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An Unexpected Highly Stereoselective Bisaziridination of (*E*,*E*)-1,4-Dialkyl-2,3-dinitrobutadienes Followed by a Nitro Group Driven Ring Enlargement

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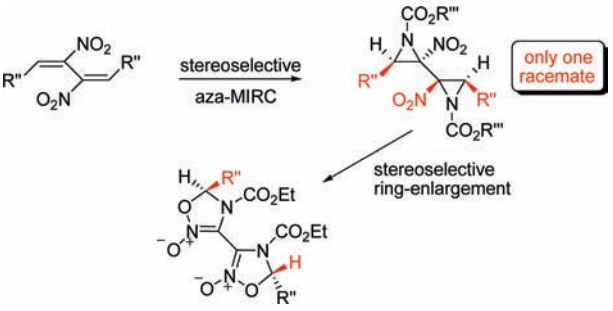

(±)-2,2′-Dinitro-2,2′-biaziridines were obtained by a direct aza-MIRC (Michael initiated ring closure) reaction on (*E*,*E*)-1,4-dialkyl-2,3-dinitro-l,3-butadienes under very mild conditions. The reactions occur with high stereoselectivity as shown by the enantioselective HPLC analyses performed on the crude mixtures. Ring enlargement to 3,3′-bi(1,2,4-oxadiazole) derivatives was easily obtained by a simple treatment with sodium iodide in DMSO, with an unforeseen regioselective aziridine C−C cleavage.

Introduction

3,4-Dinitrothiophene (**1**) represents a valuable starting molecule in organic synthesis because of its non-benzenoid behavior.[1] As a matter of fact, **1** reacts under mild experimental conditions (ethanol, room temperature) with aliphatic amines furnishing the useful building blocks (*E*,*E*)-l,4-diamino-2,3-dinitro-l,3-butadienes (**2**),[2] which in turn give (*E*,*E*)-1,4-dialkyl- or (*E*,*E*)-l,4-diaryl-2,3-dinitro-l,3-butadienes (**3**) by reaction with Grignard reagents[3] (Scheme 1). Compounds **2** and **3** can be regarded as very interesting building blocks. In fact, 2,3-dinitro-1,3-butadiene itself (**3**, R″ = H) could represent a useful scaffold because it contains twice the nitroene system which can behave as a very flexible substrate able to easily react, for example, with reducing reagents and nucleophiles.

Moreover this scaffold, eventually decorated with different substituents, can be easily and variously manipulated to produce several interesting highly functionalized linear or homocyclic as well as heterocyclic compounds.[1c] Inter alia **3** reacted with diazomethane giving mono- (**4**) and 1,1′-bi (cyclopropanes) (**5**) (Scheme 1).[4]

Results and Discussion

In line with these previous studies and with the aim of enlarging the scope of the cycloaddition reactions on

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(1) (a) Spinelli, D.; Consiglio, G.; Dell'Erba, C.; Novi, M. In *The Chemistry of Heterocyclic Compounds, Thiophene and Its Derivatives*; Gronowitz, S., Ed.; Wiley: New York, 1991; Vol. 44, pp 295−396. (b) Consiglio, G.; Spinelli, D.; Dell'Erba, C.; Novi, M.; Petrillo, G. *Gazz. Chim. Ital.* **1997**, *127*, 753–769. (c) Bianchi, L.; Dell'Erba, C.; Maccagno, M.; Morganti, S.; Petrillo, G.; Rizzato, E.; Sancassan, F.; Severi, E.; Spinelli, D.; Tavani, C. *ARKIVOC* **2006**, *vii*, 169–185. (d) Terrier, F. *Nucleophilic Aromatic Displacement: The Influence of the Nitro Group*; VCH: New York, 1991; pp 306−307.

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(4) Armaroli, T.; Dell'Erba, C.; Gabellini, A.; Gasparrini, F.; Mugnoli, A.; Novi, M.; Petrillo, G.; Tavani, C. *Eur. J. Org. Chem.* **2002**, 1284–1291.

