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# A NOVEL INVERSE TYPE DIELS-ALDER REACTION OF ETHYL (*E*)-3-(1,3-BENZOTHIAZOL-2-YL)-3-CYANOPROPENOATE AS A HIGHLY REACTIVE 1-AZA-1,3-BUTADIENE

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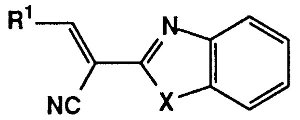
Diels-Alder reactions of ethyl (*E*)-3-(1,3-benzothiazol-2-yl)-3-cyanopropenoate (**2**) as a 1-aza-1,3-butadiene are described. The diene (**2**), bearing electron-withdrawing ester group, reacts with electron-rich dienophiles (**3a-d**) under extremely mild conditions to give corresponding cycloadducts (**4a-d**) in high yields with high regio- and *endo*-selectivities. Treatment of **2** with electron-donating allyl alcohols (**5a,b**) causes tandem transesterification and intramolecular cycloaddition to afford *cis*-fused polycyclic systems (**6a,b**) in one step.

**KEY WORDS** (*E*)-3-(1,3-benzothiazol-2-yl)-3-cyanopropenoate; regio- and *endo*-selective Diels-Alder reaction; tandem transesterification and intramolecular cycloaddition

Diels-Alder reaction of 1-aza-1,3-butadienes with olefins is now recognized as a powerful method for construction of nitrogen containing six-membered rings.[1,2] Recently, we reported that benzylidene(cyano)methyl-1,3-benzazoles (**1a,b**) as stable 1-aza-1,3-butadienes react with some dienophiles to afford Diels-Alder adducts (**Fig. 1**).[3] In the report, we also found that the dienes having more electron-withdrawing substituents (Y) exhibit higher reactivities. This observation prompted us to introduce directly electron-withdrawing ester group at 4-position in the diene system. We now report here that ethyl (*E*)-3-(1,3-benzothiazol-2-yl)-3-cyanopropenoate (**2**) acts as one of the most reactive 1-aza-1,3-dienes to electron-rich dienophiles, and also report that treatment of **2** with allyl alcohols causes tandem transesterification and intramolecular cycloaddition to afford polycyclic systems in one step.

**Fig. 1**



1a: X = S, $R^1$ = *p*-Y-$C_6H_4$-
1b: X = O, $R^1$ = *p*-Y-$C_6H_4$-
2: X = S, $R^1$ = $EtO_2C$

The diene (**2**) was readily prepared by condensation of 2-(cyano)methyl-1,3-benzothiazole with ethyl glyoxylate in ethanol in the presence of a catalytic amount of triethylamine. Treatment of **2** with electron-rich dienophiles (**3a-d**) causes Diels-Alder reaction under extremely mild conditions to give the corresponding *endo*-cycloadducts (**4a-d**) in high yields (**Chart 1** and **Table 1**). Thus, the reaction of the diene **2** with 10 equivalents of ethyl vinyl ether (**3a**) afforded *cis*-adduct (**4a**) predominantly, in almost quantitative yield (entry 1). In the same manner, cyclic vinyl ether (**3b**) or olefins bearing an electron-donating aromatic ring (**3c,d**) acted as nice dienophiles to the diene (**2**), affording exclusively *endo*-cycloadducts (**4b-d**) in high yields (entries 2-4).[4] The regio- and stereochemical assignments of the adducts (**4a-d**) were made by their $^1$H-NMR spectra including NOE experiments.[5] Since all the reactions in **Table 1** afforded *endo*-cycloadducts, they may proceed *via* transition state **A** due to secondary orbital interactions. In contrast to the reactions in **Table 1**, heating diene (**2**) with 10 equivalents of methyl acrylate in toluene at 100 °C for 56 h gave

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the corresponding cycloadducts in low yield (30%, the same regiochemstry, *cis* : *trans* = 1.9 : 1). This observation may show the electrophilic character of the diene (**2**) as an inverse type diene.[2a,b,4)]

