Orbital Distortion Arising from Remote Substituents. Nitration, Reduction, and Epoxidation of Fluorenes Bearing a Carbonyl or an Olefin Group in Spiro Geometry

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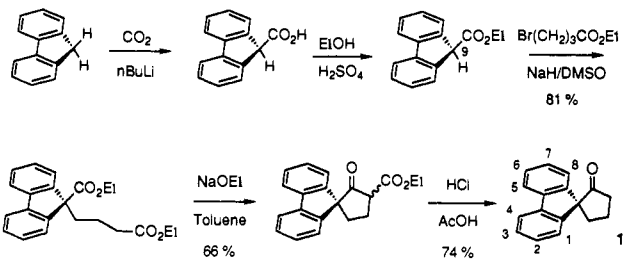
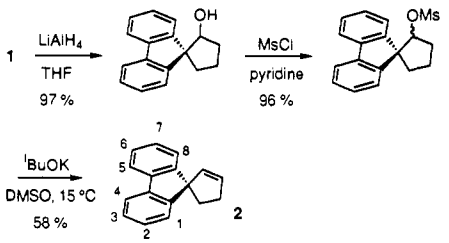
Abstract: Nitration of spiro[cyclopentane-1,9′-fluoren]-2-one with acetyl nitrate predominantly gave the 4-nitro derivative. In the reduction of substituted spiro[cyclopentane-1,9′-fluoren]-2-ones, the anti alcohols were favored in all cases. In the epoxidation of substituted spiro[cyclopent-2-ene-1,9′-fluorenes], the syn epoxides were favored. These distributions of the products can be interpreted in terms of orbital perturbations arising from interactions of the π orbitals of the aromatic and the carbonyl moieties or of the π orbitals of the aromatic and the olefin moieties, i.e., orbital mixing perturbation of the aromatic π orbitals through the π orbital of the bisected carbonyl (or olefin) group and the reciprocal perturbation of the π orbital of the carbonyl (or olefin) group arising from the orthogonal π aromatic orbitals.

Reactivities of most types of organic molecules depend upon the three-dimensional extension of particular orbitals occupied or unoccupied by electrons.[1] The orbital interactions may determine the course of attack of a reagent, particularly when the stereogenic center is free from steric bias. Such influence of electronic modifications of the inducing center has been demonstrated in recent studies on cyclohexanones,[2] methylenecyclohexanes,[2,3] 5-substituted 2-adamantanones,[4] 5-substituted 1,3-cyclopentadienes,[5] and 2,2-diarylcyclopentanones,[6] in addition to the classic examples of anomeric effects of pyranose sugars[7] and exo reactivities of norbornenes.[8] Biased reactions in nucleophilic additions, electrophilic additions, and Diels–Alder cycloadditions of those systems are the phenomenologically reasonable results of the unsymmetrical π face of the carbonyl and the olefin group arising from nonequivalent substituents. This asymmetry is an intrinsic feature of the system and is not induced by the attack of a reagent. Electronic effects stem from orbital interactions between particular orbitals of the σ and π frameworks in the molecule. In this context, substituent effects in norbornenes,[8,9] cyclopentadienes,[9] cyclohexanone,[2,3] and methylenecyclohexane systems[2,3] were postulated to be attributed to orbital interactions between a σ fragment and a π fragment. We are interested in possible interactions between two π fragments in a molecule, wherein each of the interactive fragments would be subject to efficient reciprocal perturbations in its reactivity. In this paper we will deal with some reactions of fluorene derivatives bearing a spiro substituent, i.e., nitration and epoxidation of spiro[cyclopent-2-ene-1,9′-fluorene] (**2**) and nitration and reduction of spiro[cyclopentane-1,9′-fluorene]-2-one (**1**) (Figure 1).[10,11] These reactivities of both systems can be interpreted in terms of the interactions between the π orbitals of the aromatic ring and that of the carbonyl group or the olefin group, i.e., the perturbation of the aromatic ring arising from the bisected carbonyl (or olefin) group and the reciprocal perturbation of the carbonyl (olefin) group arising from the orthogonal aromatic ring. We also discuss the orbital interaction motif underlying these biased reactions of spiro[cyclopentane-1,9′-fluorene] systems.