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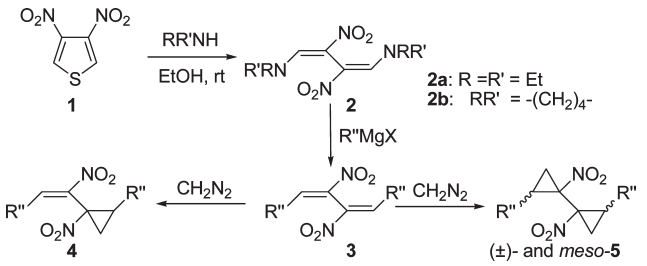
SCHEME 1. Synthesis of Substituted Mono- and 1,1′-Bi-(cyclopropanes) from 3,4-Dinitrothiophene



2,3-dinitro-1,3-butadienes, we have attempted to aziridinate them with nosyloxycarbamates ($NsONHCO_2R'''$, Ns = 4-$NO_2C_6H_4SO_2$; R‴ = Et or Bn) in the presence of CaO according to the procedure extensively developed long since[5] by an aza-MIRC (Michael initiated ring closure) reaction.[6]

Aziridines,[7] especially those polyfunctionalized,[8] are a very important class of chemical compounds and versatile building blocks for the synthesis of a variety of biologically interesting compounds.

The aziridination reactions were first performed by using the aminating agent and (*E*,*E*)-**2a** (R = R′ = Et)[2a,b] or (*E*,*E*)-**2b** [RR′ = −$(CH_2)_4$−],[2d] but we observed that the *β*-nitro enamines failed to react. Even attempts to aziridinate (*E*,*E*)-l,4-diphenyl-2,3-dinitro-l,3-butadiene[2c] did not lead to the expected products.[9] On the contrary, dialkyl derivatives (**3a**−**f**) easily reacted. Carrying on the reaction in equimolar ratio with the aim of synthesizing the monoaziridination products **6**, we obtained surprisingly only the 2,2′-biaziridines in low yields while some 2,3-dinitro-l,3-butadienes could be recovered unreacted. On the other hand, using a 2-fold excess of $NsONHCO_2R'''$, a good conversion of (*E*,*E*)-**3a**−**f** was achieved (Scheme 2) and (±)-2,2′-biaziridines **7a**−**f** and **8a** were obtained in good yields (Table 1).

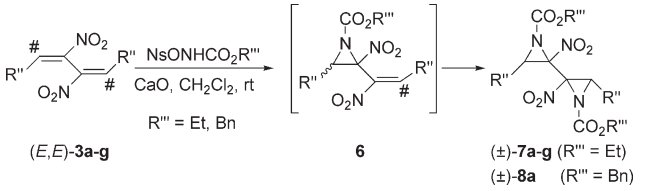
This peculiar behavior deserves some comments. The fact that intermediate **6** could not be isolated can be explained with the fact that the marked (#) carbon in **6** may also experience an inductive effect from the nitro group on the saturated carbon atom, and this makes the double addition

TABLE 1. Synthesis of (±)-2,2′-Dinitro-2,2′-biaziridines

entry	product	R″	reagent molar ratio[a]	yield (%)[b]
1	**7a**	Me	1:2:3	82
2	**7b**	Et	1:2:3	80
3	**7c**	Bu	1:2:3	76
4	**7d**	*i*-Pr	1:4:5	58
5	**7e**	2-(1,3-dioxan-2-yl)ethyl	1:4:5	66
6	**7f**	cyclopentyl	1:8:8	35
7	**8a**	Me	1:2:3	79

[a] **3**/$NsONHCO_2R'''$/base. [b] After flash chromatography.

SCHEME 2. Aza-MIRC Reactions on (*E*,*E*)-1,4-Dialkyl-2,3-dinitrobutadienes (3)



very fast and followed by the relevant ring closure. The importance of charge distribution (highly electrophilic character of the marked carbons of **3**) for the occurrence of the nucleophilic attack by the aziridinating agents is supported by the above observation that both (*E*,*E*)-l,4-diphenyl-2,3-dinitro-l,3-butadiene (**3**, R″ = Ph) and (*E*,*E*)-1,4-diamino-2,3-dinitro-1,3-butadienes (**2a**,**b**) do not react.

As shown in Table 1, the reactions have been successful for different substituents present at the C−l and C−4 ends of the dinitrobutadiene system and also in the presence of a 1,3-dioxane ring (entry 5), whose selective hydrolysis[5c] may lead to the introduction of an interesting carbonyl group on the aziridine ring.[10] The aza-MIRC reaction seems to suffer from steric effects, some cases reported in Table 1 (entries 4−6) requiring an excess of aminating reagent. The same steric effects slow the aziridination reactions and favor the decomposition of the aminating agent. The importance of steric effects is especially confirmed by the observation that butadiene **3f** (R″ = cyclopentyl) gives the aziridination reaction in lower yield upon increasing the excess of $NsONHCO_2Et$.

Noteworthy, the aza-MIRC reactions occur with high stereoselectivity, furnishing essentially *only a pair out of 10 possible stereoisomers* of the relevant (±)-2,2′-biaziridines,[11] as shown by the enantioselective HPLC analyses performed on the crude mixtures with different detectors (UV, CD, and ELSD). In Figure 1, the HPLC analyses of the crude **7c** are reported.

