Nucleophilic Reaction upon Electron-Deficient Pyridone Derivatives. XII.[1] Novel Additions of 3,5-Dinitro-2-pyridone with Ethyl Vinyl Ether: Formation and Reactions of a Six-membered Cyclic Nitronate

Yasuo TOHDA,* Keita TANI, Norihiko YAMAWAKI, Masahiro ARIGA,† Nagatoshi NISHIWAKI,† Katsuroh KOTANI,† and Eizo MATSUMURA†

Laboratory of Organic Chemistry, Division of Natural Science, Osaka Kyoiku University, Asahigaoka, Kashiwara, Osaka 582

† Department of Chemistry, Osaka Kyoiku University, Minamikawahori-cho, Tennoji-ku 4-88, Osaka 543

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Successive additions of 3,5-dinitro-2-pyridone (**1**) with three molecules of ethyl vinyl ether (EVE) were investigated. The first addition is the first example of reverse electron-demand Diels–Alder (REDA) cyclization of 2-pyridone which acts as a diene to give an unstable bicyclic intermediate **9**. Meisenheimer complexes **2a** and **2b** are isolated as a quenched intermediate of **9**. The second addition is a REDA cyclization between the nitroalkene moiety of **9** and EVE to afford a six-membered nitronate **4**, which are characterized by some chemical reactions. The third step is 1,3-dipolar addition of the nitronate with EVE to give a 1:3 adduct **3**.

In a course of our study on electron-deficient pyridone derivatives,[1] we found that 1-substituted 3,5-dinitro-2-pyridones (**1**) were susceptible to various nucleophiles. One of the pyridones, **1a** (1-methyl derivative), reacts with C-, N-, or O-nucleophiles at its C-6 position to give stable Meisenheimer complexes (**2**).[2] In some cases, the second addition of nucleophiles occurs at the C-4 position of **2**, and subsequent reactions proceed to give ring-cleaved products such as 2-nitro-1,3-propanediimines,[3] 4-nitrophenols,[4] 4-nitroanilines,[5] or 3-nitropyridines[6,7] by loss of N-substituted nitroacetamide as a common fragment. These products are formed via a general reaction course, i.e., an addition–addition–elimination–elimination mechanism (AAEE mechanism) as shown in Scheme 1. The carbon nucleophiles used in these reactions were relatively strong, e.g., enolate anions[4] or enamines.[5,6] Now, we wish to report novel successive additions of the dinitropyridone **1** with three molecules of less nucleophilic ethyl vinyl ether (EVE) involving unexpected formation of a six-membered cyclic nitronate, which is an interesting intermediate for organic syntheses.[8]

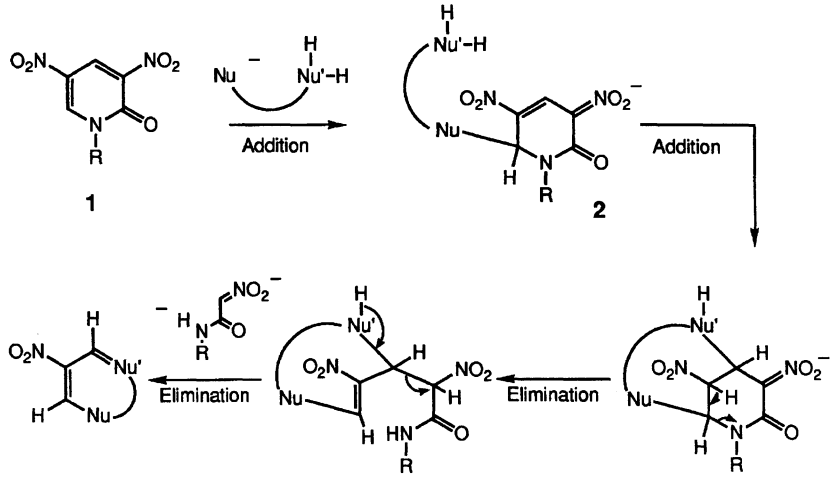
Results and Discussion

1:3 Adduct Formation via a Cyclic Nitronate Intermediate. Treatment of 1-substituted 3,5-dinitro-2-pyridones (**1a**—**1d**) with excess of ethyl vinyl ether (EVE) in DMF gave 1:3 adducts **3a**—**3d** in good yields (Table 1, Entries 1—4). Such adducts did not formed from α- or/and β-substituted vinyl ethers or enamines at all. 1-(2-Pyridyl) (**1b**), 1-(4-nitrophenyl) (**1c**), and 1-(5-bromo-2-pyridyl) derivatives (**1d**) were more reactive than 1-methyl one (**1a**). ^{1}H NMR and other spectra of **3** were too complex to determine the structure of **3**. In order to identify the structure of the adducts and to understand the mechanism of the reaction, we tried to isolate intermediates by some controlled reactions.

When **1b** and **1c** were treated with EVE at 50°C in DMF, 1:2 adducts **4b** and **4c** were obtained in 45% and 49% yields, respectively, but the corresponding adduct **4a** could not be isolated. It is obvious that **4** is an intermediate of the reaction because treatment of **4** with EVE at 60°C gave **3** in good yields (Table 1, Entries 8 and 9). ^{1}H NMR spectra of **4** show two sets of CH–CH_2–CH four spin system (see Experimental), indicating that two molecules of EVE attacked the C-4 and C-6 positions of **1**. The following three types of reactions of **4** show that **4** has one six-membered cyclic nitronate moiety (see Scheme 3).

