOX	Rt	16	35 – 34	Rac – nd

[a] Isolated yield. [b] Determined by chiral stationary HPLC. [c] 10 mol%

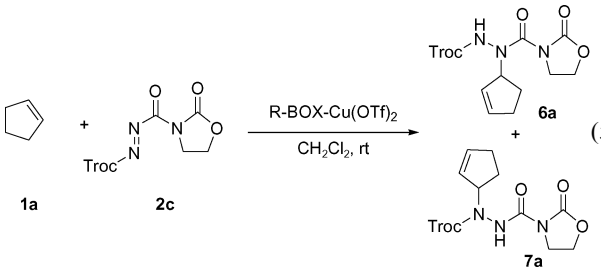
complex and thereby improve the enantioselectivity. It was also postulated that coordination to the chiral BOX–Cu(II) complex **4** would lead to an intermediates such as **5**, which might participate in the enantioselective aza-ene reaction. Adducts of this type are involved in the enantioselective enol-amination[18] in direct analogy to the previously reported Diels–Alder reactions.[17d]



4
a: R = *t*-Bu
b: R = Ph

5

Some representative screening results of the enantioselective aza-ene reaction of cyclopentene **1a** with 2,2,2-trichloroethyl-{[(2-oxo-1,3-oxazolidin-3-yl)carbonyl]diazenyl} formate (TOCDF) **2c** catalyzed by (*R*)–R–BOX–$Cu(OTf)_2$ (20 mol%) (eqn. 5) are presented in Table 3.



1a **2c** (5)

The reaction of cyclopentene **1a** with TOCDF **2c** catalyzed by $Cu(OTf)_2$ (20 mol%) gave a mixture of the allylic aminated product **6a** as a minor product and **7a** as a major product, which could be separated by flash chromatography. In contrast, the same reaction catalyzed by $Yb(OTf)_3$ (10 mol%) gave the opposite result; **6a** was formed as the major product and **7a** as the minor product (Table 3, entries 1, 2). Due to the fact that $Cu(OTf)_2$ gave a slightly better yield and our experience with chiral copper complexes in asymmetric catalysis,[19] we decided to investigate some chiral BOX ligands for the aza-ene reaction.

The (*R*)–Ph–BOX–$Cu(OTf)_2$ (20 mol%) complex catalyzed the aza-ene reaction of cyclopentene **1a** with TOCDF **2c**, giving **6a** only (Table 3, entry 3). The switch in product obtained using the chiral catalyst, compared to the use of $Cu(OTf)_2$ only, should be noted (entry 3 *vs.* 1). Product **6a** was obtained in 60% yield and 40% ee and the structure was confirmed by X-ray analysis outlined in Fig. 1. Performing the same reaction at a lower temperature (−24 °C) did not improve the enantioselectivity (entry 4). Changing the chiral bisoxazoline ligand to (*S*)-*t*–Bu–BOX (entry 5) resulted in moderate yield of the aza-ene adducts, with a 1 : 1 ratio of the regioisomers **6a** : **7a** and product **6a** was formed as a racemate (entry 5).

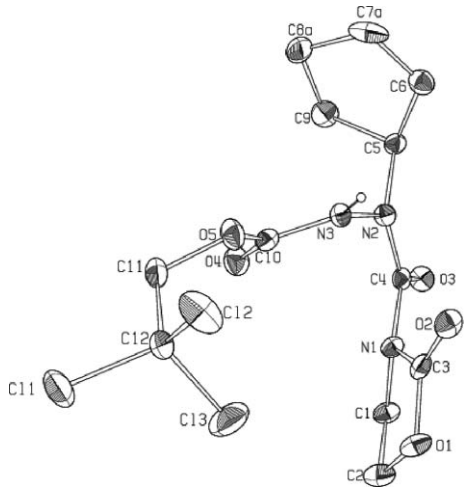
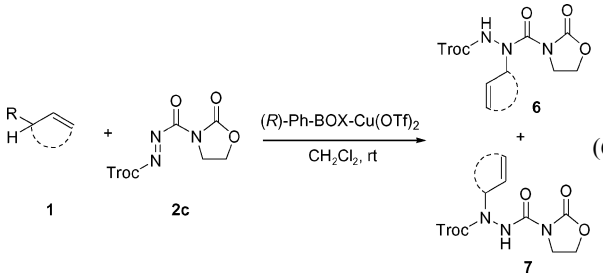


Fig. 1 X-Ray structure of **6a**.