In addition, Figure 2 shows the general trend of peculiar stereospecificity for **7c**, **7d**, and **7f** compounds, where *Rac-M* points out the major obtained racemate and *rac-m* the minor racemates.

(5) (a) Barani, M.; Fioravanti, S.; Pellacani, L.; Tardella, P. A. *Tetrahedron* **1994**, *50*, 11235–11238. (b) Fioravanti, S.; Morreale, A.; Pellacani, L.; Tardella, P. A. *J. Org. Chem.* **2002**, *67*, 4972–4974. (c) Fioravanti, S.; Marchetti, F.; Pellacani, L.; Ranieri, L.; Tardella, P. A. *Tetrahedron: Asymmetry* **2008**, *19*, 231–236.

(6) For other aza-MIRC reactions, see: Tranchant, M.-J.; Dalla, V. *Tetrahedron* **2006**, *62*, 10255−10270 and references therein.

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(8) (a) Alickmann, D.; Froehlich, R.; Wuerthwein, E.-U. *Org. Lett.* **2001**, *3*, 1527–1530. (b) Attanasi, O. A.; Favi, G.; Filippone, P.; Stanovnik, B.; Svete, J. *Synlett* **2003**, 995−996. (c) Zhou, P.; Chen, B.-C.; Davis, F. A. In *Aziridines and Epoxides in Organic Synthesis*; Yudin, A. K., Ed.; Wiley-VCH: Weinheim, Germany, 2006; Chapter 3. (d) Troisi, L.; Granito, C.; Carlucci, C.; Bona, F.; Florio, S. *Eur. J. Org. Chem.* **2006**, 775–781. (e) Filiatrault, T. D.; Lewandowski, K. M.; Anderson, K. S.; Gaddam, B. N.; Joseph, E. G. U.S. Patent 2008200587, **2008**.

(9) Also, attempts to convert **3** (R″ = Ph) into the corresponding 2,2′-biaziridines under solvent-free conditions failed, in contrast to our previously reported data on (*E*)-*β*-nitrostyrene: Fioravanti, S.; Pellacani, L.; Stabile, S.; Tardella, P. A.; Ballini, R. *Tetrahedron* **1998**, *54*, 6169–6176.

(10) Fioravanti, S.; Morreale, A.; Pellacani, L.; Tardella, P. A. *Mol. Diversity* **2003**, *6*, 177–180.

(11) They have four stereocenters: in principle, they would exist in $2^4 = 16$ stereoisomers. Indeed, the four stereocenters are stereoequivalent two by two. Therefore, only 10 stereoisomers, four racemates: [*R*,*R*,*R*,*R*/*S*,*S*,*S*,*S* (they contain a C_2 symmetry axis); *R*,*S*,*S*,*R*/*S*,*R*,*R*,*S* (they contain a C_2 symmetry axis); *R*,*S*,*S*,*S*/*S*,*R*,*R*,*R* (they do not contain a symmetry element); *R*,*S*,*R*,*R*/*S*,*R*,*S*,*S* (they do not contain a symmetry element)] and two *meso* forms (*R*,*R*,*S*,*S* = *S*,*S*,*R*,*R*; *R*,*S*,*R*,*S* = *S*,*R*,*S*,*R*) can be predicted.

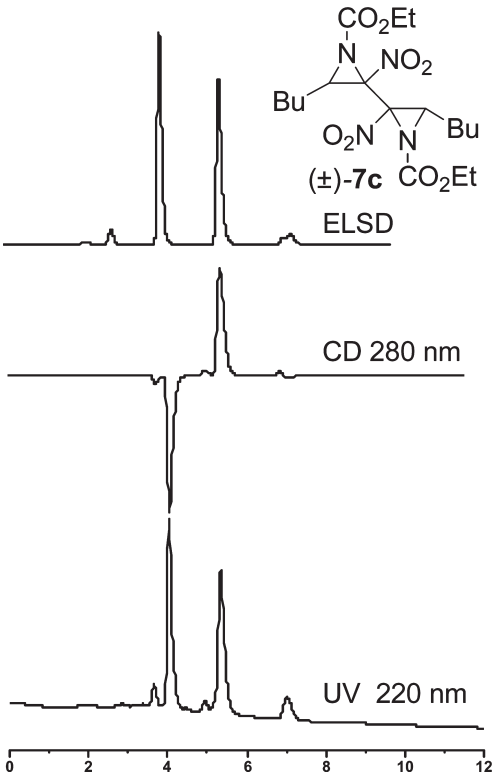


FIGURE 1. Enantioselective HPLC analyses performed on the crude mixtures obtained by aziridination of **3c**. ELSD (top), CD at 280 nm (middle), and UV at 220 nm (bottom) traces.

