by comparing the spectral data with those of the analogous compounds.[1a,15,19]

On the other hand, the reaction of **1a** with tropone in benzene at 80 °C for 20 h gave exo [4 + 6] π adduct **4** in 70% yield.[1a]

Kinetics. The reaction rate was followed at a given temperature by measuring the loss of the long-wavelength absorbance of the phencyclone chromophore in the visible spectrum (630 nm) by using a 10 × 10 mm quartz cell which was thermostated with flowing water at constant temperature. The pseudo-first-order rate constants were calculated from a plot of ln $(A_t - A_\infty)/(A_0 - A_\infty$ vs. time by a least-squares method, where A_t is the absorbance at time t and A_∞ is the absorbance after about 10 half-lives. The second-order rate constants were obtained in the usual manner. The treatment of Andrews and Keefer[7] was followed in the calculation of the equilibrium constants. The kinetic data are listed in Tables III-VII and IX-XI.

Acknowledgment. We thank Miss K. Konishi and Miss R. Kutsunai for experimental assistance.

Registry No. 1a, 5660-91-3; **1b**, 16691-79-5; **1c**, 13177-38-3; **1d**, 32683-51-5; **2a**, 1484-13-5; **2b**, 111-34-2; **2c**, 109-53-5; **2d**, 769-78-8; **2e**, 3050-69-9; **2f**, 88-12-0; **2g**, 110-87-2; **3a**, 78456-56-1; **3b**, 78456-57-2; **3c**, 78456-58-3; **3d**, 78456-59-4; **3e**, 78456-60-7; **3f**, 78456-61-8; **3g**, 78479-40-0; **4**, 57969-45-6; **5**, 78456-62-9; 1,3-diazo-1,3-diphenyl-2-propanone, 26536-34-5; tropone, 539-80-0; *p*-methoxystyrene, 637-69-4; norbornadiene, 121-46-0; cyclooctatetraene, 629-20-9.

Reagent Design and Study of *p*-Benzoquinone Derivatives. The Site-Selective Cycloaddition Reaction of Diquinones and Photochemical Cage Formation of the Adducts

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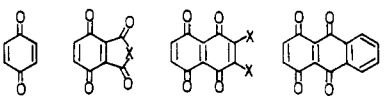
Cycloaddition reactions of naphthodiquinone derivatives and the photochemical behavior of their adducts have been investigated. Naphthodiquinone (**4**) and dichloronaphthodiquinone (**5**) reacted exclusively at the internal double bond with both cyclopentadiene and quadricyclane to give the corresponding 1:1 adducts in high yields. While anthradiquinone (**6**) reacted also only at the internal double bond with quadricyclane, the reaction with cyclopentadiene took place at both the internal and terminal double bonds of **6**. The stereochemistry of the adducts was determined by spectral inspections and chemical transformations. The cyclopentadiene adducts were photochemically converted into the cage compounds in high yields, although the quadricyclane adducts were photoinert. In the photochemical reactions, high site selectivity was observed; the intramolecular [2 + 2] π photoaddition occurred only between enedione (electron poor) and cyclopentene (electron rich) double bonds.

p-Benzoquinone (**1**, Chart I) is a versatile synthon for the preparation of cage compounds of current interest,[1] although **1** is not a powerful dienophile in the Diels-Alder reactions, and is rather inert to homodienes and conjugated medium-ring polyenes even under drastic conditions. Recently, on the basis of the concept of donor (HOMO)-acceptor (LUMO) relationships of the pericyclic reaction,[2] we were able to remarkably enhance the reactivity of *p*-benzoquinone by introducing strong electron-attracting substituents, which cause a lowering of the LUMO energy level.[3] Thus, *p*-benzoquinone-2,3-dicarboxylic anhydride (PBA, **2**) and *N*-phenylimidine (PBI, **3**) showed high reactivities toward the electron-rich dienes, homodienes, and trienes.[3] As a reasonable extension of our studies on the reagent design by FMO control, a series of diquinones such as 1,4,5,8-naphthodiquinone (NDQ, **4**),[4] 2,3-dichloronaphthodiquinone (DNDQ, **5**), and 1,4,9,10-anthradiquinone (ADQ, **6**)[5] were prepared, and their cycloaddition reactions with electron-rich dienes were investigated.

Due to their direct applicability to a total synthesis of biologically important anthracycline antibiotics, there is

Chart I



great current interest in the Diels-Alder reactions of naphthoquinone derivatives.[6-11] However, there still remains the ambiguity concerning the site selectivity in the cycloaddition reactions of bifunctional dienophiles such as ADQ (**6**) which can undergo initial Diels-Alder addition at the internal or terminal double bond.[6,11,12] Apparently, more experimental results are needed in order to clarify

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0022-3263/81/1946-3841$01.25/0