1 **2c** (6)

To further explore the scope of the reaction, a few other alkenes were reacted with TOCDF **2c** in the presence of (*R*)–Ph–BOX–$Cu(OTf)_2$ (20 mol%) (eqn. 6). The results are presented in Table 4. Ethylidenecyclohexane **1c** (entry 2) reacts with **2c** to give **7b** as the major product in high yields (94%) and 60% ee. (*E*)-hex-3-ene **1e** (entry 3) gave adduct **6c** as the minor product in 15% yield and 7% ee, in contrast to adduct **7c**, which were formed in 50% yield and 33% ee.

Table 4 Catalytic enantioselective aza-ene reactions of the alkenes **1a, c** and **e** with TOCDF **2c** catalyzed by (*R*)–Ph–BOX–$Cu(OTf)_2$ (20 mol%) at rt in CH_2Cl_2

Entry	Alkene	Time/h	Yield[a] (%)	Ee[b] (%) **6 – 7**
1	 **1a**	17	**6a** 60 –	40 – nd
2	 **1c**	19	– **7b** 94	Nd – 60
3	 **1e**	20	**6c** 15 – **7c** 50	7 – 33

[a] Isolated yield. [b] Determined by chiral stationary HPLC.

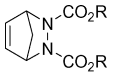
Table 5 Catalytic enantioselective hetero-Diels–Alder reaction of cyclopentadiene **9** with azodicarboxylates **2c, d** catalyzed by (*R*)–Ph–BOX–Cu(OTf)$_2$

Entry	Azodicarboxylate	Catalyst load (%)	Temp/°C	Time/min	Yield[a] (%)	Ee[b] (%)
1	**2c**	10	Rt	10	**8a** – 90	22
2	**2c**	10	−20	30	**8a** – 92	22
3	**2d**	5	Rt	10	**8b** – 71	20
4	**2d**	10	−20	60	**8b** – 73	20

[a] Isolated yield. [b] Determined by chiral stationary HPLC.

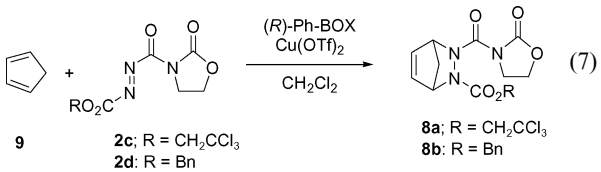
Azodicarboxylates in Lewis-acid catalyzed enantioselective hetero-Diels–Alder reactions

Polysubstituted cyclopentanes are key intermediates in the preparation of various natural or synthetic biologically active compounds, including glycosidase inhibitors,[20] antiviral and antitumor carbonucleoside[21] or kinase inhibitors.[22] Recently, it has been described that polysubstituted cyclopentene can be obtained by desymetrization and ring opening[23] of hydrazine **8**.



8

We wish to present that the catalytic and enantioselective aza-aene reaction presented above can be extended to the hetero-Diels–Alder reaction of cyclopentadiene **9** (eqn. 7). Some representative results for the reaction of **9** with TOCDF **2c** and phenymethyl{[(2-oxo-1,3-oxazolidin-3-yl)carbonyl]diazenyl} formate **2d** in the presence of (*R*)–Ph–BOX–Cu(OTf)$_2$ are presented in Table 5.



9 **2c**; R = CH_2CCl_3 **2d**: R = Bn **8a**; R = CH_2CCl_3 **8b**: R = Bn (7)

Cyclopentadiene **9** reacted with TOCDF **2c** catalyzed by (*R*)–Ph–BOX–Cu(OTf)$_2$ (10 mol%) to give the hetero-Diels–Alder adduct **8a** in high yield (up to 92%) with 22% ee. The reaction proceeded in CH_2Cl_2 at different temperatures (rt, −20 °C, entries 1, 2) with no improvement of enantioselectivity. Using benzyl azodycarboxylate derivative **2d**, adduct **8b** was obtained in a good yield and 20% ee (entries 3, 4). Unfortunately, changing the chiral ligand to more steric hindered ligand did not improved the enantioselectivity.