Furthermore, the ^{1}H NMR signals of the two aziridine protons are shifted ca. 0.45 ppm between themselves, thus suggesting a different configuration of the two aziridine rings, due to the free rotation around the C−C single bond of the intermediate Michael adduct. A change of the aziridine configuration with respect to the starting nitro alkenes has previously been observed in related aminations.[5c]

To examine the influence of reagents on the outcome of bisaziridinations, the aza-MIRC reaction was performed on **3a** by changing the aminating agent ($NsONHCO_2Bn$, Table 1, entry 7), the inorganic base (NaH), and the solvent (THF), but no significant variation was observed on the yield and on the stereochemistry as confirmed by stereoselective HPLC analyses and ^{1}H NMR spectra.

On the other hand, in all tested conditions, no trace of monoaziridines and only very limited amounts of *meso*-2,2′-biaziridines were found. These experimental findings represent an unexpected and valuable novelty with respect to previously reported synthesis of homocyclic analogues (**4** and **5**) starting from the same dinitro dienes.[4]

Taking in mind the behavior of compounds **5** that rearrange into 5,5′-disubstituted-4,5,4′,5′-tetrahydro[3,3′]biisoxazole 2,2′-dioxides with sodium iodide,[12] **7a** and **7c** were treated with sodium iodide in DMSO (Scheme 3), thus quantitatively obtaining the relevant bis(4,5-dihydro-l,2,4-oxadiazole-2-oxides) (**9a**,**c**), once more again via a highly stereoselective isomerization (Scheme 3).

This ring enlargement happens with the quite unusual cleavage of the C−C bonds of the aziridine rings,[13] with

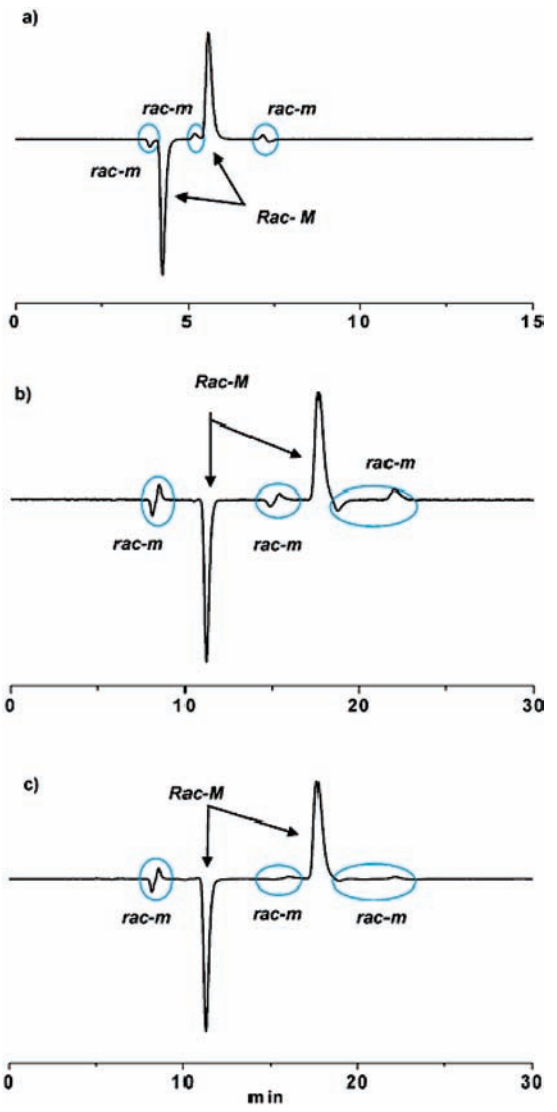


FIGURE 2. Chiroptical detection (CD at 280 nm) of crude mixtures of **7c** (top, a), **7d** (middle, b), and **7f** (bottom, c) by enantioselective HPLC analysis. *Rac-M* and *rac-m* were used for major and minor racemates, respectively.

the C−N cleavage[14] being more common. This kind of ring opening could occur because of the driving effect of the nitro group which is able to delocalize the negative charge in the intermediate anion (Scheme 4) that in turn gives the final 5,5′-dialkyl-4,4′-bis(ethoxycarbonyl)-4,4′,5,5′-tetrahydro-3,3′-bi(1,2,4-oxadiazole) 2,2′-dioxides **9a**,**c** with complete stereoselectivity.