Table I. ^{1}H NMR and IR Data for Adducts

compd	^{1}H NMR,[a] δ ($CDCl_3$)	IR (Nujol), cm^{-1}
7	1.28, 1.57 (AB q, J = 10.0, 2 H), 4.04 (m, 2 H), 6.23 (m, 2 H), 6.64 (s, 2 H), 6.87 (s, 2 H)	1699
8	0.84, 1.31 (AB q, J = 11.0, 2 H), 2.50 (s, 2 H), 3.28 (br s, 2 H), 6.01 (br s, 2 H), 6.81 (s, 2 H), 6.88 (s, 2 H)	1700
9	5.55 (s, 2 H), 6.46 (s, 4 H), 7.04-7.32 (m, 8 H)	1700
10	1.34, 1.60 (AB q, J = 10.0, 2 H), 4.11 (m, 2 H), 6.25 (m, 2 H), 6.90 (s, 2 H)	1700
11	1.20-1.70 (m, 2 H), 4.07-4.18 (m, 2 H), 6.25 (m, 2 H), 6.64 (s, 2 H)	1700
12	0.84, 1.36 (AB q, J = 12.2, 2 H), 2.53 (s, 2 H), 3.30 (s, 2 H), 6.05 (m, 2 H), 6.84 (s, 2 H)	1715
13	0.68, 1.36 (AB q, J = 12.2, 2 H), 2.53 (s, 2 H), 3.30 (s, 2 H), 6.05 (m, 2 H), 6.92 (s, 2 H)	1715
14	1.32, 160 (AB q, J = 10.0, 2 H), 4.25 (m, 2 H), 6.28 (m, 2 H), 6.59 (s, 2 H), 7.65-7.99 (m, 4 H)	1700
15	1.32, 1.58 (AB q, J = 10.0, 2 H), 4.18 (m, 2 H), 6.20 (m, 2 H), 6.79 (s, 2 H), 7.65-7.98 (m, 4 H)	1700
16	0.82, 1.63 (AB q, J = 10.0, 2 H), 1.13, 1.64 (AB q, J = 10.0, 2 H), 3.20 (m, 2 H), 3.28 (d, J = 1.2, 2 H), 4.04 (m, 2 H), 6.00 (m, 2 H), 6.20 (m, 2 H), 7.76-8.14 (m, 4 H)	1728
18	0.79, 1.29 (AB q, J = 11.0, 2 H), 2.60 (s, 2 H), 3.37 (br s, 2 H), 6.05 (m, 2 H), 6.85 (s, 2 H), 7.70-8.02 (m, 4 H)	1700
19	0.89, 1.34 (AB q, J = 11.0, 2 H), 2.56 (s, 2 H), 3.34 (br s, 2 H), 6.04 (m, 2 H), 6.80 (s, 2 H), 7.76-8.08 (m, 4 H)	1700

[a] J values are given in hertz.

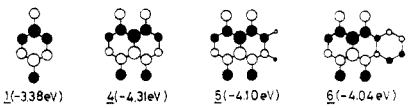


Figure 1. LUMO energy levels and coefficients by PPP method.

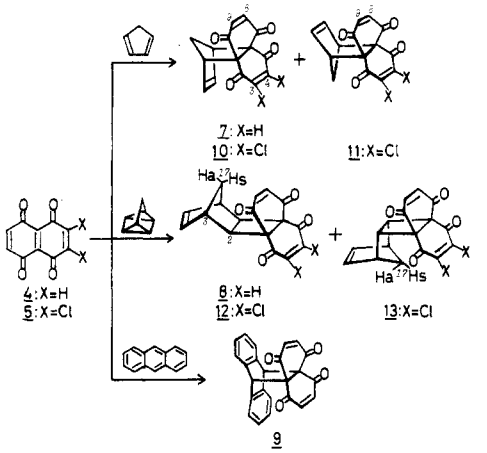
the controlling factors of site selection. Except for those for **6**, to the best of our knowledge there are few reports concerning the Diels–Alder reactions of diquinones (**4** or **5**).[6,11,12] In this article, we describe the site-selective cycloaddition reactions of **4–6** and photochemical transformation of the adducts to the cage compounds. The results are discussed in terms of frontier molecular orbital (FMO) theory.[13]

Results and Discussion

Preparation of NDQ (4), DNDQ (5), and ADQ (6). Naphthodiquinone derivatives **4–6** were prepared in good yields by the improved method. Thus, oxidation of the corresponding hydroquinones[14] with an excess of phenyliodine bis(trifluoroacetate) [$C_6H_5I(OCOCF_3)_2$][15] in acetone at room temperature afforded **4** (81%), **5** (81%), and **6** (66%). Structural proof was based on the spectral data and elemental analyses for the new compounds (see Experimental Section). The MO calculations of π electron systems of these diquinones by means of SCF Pariser–Parr–Pople method[16] indicated that LUMO energies of **4–6** are remarkably lowered, as for PBA (**2**, −4.44 eV) and PBI (**3**, −4.09 eV),[17] compared with that of **1** (−3.38 eV), suggesting the similar increase in their cycloadditivity toward electron-rich dienes (see Figure 1).