Conclusion

In summary, bis(2,2,2,-trichloroethyl)azodicarboxylate is an efficient amination reagent for the aza-ene reaction with alkenes catalyzed by Cu(OTf)$_2$, Zn(OTf)$_2$, Yb(OTf)$_3$ and Nd(OTf)$_3$. The scope of the Lewis-acid catalyzed aza-ene reaction is demonstrated for different alkenes with formation of the allylic amines in up to 99% yield. The reactions can also be catalyzed by chiral Ph–BOX–Cu(OTf)$_2$ and proceed with good yield and moderate enantiomeric excess. Furthermore, chiral Ph–BOX–Cu(OTf)$_2$ can catalyze the hetero-Diels–Alder reaction of cyclopentadiene with azodicarboxylate derivatives giving high yields and low enantioselectivities.

Experimental

General methods

The ^{1}H and ^{13}C NMR spectra were recorded at 400 MHz and 100 MHz, respectively. The chemical shifts are reported in ppm downfield to $CDCl_3$ (δ = 7.25) for ^{1}H NMR and relative to the central $CDCl_3$ resonance (δ = 77.0) for ^{13}C NMR. The NMR spectra were run at 60 °C due to line broading. Coupling constants in ^{1}H NMR are in Hz. Solvents were dried according to standard procedures. Flash chromatography (FC) was carried out using Merck silica gel 60 (230–400 mesh). Optical rotations were measured on Perkin-Elmer 241 polarimeter and $CHCl_3$ was used as solvent. The enantiomeric excess (ee) of the products was determined by HPLC using Daicel Chiralpack AD with *i*-PrOH–hexane as eluent or Chiralcel OD–R with MeCN–MeOH as eluent.

Materials

Diethyl azodicarboxylate, (*E*)-hex-3-ene 1-pentene, were purchased from Lancaster and used as received. Bis(2,2,2,-trichloroethyl) azodicarboxylate, 2,4,4-trimethyl-2-pentene were purchased from Fluka and used as received. Cyclopentene, cyclohexene, ethylidenecyclohexan, (*R*)–(+)-2,2′-isopropylidenebis(4-phenyl-2-oxazoline), 2,2′-isopropylidenebis[(4*R*)-4-*tert*-butyl-2-oxazoline], Yb(OTf)$_3$, Cu(OTf)$_2$, Sn(OTf)$_2$, Nd(OTf)$_3$ and Zn(OTf)$_2$, were purchased from Aldrich and used as received. 2,2,2-Trichloroethyl{[(2-oxo-1,3-oxazolidin-3yl)carbonyl]diazenyl} formate and phenylmethyl{[(2-oxo-1,3-oxazolidin-3yl)carbonyl]diazenyl} formate were prepared following a literature procedure.[18]

General procedure for catalytic aza-ene reactions of alkenes with BTCEAD

To a glass tube with a magnetic stirring bar and 2 mL of CH_2Cl_2 was added BTCEAD **2b** (190 mg, 0.5 mmol) cyclopentene **1a** (68.3 mg, 1 mmol) and catalyst (0.05–0.1 mmol) and stirred at rt. The yellow solution turned colorless after the time indicated in the tables. The crude mixture was then purified by FC (hexane : EtOAc 4 : 1) to give the aza-ene adduct.

Diethyl 1-(2-cyclopenten-1-yl)-1,2-hydrazinedicarboxylate 3a.[24]

1-(2-Cyclopentene-1-yl)-1,2-hydrazinedicarboxylic acid bis(2,2,2-trichloroethyl) ester 3b. Colorless oil. ^{1}H NMR (CD_3CN 353 K);[3] ^{13}C NMR ($CDCl_3$, 333 K) δ 27.5, 31.6, 65.8, 75.4, 76.0, 95.1, 95.2, 128.0, 137.0, 154.0, 154.7; HRMS $C_{11}H_{12}Cl_6N_2O_4$ $[M + Na]^+$ calcd 468.8826, found 468.8834.