Interestingly, they allow one to furnish a stereochemical evidence for the definitive assignment of the configuration of the parent 2,2′-biaziridine **7**.

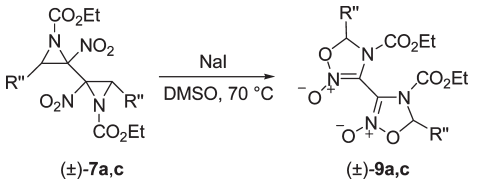
In fact, the S_N2−S_N2 iodide induced domino ring opening−ring closure of **7**, giving only a racemate of **9** (Figure 3),

(12) Bianchi, L.; Dell'Erba, C.; Gasparrini, F.; Novi, M.; Petrillo, G.; Sancassan, F.; Tavani, C. *ARKIVOC* **2002**, *xi*, 142–158.

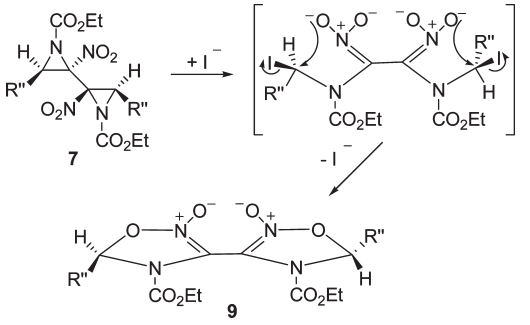
(13) (a) Attanasi, O. A.; Davoli, P.; Favi, G.; Filippone, P.; Forni, A.; Moscatelli, G.; Prati, F. *Org. Lett.* **2007**, *9*, 3461–3464. (b) Wang, J.-Y.; Hu, Y.; Wang, D.-X.; Pan, J.; Huang, Z.-T.; Wang, M.-X. *Chem. Commun.* **2009**, 422–424.

(14) (a) Yu, R.; Yamashita, Y.; Kobayashi, S. *Adv. Synth. Catal.* **2009**, *351*, 147–152. (b) Pineschi, M. *Eur. J. Org. Chem.* **2006**, 4979–4988. (c) Hu, X. E. *Tetrahedron* **2004**, *60*, 2701–2743.

SCHEME 3. Stereoselective Isomerization of (±)-2,2′-Dinitro-2,2′-biaziridines 7



SCHEME 4. Ring Enlargement Pathway of (±)-2,2′-Dinitro-2,2′-biaziridines 7



allows one to deduce that the surviving two chiral centers must be homochiral.

Thus, the same configuration can be attributed to the corresponding carbon atoms in **7**. As a matter of fact, of the 10 stereoisomers,[11] the two *meso* forms are excluded by enantioselective HPLC analyses. The other two chiral pairs can be excluded on the basis of their ^{1}H NMR spectra that do not show signals arising from equivalent aziridine protons and rule out C_2-symmetric species. In addition, the ring enlargement product **9c** has been shown to be chiral by enantioselective HPLC, and this implies that the two residual stereogenic carbons on **9c** are homochiral (the heterochiral combination giving rise to a *meso*-oxadiazoline). Clearly, the corresponding carbons of the parent biaziridine **7c** must also be homochiral since they are not involved in the ring enlargement process. Combining all of the above stereochemical findings leads to the assignment of the *R*,*S*,*R*,*R*/*S*,*R*,*S*,*S* configuration to the major racemate *Rac*-*M* generated by the aza-MIRC reaction.

Conclusions

In conclusion, (*E*,*E*)-1,4-dialkyl-2,3-dinitro-l,3-butadienes (**3**) carrying linear, branched, functionalized, or cyclic alkyl residues undergo a direct and highly stereoselective aza-MIRC reaction under very mild conditions, easily giving the corresponding 2,2′-dinitro-2,2′-biaziridines with good yields. As is well known, biaziridines are rarely reported in the literature,[15] although they can represent an interesting

