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MOLECULAR DESIGN BY CYCLOADDITION REACTIONS—XXVIII[1]

CONTROLLING FACTORS IN STEREOSPECIFIC CYCLOADDITION REACTIONS OF PHENANTHRENO[9,10-c]-FURAN AND AZULENOCYCLONE WITH SOME DIENOPHILES

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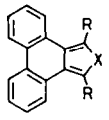
Abstract—The cycloaddition reactions of 1,3-diphenylphenanthreno[9.10-c]furan and azulenocyclone, which are phencyclone and dibenzo[4,5-c]furotropone related compounds, with some electron-rich and electron-deficient dienophiles are extensively investigated. The structures of these adducts were determined by spectral inspections. The sterespecificity of these compounds were observed. The formation mechanisms for these adducts are discussed by the frontier orbital analyses and some interaction factors.

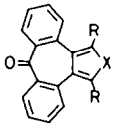
We investigated the thermal cycloaddition reactions of phencyclone (**1**)[2] and dibenzo[4,5-c]furotropone (**2**)[3] with some electron-rich and electron-deficient olefins and triene compounds such as tropone, cycloheptatriene and N-carbethoxyazepine. The high peri-, regio- and stereospecificity of these compounds was observed.

It was of interest to examine reactivity and specificity of these related compounds for the cycloaddition reactions; e.g. controlling factors over the modes of cycloadditions needed clarification.

We now describe the cycloaddition reactions of 1,3-diphenylphenanthreno[9,10-c]furan (**3**)[4] and azulenocyclone (1,3-diphenyl-2,8-dihydrodibenzo[e,h]azulen-2,8-dione) (**4**)[5] with some electron-rich and electron-deficient dienophiles.



1 R=Ph, X=CO (Phencyclone)
3 R=Ph, X=O (1.3-Diphenylphenanthreno-[9.10-c] furan)



2 R=H, X=O (Dibenzo[4.5-c] furotropone)
4 R=Ph, X=CO (Azulenocyclone)

Chart 1.

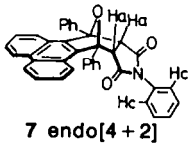
RESULTS

Cycloaddition reactions of 1,3-*diphenylphenanthreno* [9,10-c]*furan* (**3**) *with some dienophiles.* The cycloadditions of 1,3-diphenylphenanthreno[9,10-c]furan (**3**) with N-phenylmaleimide (**5**) and maleic anhydride (**6**) as electron-deficient dienophiles afforded [4+2]cycloadducts, **7** and **8** in 95% and 71% yields, respectively. The NMR spectrum of **7** showed two center bridgehead proton (Ha) signals as a singlet at δ 4.57, which might be deshielded by the anisotropy of the oxa-bridged moiety,[6] and two aromatic proton (Hc) signals as a multiplet at δ 5.70, which might be shielded owing to lying over the phenanthrene ring.[2]

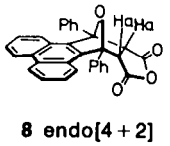
Similarly, the NMR spectrum of **8** exhibited two center bridgehead proton (Ha) signals as a singlet at δ 5.00. Thus, it is concluded that both adducts **7** and **8** were assigned the *endo* configuration. However, the cycloadditions of **3** with other electron-deficient dienophiles such as *p*-benzoquinone and tetracyanoethylene gave no adducts. On the other hand, the reaction of **3** with oxabenzonorbornadiene (**9**) as a electron-rich and strained olefin gave a mixture of isomeric 1:1 adducts (**10** and **11**) with the ratio of 2:1 in total yield of 76%.

5 X=N—Ph
6 X=O

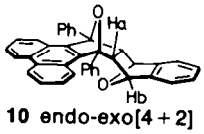
9



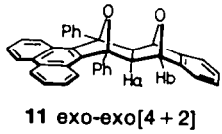
7 endo[4+2]



8 endo[4+2]



10 endo-exo[4+2]



11 exo-exo[4+2]

Chart 2.