In the first place, treatment of **4b** with KOBu^t gave an α,β-unsaturated oxime **5b** in 78% yield by loss of one molecule of ethyl formate. Less basic NaOEt gave **5b** in a poorer yield of 28%. Structure of **5b** was indicated by its ^{1}H NMR and IR spectra. Two singlet protons at δ=5.51 and 6.25 and a strong absorption at 3360 cm^{-1} are attributed to a methylene group and an oxime hydroxy group, respectively. The ^{1}H NMR spectrum showed the presence of one set of the CH–CH_2–CH four spin system. Previously we had found some characteristic reactions of a six-membered cyclic nitronate **6** which had been obtained by a reverse electron-demand Diels–Alder (REDA) reaction of a highly electron-deficient nitroalkene, methyl α,*p*-dinitrocinnamate, with vinyl ethers. (Scheme 2, Eq. 1)[9] One of the characteristic reactions of **6** is a base-promoted fragmentation which gives the α,β-unsaturated oxime **5** and an ester. (Scheme 2, Eq. 2) Thus the conversion of **4b** to **5b** is one of the chemical evidences that **4** is a six-membered cyclic nitronate, although other base promoted fragmentations of such nitronates have been reported.[10]

In the second place, **4** reacted with acrylonitrile even in the presence of excess EVE to give compounds **7**, which are found to be 1:2:1 adducts of the pyridone, EVE and the acrylic acid derivatives (Table 1, Entry 13). Furthermore, adducts **7** were exclusively obtained by direct reaction of **1a**—**1d** with EVE and the acrylic acid derivatives (Table 1, Entries 10—12). Since 1,3-



Scheme 1. A typical reaction of **1** with nucleophiles.

Table 1. Reactions of **1** with Ethyl Vinyl Ether

Entry	Substrate	Reagent[a)]	Temp/°C	Products[b)]	Yields[c)]/%
1	**1a**	EVE	80	**3a**	67
1	**1b**	EVE	60	**3b**	85
3	**1c**	EVE	60	**3c**	90
4	**1d**	EVE	60	**3d**	82
5	**1a**	EVE	60	—	d)
6	**1b**	EVE	50	**4b**	45
7	**1c**	EVE	50	**4c**	49
8	**4b**	EVE	60	**3b**	84
9	**4c**	EVE	60	**3c**	87
10	**1a**	EVE+AN	80	**7a**	77
11	**1b**	EVE+AN	60	**7b**	86
12	**1d**	EVE+MA	60	**7d**	71
13	**4b**	EVE+AN	60	**7b**	75
14	**4b**	MA	60	**7b′**	58

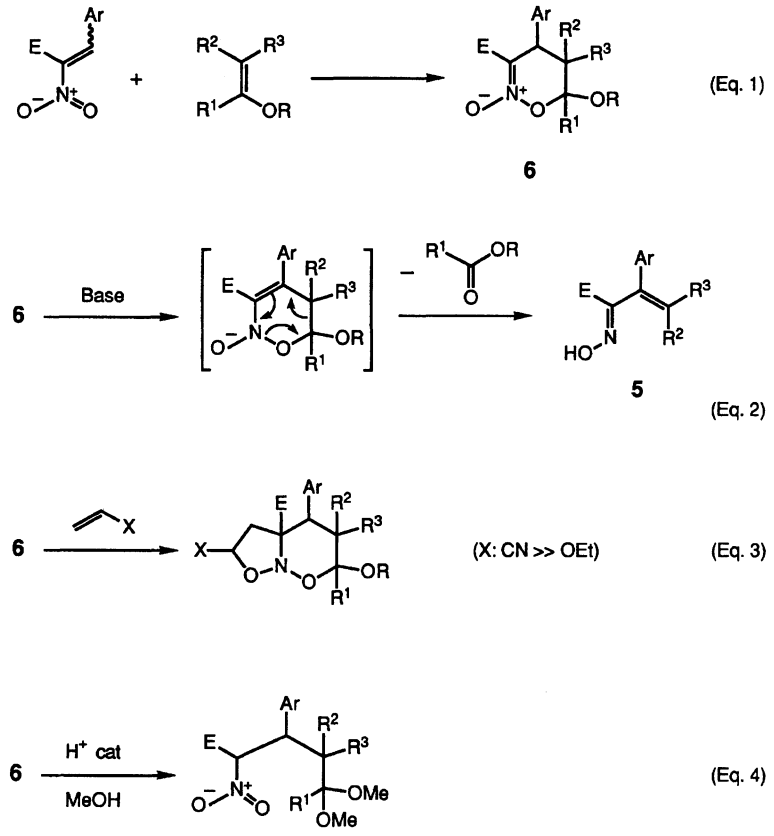
a) AN=acrylonitrile, MA=methyl acrylate. b) **3**=the 1 : 3 adducts, **4**=the 1 : 2 adducts, **7**=the 1 : 2 : 1 adducts. c) Isolated yields are shown. d) Any product was not isolated and **1a** was recovered in 85% yield.

dipolar addition of cyclic nitronates with electron-deficient dipolarophile occurs faster than that with electron-rich one (Scheme 2, Eq. 3),[9,11] the above reactions are another chemical evidence that **4** is a cyclic nitronate. Structure of **7d** had been identified by X ray crystallography by Namba and his co-workers[12] (Fig. 1) and supported the identification of the other adducts **3**—**9**. (vide infra)

In the last place, treatment of **4b** with catalytic amount of *p*-toluenesulfonic acid in methanol gave an acetal **8** by a ring opening reaction of the cyclic nitronate into the corresponding Michael adduct of the original nitroalkenes with the vinyl ether (Eq. 4).[9] The similar ring opening of cyclic nitronates obtained from nitroalkenes and enamines are well-known.[13]

Isolation of Anionic σ-Adduct Intermediates. When **1a** was treated with EVE in pyridine at room temperature, orange-red precipitates **2a** were obtained quantitatively which were composed of **1a**, EVE and pyridine in a ratio of 1 : 1 : 1. The compound is so labile that it decomposes to **1a** quantitatively on heating without EVE in methanol for an hour. Half-life of **2a** is about 20 min in methanol at ambient temperature. Its insolubility and instability prevent **2a** from measuring ^{1}H NMR spectrum. It can be concluded that **2a** is an anionic σ-complex in which β-carbon of EVE adds at the C-6 position of **1a** by comparing its electronic and IR spectra with those of known anionic σ-adducts of **1a** (Fig. 2).[2] Similarly, **2c** was obtained by a reaction of **1c** and EVE in pyridine. Treatment of **1b** with EVE in DMF at ambient temperature also gave orange precipitates **2b** which were composed of **1b** and EVE in a ratio of 1 : 1. Heating **2a**—**2c** with EVE also afforded **3a**—**3c** in good yields. The color and the chemical behavior of **2b** and **2c** strongly indicate that the compounds are also anionic σ-complexes. Because the compound **2b** has no extra pyridine moiety, the counter cation of the complex must be constructed by intramolecular coordination of the nitrogen in the 1-(2-pyridyl) group of **1b** to the α-carbon of the EVE as shown in Fig. 2. Thus the addition site of EVE on **1b** must be the C-6 position rather than the C-4 one.