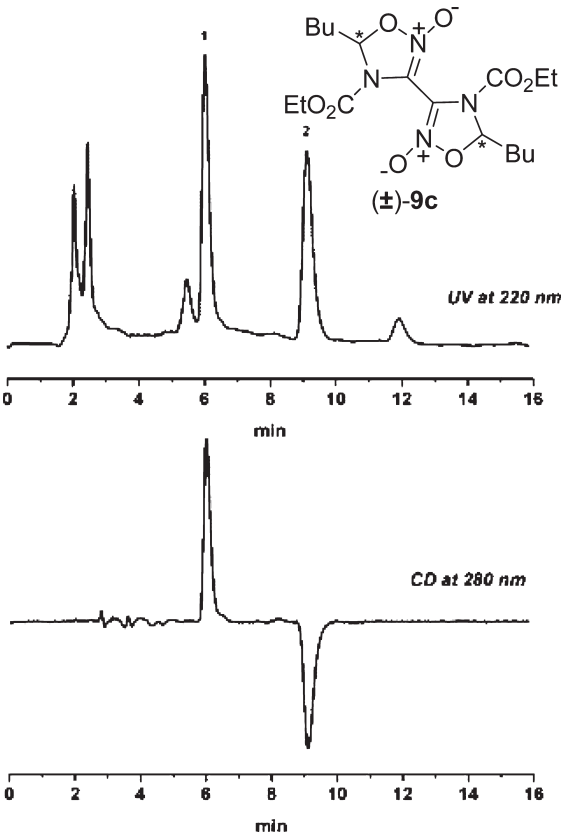


FIGURE 3. Enantioselective HPLC analyses performed on the crude mixtures obtained by isomerization of **7c**. UV at 220 nm (top) and CD at 280 nm (bottom) traces.

tool in asymmetric synthesis because of their aptitude to behave as ligands with some cations, thus mediating asymmetric transformations.[16] The isomerization reactions lead to valuable 4,5-dihydro-1,2,4-oxadiazoles which represent a good skeleton showing interesting pharmacological properties,[17] and their use can be foreseen. On the other hand, several 1,2,4-oxadiazolone derivatives represent very promising hits as LTCC blockers[18] as well as MDR agonists.[19]

Experimental Section

Synthesis of (*E*,*E*)-2,3-Dinitro-l,3-butadienes (3). General Procedure. To a stirring solution of (*E*,*E*)-1,4-bis(diethylamino)-2,3-dinitro-1,3-butadiene **2** (1 mmol) in 130 mL of anhydrous THF under Ar and cooled to 0 °C was slowly added 2.3 mmol of the suitable alkylmagnesium bromide reagent (1 M in THF). After 2 h, the reaction mixture was poured into ice/3% HCl, stirred for additional 1 h at room temperature, and extracted with CH_2Cl_2. The organic phase was dried over Na_2SO_4 overnight. Then, after solvent evaporation, **3** was purified by a silica

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gel column using a gradient of CH_2Cl_2 and $(CH_3CH_2)_2O$ as eluent.

(3*E*,5*E*)-2,7-Dimethyl-4,5-dinitroocta-3,5-diene (3d): 78% yield; IR ($CHCl_3$) 1603, 1526 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.13 (d, J = 5.8 Hz, 12 H), 2.38−2.45 (m, 2 H), 7.63 (d, J = 11.0 Hz, 2 H); ^{13}C NMR ($CDCl_3$) δ 21.1, 21.2, 29.2, 29.4, 139.1, 150.3, 150.6; HRMS-ESI (m/z) $[M]^+$ calcd for $C_{10}H_{16}N_2O_4$ 228.1110, found 228.1112.

[(1*E*,3*E*)-2,3-Dinitrobuta-1,3-diene-1,4-diyl]dicyclopentane (3f): 75% yield; IR ($CHCl_3$) 1603, 1524 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.53−1.90 (m, 16 H), 2.44−2.50 (m, 2 H), 7.55 (d, J = 11.0 Hz, 2 H); ^{13}C NMR ($CDCl_3$) δ 25.6, 32.8, 39.6, 39.8, 139.4, 149.4, 149.7; HRMS-ESI (m/z) $[M]^+$ calcd for $C_{14}H_{20}N_2O_4$ 280.1423, found 280.1422.

Synthesis of (±)-2,2′-Dinitro-2,2′-biaziridines 7a−f. General Procedure. To a stirred CH_2Cl_2 (3 mL) solution of (*E*,*E*)-2,3-dinitro-1,3-butadienes **3a−f** (1 mmol) were added CaO (3 mmol for **3a−c**, 5 mmol for **3d**,**e**, and 8 mmol for **3f**) and NsONH−CO_2Et (2 mmol for **3a−c**, 4 mmol for **3d**,**e**, and 8 mmol for **3f**) at room temperature. After the reactions were complete (TLC), the crude mixtures were filtered through plugs filled with silica gel using CH_2Cl_2 as eluent, and the solvent was removed in vacuo. The diastereomeric crude mixtures of 2,2′-biaziridines **7a−f** were analyzed by enantioselective HPLC analyses.