The NMR spectrum of major product **10** showed signals at δ 3.50 (s, 2H, Ha) and 4.78 (s, 2H, Hb). On the other hand, the NMR spectrum of minor product **11** exhibited signals at δ 2.87 (s, 2H, Ha) and 5.68 (s, 2H, Hb). The absence of vicinal couplings (Ja, b) for the adducts **10** and **11** indicated that the dihedral angles between Ha and Hb are to be approximately 90°.[3,6] Besides, significant differences of the chemical shifts for the protons of Ha at δ 3.50 and 2.87 were observed in the NMR spectrum of **10** and **11**, indicating clearly the anisotropy effects due to aromatic rings or to the bridged oxygen. Therefore, the adducts **10** and **11** were assigned structures *endo–exo* and *exo–exo* configuration.

Cycloaddition reactions of azulenocyclone with some electron-rich and electron-deficient dienophiles

With electron-rich olefins. The cycloadditions of azulenocyclone (**4**) with oxabenzonorbornadiene (**9**), norbornadiene (**12**), and acenaphthylene (**13**) afforded [4 + 2]cycloadducts, **14** (68%), **15** (41%) and **17** (73%), and a decarbonylated products (**16**) (43%), respectively. The IR spectra of these adducts (**14**, **15**, **17**) showed common characteristic bands at 1780–1790 cm^{-1} due to a CO group of bicyclo[2.2.1]hepta-7-one. The NMR spectrum of **14** exhibited signals at δ 3.40 (s, 2H, Ha), which might be deshielded by the anisotropy effect of the bridged CO moiety, and at δ 5.88 (s, 2H, Hb). Similarly, the NMR spectrum of **15** showed signals at δ 3.16 (s, 2H, Ha), 3.48 (*m*, 2H, Hb), 1.10 (*double m*, 1H, J = 9.0 Hz, Hc), and 1.78 (double m, 1H, J = 9.0 Hz, Hd). The absence of vicinal couplings (Ja,b) for the adducts **14** and **15** were observed. The NMR spectrum of **17** exhibited also center bridged proton (Ha) signals as a singlet at δ 5.42.

Thus, it is concluded that the adducts **14** and **15** were assigned the *endo-exo* configuration and the adduct **17** was assigned the *endo* configuration.

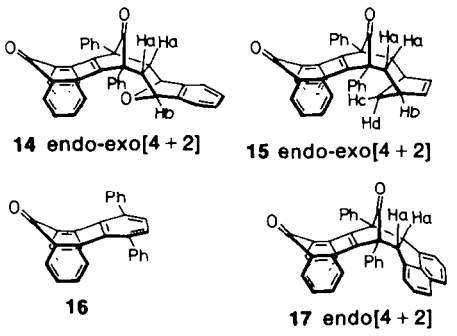
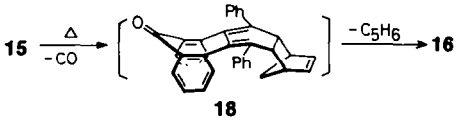


Chart 3.

On the other hand, the IR spectrum of **16** showed only one CO band at 1663 cm^{-1} (dibenzotropone group) and the NMR spectrum displayed only aromatic proton signals.

Thus, the formation of compound **16** might proceed initially producing a decarbonylated intermediate (**18**) followed by the retrogressive Diels–Alder reaction, which was further confirmed by the formation of **16** in the pyrolysis of **15** in chlorobenzene at 130° for 2 hr.



Scheme 1.

With electron-deficient olefins. The cycloaddition of azulenocyclone (**4**) with N-phenylmaleimide (**5**), maleic anhydride (**6**), and *p*-benzoquinone (**19**) afforded [4 + 2]cycloadducts, **20** (87%), **21** (70%), and **22** (58%), respectively. The IR spectrum of these adducts (**20–22**) showed common characteristic bands at 1785–1800 cm^{-1} due to CO group of bicyclo[2.2.1]hepta-7-one.