Since anionic σ-complexes are known as important intermediates in many nucleophilic reactions upon aromatic compounds, they have been widely investigated.[14] In spite of these efforts, isolation of EVE-added anionic σ-complexes of any electron-deficient aromatics have been not known in our knowledge.[15] In order to compare the reactivity of **1** with that of 1,3,5-trinitrobenzene (TNB), one of the most popular electron-deficient aromatics, or with 2-methoxy-3,5-dinitropyridine, the pyridine isomer of **1a**, these substrates were heated with EVE in pyridine but even color of the mixtures did not change at all. These findings also indicate the high affinity of **1** with EVE.



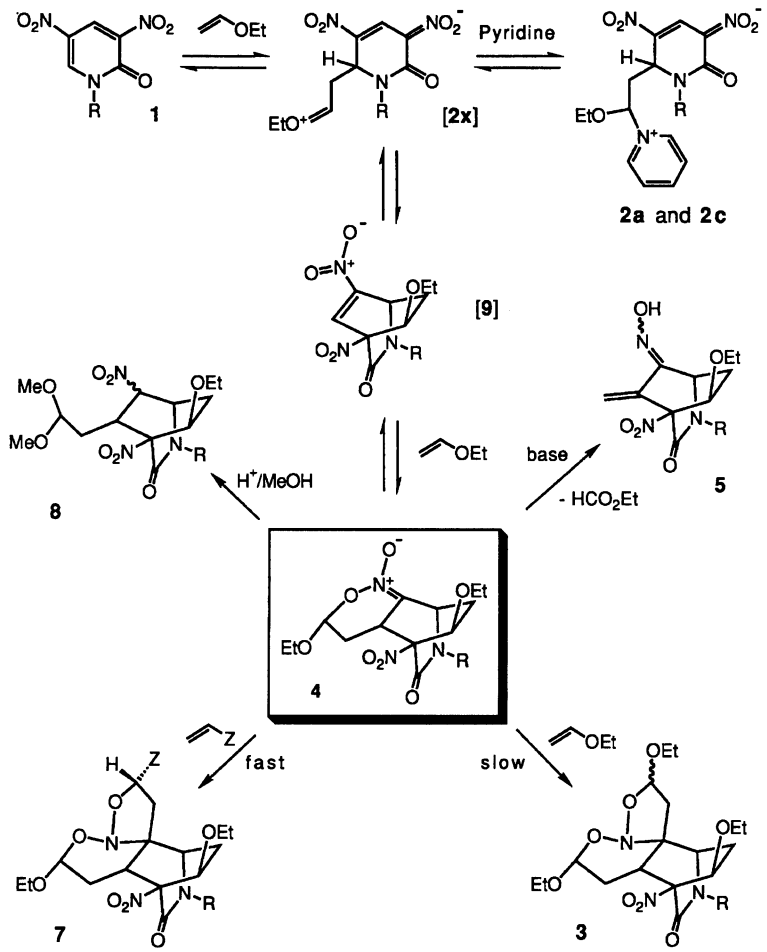
Scheme 2. Characteristic reactions of the cyclic nitronate **6**. (E=CO_2Me, Ar=$C_6H_4NO_2$-*p*)

Mechanism of the Addition Reaction. A mechanism of the adducts formation and the chemical transformations of **4** are proposed as follow on the basis of these chemical reactions and the determined structure of **7d** (Scheme 3).

The first addition of EVE occurs at the C-6 position of **1** to give an anionic σ-complex **2x** in which the counter cation is located on the ether oxygen atom. The labile complex is reversibly quenched by pyridine bases intermolecularly (in the case of **2a** or **2c**) or intramolecularly (in the case of **2b**).

Intramolecular cyclization of **2x** leads to a 2-azabicyclo[2.2.2]oct-5-ene intermediate **9**, although it cold not be detected or isolated probably due to its instability. The formation of **9** from **1** is obviously a typical stepwise reverse electron-demand Diels–Alder (REDA) addition. While many stable 2-azabicyclo-[2.2.2]oct-5-enes have been reported which are formed from normal Diels–Alder addition of 2-pyridones with electron-deficient dienophiles,[16] such bicyclic adducts are not known at all which are formed by the REDA cyclization of 2-pyridones with electron rich alkenes or alkynes. Indeed, only a few electron-deficient aromatic compounds can act as the diene of the REDA cyclization. They are all highly electron-deficient polyazines[17] or benzo[*b*]quinolizinium (acridizinium) cations.[18] But the mechanism of the cyclizations of these electron-deficient aromatic compounds via the cationic polar cycloaddition is quite different from that of the present one. The cationic polar addition proceeds via a charge-transfer complex without an intermediate carbonium ion.[18] On the other hand, one of the factors which make the present cyclization possible is high stability of the Meisenheimer intermediate **2x**. From the determined structure of **7d**, the cyclization of **2x** occurs steroselectively in an endo manner, which is interpreted in terms of electrostatic attraction between its 1,3-dinitropropenyl anion part and its oxonium cation one.