Diethyl 3,3′-dimethyl-2,2′-dinitro-2,2′-biaziridine-1,1′-dicarboxylate (7a): pale yellow oil; IR ($CHCl_3$) 1743, 1576 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.23 (t, J = 7.1 Hz, 3 H), 1.31 (t, J = 7.1 Hz, 3 H), 1.35 (d, J = 5.7 Hz, 3 H), 1.52 (d, J = 5.7 Hz, 3 H), 3.18 (q, J = 5.7 Hz, 1 H), 3.63 (q, J = 5.7 Hz, 1 H), 4.15−4.38 (m, 4 H); ^{13}C NMR ($CDCl_3$) δ 13.8, 14.0, 14.2, 14.5, 49.1, 64.3, 76.0, 76.1, 155.3, 155.7; HRMS-ESI (m/z) $[M + H]^+$ calcd for $C_{12}H_{19}N_4O_8$ 347.1203, found 347.1214.

Diethyl 3,3′-diethyl-2,2′-dinitro-2,2′-biaziridine-1,1′-dicarboxylate (7b): pale yellow oil; IR ($CHCl_3$) 1748, 1578 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.06−1.34 (m, 12 H), 1.92−2.24 (m, 4 H), 3.06 (dd, J = 6.5 Hz, J = 13.2 Hz, 1 H), 3.46 (dd, J = 4.0 Hz, J = 8.8 Hz, 1 H), 4.09−4.31 (m, 4 H); ^{13}C NMR ($CDCl_3$) δ 13.9, 14.0, 28.4, 49.2, 50.1, 63.8, 64.2, 75.8, 76.2, 154.9, 155.6; HRMS-ESI (m/z) $[M + H]^+$ calcd for $C_{14}H_{23}N_4O_8$ 375.1516, found 375.1509.

Diethyl 3,3′-dibutyl-2,2′-dinitro-2,2′-biaziridine-1,1′-dicarboxylate (7c): pale yellow oil; IR ($CHCl_3$) 1745, 1578 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.77−0.95 (m, 6 H), 1.15−1.64 (m, 14 H), 1.77−2.14 (m, 4 H), 2.98−3.13 (m, 1 H), 3.42−3.55 (m, 1 H), 4.11 (q, J = 7.1 Hz, 2 H), 4.21 (q, J = 7.1 Hz, 2 H); ^{13}C NMR ($CDCl_3$) δ 13.5, 13.7, 13.8, 14.2, 21.9, 22.0, 25.9, 28.3, 28.5, 48.2, 64.2, 64.3, 75.8, 77.6, 155.0, 155.7; HRMS-ESI (m/z) $[M + H]^+$ calcd for $C_{18}H_{31}N_4O_8$ 431.2142, found 431.2155.

Diethyl 3,3′-diisopropyl-2,2′-dinitro-2,2′-biaziridine-1,1′-dicarboxylate (7d): pale yellow oil; IR ($CHCl_3$) 1746, 1576 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.83−1.12 (m, 12 H), 1.16−1.30 (m, 6 H), 2.22−2.46 (m, 2 H), 2.89 (d, J = 9.4 Hz, 1 H), 3.23 (d, J = 9.4 Hz, 1 H), 4.08 (q, J = 7.1 Hz, 2 H), 4.17 (q, J = 7.1 Hz, 2 H); ^{13}C NMR ($CDCl_3$) δ 13.9, 14.0, 17.1, 17.2, 30.9, 31.0, 49.0, 49.1, 63.1, 75.8, 77.6, 154.2, 155.0; HRMS-ESI (m/z) $[M + H]^+$ calcd for $C_{16}H_{27}N_4O_8$ 403.1829, found 403.1796.

Diethyl 3,3′-bis[(1,3-dioxan-2-yl)ethyl]-2,2′-dinitro-2,2′-biaziridine-1,1′-dicarboxylate (7e): pale yellow oil; IR ($CHCl_3$) 1749, 1573 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.16−1.41 (m, 10 H), 1.55−2.22 (m, 8 H), 3.09−3.26 (m, 1 H), 3.56 (dd, J = 3.8 Hz, J = 9.4 Hz, 1 H), 3.62−3.74 (m, 4 H), 3.91−4.22 (m, 8 H), 4.45−4.61 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 14.4, 25.5, 29.6, 31.7, 48.1, 66.7, 66.9, 67.8, 77.2, 82.7, 155.6; HRMS-ESI (m/z) $[M + H]^+$ calcd for $C_{22}H_{35}N_4O_{12}$ 547.2251, found 547.2238.