Cycloaddition Reaction of NDQ (4) and DNDQ (5). When NDQ (**4**) suspended in benzene was allowed to react with excess of cyclopentadiene (25 °C, 10 min), quadricyclane (80 °C, 2 h), and anthracene (25 °C, 3 days), only

Scheme I



1:1 Diels–Alder adducts **7** (95%), **8** (85%), and **9** (75%) were obtained, respectively. In the ^{1}H NMR spectrum (Table I) of each adduct, the appearance of two kinds of characteristic singlets for enedione olefinic protons clearly indicated that the addition took place at the internal double bond of **4**. In the case of adduct **7**, the upfield shift of the endo enedione protons [δ 6.64 (s, 2 H, H-3,4)] relative to the exo one [δ 6.87 (s, 2 H, H-8,9)] can be attributed to the shielding effect of the proximate cyclopentene double bond, since the signals for enedione moieties in **8** appear at δ 6.81 and 6.88 (each s, 2 H). This assignment was further confirmed by the disappearance of the singlet at δ 6.64 in **7** upon photochemical transformation to the cage compound (see below). The enedione proton signal of adduct **9** appeared at even higher field [δ 6.46 (s, 4 H)] due to the anisotropic effect of the proximate aromatic ring. The exo configuration of the norbornene moiety in **8** was deduced from the absence of measurable coupling between H-2 and H-3 and the spectral similarity to the reported exo adducts of quadricyclane.[3,18]

Reaction of DNDQ (**5**) with cyclopentadiene at 25 °C in benzene resulted in the formation of a mixture (95%)

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(17) These values are higher than those calculated by the MNDO method:[3c] **1**, −1.51 eV; **2**, −2.81 eV; **3**, −2.41 eV.
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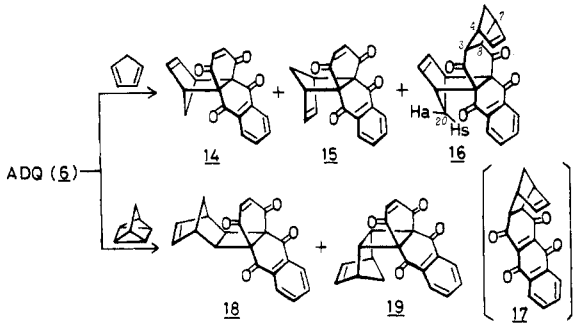
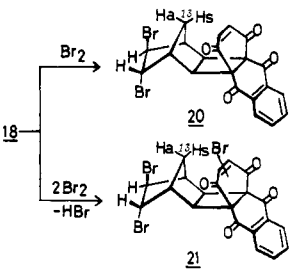
Scheme II



Scheme III



of two 1:1 adducts, **10** and **11** (Scheme I). The product ratio (86:14 **10**:**11**) was determined by the ^1H NMR analysis of the crude product. In the major product **10**, which was isolated in a pure form by repeated recrystallization from chloroform, the enedione protons (H-8,9) appeared as a singlet at δ 6.90, while those of the minor product **11** appeared at δ 6.64 (s, 2 H). The shielded nature of the latter signal revealed the proximity of H-8 and H-9 to the cyclopentene double bond in **11**. Therefore, the major product was assigned to the endo compound **10** and the minor one the exo compound **11**. Further support for the stereochemical assignment was obtained by photochemical transformation of **10** to the cage compound (see below). Reaction of DNDQ (**5**) with quadricyclane (80 °C, 10 min) gave rise to an inseparable mixture (89%) of two 1:1 adducts (50:50 **12**:**13**). Both products were identified as the internal adducts (**12** and **13**; Scheme I) on the basis of the ^1H NMR spectra (see Table I). The stereochemical assignments were achieved by spectral comparison with that of **8**: while the H_{syn}-17 signal of **12** appears at the same position (δ 0.84) as that of **8**, the corresponding signal of **13** is shifted upfield (δ 0.68) due to the induced shielding effect of the chlorine-substituted double bond.

It is interesting to note that DNDQ (**5**) shows the different stereoselectivities in the reactions with cyclopentadiene (6:1 **10**:**11**) and quadricyclane (1:1 **12**:**13**). In the reaction with cyclopentadiene, both the endo and exo approaches are considered to experience almost the same magnitude of bonding secondary orbital interactions on the basis of the calculated LUMO coefficients of **5** (Figure 1). Therefore, the preferred formation of **10** over **11** should be attributed to the increased steric hindrance between hydrogen attached to the sp^3 carbon of cyclopentadiene and chlorine substituents of **5** in the exo transition state. On the other hand, the sterically less requiring addition of quadricyclane to **5**, in which the exo configuration with regard to the norbornene moiety was favored by the secondary orbital interaction,[3] resulted in the equal formation of **12** and **13** regardless of the substituents (X).

Cycloaddition Reaction of ADQ (6). Brief treatment of ADQ (**6**) with 1.1 equiv of cyclopentadiene (25 °C, 10 min) in benzene gave a mixture of 1:1 adducts **14** and **15** and 1:2 adduct **16** (Scheme II). The adducts **14** and **15** were obtained as an inseparable crystalline mixture (49%, 50:50 **14**:**15**), and their structural assignments were deduced by comparison of their ^1H NMR spectra with those of **7**, **10**, and **11**. Selective cage formation of **14** on irradiation of this mixture also supported the above assignments (see below).