1-(2-Cyclohexene-1-yl)-1,2-hydrazinedicarboxylic acid bis(2,2,2-trichloroethyl) ester 3c. Colorless solid. Mp = 118–120 °C. ^{1}H NMR (CD_3CN 353 K);[3] ^{13}C NMR ($CDCl_3$, 333 K) δ 20.7, 24.4, 26.8, 55.8, 75.3, 75.8, 95.0, 95.1, 125.5, 132.6, 154.1, 154.6; HRMS $C_{12}H_{14}Cl_6N_2O_4$ $[M + Na]^+$ calcd 482.8982, found 482.8994.

1-[1-(1-Cyclohexen-1-yl)ethyl]-1,2-hydrazinedicarboxylic acid bis(2,2,2-trichloroethyl) ester 3d. Colorless foam. ^{1}H NMR (CD_3CN 353 K);[10] ^{13}C NMR ($CDCl_3$, 333 K) δ 15.1, 22.1, 22.6, 25.1, 26.7, 58.9, 75.1, 75.7, 95.1, 124.6, 135.4, 154.1, 154.3; HRMS $C_{14}H_{18}Cl_6N_2O_4$ $[M + Na]^+$ calcd 510.9295, found 510.9284.

1(4,4-Dimethyl-2-methyl-penten-1-yl)-1,2-hydrazinedicarboxylic acid bis(2,2,2-trichloroethyl)ester 3e. Colorless solid. Mp = 118–121 °C. ^{1}H NMR ($CDCl_3$ 333 K) δ 0.91 (s, 9H), 1.93 (s, 3H), 4.17 (s, 2H), 4.75 (d, J = 8 Hz, 2H), 4.93 (s, 1H), 5.01

(s, 1H), 7.03 (br, 1H); ^{13}C NMR ($CDCl_3$ 333 K) δ 29.8, 31.5, 47.1, 56.7, 75.2, 75.9, 94.9, 116.6, 140.9, 153.7, 154.4; HRMS $C_{14}H_{20}Cl_6N_2O_4$ [M + Na]$^+$ calcd 512.9452, found 512.9803

1-(4,4-Dimethyl-2-methylene-penten-1-yl)-1,2-hydrazinedicarboxylic acid bis(2,2,2-trichloroethyl) ester 3e and 1-(1-*tert*-butyl-2-methyl-allyl)-1,2-hydrazine dicarboxylic acid bis(2,2,2-trichloroethyl) ester 3f. Colorless solid. ^{1}H NMR ($CDCl_3$ 333 K) δ 0.94 and 1.02 (s, **3f** and s, **3e**, 9H), 1.88 and 1.93 (2s, **3e** and **3f**, 3H), 4.20 and 4.52 (br, **3e** and br s, **3f**, 2H), 4.77 and 4.79 (2s, **3e** and **3f**, 4H), 4.96 (s, **3e**, 1H), 5.03 (s, **3e**, 1H), 5.12 (br, **3f**, 1H), 5.17 (br, **3f** 1H), 6.60 (br, **3e**, 1H), 6.87 (br, **3f**, 1H); HRMS $C_{14}H_{20}Cl_6N_2O_4$ [M + Na]$^+$ calcd 512.9452, found 512.9451.

(*E*)-1-(2-Hexen-4-yl)-1,2-hydrazinedicarboxylic acid bis(2,2,2-trichloroethyl) ester 3g. Colorless oil. ^{1}H NMR ($CDCl_3$ 333 K) δ 0.93 (t, J = 7.6 Hz, 3H), 1.53–1.62 (m, 1H), 1.67 (d, J = 6 Hz, 3H), 1.70–1.78 (m, 1H), 4.46–4.52 (m, 1H), 4.76–4.79 (m, 4H), 5.44 (dd, J = 15.2, 7.2 Hz, 1H), 5.70 (dq, J = 15.6, 6.8 Hz, 1H), 6.62 (br, 1H); ^{13}C NMR ($CDCl_3$, 333 K) δ 10.8, 17.7, 24.9, 63.1, 75.3, 75.8, 94.9, 95.1, 128.0, 129.7, 154.1, 154.6; HRMS $C_{12}H_{16}Cl_6N_2O_4$ [M + Na]$^+$ calcd 484.9139, found 484.9102.