Scheme I



Scheme II



Synthesis of Fluorenes Bearing Spiro Substituents. The preparation of the parent spiro[cyclopentane-1,9′-fluoren]-2-one (**1**) is shown in Scheme I. Starting from 9-(ethoxycarbonyl)fluorene, alkylation of C-9 with a bromoalkane bearing an ethoxycarbonyl group was carried out by the use of sodium hydride in DMSO at 17 °C. The spiro ketone was prepared by the Dieckmann condensation of the diester in the presence of sodium ethoxide or potassium *tert*-butoxide, followed by hydrolysis and decarboxylation in aqueous hydrochloric acid and acetic acid.[12] Spiro

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(3) Johnson, C. R.; Tait, B. D.; Cieplak, A. S. *J. Am. Chem. Soc.* **1987**, *109*, 5875. Frenking, G.; Koehler, K. F.; Reetz, M. T. *Angew. Chem., Int. Ed. Engl.* **1991**, *30*, 1146.
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(5) (a) Williamson, K. L.; Li. Hsu, Y.-F. *J. Am. Chem. Soc.* **1970**, *92*, 7385. (b) Mavaulay, J. B.; Fallis, A. G. *J. Am. Chem. Soc.* **1990**, *112*, 1136.
(6) Halterman, R. L.; McEvoy, M. A. *J. Am. Chem. Soc.* **1990**, *112*, 6690.
(7) Lemieux, R. U.; Koto, S. *Tetrahedron* **1974**, *30*, 1933. Reference 1, Chapter 2. Inagaki, S.; Mori, Y.; Goto, N. *Bull. Chem. Soc. Jpn.* **1990**, *63*, 1098.
(8) (a) Alder, K.; Stein, G. *Liebigs Ann. Chem.* **1931**, *485*, 211. *Ibid.* **1935**, *515*, 185. (b) Brown, H. C. *Chem. Ber.* **1966**, *2*, 199. (c) Huisgen, R.; Ooms, P. H.; Mingin, M.; Allinger, N. L. *J. Am. Chem. Soc.* **1980**, *102*, 3951. (d) Spanget-Larsen, J.; Gleiter, R. *Tetrahedron Lett.* **1982**, *23*, 2435. Gleiter, R.; Spanget-Larsen, J. *Tetrahedron* **1983**, *39*, 3345. (e) Schleyer, P. v. R. *J. Am. Chem. Soc.* **1967**, *89*, 701. (f) Mehta, G.; Khan, F. A. *J. Am. Chem. Soc.* **1990**, *112*, 6140.
(9) (a) Inagaki, S.; Fukui, K. *Chem. Lett.* **1974**, 509. Inagaki, S.; Fujimoto, H.; Fukui, K. *J. Am. Chem. Soc.* **1976**, *98*, 4054. (b) Washburn, W. N.; Hillson, R. A. *J. Am. Chem. Soc.* **1984**, *106*, 4575.
(10) A part of the work was communicated in Ohwada, T.; Shudo, K. *Chem. Pharm. Bull.* **1991**, *39*, 2176.
(11) For simple numbering of the aromatic positions of spiro[cyclopentane-1,9′-fluorene] systems, dash suffixes are omitted except for the ipso positions (1′ and 8′) throughout this paper.
(12) Stauffer, D. A.; Fancher, O. E. *J. Org. Chem.* **1960**, *25*, 935.

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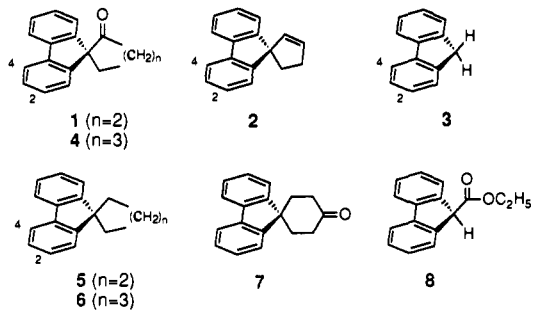


Figure 1.

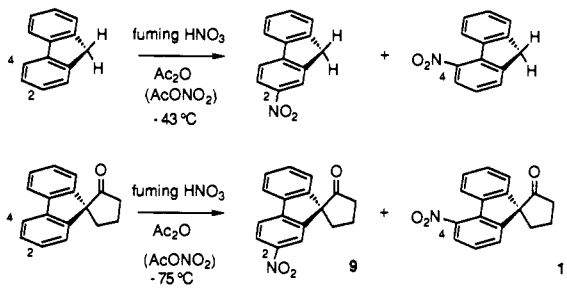


Figure 2.

Table I. Distributions of Isomers in Mononitro Derivatives Formed by Nitration in Acetic Anhydride

substrate	temp (°C)	time (h)	nitro products (%) 2-nitro	4-nitro	4/2 ratio
1	−75	5	11	77	7.0
2	−43	8	30	8[a]	0.3
3	−43	6	56	28	0.5
4	−43	10	26	52[b]	2.0
5	−43	8	81	14	0.2
6	−43	7	74	26	0.4
7	−22	5	65	17	0.3
8	−22	3	54	34	0.6

[a] Recovery (55% yield). [b] Recovery (14% yield).

ketones substituted with 2-fluoro and 2-methoxy groups were prepared similarly from 2-fluorofluorene and 2-methoxyfluorene, respectively.[11] The 2- and 4-nitro spiro ketones were obtained by the nitration of the parent spiro ketone **1**.