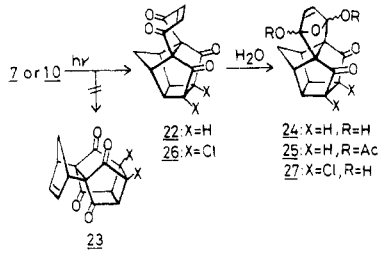
The 1:2 structure of adduct **16**, which was isolated in a pure form (17%) by column chromatography on silica gel, was apparent from its elemental analysis and mass spectrum (M^+, m/z 370). The gross structure of **16** was determined by the careful analysis of its ^1H NMR spectrum and the spin-decoupling experiments. The presence of appreciable coupling (J = 1.2 Hz) between H-3 (H-8) and H-4 (H-7) suggested the endo configuration at C-3 (C-8), and the upfield shift of H_{syn}-20 (δ 0.82) was indicative of the proximity of this bridge (C-20) to the aromatic ring. Interestingly, the reaction of **6** with a large excess of cyclopentadiene led to the same results. Furthermore, treatment of **14** and **15** with excess of cyclopentadiene for a prolonged period under the same conditions gave none of **16** and resulted in the recovery of **14** and **15**. This fact suggested that 1:2 adduct **16** was formed by the initial endo addition to the terminal double bond of **6** (i.e., **17**), followed by the rapid exo addition of a second cyclopentadiene molecule to the internal double bond from the opposite side which is controlled by steric factors. It should be noted that the internal Diels–Alder adducts (**7**, **10**, **11**, **14**, **15**) undergo no further addition reactions because of their bent structures which cause a severe steric hindrance for the approach of a second diene molecule.

Reaction of ADQ (**6**) with quadricyclane (80 °C, 10 min) gave a mixture (94%) of two internal 1:1 adducts (**18** and **19**), of which **18** could be isolated in a pure form by repetition of recrystallization. The product ratio (50:50 **18**:**19**) was determined in the crude product by ^1H NMR integration of the olefinic proton region unique to each isomer. Stereochemical assignment of these adducts was based on the chemical transformations. Treatments of pure **18** with 1 and 2 equiv of Br_2 in methylene chloride at room temperature afforded **20** (88%) and **21** (76%), respectively (Scheme III). The tribromide **21** was possibly derived from the initially formed tetrabromide by loss of HBr. The ^1H NMR spectra of **20** and **21** differ only in the olefinic region [**20**, δ 6.81 (s, 2 H); **21**, δ 7.31 (s, 1 H)] and a slight upfield shift of H_{syn}-13 in **21** (δ 1.14) relative to that in **20** (δ 1.26), indicating the proximity of the bridge (C-13) to the bromine-substituted enedione moiety in **21**. Therefore, **18** was assigned to the exo-trans configuration as shown in Scheme II.

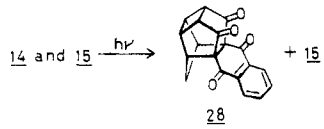
As the above results indicated, NDQ (**4**) and DNDQ (**5**) reacted exclusively at the internal double bond with both cyclopentadiene and quadricyclane. This high site selectivity in their cycloaddition reactions is in good agreement with the results of MO calculations which show the largest LUMO coefficients at the internal double bond of these diquinones (Figure 1). However, ADQ (**6**) reacted with cyclopentadiene at both internal and terminal double bonds, while the reaction with less reactive quadricyclane took place only at the internal double bond as expected from FMO considerations. The similar divergency in the site-selectivity has been recognized in the cycloaddition reactions of ADQ (**6**) with various dienes.[6,11,12]

Photochemistry of the Adducts. The unique structural features of the above obtained adducts led us to investigate their photochemical behavior. Since the Diels–Alder adducts (**7**, **10**, **14**) contain three double bonds in the longicyclic system, two different types of intramolecular [2 + 2] π photoadditions are possible depending on the sort of participating double bonds.

Scheme IV



Scheme V

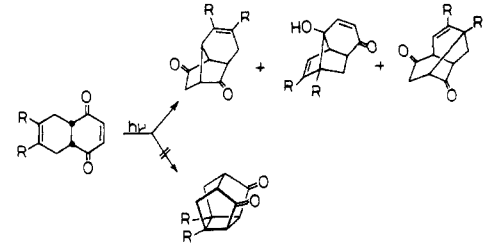


Irradiation of **7** in ethyl acetate with a 100-W high-pressure mercury lamp through a filter of I_2/CCl_4 solution (>350 nm) for 15 min afforded the sole product **22** in 93% yield (Scheme IV). The similar irradiation of **7** through a Pyrex filter in various solvents such as acetone and methylene chloride also gave **22** in high yields. The reaction could also be smoothly effected by sunlight. Structure elucidation of **22** (M^+, m/z 254) was based on spectral inspections and chemical conversions. The IR spectrum showed two characteristic carbonyl bands at 1760 (five-membered carbonyl) and 1672 cm^{-1} (enedione carbonyl). The ^1H NMR spectrum of **22** was characterized by a singlet at δ 6.87 (2 H) due to the exo enedione moiety, but no signals for the cyclopentene and the endo enedione moietites were observed. Thus, the alternative structure **23** was clearly ruled out.