The second addition is also a step-wise REDA reaction of the nitroalkene moiety of **9** with EVE to form the cyclic nitronate **4**.[9] It is well-known that in the presence of Lewis acid catalyst, simple nitroalkenes which have no electron-withdrawing groups readily react with simple alkenes to give the cyclic nitronates,[19] while in the absence of the catalysts such simple nitroalkenes do not react with simple alkenes or even with weakly nucleophilic vinyl ethers. Without any Lewis acid catalyst, only sufficiently electron-deficient nitroalkenes such as methyl α,*p*-dinitrocinnamate can cyclize with weakly nucleophilic vinyl ethers[9] or simple nitroalkenes form the cyclic adducts with strongly nucleophilic enamines.[13] The intermediate **9** is apparently a nitroalkene which has no electron-withdrawing group. The above discussion indicates the cyclization of **9** with EVE is assisted by a neighboring group participation. From the fact that the second addition of EVE occurs at



Scheme 3. Formation and reactions of the cyclic nitronate **4**. (Z=an electron-withdrawing group)

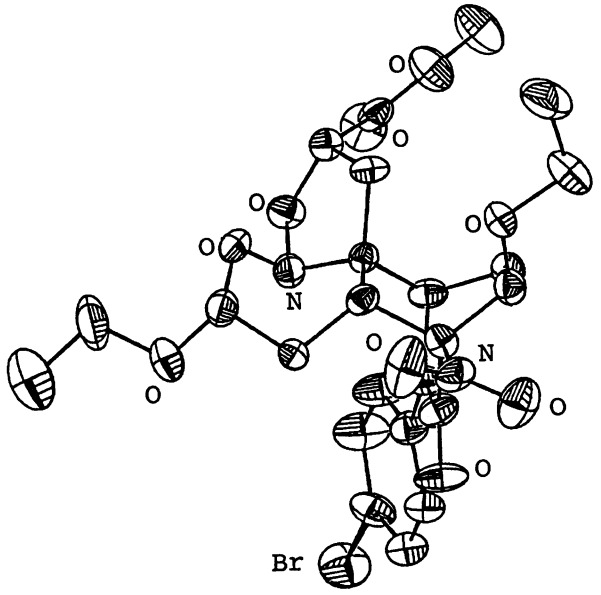


Fig. 1. A perspective view of the adduct **7d**.

the endo site of **9**, the amide moiety of the bicyclooctene **9** may assist the cyclization. The higher reactivity of **1b** or **1c** [*N*-(2-pyridyl) or *N*-(4-nitrophenyl) derivatives] compared with that of **1a** (*N*-methyl derivative) is explained in terms of the higher Lewis acidity of the amide group. Steric hindrance of the amide moiety may be one of the reasons why bulky α- or β-substituted vinyl ethers do not react with **1**. The structure of **4** and other products derived form **4** are reasonably identified as shown in Scheme 3.

In conclusion, the reaction of 3,5-dinitro-2-pyridone (**1**) with ethyl vinyl ethers (EVE) involves some novel types of additions. The conversion of **1** to 2-azabicyclo-[2.2.2]oct-5-ene intermediate **9** is the first example of a reverse electron-demand Diels–Alder addition in which an azine acts as the diene. One of driving forces of the addition is formation of an extremely stable anionic σ-complex intermediate **2x**, which is reversibly quenched by pyridine bases. The formation of the six-membered nitronate **4** from **9** and EVE is catalyzed by the intramolecular amide group. Finally, some characteristic conversions of the six-membered nitronate **4** are found involving the unique base-catalysed fragmentation into α,β-unsaturated oxime **5**.

Experimental

The ^{1}H NMR spectra were measured by a Hitachi R-20B (60 MHz) or a JEOL FX 100 spectrometer (100 MHz), the

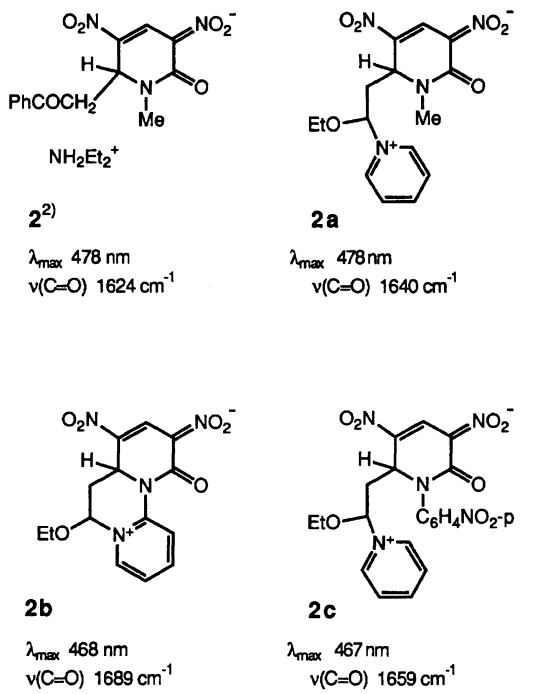


Fig. 2. Structures and spectra of anionic σ-complexes **2**.

IR spectra by a Hitachi 260-10 spectrophotometer, and the electronic spectra by a Shimadzu UV-240 spectrophotometer.

1-(5-Bromo-2-pyridyl)-3,5-dinitro-2-pyridone (1d). This compound was prepared by the similar method as that of **1b**.[4] Mp 190.5—191°C. Found: C, 34.95; H, 1.18; N, 16.35%. Calcd for $C_{10}H_5BrN_4O_5$: C, 35.21; H, 1.48; N, 16.43%. ^{1}H NMR (60 MHz, acetone-d_6) δ=7.96 (1H, d, J=8.3 Hz), 8.33 (1H, dd, J=8.3 and 2.6 Hz), 8.81 (1H, d, J=2.6 Hz), 9.09 (1H, d, J=3.2 Hz), 9.55 (1H, d, J=3.2 Hz). IR (Nujol) 1685 (C=O), 1616 (C=C), 1542 (NO_2), 1370 (NO_2), 1286, 1131, 1000, 834, 752 cm^{-1}.