Spiro[cyclopent-2-ene-1,9′-fluorene] (**2**) was prepared from the corresponding spiro ketone **1** (Scheme II). The mesylate of the alcohol, obtained by reduction of the spiro ketone, was subjected to elimination in the presence of potassium *tert*-butoxide in DMSO.[13] 2-Fluoro and 2-methoxy derivatives were also prepared from the corresponding ketones.[11] The 2- and 4-nitro derivatives were obtained by the nitration of **2**.

Reactions of Fluorenes Bearing a Ketone in Spiro Geometry. Nitration of the Fluorene Ring. Fluorene exhibits more nucleophilicity at C-2 than at C-4, due to increased conjugation of the aromatic rings and steric congestion at C-4. In the nitration of the parent fluorene **3** at −43 °C with acetyl nitrate, the isomer distribution was observed to be 67% at C-2 and 33% at C-4 (Figure 2).[14] A spiro substitution, on the other hand, was found to have an unexpectedly large effect on the nitration, resulting in a great change of the distribution of products: instead of the 2-nitro derivative (**9**, 11%), spiro[cyclopentane-1,9′-fluoren]-2-one (**1**) predominantly gave the 4-nitro derivative (**10**; 77%) with the nitrating reagent at −75 °C (Figure 2 and Table I). The nitration reaction of the spiro ketone at a higher temperature, −43 °C, did not alter the result. A similar divergence in the distributions of nitrated compounds was also observed in the case of the reactions

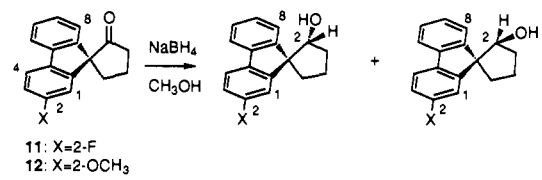


Figure 3.

Table II. Distributions of Isomers in Alcohols Formed by Reduction of Substituted Spiro[cyclopentane-1,9′-fluoren]-2-ones at −43 °C

	substituent (X)	yield of alcohol (%)	anti/syn ratio
1	H	75	50:50
9	2-NO_2	81	68:32
10	4-NO_2	67	71:29
11	2-F	58	72:28
12	2-OCH_3	73	74:26

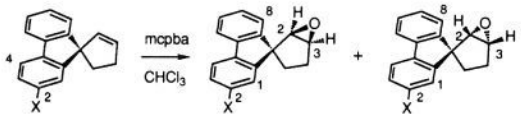
of the spiro fluorene bearing a six-membered ring, spiro[cyclohexane-1,9′-fluoren]-2-one (**4**) (Figure 1). The bisected carbonyl group of **1** and **4** plays a significant role in these divergent nitrations: the nitration of spiro[cyclopentane-1,9′-fluorene] (**5**) and spiro[cyclohexane-1,9′-fluorene] (**6**), the decarbonylated compounds, resulted in the commonly expected distributions of nitrated fluorenes (Table I). Judging from the ratios of 4-/2-nitration, a less flexible conformation, i.e., a more rigid planarity of the five-membered ring of **1** and **5**, strongly perturbed the nitration. Neither the cyclohexane ring nor the cyclopentane ring in the spiro-geometry encouraged the nitration at C-4; rather both enhanced the reactivities at the C-2 position of the fluorene ring. These results also exclude possible steric congestion around the C-2 position owing to the spiro substitution of the C-9 position. Moreover, the nitration of spiro[cyclohexane-1,9′-fluoren]-4-one (**7**) also favored the 2-nitro derivative (65%) rather than the 4-nitro derivative (17%), suggesting the requisite proximity for interaction between the carbonyl and the aromatic moieties. An indirect effect on the nitration reaction arising from a carbonyl substituent at the C-9 position of the fluorene was indicated by the nitration of 9-(ethoxycarbonyl)fluorene (**8**) (Table I). The 4/2 ratio (0.6) is very similar to that of fluorene (**3**) (0.5). All the results, therefore, indicate perturbation of the fluorene ring arising from the bisected carbonyl group of **1**.

Reduction of the Ketone. In the reverse direction, the perturbation on the fluorene ring in the spiro[cyclopentane-1,9′-fluoren]-2-one system should transfer to the carbonyl group. This reciprocal perturbation of the carbonyl group can be demonstrated by the biased reduction of the carbonyl groups of substituted spiro[cyclopentane-1,9′-fluoren]-2-ones **9**, **10**, **11**, and **12** (Figure 3).[10] The ketones were reduced to the alcohols by the action of sodium borohydride in methanol at −43 °C. Although the yields of the products depend to some degree on the substituent at C-2 or C-4 of the fluorene ring (Table II), the anti alcohol, i.e., the syn addition of the reducing reagent with respect to the substituent, is favored in all cases. The configurations of the alcohols were elucidated after isolation, on the basis of NOE detection and characteristic lower-field shift of H-1 or H-8 owing to the anisotropic effect of the hydroxy group.[15] The ratios were determined from NMR spectra before isolation.