The NMR spectrum of **20** and **22** exhibited center bridged proton (Ha) signals as each singlet at δ 4.96 and 4.70, which might be deshielded by the anisotropy of the bridged CO moiety, and two aromatic proton (Hc) signals of **20** as a multiplet at δ 6.75, which might be shielded

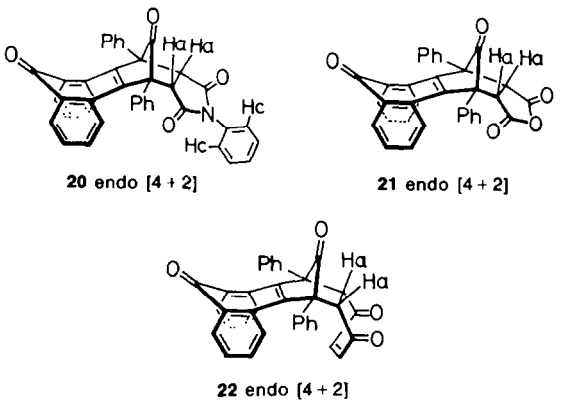


Chart 4.

owing to lying over the dibenzo moiety.[2] Thus, it is concluded that these adducts (**20–22**) were assigned the *endo* configuration.

DISCUSSION

As described our previous work,[2] phencyclone (**1**) was very reactive diene component for various olefinic dienophiles and cyclic triene compounds in the cycloaddition reactions. On the other hand, 1,3-diphenylphenanthreno[9,10-c]furan, similar structure to **1**, was shown to be less reactive for olefinic dienophiles, and to be inert for cyclic triene compounds such as tropone and cycloheptatriene in the cycloaddition reactions. The cycloadditions of **3** with N-phenylmaleimide (**5**) and maleic anhydride (**6**) gave the stereospecific [4 + 2]adducts **7** and **8**, however, the reaction of **3** with oxabenzonorbornadiene (**9**) gave the stereoselective [4 + 2] adducts **10** and **11**. By contrast, dibenzo[4,5-c]furotropone (**2**) was reactive for electron-deficient olefins.[3] However, azulenocyclone (**4**), similar structure to **2**, was more reactive for electron-rich olefins than electron-deficient olefins, but azulenocyclone (**4**) is shown to be inert for cyclic triene compounds.

The cycloadditions of **4** with electron-rich (**9**, **12**, **13**) and electron-deficient olefins (**5**, **6**, **19**) gave all the stereospecific *endo* [4 + 2]adducts.

In order to account for the formation of stereospecific *endo* [4 + 2] isomers in the cycloadditions of **3** and **4**, we have considered some common interactions such as secondary-orbital, geometrical primary effect, steric and dipole–dipole interactions between reactants.

In the cycloadditions of **1** and **3** which have coplanar structures, the secondary-orbital and the geometrical primary interactions controlled mainly the stereospecificity. Furthermore, steric interactions between the "X" portion of the diene components (**1**, **3**) and the "Y"

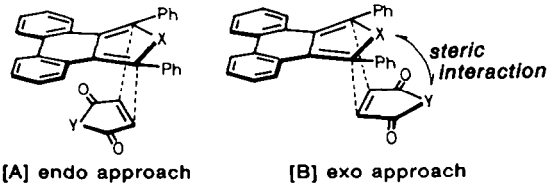


Fig. 1.

portion of the dienophiles would be favorable to *endo* approach [A] as depicted in Fig. 1. On the other hand, in the cycloadditions of 2 and 4 which have nonplanar structures, steric and dipole–dipole interactions controlled mainly the stereospecificity as depicted in Fig. 2.

However, in the cycloaddition of 3 with sterically bulky olefin such as oxabenzonorbornadiene (9), steric interaction between the "oxa-bridged" moiety of 9 and the phenanthrene moiety of 3 would be made possible to the both approaches ([G] and [H]) as depicted in Fig. 3.

Furthermore, it is found that phencyclone (1) and azulenocyclone (4) reacted with both electron-rich and electron-deficient olefins. On the contrary, dibenzo[4,5-c]furotropone (2) and 1,3-diphenylphenanthrens[9,10-c]furan (3) reacted only with electron-deficient olefins, exceptionally with oxabenzonorbornadiene (9). In order to account for the reactivities in the cycloadditions of compounds (2–4), we have estimated by the consideration of frontier orbital analyses in comparison with that of 1.[2] It is to be noted that 1 and 4 have estimated to lower energy LUMO (lowest unoccupied molecular orbital) and higher energy HOMO (highest occupied molecular orbital), which have two phenyl groups and a fused phenanthrene ring or dibenzotropone ring. In general, the electron-rich olefins have relatively higher LUMO and HOMO energy levels, and the electron-deficient olefins have relatively lower LUMO and HOMO energy levels. Therefore, both interactions of 1 or 4-HOMO-electron-deficient olefin-LUMO and 1 or 4-LUMO-electron-rich olefin-HOMO are expected as depicted in Fig. 4.