Formation of 1 : 3 Adducts 3. A solution of **1a** (1.00 g, 4 mmol) and EVE (2.00 g, 28 mmol) in DMF (40 ml) was heated at 80°C for 3 h. After removal of the solvent in vacuo, the residue was column-chromatographed on silica gel. A benzene–ethyl acetate (20 : 1) eluate was recrystallized from benzene to give 1.20 g (67%) of ($1R^*$,$2S^*$$4RS^*$,$8R^*$,$10R^*$,$11S^*$,$15R^*$)-4,8,15-triethoxy-13-methyl-11-nitro-5,7-dioxa-6,13-diazatetracyclo-[9.2.2.$0^{2,6}$.$0^{2,10}$]pentadecan-12-one (**3a**). Mp (decomp) 166—167°C. Found: C, 52.17; H, 7.19; N, 9.98%. Calcd for $C_{18}H_{29}N_3O_8$: C, 52.04; H, 7.04; N, 10.12%. ^{1}H NMR (60 MHz, $CDCl_3$) δ=1.11 (3H, t, J=7.0 Hz), 1.17 (6H, t, J=7.0 Hz), 1.5—2.8 (6H, m), 3.01 (3H, s), 3.0—4.0 (8H, m), 3.53 (1H, t, J=5.0 Hz), 4.87 (1H, dd, J=9.0 and 7.0 Hz), 5.09 (1H, dd J=6.0 and 1.2 Hz). IR (Nujol) 1705 (C=O), 1562 (NO_2), 1363 (NO_2), 1238, 1112, 1090, 831 cm^{-1}.

Similarly, ($1R^*$,$2S^*$,$4RS^*$,$8R^*$,$10R^*$,$11S^*$,$15R^*$)-4,8,15-triethoxy-11-nitro-13-(2-pyridyl)-5,7-dioxa-6,13-diazatetracyclo[9.2.2.$0^{2,6}$.$0^{2,10}$]-pentadecan-12-one (**3b**) was obtained by a reaction of **1b** with EVE at 60°C for 3 h. Yield 85%. Mp (decomp) 225°C. Found: C, 55.14; H, 6.47; N, 11.82%. Calcd for $C_{22}H_{30}N_4O_8$: C, 55.22; H, 6.32; N, 11.70%. ^{1}H NMR (100 MHz, $CDCl_3$) δ=1.18 (3H, J=7.1 Hz), 1.24 (3H, J=7.1 Hz), 1.26 (3H, J=7.1 Hz), 2.0—2.5 (5H, m), 2.93 (1H, dd, J=18.4 and 10.5 Hz), 3.5—4.0 (8H, m), 4.7—4.8 (3H, m), 7.22 (1H, ddd, J=5.8, 5.2, and 1.7 Hz), 7.7—7.9 (2H, m), 8.4 (1H, m). IR (Nujol) 1720 (C=O), 1605, 1560 (NO_2), 1370 (sh) (NO_2), 1135, 1060, 910, 780 cm^{-1}.

($1R^*$,$2S^*$,$4RS^*$,$8R^*$,$10R^*$,$11S^*$,$15R^*$)-4,8,15-triethoxy-11-nitro-13-(4-nitrophenyl)-5,7-dioxa-6,13-diazatetracyclo-[9.2.2.$0^{2,6}$.$0^{2,10}$]pentadecan-12-one (**3c**) was obtained by a reaction of **1c** with EVE at 60°C for 3 h. Yield 90%. Mp (decomp) 228—230°C. Found: C, 52.98; H, 5.79; N, 10.68%. Calcd for $C_{23}H_{30}N_4O_{10}$: C, 52.87; H, 5.79; N, 10.72%. ^{1}H NMR (60 MHz, $CDCl_3$) δ=1.18 (9H, J=7.3 Hz), 1.4—2.0 (2H, m), 2.3—3.0 (4H, m), 3.0—4.0 (7H, m), 4.38 (1H, t, J=2.8 Hz), 4.77 (1H, t, J=5.0 Hz), 4.96 (1H, dd, J=8.9 and 6.5 Hz), 5.73 (1H, d, J=5.6 Hz), 7.75 (2H, d, J=8.6 Hz), 8.27 (2H, d, J=8.6 Hz). IR (Nujol) 1699 (C=O), 1546 (NO_2), 1521, 1347 (NO_2), 1110, 1045, 697 cm^{-1}.

($1R^*$,$2S^*$,$4RS^*$,$8R^*$,$10R^*$,$11S^*$,$15R^*$)-13-(5-bromo-2-pyridyl)-4,8,15-triethoxy-11-nitro-5,7-dioxa-6,13-diazatetracyclo[9.2.2.$0^{2,6}$.$0^{2,10}$]-pentadecan-12-one (**3d**) was obtained by a reaction of **1d** with EVE at 60°C for 3 h. Yield 82%. Mp (decomp) 221°C. Found: C, 47.16; H, 5.29; N, 10.12%. Calcd for $C_{22}H_{29}BrN_4O_7$: C, 47.40; H, 5.24; N, 10.05%. ^{1}H NMR (60 MHz, $CDCl_3$) δ=1.17 (3H, J=6.9 Hz), 1.24 (6H, J=7.2 Hz), 1.9—3.1 (7H, m), 3.3—4.0 (7H, m), 4.6—4.9 (3H, m), 7.22 (1H, d, J=8.4 Hz), 7.36 (1H, dd, J=8.4 and 2.4 Hz), 8.38 (1H, broad d, J=2.4 Hz). IR (Nujol) 1706 (C=O), 1692 (C=O), 1558 (NO_2), 1417, 1365 (NO_2), 1279, 1096, 1058, 830, 788 cm^{-1}.