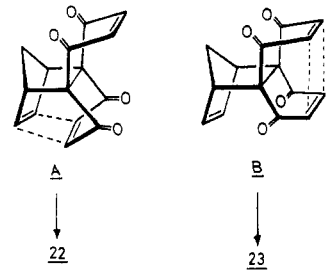
This yellow cage compound, **22**, was converted into the colorless monohydrate **24** (M^+, m/z 272) gradually in chloroform or rapidly in aqueous dioxane. The IR spectrum of **24** exhibited the absorptions of the hydroxyl group at 3420 cm^{-1} and the five-membered carbonyl at 1760 cm^{-1} but none for the conjugated carbonyl. Most revealing in the ^1H NMR spectrum (Me_2SO-d_6) is the appearance of olefinic protons at δ 6.28 (s, 2 H) and hydroxyl protons at δ 8.41 (s, 2 H, exchangeable). Treatment of **24** with acetic anhydride and 4-(dimethylamino)pyridine afforded the diacetate **25** (48%): mass spectrum, m/z 356 (M^+); IR (Nujol) 1778, 1765 cm^{-1}. These data are fully compatible with the oxa-bridged structure of **24** (Scheme IV), although the stereochemistry remains unclear. It is rather surprising that the transannular cyclization of **22** occurred between enedione carbonyls instead of cage carbonyls, since such reaction has been known to often occur to the cage diketones.[19-21] This is indicative of the "twist" conformation of cyclohexenedione ring in **22** which holds two carbonyls in close distance.

The similar irradiation of **10** afforded **27** as the exclusive product in 85% yield; IR (Nujol) 3780 and 1780 cm^{-1}; ^1H NMR (Me_2SO-d_6) δ 6.38 (s, 2 H). In this case the initial photoproduct **26** was not isolated. Irradiation of a 1:1 mixture of **14** and **15** resulted in the formation of singular product **28** in 45% yield (i.e., 90% from **14**) along with the recovery of unchanged **15** (Scheme V). Photoinactivity of **15** (as well as **9**) is a contrast to the known aromatic participation in the photochemical reactions.[22,23] The

Scheme VI



Scheme VII



structural identification of **28** was based on mass (M^+, m/z 304), IR (1790 and 1660 cm^{-1}), and ^1H NMR spectra (Experimental Section). In sharp contrast to **22** or **26**, compound **28** was very stable to moisture and was recovered unchanged even after a prolonged treatment with aqueous dioxane. This inactivity of **28** to transannular cyclization can be attributed to the presence of the aromatic ring which renders two carbonyls more distant by flattening the cyclohexene ring.

Essentially the same results were obtained from irradiation of the above adducts in the solid states, although the yields were lowered. Oxetane formation was not observed even in the solution photochemistry.[1] The facile photochemical cage formation of these adducts should be noted, since Scheffer and co-workers[24] reported that the structurally related Diels–Alder adducts of *p*-benzoquinones and 1,3-dienes gave no intramolecular [2 + 2] π photoproducts but instead a mixture of tricyclic products derived from the hydrogen abstraction by carbonyl oxygen (Scheme VI). This was attributed to the conformational mobility of these molecules and the presence of allylic hydrogen available in a favorable position for the abstraction reaction by a carbonyl group. In contrast, adducts **7**, **10**, and **14** possess the "fixed" double bond in the endo position to the enedione moiety. In addition, the spatially crowded propellane structure seems to be a reason for the reactivity enhancement of these adducts for intramolecular [2 + 2] π addition compared with that of the endo Diels–Alder adduct of cyclopentadiene and *p*-benzoquinone.[20]

It is also interesting to note that the above-mentioned intramolecular [2 + 2] π photoreactions are highly site selective. The reaction occurred exclusively between enedione and cyclopentene double bonds to give the cage compounds like **22**, but no reactions between two enedione moieties leading to the cage products like **23** were observed, although both reactions are geometrically feasible. Nonreactivity between two enedione double bonds was uniquely shown by the recovery of quadricyclane adducts (**8**, **12**, **13**) and an anthracene adduct (**9**) from their photolyses.

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The observed site selectivity can be most reasonably explained by conformational analysis of these adducts. Considering the two extreme conformations (A and B, Scheme VII) in the transition states leasing to each product, conformer A seems to be much favored by a charge-transfer interaction between the cyclopentene double bond and the excited enedione system. Conformer A is also favorable from the viewpoint of dipole–dipole interactions. The importance of a similar charge-transfer interaction for the subsequent photochemical reaction has been recently reported by Scheffer et al.[25]

The results stated above provide important suggestions for the further reagent design of new type of cage compounds.

Experimental Section

The melting points were measured with a Yanagimoto micro melting point apparatus and are uncorrected. The UV spectra were determined with a Hitachi EPS-3T spectrophotometer. The ^{1}H NMR spectra were taken with a JEOL PS-100 spectrometer with tetramethylsilane as an internal standard, and the chemical shifts are expressed in δ values. The IR spectra were taken with a JASCO IR A-1 infrared spectrophotometer. Mass spectra were obtained with a JEOL-01SG double-focusing spectrometer operating at an ionization potential of 75 eV. The solid samples were ionized by electron bombardment after sublimation directly into the electron beam at 150–200 °C.