**Chart 1**

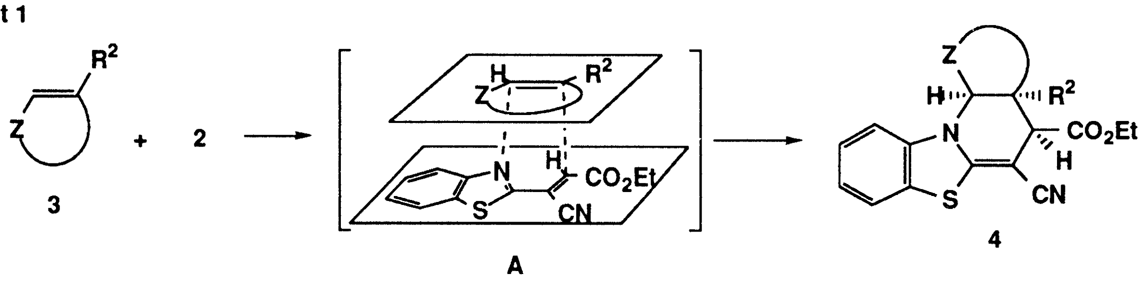
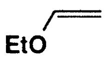
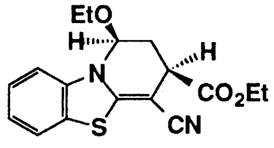
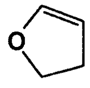
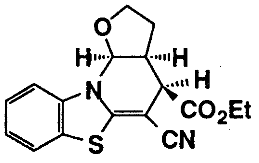
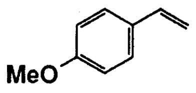
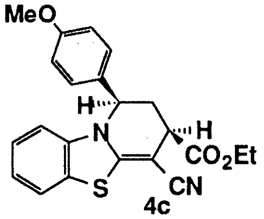
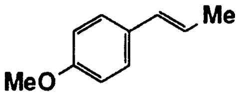
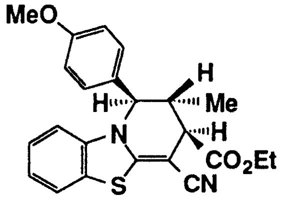
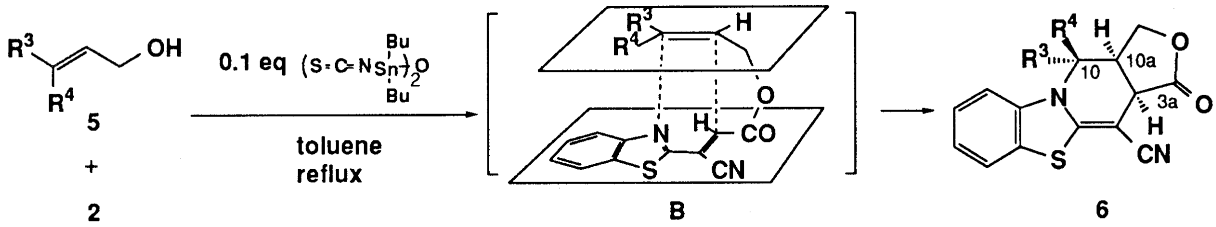


**Table 1**

| Entry | Dienophile | Conditions | Yield (%) | Product |
|---|---|---|---|---|
| 1 | <br>**3a** | $CH_2Cl_2$<br>r.t., 5 h | 98 | <br>**4a** (*cis* : *trans* = 10 : 1) |
| 2 | <br>**3b** | $ClCH_2CH_2Cl$<br>50 °C, 5 h | 87 | <br>**4b** |
| 3 | <br>**3c** | $CH_2Cl_2$<br>r.t., 24 h | 98 | <br>**4c** |
| 4 | <br>**3d** | $CH_2Cl_2$<br>r.t., 14 h | 76 | <br>**4d** |