From our experimental results, it is suggested that the interaction between 4-LUMO and electron-rich olefin-HOMO are stronger than the interaction between 4-HOMO and electron-deficient olefin-LUMO different from that of 1; the HOMO energy level of 4 is lower than that of 1 owing to the dibenzotropone moiety which is

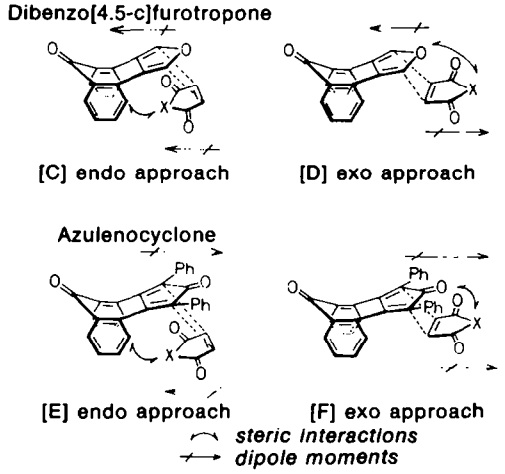


Fig. 2.

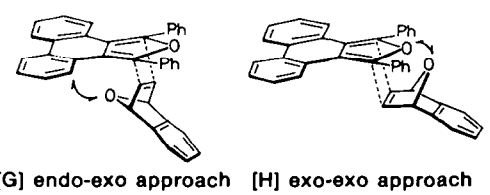


Fig. 3.

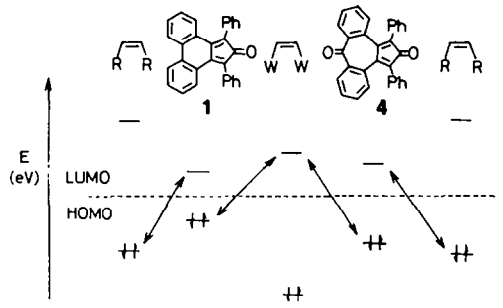


Fig. 4. Frontier orbital interactions for cyclopentadienones and olefins. R: electron-donating groups; W: electron-withdrawing groups.

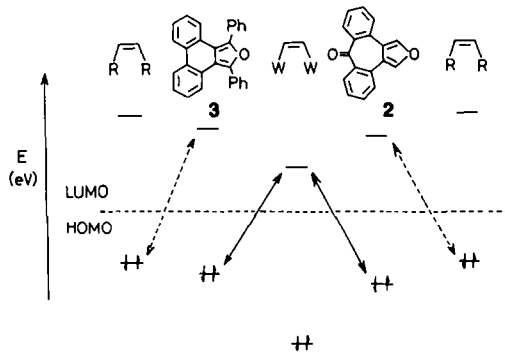


Fig. 5. Frontier orbital interactions for furans and olefins.

electron-deficient substituent as depicted in Fig. 4. On the other hand, 2 and 3 which are electron-rich diene compounds have relatively larger energy gap of the LUMO and HOMO. Therefore, only interaction of the furans (2 and 3) HOMO-electron-deficient olefin-LUMO are expected as depicted in Fig. 5. A more theoretical molecular orbital calculation for these compounds will be presented in the near future.

EXPERIMENTAL

The m.ps were measured with a Yanagimoto micromelting point apparatus and are uncorrected. Microanalyses were performed with a Perkin–Elmer 240 elemental analyzer. The NMR spectra were taken with a JEOL C-60-XL spectrometer with tetramethylsilane as an internal standard and the chemical shifts are expressed in δ values. The IR spectra were taken with a Jasco Model IRA-1 grating infrared spectrophotometer.