Preparation of NDQ (4). A mixture of naphthazarin[4] (1.9 g, 10 mmol) and phenyliodine bis(trifluoroacetate) (6.45 g, 15 mmol) in 60 mL of acetone was stirred for 1 h at room temperature. The precipitated brown solids were filtered and purified by recrystallization from benzene to give **4** (1.52 g, 81%) as pale yellow prisms: mp 224–227 °C (lit.[4] mp 200 °C dec; IR (Nujol) 1690 cm^{-1}; ^{1}H NMR (Me_2SO-d_6) δ 6.88 (s); UV (dioxane) 324 nm (ϵ 1100), 446 (44); mass spectrum, m/z 188 (M^+).

Preparation of DNDQ (5). A mixture of dichloronaphthazarin[14] (2.59 g, 10 mmol) and phenyliodine bis(trifluoroacetate) (6.45 g, 15 mmol) in 70 mL of acetone was stirred at room temperature for 1 h. Workup as described as above gave **5** (2.08 g, 81%) as light green needles: mp 190 °C dec (chloroform); IR (Nujol) 1706, 1699 cm^{-1}; ^{1}H NMR (CD_3COCD_3) δ 6.95 (s); UV (dioxane) 360 nm (ϵ 1680); mass spectrum, m/z 260 (M + 4), 258 (M + 2), 256 (M^+). Anal. ($C_{10}H_2O_4Cl_2$) C, H.

General Procedure for Cycloadditions. (a) With Cyclopentadiene. A suspension of NDQ (**4**), DNDQ (**5**), or ADQ (**6**) and a slight excess (1.3 equiv) of cyclopentadiene in dry benzene was stirred for 10–20 min at room temperature. The precipitates were filtered off and purified by recrystallization from the appropriate solvents.

(b) With Quadricyclane. A suspension of **4**, **5**, or **6** and a slight excess (1.2 equiv) of quadricyclane in dry benzene was heated at 80 °C in a sealed tube under nitrogen until the color of the diquinones disappeared (10 min to 2 h). After the mixture cooled, the precipitates were filtered and purified by recrystallization. The ^{1}H NMR and characteristic carbonyl absorptions by IR are summarized in Table I. The NMR assignments for the inseparable products were achieved by the spin decoupling experiments or changing component ratios of the mixture by the repetition of recrystallizations.

Reaction of NDQ (4). (a) Reaction with cyclopentadiene gave **tetracyclo[4.4.4.1^{11,14}.0]pentadeca-3,8,12-triene-2,5,7,10-tetraone (7)** as yellow crystals: 95%; mp 140 °C dec; UV (CH_3CN) 284 nm (ϵ 390, sh), 421 (270); mass spectrum, m/z 254 (M^+). Anal. ($C_{15}H_{10}O_4$) C, H.

(b) Reaction with quadricyclane gave **pentacyclo[6.4.4.1^{3,6}.0.0^{2,7}]heptadeca-4,10,14-triene-9,12,13,16-tetraone (8)** as yellow crystals: 85%, mp >300 °C (benzene–chloroform); UV (CH_3CN) 281 nm (ϵ 440, sh), 420 (330); mass spectrum, m/e 280 (M^+). Anal. ($C_{17}H_{12}O_4$) C, H.

(c) Reaction with anthracene (2 equiv) at room temperature (3 days) gave adduct **9** as yellow needles: 75%; mp 159–162 °C dec (benzene); UV (CH_3CN) 251 nm (ϵ 3900, sh), 296 (1000, sh), 358 (300), 378 (280), 422 (290); mass spectrum m/z 366 (M^+). Anal. ($C_{24}H_{14}O_4$) C, H.

Reaction of DNDQ (5). (a) Reaction with cyclopentadiene gave yellow solid (93%) which was shown by ^{1}H NMR analysis to be composed of **10** and **11** (86:14). Recrystallization from chloroform gave pure ***endo*-3,4-dichlorotetracyclo[4.4.4.1^{11,14}.0]pentadeca-3,8,12-triene-2,5,7,10-tetraone (10)** as yellow crystals: mp 170 °C dec; UV (CH_3CN) 233 nm (ϵ 15 100), 279 (6700), 410 (290); mass spectrum, m/z 326 (M + 4), 324 (M + 2), 322 (M^+). Anal. ($C_{15}H_8O_4Cl_2$) C, H.

(b) Reaction with quadricyclane gave yellow solid (89%) which was shown by ^{1}H NMR analysis to be composed of **12** and **13** (50:50). Attempted separation by recrystallization was unsuccessful: mass spectrum, m/z 352 (M + 4), 350 (M + 2), 348 (M^+). Anal. ($C_{15}H_{10}O_4Cl_2$) C, H.