Formation of 1 : 2 Adducts 4. A solution of 1-(2-pyridyl)-3,5-dinitro-2-pyridone (**1b**) (1.31 g, 5 mmol) and EVE (1.80 g, 25 mmol) in DMF (65 ml) was heated at 50°C for 3 h. After removal of the solvent, the residual oil was rinsed with ether and column-chromatographed on silicagel. A chloroform eluate was recrystallized from benzene–hexane to give 0.914 g (45%) of ($1R^*$,$5R^*$,$7S^*$,$8S^*$,$12R^*$)-5,12-diethoxy-8-nitro-9-oxo-10-(2-pyridyl)-4-oxa-3,10-diazatricyclo[6.2.2.$0^{2,7}$]dodecan-2(3)-en-3-ylium-3-olate (**4b**). Mp (decomp) 208°C. Found: C, 53.16; H, 5.17; N 13.88%. Calcd for $C_{18}H_{22}N_4O_7$: C, 53.20; H, 5.46; N, 13.79%. ^{1}H NMR (100 MHz, $CDCl_3$) δ=1.01 (3H, t, J=7.1 Hz), 1.16 (3H, t, J=7.1 Hz), 1.80 (H-6, ddd, J=14.0, 11.1, and 3.1 Hz), 2.15 (H-11, dt, J=14.2 and 2.6 Hz),2.80 (H-11′, ddd, J=14.2, 9.3, and 3.4 Hz), 3.36 (H-6′, dt, J=14.0 and 7.3 Hz), 3.5—4.1 (5H, m), 4.80 (H-12, dd, J=9.3 and 2.5 Hz), 5.48 (H-5, dd, J=7.3 and 3.2 Hz), 6.50 (H-1, t, J=3.1 Hz), 7.15 (1H, ddd, J=7.4, 4.9, and 1.0 Hz), 7.72 (1H, ddd, J=8.6, 7.3, and 2.0 Hz), 8.00 (1H, dt, J=8.4 and 1.0 Hz), 8.43 (1H, ddd, J=4.9, 1.9, and 1.0 Hz). IR (Nujol) 3050, 1707 (C=O), 1645 (C=N), 1586, 1563 (NO_2), 1370, 1352 (NO_2), 1240, 1174, 1120 cm^{-1}.

Similarly, ($1R^*$,$5R^*$,$7S^*$,$8S^*$,$12R^*$)-5,12-diethoxy-8-nitro-10-(4-nitrophenyl)-9-oxo-4-oxa-3,10-diazatricyclo[6.2.2.$0^{2,7}$]-dodecan-2(3)-en-3-ylium-3-olate (**4c**) was obtained by the reaction of **1c** with EVE in 49% yield. Mp (decomp) 206—208°C. Found: C, 50.68; H, 4.95; N 12.38%. Calcd for $C_{19}H_{22}N_4O_9$: C, 50.67; H, 4.92; N, 12.44%. ^{1}H NMR (60 MHz, $CDCl_3$) δ=1.12 (3H, t, J=7.0 Hz), 1.17 (3H, t, J=7.0 Hz), 1.68 (H-6, ddd, J=14.2, 10.8, and 2.6 Hz), 2.17 (H-11, dt, J=14.4 and 2.5 Hz), 2.83 (H-11′, ddd, J=14.4, 9.3, and 3.4 Hz), 3.0—4.0 (5H, m), 4.04 (H-6′, dd, J=10.8 and 7.4 Hz), 4.87 (H-12, dd, J=9.3 and 2.5 Hz), 5.27 (H-1, t, J=3.2

Hz), 5.53 (H-5, dd, J=7.4 and 2.6 Hz), 7.57 (2H, d, J=9.1 Hz), 8.28 (2H, d, J=9.1 Hz). IR (Nujol) 3115, 3090, 1706 (C=O), 1644 (C=N), 1577 (NO_2), 1346 (NO_2), 1260, 1109, 783 cm^{-1}.

Reaction of 4 with Ethyl Vinyl Ether. Mixtures of **4b** or **4c** (1 mmol) with EVE (10 mmol) in DMF (10 ml) were heated at 60°C for 3 h. After removal of the solvent in vacuo, residual solids were recrystallized from benzene to give **3b** or **3c** in 84 or 87% yields, respectively.

Formation of 1 : 2 : 1 Adducts 7 from 4. A mixture of **4b** (0.20 g, 0.50 mmol), EVE (0.14 g, 2.0 mmol) and acrylonitrile (0.11 g, 2.0 mmol) in DMF (5 ml) was heated at 60°C for 3h. The solvent was removed in vacuo and residual solid was recrystallized from benzene to give 0.17 g (75%) of ($1R^*$,$2S^*$,$4S^*$,$8R^*$,$10R^*$,$11S^*$,$15R^*$)-4-cyano-8,15-diethoxy-11-nitro-13-(2-pyridyl)-5,7-dioxa-6,13-diazatetracyclo[9.2.2.$0^{2,6}$.$0^{2,10}$]pentadecan-12-one (**7b**). Mp (decomp) 214—217°C. Found: C, 54.93; H, 5.45; N 14.92%. Calcd for $C_{21}H_{25}N_5O_7$: C, 54.89; H, 5.48; N, 15.24%. ^{1}H NMR (60 MHz, DMSO-d_6) δ=1.07 (3H, t, J=6.7 Hz), 1.11 (3H, t, J=6.7 Hz), 1.3—1.7 (1H, m), 2.6—3.9 (10H, m), 4.6—5.6 (4H, m), 7.1—7.3 (1H, m), 7.8—8.0 (2H, m), 8.3—8.5 (1H, m). IR (Nujol) 1720 (C=O), 1560 (NO_2), 1413, 1370 (NO_2), 1276, 1107, 1060 cm^{-1}.