General procedure for cycloaddition. A soln of 4 and 1.1 equimolar of olefins was heated under N_2 or argon in a sealed tube. The solvent was removed under reduced pressure and the residue was purified by recrystallization or silica gel chromatography and then analysed by NMR.

Cycloaddition reactions of 1,3-*diphenylphenanthreno* [9,10-c] *furan* (3) *with dienophiles*

With N-*phenylmaleimide* (5). A soln of 3 (346 mg) and 5 (190 mg) in toluene (5 ml) was heated at 80° for 3 hr. The solvent was removed under reduced pressure and the residue was recrystallized from CH_2Cl_2–MeOH to give 7 (483 mg, 95%) as colorless crystals, m.p. 225–226°; ν_{max} (KBr) 1780 and 1710 cm^{-1}; δ ($CDCl_3$) 4.57 (2H, s, Ha), 5.75 (2H, m, Hc) and 6.8–8.75 (21H, m, aromatic-H). (Found: C, 83.68; H, 4.94; N, 2.56. $C_{38}H_{25}O_3N$ requires: C, 83.96; H, 4.64; N, 2.58%).

With maleic anhydride (6). A soln of 3 (370 mg) and 6 (108 mg) in toluene (5 ml) was heated at 110° at 4 hr. Work-up as described above gave 8 (330 mg, 71%) as colorless crystals, m.p. 176–178° (benzene); ν_{max} (KBr) 1870 and 1800 cm^{-1} (CO–O–CO); δ

(DMSO-d_6–$CDCl_3$) 5.00 (2H, s, Ha) and 7.0–8.85 (18H, m, aromatic-H). (Found: C, 81.74; H, 4.95. $C_{32}H_{20}O_4$ requires: C, 82.04; H, 4.30%).

With oxabenzonorbornadiene (**9**). A soln of **3** (370 mg) and **9** (156 mg) in chlorobenzene (5 ml) was heated at 140° for 22 hr. The solvent was removed under reduced pressure and the residue was subjected to silica gel chromatography using benzene–n-hexane (1:1). The first fraction gave the 1:1 adduct (**10**) (253 mg, 50%) as colorless cubics, m.p. >300° (CH_2Cl_2–MeOH); ν_{max} (KBr) 1600, 1580 and 1500 cm^{-1}; δ ($CDCl_3$) 3.50 (2H, s, Ha), 4.78 (2H, s, Hb), and 6.95–8.75 (22H, m, aromatic-H). (Found: C, 81.6; H, 5.1. $C_{38}H_{26}O_2 \cdot 2/3CH_2Cl_2$ requires: C, 81.3; H, 4.8%). The second fraction gave the 1:1 adduct (**11**) (130 mg, 26%) as colorless crystals, m.p. >300° (CH_2Cl_2–MeOH); ν_{max} (KBr) 1600, 1580 and 1500 cm^{-1}; δ (CD_2Cl_2–DMSO-d_6) 2.87 (2H, s, Ha), 5.68 (2H, s, H_b) and 7.0–8.7 (22H, m, aromatic-H). (Found: C, 85.75; H, 6.5. $C_{38}H_{26}O_2 \cdot 1/4CH_2Cl_2$ requires: C, 85.75; H, 6.6).

Cycloaddition reactions of azulenocyclone (**4**) *with dienophiles*

With oxabenzonorbornadiene (**9**). A soln of **4** (205 mg) and **9** (80 mg) in toluene (5 ml) was heated under argon in a sealed tube at 110° for 2 hr. The solvent was removed under reduced pressure and the residue was recrystallized from CH_2Cl_2–MeOH to give **14** (187 mg, 68%) as colorless needles, m.p. 277–278°; ν_{max} (KBr) 1780 (C=O), 1660, 1650 cm^{-1} (C=O); δ ($CDCl_3$) 3.40 (2H, s, Ha), 5.88 (2H, s, Hb) and 6.8–7.8 (22H, m, aromatic-H). (Found: C, 86.3; H, 5.05. $C_{40}H_{26}O_3$ requires; C, 86.6; H, 4.75%).