Reaction of ADQ (6). (a) Reaction with cyclopentadiene gave a yellow precipitate (48%) which was shown by ^{1}H NMR analysis to be composed of **14** and **15** (50:50). Attempted separation by recrystallization was unsuccessful; mass spectrum, m/z 304 (M^+). Anal. ($C_{19}H_{12}O_4$) C, H.

Chromatography of the filtrate on silica gel with chloroform as an eluant afforded **16** as colorless crystals: 17%; mp 160 °C dec; mass spectrum, m/z 370 (M^+). Anal. ($C_{24}H_{18}O_4$) C, H.

(b) Reaction with quadricyclane gave yellow solid (94%) which was shown by ^{1}H NMR analysis to be composed of **18** and **19** (50:50). Several recrystallizations from benzene–chloroform gave pure **18** as yellow crystals: mp 233–234 °C; UV (CH_3CN) 228 nm (ϵ 31 000), 301 (1560), 405 (350); mass spectrum, m/z 330 (M^+). Anal. ($C_{21}H_{14}O_4$) C, H.

Bromination of Compound 18. To a solution of **18** (140 mg, 0.42 mmol) in methylene chloride (5 mL) was added dropwise bromine (68 mg, 0.42 mmol) dissolved in methylene chloride (1 mL). The color of bromine immediately disappeared. After being stirred at room temperature for 1 h, the solution was evaporated under reduced pressure to give solid residue which was recrystallized from carbon tetrachloride to give **20** (160 mg, 88%) as yellow crystals: mp 152–154 °C; IR (Nujol) 1706 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.26, 2.03 (AB q, J = 13.0 Hz, 2 H), 2.91 (d, J = 6.0 Hz, 1 H), 2.95 (s, 2 H), 3.50 (d, J = 6.0 Hz, 1 H), 3.63 (t, J = 3.0 Hz, 1 H), 4.35 (t, J = 3.0 Hz, 1 H), 6.81 (s, 2 H), 7.79–8.07 (m, 4 H); mass spectrum, m/z 492 (M + 4), 490 (M + 2), 448 (M^+). Anal. ($C_{21}H_{14}O_4Br_2$) C, H.

Similar treatment of **18** (140 mg, 0.42 mmol) with bromine (135 mg, 0.84 mmol) in methylene chloride at room temperature for 3 h gave **21** (182 mg, 76%) as yellow prisms: mp 222–224 °C (carbon tetrachloride); IR (Nujol) 1710 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.14, 2.06 (AB q, J = 13.0 Hz, 2 H), 2.91 (d, J = 6.0 Hz, 1 H), 2.95 (s, 2 H), 3.50 (d, J = 6.0 Hz, 1 H), 3.63 (t, J = 3.0 Hz, 1 H), 4.35 (t, J = 3.0 Hz, 1 H), 7.31 (s, 1 H), 7.81–8.09 (m, 4 H); mass spectrum, m/z 572 (M + 6), 570 (M + 4), 568 (M + 2), 566 (M^+). Anal. ($C_{21}H_{13}O_4Br_3$) C, H.

General Procedure for Photochemical Reaction of the Adducts. A solution of the adduct (0.03 M) in various solvents was irradiated with a 100-W high-pressure mercury lamp fitted with an I_2–CCl_4 filter solution under nitrogen at room temperature. After the consumption of starting materials was confirmed by TLC, the solvent was removed under reduced pressure at room temperature. The residual solids were purified by recrystallization.

Photochemical Reaction of 7. Irradiation of **7** (100 mg, 0.39 mmol) in ethyl acetate for 15 min gave **hexacyclo[4.4.4.1^{7,10}.0.0^{3,4}.0^{8,9}]pentadeca-13-ene-2,5,12,15-tetraone (22)** (93 mg, 93%) as yellow needles: mp 253–255 °C (ethyl acetate); IR (Nujol) 1760, 1738, 1672 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.94 (br s, 2 H), 3.13–3.33 (m, 4 H), 3.57 (m, 2 H), 6.87 (s, 2 H); mass spectrum, m/z 254 (M^+). Anal. ($C_{15}H_{10}O_4$) C, H.

Similar irradiation of **7** through a Pyrex filter in methylene chloride and acetone gave **22** in 92% and 95% yields, respectively. Exposure of **7** in ethyl acetate to sunlight (30 min) also afforded **22** in 95% yield.

Photochemical Reaction of 10. Irradiation of **10** (80 mg, 0.25 mmol) in ethyl acetate for 15 min gave **27** (69 mg, 85%) as colorless prisms: mp 263–265 °C dec (ethyl acetate); IR (Nujol) 3440–3320, 1780 cm^{-1}; ^{1}H NMR (Me_2SO-d_6) δ 1.52, 1.80 (AB q, J = 9.0 Hz, 2 H), 3.05–3.76 (m, 4 H), 6.38 (s, 2 H); mass spectrum, m/z 344 (M + 4), 342 (M + 2), 340 (M^+). Anal. ($C_{15}H_{10}O_5Cl_2$) C, H.