Diethyl 3,3′-dicyclopentyl-2,2′-dinitro-2,2′-biaziridine-1,1′-dicarboxylate (7f): pale yellow oil; IR ($CHCl_3$) 1748, 1578 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.12−1.27 (m, 6 H), 1.38−1.99 (m, 16 H), 2.32−2.54 (m, 2 H), 2.99 (d, J = 8.8 Hz, 1 H), 3.34 (d, J = 8.8 Hz, 1 H), 4.00−4.25 (m, 4 H); ^{13}C NMR ($CDCl_3$) δ 13.9, 14.0, 25.0, 25.5, 32.7, 39.6, 53.8, 60.2, 63.6, 77.2, 149.4; HRMS-ESI (m/z) $[M + H]^+$ calcd for $C_{20}H_{31}N_4O_8$ 455.2142, found 455.2135.

Synthesis of (±)-2,2′-Dinitro-2,2′-biaziridines 8a. The same procedure for the synthesis of **7a** was followed, but using NsONH−CO_2Bn (2 mmol) as aminating agent, NaH (3 mmol) as inorganic base, and THF (3 mL) as solvent. After workup, the diastereomeric crude mixture of 2,2′-biaziridines **8a** was analyzed by enantioselective HPLC analyses.

Dibenzyl 3,3′-dimethyl-2,2′-dinitro-2,2′-biaziridine-1,1′-dicarboxylate (8a): yellow oil; IR ($CHCl_3$) 1746, 1600, 1577 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.33 (d, J = 5.7 Hz, 3 H), 1.51 (d, J = 5.7 Hz, 3 H), 3.23 (q, J = 5.7 Hz, 1 H), 3.67 (q, J = 5.7 Hz, 1 H), 5.17 (s, 2 H), 5.26 (s, 2 H), 7.32−7.37 (m, 10 H); ^{13}C NMR ($CDCl_3$) δ 14.3, 14.4, 49.1, 50.0, 68.9, 76.0, 76.2, 127.1, 127.7, 129.0, 143.5, 154.80, 155.0; HRMS-ESI (m/z) $[M + H]^+$ calcd for $C_{22}H_{23}N_4O_8$ 471.1516, found 471.1524.

Ring Enlargement of 7a and 7c into 9a and 9c. General Procedure. A stirred solution of **7** (1 mmol) and dry NaI (2 mmol) in anhydrous DMSO (20 mL) was heated at 70 °C under atmosphere of Ar overnight. Then, the mixtures were cooled at room temperature, diluted with brine, and extracted with diethyl ether. After drying over Na_2SO_4 and solvent evaporation, the products were analyzed by enantioselective HPLC analyses.

4,4′-Bis(ethoxycarbonyl)-5,5′-dimethyl-4,4′,5,5′-tetrahydro-3,3′-bi(1,2,4-oxadiazole) 2,2′-dioxide (9a): brown viscous oil; IR ($CHCl_3$) 1725, 1500 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.29 (t, J = 7.1 Hz, 3 H), 1.31 (t, J = 7.1 Hz, 3 H), 1.58 (d, J = 5.3 Hz, 6 H), 4.25 (q, J = 7.1 Hz, 2 H), 4.26 (q, J = 7.1 Hz, 2 H), 6.16 (q, J = 5.3 Hz, 2 H); ^{13}C NMR ($CDCl_3$) δ 14.0, 14.1, 20.4, 63.0, 63.6, 92.1, 145.8, 149.4, 151.0, 155.9; HRMS-ESI (m/z) $[M + H]^+$ calcd for $C_{12}H_{19}N_4O_8$ 347.1203, found 347.1198.

5,5′-Dibutyl-4,4′-bis(ethoxycarbonyl)-4,4′,5,5′-tetrahydro-3,3′-bi(1,2,4-oxadiazole) 2,2′-dioxide (9c): brown viscous oil; IR ($CHCl_3$) 1728, 1499 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.85−0.92 (m, 6 H), 1.18−1.65 (m, 18 H), 4.16−4.29 (m, 4 H), 6.02 (q, J = 5.0 Hz, 2 H); ^{13}C NMR ($CDCl_3$) δ 13.7, 13.9, 14.0, 22.1, 24.6, 29.5, 62.6, 63.3, 94.5, 145.8, 149.4, 151.0, 155.9; HRMS-ESI (m/z) $[M + H]^+$ calcd $C_{18}H_{31}N_4O_8$ 431.2142, found 431.2136.

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Supporting Information Available: ^1H and ^{13}C NMR spectra of compounds (*E*,*E*)-**3d**,**f** as well as ^1H and ^{13}C NMR spectra and chiral HPLC data of compounds (±)-**7a−f**, (±)-**8a**, and (±)-**9a**,**c** were reported. This material is available free of charge via the Internet at http://pubs.acs.org.