With norbornadiene (**12**). A soln of **4** (205 mg) and **12** (92 mg) in toluene (5 ml) was heated under argon in a sealed tube at 110° for 3 hr. The solvent was removed under reduced pressure and the residue was subjected to silica gel chromatography using benzene–CH_2Cl_2 (2:1). The first fraction gave **16** (88 mg, 43%) as colorless crystals, m.p. 280–281° (CH_2Cl_2–MeOH); ν_{max} (KBr) 1663 cm^{-1} (C=O); δ (CD_2Cl_2) 6.8–7.5 (20H, m, aromatic-H). (Found: C, 88.2; H, 5.45. $C_{31}H_{20}O$ requires: C, 88.4; H, 5.2%). The second fraction gave **15** (102 mg, 41%) as colorless needles, m.p. 237–239° (CH_2Cl_2–MeOH); ν_{max} (KBr) 1780 (C=O), 1660 cm^{-1} (C=O); δ (CD_2Cl_2) 1.10 (1H, d, J = 9.0 Hz, bridged methylene-H), 1.78 (1H, d, J = 9.0 Hz, bridged methylene-H), 3.16 (2H, s, Ha), 3.48 (2H, m, Hb), 6.66 (2H, br s, olefinic-H) and 6.8–7.75 (18H, m, aromatic-H). (Found: C, 91.05; H, 5.25. $C_{37}H_{26}O_2$ requires: C, 91.15; H, 4.95%). Furthermore, **15** was heated in chlorobenzene at 130° for 3 hr and chromatographed on silica gel using benzene to give **16** in quantitative yield.

With acenaphthylene (**13**). A soln of **4** (205 mg) and **13** (84 mg) in toluene (5 ml) was heated under argon in a sealed tube at 100° for 5 hr. The solvent was removed under reduced pressure and the residue was recrystallized from CH_2Cl_2–MeOH to give **17** (205 mg, 73%) as colorless crystals, m.p. 272–274°; ν_{max} (KBr) 1790 (C=O), 1650 cm^{-1} (C=O); δ ($CDCl_3$–CD_2Cl_2) 5.42 (2H, s, Ha) and 6.8–8.0 (24H, m, aromatic-H). (Found: C, 89.4; H, 4.95. $C_{42}H_{26}O_2$ requires: C, 89.65; H, 4.65%).

With N-phenylmaleimide (**5**). A soln of **4** (205 mg) and **5** (90 mg) in toluene (5 ml) was heated at 100 for 3 hr. Work-up gave **20** (254 mg, 87%) as colorless prisms, m.p. 258–260° (CH_2Cl_2–MeOH); ν_{max} (KBr) 1795, 1700, and 1645 cm^{-1} (imide and C=O); δ ($CDCl_3$–DMSO-d_6) 4.96 (2H, s, Ha), 6.75 (2H, m, Hc), and 7.05–7.75 (21H, m, aromatic-H). (Found: C, 82.05; H, 4.55; N, 2.2. $C_{40}H_{25}O_4N$ requires: C, 82.3; H, 4.3: N, 2.4%).

With p-benzoquinone (**19**). A soln of **4** (205 mg) and **19** (60 mg) in toluene (5 ml) was heated at 100° for 20 hr. Work-up gave **22** (146 mg, 58%) as yellow needles, m.p. 238–243° (CH_2Cl_2–MeOH); ν_{max} (KBr) 1800 (C=O) and 1670 cm^{-1} (C=O); δ (CD_2Cl_2) 4.70 (2H, s, Ha), 6.55 (2H, s, olefinic-H) and 6.8–7.85 (18H, m, aromatic-H). (Found: C, 83.15; H, 4.5. $C_{36}H_{22}O_4$ requires: C, 83.4; H, 4.3%).

With maleic anhydride (**6**). A soln of **4** (205 mg) and **6** (60 mg) in toluene (5 ml) was heated at 100° for 10 hr. Work-up gave **21** (176 mg, 70%) as colorless crystals, m.p. 255–258° (CH_2Cl_2); ν_{max} (KBr) 1860, 1785 and 1650 cm^{-1} (C=O). (Found: C, 80.0; H, 4.25. $C_{34}H_{20}O_5$ requires: C, 80.3; H, 3.95%).

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