(*E*)-1-(2-Penten-1-yl)-1,2-hydrazinedicarboxylic acid bis(2,2,2-trichloroethyl) ester 3h. Colorless oil. ^{1}H NMR ($CDCl_3$ 333 K) δ (t, J = 7.6 Hz, 3H), 2.04 (quintet, J = 7.6 Hz, 2H), 4.13 (d, J = 6 Hz, 2H), 4.74 (s, 4H), 5.44–5.51 (m, 1H), 5.69–5.76 (m, 1H), 7.03 (br, 1H); ^{13}C NMR ($CDCl_3$, 333 K) δ 13.2, 25.2, 52.7, 75.2, 75.8, 94.9, 95.0, 121.8, 138.4, 153.9, 154.0; HRMS $C_{11}H_{14}Cl_6N_2O_4$ [M + Na]$^+$ calcd 470.8982, found 470.8979.

General procedure for catalytic enantioselective aza-ene reactions

In an oven dried Schlenk tube equipped with a magnetic stirrer bar, $Cu(OTf)_2$ (36.2 mg, 0.1 mmol) and (*R*)-(+)-2,2-isopropylidene-bis(4-phenyl-2-oxazoline) (36.8 mg, 0.11 mmol) were added. The mixture was stirred under a vacuum for 2 h and filled with N_2. Dry CH_2Cl_2 (1 mL) was added and the solution stirred for 1 h. 160 mg (0.5 mmol) of 2,2,2-trichloroethyl{[(2-oxo-1,3-oxazolidin-3-yl)carbonyl]diazenyl}-formate **2c** was added, followed by the addition of the alkene (1 mmol) and stirred at rt. After the time indicated in the table the product was isolated by FC (CH_2Cl_2 : EtOAc 4 : 1).

***N*′-Cyclopent-2-enyl-*N*′-(2-oxo-oxazolidine-3-carbonyl)-hydrazinecarboxylic acid 2,2,2-trichloro-ethyl ester 6a.** Colorless solid. Mp = 88–90 °C. The enantiomers were separated by HPLC using a Chiralpak AD chiral stationary phase in hexane–*i*-PrOH 80 : 20 (τ_{major} = 10.13 min, τ_{minor} = 9.04 min). $[\alpha]_D^{rt} = -16.3$ (c = 1.0, $CHCl_3$, 40% ee); ^{1}H NMR ($CDCl_3$ 333 K) δ 2.17–2.42 (m, 4H), 4.01–4.89 (m, 6H), 5.39 (br s, 1H), 5.67 (br s, 1H), 6.01 (br s, 1H), 7.74 (br s, 1H); ^{13}C NMR ($CDCl_3$ 333 K) δ 27.1, 31.4, 44.1, 63.1, 65.6, 74.9, 94.0, 127.8, 136.6, 150.0, 153.5, 153.9; HRMS $C_{12}H_{14}Cl_3N_3O_5$ [M + Na]$^+$ calcd 407.9879, found 407.9907.

***N*-Cyclopent-2-enyl-*N*'-(2-oxo-oxazolidine-3-carbonyl)-hydrazinecarboxylic acid 2,2,2-trichloro-ethyl ester 7a.** Colorless solid. ^{1}H NMR ($CDCl_3$ 333 K) δ 1.91 (br s, 1H), 2.22–2.31 (m, 2H), 2.39–2.49 (m, 1H), 4.02 (t, J = 8.4 Hz, 2H), 4.44 (t, J = 8.6 Hz, 2H), 4.74 (s, 2H), 5.37–5.40 (m, 1H), 5.68–5.70 (m, 1H), 5.99–6.02 (m, 1H), 9.21 (s, 1H); ^{13}C NMR ($CDCl_3$, 333 K) δ 27.5, 31.4, 42.5, 63.0, 65.7, 75.8, 95.2, 128.1, 136.5, 151.9, 155.2; HRMS $C_{12}H_{14}Cl_3N_3O_5$ [M + Na]$^+$ calcd 407.9879, found 407.9886.