($1R^*$,$2S^*$,$4S^*$,$8R^*$,$10R^*$,$11S^*$,$15R^*$)-8,15-diethoxy-4-methoxycarbonyl-11-nitro-13-(2-pyridyl)-5,7-dioxa-6,13-diazatetracyclo[9.2.2.$0^{2,6}$.$0^{2,10}$]pentadecan-12-one (**7b′**) was obtained by a reaction of **4b** (0.10 g, 0.25 mmol), methyl acrylate (0.10 g, 1.3 mmol) in DMF (5 ml) at 60°C for 4 h. After removal of the solvent, residual solids were recrystallized from ethanol to give 0.071 g (58%) of **7b′**. Mp (decomp) 205°C. Found: C, 53.06; H, 5.60; N, 11.17%. Calcd for $C_{22}H_{28}N_4O_9$: C, 53.65; H, 5.73; N, 11.38%. ^{1}H NMR (60 MHz, DMSO-d_6) δ=1.16 (3H, t, J=7.2 Hz), 1.18 (3H, t, J=7.2 Hz), 1.3—1.8 (1H, m), 2.2—2.5 (4H, m), 2.6—2.9 (2H, m), 3.2—3.8 (4H, m), 3.72 (3H, s), 4.6—5.3 (4H, m), 7.1—7.3 (1H, m), 7.7—7.9 (2H, m), 8.38 (1H, broad d, J=4.8 Hz). IR (Nujol) 1758 (ester C=O), 1710 (amide C=O), 1160 cm^{-1}.

Formation of 1 : 2 : 1 Adduct 7 from 1. A mixture of **1a** (0.40 g, 2.0 mmol), EVE (0.72 g, 10 mmol), and acrylonitrile (0.27 g, 5.0 mmol) in DMF (10 ml) was heated at 80°C for 3 h. After removal of the solvent in vacuo, the residual solid was recrystallized from benzene to give 0.61 g (77%) of ($1R^*$,$2S^*$,$4S^*$,$8R^*$,$10R^*$,$11S^*$,$15R^*$)-4-cyano-8,15-diethoxy-13-methyl-11-nitro-5,7-dioxa-6,13-diazatetracyclo[9.2.2.$0^{2,6}$.$0^{2,10}$]pentadecan-12-one (**7a**). Mp (decomp) 200—202°C. Found: C, 51.32; H, 6.08; N 13.92%. Calcd for $C_{17}H_{24}N_4O_7$: C, 51.51; H, 6.10; N, 14.14%. ^{1}H NMR (60 MHz, $CDCl_3$) δ=1.13 (3H, t, J=7.1 Hz), 1.20 (3H, t, J=7.1 Hz), 1.4—1.9 (1H, m), 2.1—2.7 (3H, m), 2.7—4.0 (8H, m), 3.03 (3H, s), 4.59 (1H, dd, J=6.6 and 3.0 Hz), 4.94 (1H, dd, J=8.6 and 6.2 Hz), 5.14 (1H, dd, J=8.0 and 5.3 Hz). IR (Nujol) 1690 (C=O), 1552 (NO_2), 1370 (sh) (NO_2), 1242, 1105, 1080, 1005, 850 cm^{-1}.

Similarly, **7b** was obtained in 86% yield by a reaction of **1b** (0.50 g, 1.8 mmol), EVE (0.40 g, 5.4 mmol), and acrylonitrile (0.29 g, 5.4 mmol) in DMF (10 ml) at 60°C for 3 h.

($1R^*$,$2S^*$,$4S^*$,$8R^*$,$10R^*$,$11S^*$,$15R^*$)-13-(5-bromo-2-pyridyl)-4-methoxycarbonyl-8,15-diethoxy-11-nitro-5,7-dioxa-6,13-diazatetracyclo[9.2.2.$0^{2,6}$.$0^{2,10}$]pentadecan-12-one (**7d**) was afforded by a reaction of **1d** (0.34 g, 1 mmol), EVE (0.29 g, 4 mmol), and methyl acrylate (0.26 g, 4 mmol) in 71% yield. Mp (decomp) 227—229°C. Found: C, 46.04; H, 4.71; N 9.96%. Calcd for $C_{22}H_{27}BrN_4O_9$: C, 46.24; H, 4.76; N, 9.81%. ^{1}H NMR (60 MHz, $CDCl_3$) δ=1.15 (6H, t, J=7.2 Hz), 1.69 (1H, td, J=13.4 and 8.5 Hz), 2.3—2.9 (5H, m), 3.2—4.0 (5H, m), 3.78 (3H, s), 4.65 (1H, t, J=4.8 Hz), 4.89 (1H, dd, J=6.4 and 3.7 Hz), 5.02 (1H, dd, J=5.7 and 2.4 Hz), 5.36 (1H, t, J=2.7 Hz), 7.72 (1H, dd, J=8.7 and 2.2 Hz), 7.89 (dd, J=8.7 and 0.9 Hz). 8.33 (1H, dd, J=2.2 and 0.9 Hz). IR (Nujol) 1747 (C=O, ester), 1696 (C=O, amide), 1551 (NO_2), 1362 (NO_2), 1267, 1213, 1100, 1003, 807 cm^{-1}.

Fragmentation of Nitronate 4b with Base. A suspension of *t*-BuOK (1 mmol) in THF (35 ml) was added to a solution of **4b** (0.405 g, 1 mmol) in THF (50 ml) at −15°C during 5 min, and stirred at room temperature for 4 h. Acetic acid (0.070 g, 1.1 mmol) in methanol (6 ml) was added to the pale red solution. Benzene (70 ml) was added to the mixture and it was washed with water and dried by Na_2SO_4. After removal of the solvent, residual solid was recrystallized from benzene to give 0.260 g (78%) of ($1R^*$,$4S^*$,$8R^*$)-8-ethoxy-6-hydroxyimino-5-methylene-4-nitro-2-(2-pyridyl)-2-azabicyclo[2.2.2]-octan-3-one (**5b**). Mp (decomp) 146—150°C. Found: C, 54.24; H, 4.86; N 16.25%. Calcd for $C_{15}H_{16}N_4O_5$: C, 54.21; H, 4.85; N, 16.86%. ^{1}H NMR (100 MHz, CD_3COCD_3) δ=1.14 (3H, t, J=6.6 Hz), 1.9 (H-7′, m), 2.86 (H-7, ddd, J=13.5, 9.1, and 3.7 Hz), 3.4—3.9 (2H, m), 4.99 (H-8, dd, J=9.1 and 2.4 Hz), 5.51 (1H, s), 6.25 (1H, s), 6.92 (H-1, t, J=3.5 Hz), 7.1—7.3 (1H, m), 7.7—8.1 (2H, m), 8.49 (1H, broad d, J=4.9 Hz), 11.02 (1H, s). IR (Nujol) 3360 (OH), 3065, 1710 (C=O), 1658 (C=N and C=C), 1580, 1565 (NO_2), 1355 (NO_2), 1075, 907 cm^{-1}.