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Photochemical Reaction of 14. Irradiation of a 1:1 mixture of **14** and **15** (100 mg, 0.33 mmol) in methylene chloride for 1 h gave **28** (45 mg, 90%) as yellow crystals: mp >300 °C (ethyl acetate); IR (Nujol) 1790, 1660 cm^{-1}; ^1H NMR ($CDCl_3$) 1.55, 2.14 (AB q, J = 10.0 Hz, 2 H), 3.58 (br s, 4 H), 3.89 (br s, 2 H), 7.70, 8.10 (AA'BB', 4 H); mass spectrum, m/z 304 (M^+). Anal. ($C_{19}H_{12}O_4$) C, H.

The filtrate was shown to be mainly composed of **15** by ^1H NMR and IR spectra.

Transannular Cyclization of 22. Compound **22** (65 mg, 0.25 mmol) was dissolved in chloroform (1 mL) and exposed to atmospheric moisture for 3 days. The precipitated solids were collected by filtration and recrystallized from ethyl acetate to give **24** (66 mg, 95%) as colorless crystals: mp >300 °C; IR (Nujol) 3420, 1760 cm^{-1}; ^1H NMR (Me_2SO-d_6) δ 1.36, 1.68 (AB q, J = 9.2 Hz, 2 H), 3.24-3.60 (m, 6 H), 6.28 (s, 2 *H*), 8.41 (s, D_2O exchangeable, 2 H); UV (CH_3CN) 303 nm (ϵ 4500); mass spectrum, m/z 272 (M^+), 254 (M - 18). Anal. ($C_{15}H_{12}O_5$) C, H.

Acetylation of 24. To a solution of **24** (95 mg, 0.35 mmol) in pyridine (5 mL) were added acetic anhydride (5 mL) and a trace of 4-(dimethylamino)pyridine. The resulting solution was stirred at room temperature for 3 days and then diluted with water. The mixture was extracted with ethyl acetate, dried over anhydrous Na_2SO_4, evaporated under reduced pressure, and crystallized from ether to give **25** (60 mg, 48%) as colorless needles: mp 283-285 °C; IR (Nujol) 1778, 1765 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.54, 2.18 (AB q, J = 10.0 Hz, 2 H), 2.34 (s, 6 H), 3.44 (br s, 4 H), 3.62 (br s, 2 H), 7.05 (s, 2 H); mass spectrum, m/z 356 (M^+). Anal. ($C_{19}H_{16}O_7$) C, H.

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Supplementary Material Available: Table II, LUMO energies and coefficients (1 page). Ordering information is given on any current masthead page.

Potential Diuretic-β-Adrenergic Blocking Agents: Synthesis of 3-[2-[(1,1-Dimethylethyl)amino]-1-hydroxyethyl]-1,4-dioxino[2,3-*g*]quinolines

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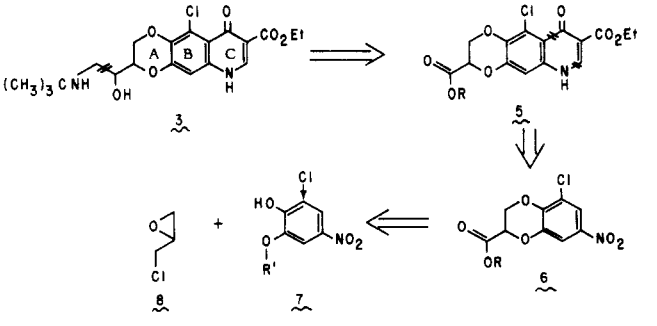
A series of hybrid structures were designed as potential diuretic-β-adrenergic blocking agents on the basis of the structures of the diuretic quincarbate (**2**) and a benzodioxane β blocker, **1**. Synthesis of the hybrids **50** and **51** as well as improved synthesis of the parent drugs **1** and **2** were developed. The key intermediate in the synthesis of **50** and **51** was the tricyclic diester **29** in which the quinolone functionality was masked as the corresponding 4-chloroquinoline. Discrimination between the methyl and ethyl esters in **29** was achieved by selective hydrolysis of the methyl ester and set the stage for attachment of the amino alcohol side chain and subsequent unmasking of the quinolone. Phosphoryl chloride induced cyclization of the adduct **25** afforded the tricyclic diester **29** along with the dioxino[2,3-*f*]quinoline **27** as the minor side product. The adduct **25** was prepared from the 2-(hydroxymethyl)-7-nitrobenzodioxane **15** which, in turn, was available from the monoprotected catechols **11** and **12**. Construction of the monoprotected catechols solved most of the regiochemical problems posed by the structures **50** and **51**. The tricyclic amino alcohols **50** and **51** were essentially devoid of diuretic and β-adrenergic blocking activity.

The most important first-line drug therapies for essential hypertension are diuretics[2] and β-adrenergic blocking agents.[3] In many instances, neither of these drugs alone adequately controls blood pressure, and, as a result, combinations of β blockers and diuretics have been subjected to extensive clinical trials with encouraging results.[4] An attractive alternative to this combination therapy would be a single entity exhibiting both of the desired pharmacological actions. The tricyclic amino alcohols **3** and **4** were designed as potential β-blocker diuretics after considering the structures of the known β blocker **1**[5] and the diuretic

Scheme I



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