***N*-(1-Cyclohex-1-enyl-ethyl)-*N*'-(2-oxo-oxazolidine-3-carbonyl)-hydrazinecarboxylic acid 2,2,2-trichloro-ethyl ester 7b.** Colorless oil. The enantiomers were separated by HPLC using a Chiralpak AD chiral stationary phase in hexane–*i*-PrOH 80 : 20 (τ_{minor} = 8.09 min, τ_{major} = 9.59 min). $[\alpha]_D^{rt} = -19.2$ (c = 1.0, $CHCl_3$, 60% ee); ^{1}H NMR ($CDCl_3$ 333 K) δ 1.30 (d, J = 6.8 Hz, 3H), 1.50–1.64 (m, 4H), 1.88–2.09 (m, 4H), 4.02 (t, J = 8.4 Hz, 2H), 4.43 (t, J = 8.8 Hz 2H), 4.69–4.79 (m, 3H), 5.64–5.66 (m, 1H), 9.14 (s, 1H); ^{13}C NMR ($CDCl_3$, 333 K) δ 15.1, 22.1, 22.6, 25.1, 26.7, 42.4, 58.9, 62.9, 75.6, 95.1, 124.7, 135.5, 151.5, 153.7, 155.2; HRMS $C_{15}H_{20}Cl_3N_3O_5$ [M + Na]$^+$ calcd 450.0366, found 450.0365.

***N*′-(1-Ethyl-but-2-enyl)-*N*′-(2-oxo-oxazolidine-3-carbonyl)-hydrazinecarboxylic acid 2,2,2-trichloro-ethyl ester 6c.** Colorless oil. The enantiomers were separated by HPLC using a Chiralpak AD chiral stationary phase in hexane–*i*-PrOH 80 : 20 (τ_{major} = 6.07 min, τ_{minor} = 6.90 min). $[\alpha]_D^{rt} = -2.1$ (c = 1.0, $CHCl_3$, 7% ee); ^{1}H NMR ($CDCl_3$ 333 K) δ 0.94 (t, J = 6.4 Hz, 3H), 1.47–1.77 (m, 5H), 4.11–4.84 (m, 7H), 5.43–5.49 (m, 1H), 5.69–5.78 (m, 1H), 7.76 (br s, 1H); HRMS $C_{13}H_{18}Cl_3N_3O_5$ [M + Na]$^+$ calcd 424.0210, found 424.0221.

***N*-(1-Ethyl-but-2-enyl)-*N*′-(2-oxo-oxazolidine-3-carbonyl)-hydrazinecarboxylic acid 2,2,2-trichloro-ethyl ester 7c.** Colorless oil. The enantiomers were separated by HPLC using a Chiralpak AD chiral stationary phase in hexane–*i*-PrOH 80 : 20 (τ_{minor} = 7.93 min, τ_{major} = 9.20 min). $[\alpha]_D^{rt} = +2.1$ (c = 1.0, $CHCl_3$, 33% ee); ^{1}H NMR ($CDCl_3$ 333 K) δ 0.96 (t, J = 7.6 Hz, 3H), 1.53–1.77 (m, 5H), 4.04 (t, J = 8.4 Hz, 2H), 4.42–4.53 (m, 3H), 4.74 (br, 2H), 5.44 (dd, J = 15.6, 7.6 Hz, 1H), 5.67–5.73 (m, 1H), 9.22 (s, 1H); ^{13}C NMR ($CDCl_3$, 333 K) δ 10.7, 17.6, 25.0, 42.5, 62.1, 63.0, 75.7, 95.2, 128.1, 129.6, 151.8, 153.7, 155.3; HRMS $C_{13}H_{18}Cl_3N_3O_5$ [M + Na]$^+$ calcd 424.0210, found 424.0209.

General procedure for catalytic enantioselective hetero-Diels–Alder reactions

In a oven dried Schlenk tube equipped with a magnetic stirrer bar, $Cu(OTf)_2$ (18,1 mg, 0.05 mmol) and (*R*)-(+)-2,2-isopropilidene-bis(4phenyl-2-oxazoline) (18.4 mg, 0.055 mmol) were added. The mixture was stirred under a vacuum for 2 h and filled with N_2. Dry CH_2Cl_2 (1 mL) was added and the solution stirred for 1 h. 160 mg (0.5 mmol) of 2,2,2-trichloroethyl{[(2-oxo-1,3-oxazolidin-3-yl)carbonyl]diazenyl}-formate **2c** was added, followed by the addition of cyclopentadiene **9** (33 mg, 0.5 mmol) and stirring at rt. After the time indicated in the table the product was isolated by FC (CH_2Cl_2 : EtOAc 4 : 1).