With the results of the intermolecular reaction of **2** with **3** in hand, our attention turned to the application of this reaction to an intramolecular version. To achieve this, we took a tandem transesterification-intramolecular cycloaddition approach as shown in **Chart 2**.[6)] First, heating diene **2** with allyl alcohol (**5**, $R^3$ = $R^4$ = H) in the presence of a catalytic amount of distannoxane catalyst[7)] gave only a transesterification product. Taking into account the electrophilic character of the diene (**2**), more electron-donating allyl alcohols (**5a,b**) were next examined. In both cases, *cis*-fused lactones (**6a,b**) were obtained exclusively. Thus, reactions of **2** with **5a** and **5b** gave 3a,10a-*cis*-10,10a-*trans*-cycloadduct (**6a**) and 3a,10a-*cis*-10,10a-*cis*-cycloadduct (**6b**), respectively.[8)] These facts clearly show that the present intramolecular process is concerted because of the reflection of the olefinic geometries of dienophiles into the products, and also suggested that both reactions took place *via* the tether-*endo* transition state (**B**).

**Chart 2**



a: $R^3$ = *p*-$MeOC_6H_4$, $R^4$ = H, 4 h, 49%; b: $R^3$ = H, $R^4$ = *p*-$MeOC_6H_4$, 10 h, 75%

The diene (**2**) would be one of the most reactive 1-aza-butadienes.[2a,b] In this work, especially, the tandem process may be applicable to other inverse type 1-azadiene systems.[2a,b]

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3) Sakamoto M., Nozaka A., Shimamoto M., Ozaki H., Suzuki Y., Yoshioka S., Nagano M., Okamura K., Date T., Tamura O., *Chem. Pharm. Bull.*, **42**, 1367-1369 (1994); idem, *J. Chem. Soc., Perkin Trans. 1*, **1995**, 1759-1770.

4) Brief AM1 calculation on *s-cis* conformation of **1a** (Y = H) and **2** supports this difference in reactivities. Thus, the calculation shows that the diene (**2**) has lower LUMO (-1.6 eV) than **1a** (Y = H) (-1.2 eV). In addition, the magnitude of C4 coefficient of **2** (0.47) is larger than that of **1a** (0.44). These values in the calculation of **2** are favorable for regio-selective diene-LUMO controlled (inverse type) Diels-Alder reaction with high regioselectivity. Accordingly, diene (**2**) smoothly reacts with electron-rich dienophiles (**3a-d**) (HOMO: between -9.5 and -8.5 eV). See also, ref. 4b) and 6b). For AM1, see, Dewar, M. J. S.; Zoebisch, E. G.; Healy, E. F.; Stewart, J. J. P. *J. Am. Chem. Soc.* **1985**, *107*, 3902.

5) For example, $^1$H-NMR of **4d** as follows, $^1$H-NMR ($CDCl_3$, 270 MHz): 1.02 (3 H, t, $J$ = 7.3 Hz, $CO_2CH_2C\mathit{H}_3$), 1.26 (3 H, d, $J$ = 7.0 Hz, $CHC\mathit{H}_3$), 3.01 (1 H, br s, $C\mathit{H}CO_2Et$, spin saturation at $\delta$ = 1.26; NOE → 11.3%), 3.22 (1 H, br qt, $J$ = 7.0, 1.6 Hz, $C\mathit{H}CH_3$, spin saturation at $\delta$ = 1.26; NOE → 9.0%), 3.55 (2 H, q, $J$ = 7.3 Hz, $CO_2C\mathit{H}_2CH_3$), 3.73 (3 H, s, $OC\mathit{H}_3$), 5.00 (1 H, br s, $NC\mathit{H}Ar$, spin saturation at $\delta$ = 1.26; NOE → 6.7%), 6.58 (1 H, d, $J$ = 7.6 Hz, ArH), 6.77 (2 H, d, $J$ = 8.6 Hz, ArH), 6.92 (2 H, d, $J$ = 8.6 Hz, ArH), 7.01-7.14 (2 H, m, ArH), 7.44 (1 H, dd, $J$ = 7.4, 1.3 Hz, ArH).

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8) In contrast to the reactions, treatment of **2** with **5a** in the absence of the catalyst in refluxing toluene did not give the intramolecular cycloadduct (**6a**) at al. Accordingly, the present cycloaddition should occur by way of transesterification and intramolecular cycloaddition instead of intermolecular cycloaddition and lactonization.

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