Decomposition of 4b with Acid. A suspension of **4b** (0.405 g, 1 mmol) in dry methanol containing 20 mg of *p*-toluenesulfonic acid was stirred at 45°C. After 1 h, all the substrate was dissolved. Benzene (40 ml) was added to the solution and washed with water, dried by $MgSO_4$. The residual solid was recrystallized from benzene-hexane to give 0.35 g (83%) of ($1R^*$,$4S^*$,$5R^*$,$6RS^*$,$8R^*$)-8-ethoxy-5-(2,2-dimethoxyethyl)-4,6-dinitro-2-(2-pyridyl)-2-azabicyclo-[2.2.2]octan-3-one (**8b**). Mp (decomp) 162—165°C. Found: C, 51.20; H, 5.78; N 13.08%. Calcd for $C_{18}H_{24}N_4O_8$: C, 50.94; H, 5.69; N, 13.20%. ^{1}H NMR (60 MHz, $CDCl_3$) δ=1.15 (3H, t, J=7.0 Hz), 1.3—1.7 (2H, m), 2.01 (1H, dt, J=15.0 and 2.6 Hz), 2.36 (1H, ddd, J=15.0, 3.9, and 1.7 Hz), 3.28 (3H, s), 3.32 (3H, s), 3.3—3.7 (1H, m), 4.3 (2H, m), 4.5—4.8 (2H, m), 5.15 (1H, ddd, J=4.5, 3.2, and 1.6 Hz), 6.05 (1H, ddd, J=5.0, 4.5, and 3.0 Hz), 7.2 (1H, m), 7.8 (1H, m), 8.0 (1H, m), 8.4 (1H, m). IR (Nujol) 1705 (C=O), 1587, 1560, 1553 (NO_2), 1363 (NO_2), 1123 (C–O), 1073 (C–O), 1045 cm^{-1}.

Isolation of Anionic σ-Adducts 2a and 2c. A solution of **1a** (0.50 g, 2 mmol) and EVE (1.00 g, 14 mmol) in pyridine (10 ml) was allowed to stand for 12 h. Orange-red precipitates were washed with pyridine and ether. This material was analytically pure 6-[2-ethoxy-2-(1-pyridino)-ethyl]-1-methyl-5-nitro-2-oxo-1,2,3,6-tetrahydropyridine-3-nitronate (**2a**) (0.67 g, 94%). Mp (decomp) 128—131°C. Found: C, 51.60; H, 5.45; N 16.26%. Calcd for $C_{15}H_{18}N_4O_6$: C, 51.42; H, 5.18; N, 15.99%. IR (Nujol) 1640 (C=O), 1590, 1375 (NO_2), 1320, 1218, 1170, 942, 780 cm^{-1}. Electronic spectra (MeOH) λ=325 (ε>8.1×10^3) and 478 (ε>1.9×10^4)

nm. Half life of **2a** in methanol at room temperature was measured with its electronic spectrum to be ca. 20 min.

Similarly, 6-[2-ethoxy-2-(1-pyridino)ethyl]-5-nitro-1-(4-nitrophenyl)-2-oxo-1,2,3,6-tetrahydropyridine-3-nitronate (**2c**) was obtained in 76% yield. Mp (decomp) 253—256°C. Found: C, 52.28; H, 4.08; N 15.13%. Calcd for $C_{20}H_{19}N_5O_8$: C, 52.52; H, 4.19; N, 15.31%. IR (Nujol) 1659 (C=O), 1612, 1600, 1517, 1350 (NO_2), 1313, 1207, 1170, 1115, 1051, 942, 852, 774 cm^{-1}. Electronic spectra (MeOH) $\lambda=349$ ($\varepsilon>2.0\times10^3$) and 467 ($\varepsilon>3.6\times10^3$) nm.

Isolation of Anionic σ-adduct 2b. A mixture of **1b** (0.50 g, 1.8 mmol) and EVE (1.00 g, 14 mmol) in DMF (10 ml) was allowed to stand at room temperature for 12 h. Orange precipitates were washed with DMF and ether to give analytically pure 9-ethoxy-1-nitro-4-exo-3,4,4a,9,10,10a-hexahydro-4a-aza-8a-azoniaphenanthrene-3-nitronate (**2b**) (0.32 g, 50%). Mp (decomp) 177°C. Found: C, 50.18; H, 3.93; N, 17.03%. Calcd for $C_{14}H_{14}N_4O_6$: C, 50.30; H, 4.22; N, 16.76%. Electronic spectra (MeOH) $\lambda=399$ ($\varepsilon>3.4\times10^3$), 468 ($\varepsilon>6.1\times10^3$) nm. Due to insolubility and lability of **2b**, exact absorbances of these peaks could not be measured. IR (Nujol) 1689 (C=O), 1614, 1574, 1502, 1360 (NO_2), 1314, 1203, 1187, 1160, 780 cm^{-1}. The solvent of the filtrate was removed in vacuo and the residue was rinsed with ethanol. Residual solid was recrystallized from benzene to give 0.18 g (23%) of **4b**. The ethanol solution was condensed to give 0.11 g (14%) of **3b**.

Reaction of Anionic σ-Adducts 2a—2c with EVE. A suspension of either **2a**, **2b**, or **2c** (each 0.5 mmol) in DMF (5 mmol) containing EVE (5 mmol) was heated at either 80, 60, or 60°C for 3 h. After removal of the solvent in vacuo, residual oil was crystallized from benzene to afford **3a**, **3b**, or **3c** in 67, 74, or 70% yield, respectively.

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