3-(2-Oxo-oxazolidine-3-carbonyl)-2,3-diaza-bicyclo-[2.2.1]-hept-5-ene-2-carboxylic acid 2,2,2-trichloro-ethyl ester 8a. Colorless solid. Mp = 159–160 °C. The enantiomers were separated by HPLC using a Daicel Chiralcel OD–R chiral stationary phase in MeOH–MeCN 90 : 10, 22% ee (τ_{major} = 8.86 min, τ_{minor} = 11.11 min). $[\alpha]_D^{rt} = -10.9$ (c = 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$ 333 K) δ 1.82 (d, J = 8.8 Hz, 1H), 1.97 (d, J = 8.8 Hz, 1H), 3.92–3.98 (m, 1H), 4.12 (q, J = 9.2 Hz, 1H), 4.35–4.46 (m, 2H), 4.68 (d, J = 12 Hz, 1H), 4.79 (d, J = 12 Hz, 1H), 5.20 (br, 2H), 6.57–6.62 (m, 2H); ^{13}C NMR ($CDCl_3$, 333 K) δ 44.1, 47.5, 62.4, 64.9, 69.1, 75.5, 95.0, 135.7, 137.1, 152.5, 153.5, 155.1; HRMS $C_{12}H_{12}Cl_3N_3O_5$ [M + K]$^+$ calcd 405.9530, found 405.9594.

3-(2-Oxo-oxazolidine-3-carbonyl)-2,3-diaza-bicyclo-[2.2.1]-hept-5-ene-2-carboxylic acid benzyl ester 8b. Colorless foam. The enantiomers were separated by HPLC using a Daicel Chiralcel OD–R chiral stationary phase in MeOH–MeCN 90 : 10, 20% ee (τ_{minor} = 15.94 min, τ_{major} = 17.51 min). $[\alpha]_D^{rt} = -6.9$ (c = 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$ 333 K) δ 1.70 (d, J = 8.8 Hz, 1H), 1.85 (d, J = 8.8 Hz, 1H), 3.82–3.88 (m, 1H), 4.05 (q, J = 9.2 Hz, 1H), 4.24–4.36 (m, 2H), 5.06–5.21 (m, 4H), 6.43–6.47 (m, 2H), 7.23 (br, 5H); ^{13}C NMR ($CDCl_3$, 333 K) δ 43.9, 47.3, 62.3, 64.5, 67.7, 68.7, 127.5, 127.9, 128.3, 135.3, 136.9, 152.6, 153.4, 157.1; HRMS $C_{17}H_{17}N_3O_5$ [M + K]$^+$ calcd 366.0879, found 366.0879.

X-Ray structure analysis of *N′*-cyclopent-2-enyl-*N′*-(2-oxo-oxazolidine-3-carbonyl)-hydrazinecarboxylic acid 2,2,2-trichloro-ethyl ester 6a

Crystals of **6a** are orthorhombic, Pbca, with unit cell at 100 K: $a = 11.4775(5)$ Å, $b = 11.1987(5)$ Å, $c = 24.918(1)$ Å, $V = 3202.8(2)$ Å^3, $Z = 8$, $\rho_{calcd} = 1.604$, $\mu = 0.600$ cm^{-1} (MoKα radiation, $\lambda = 0.71073$ Å), $F(000) = 1584$, $T = 100$ K. 49 125 reflections collected on a SMART diffractometer, 4589 independent, 3282 significant ($I > 3\sigma(I)$). Structure solved by means of the SIR97 program system.[25] 205 parameters were refined, final $R = 0.048$, $R_w = 0.054$. The cyclopentene ring is disordered (rotated 180° around the N–C bond) and the outer carbon atoms are split into two each with occupancies constrained to add up to 1.0.†

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