A coordinative interaction of the substituent with the reducing agent can be excluded, in view of the great distances between the substituents and the carbonyl group. The distance between the fluorine atom at C-2 and the carbonyl carbon atom in **11**, for

(13) Snyder, C. H.; Soto, A. R. *J. Org. Chem.* **1964**, *29*, 742.
(14) Dewar, M. J. S.; Urch, D. S. *J. Chem. Soc.* **1958**, 3079. Schofield, K. *Aromatic Nitration*; Cambridge Univ. Press: London, 1980; Chapter 13.

(15) The configurations of substituted spiro[cyclopentane-1,9′-fluoren]-2-ols were elucidated on the basis of NOE experiments and the characteristic lower-field shift of H-1 or H-8 (as compared with those of the corresponding ketones) owing to the anisotropic effect of the hydroxy group. The chemical shifts of the aromatic protons (the $H_{5,6,7,8}$ protons of the unsubstituted ring), both of the syn alcohols and of the starting ketones themselves, are unperturbed, in good accordance with those of the aromatic protons of the parent spiro[cyclopentane-1,9′-fluoren]-2-one (**1**). This provided a supporting evidence for the assignments of the configurations of the alcohols. See Experimental Section.



13: X=2-NO_2 **14**: X=4-NO_2
15: X=2-F **16**: X=2-OCH_3

Figure 4.

Table III. Distributions of Isomers in Epoxides Formed by MCPBA of Substituted Spiro[cyclopent-2-ene-1,9′-fluorenes] at 3 °C

	substituent (X)	yield of epoxides (%)	syn/anti ratio
2	H	92	50:50
13	2-NO_2	86	63:37
14	4-NO_2	97	65:35
15	2-F	77	61:39
16	2-OCH_3	67	69:31

example, is more than 5 Å based on molecular models. The oxygen atoms of the nitro group at the 4-position are too far away to interact directly, or even in a coordinative manner, with the carbonyl group. Furthermore, the similar behavior of the two isomeric nitro fluorenes (2-nitro **9** and 4-nitro **10**) also excluded this possibility.

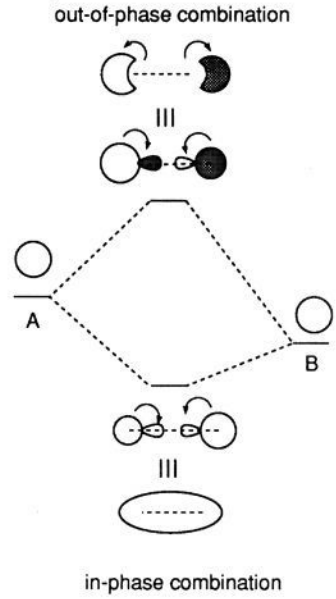
Simple considerations based on electron delocalization theory allow us to predict the divergent reaction depending on the nature of the substituents, i.e., electron-withdrawing (such as a nitro group) or electron-donating (such as a methoxy group). In the case of biased reductions of 2,2-diarylcyclopentanones,[5] preferential attack of a hydride opposite the more electron-rich aromatic ring was consistent with this kind of simple delocalization theory. The result of the reduction of the methoxy-substituted **12** is, however, apparently in conflict with this idea. Molecular orbital calculations can estimate the ring charge of an aromatic compound (C_6H_5X) as the summation of charges of carbons and hydrogens except for those of the C–X moiety. The calculations based on STO-3G basis sets showed that the rings of substituted benzenes (fluorobenzene, phenol, nitrobenzene) are positively charged (+0.13, +0.08, and +0.24, respectively), whereas the ring of the parent benzene is rather negatively charged (−0.06).[16] The predominant alcohol, in all cases, can be regarded as the product arising from the addition of hydride to the face opposite the negatively charged aromatic ring. This modification of the electron delocalization theory, however, is not valid in the case of the epoxidation of olefins in spiro geometry (vide post).

Reactions of Fluorenes Bearing an Olefin in Spiro Geometry. Nitration of the Fluorene Ring. Nitration reaction with acetyl nitrate at −43 °C of spiro[cyclopent-2-ene-1,9′-fluorene] (**2**) gave the 4-nitro derivative (8%) and the 2-nitro derivative (30%), accompanied with recovery (55%) of unchanged **2** (Figure 1 and Table I). A long reaction time and high reaction temperature degrade the olefin moiety, probably by nitration of the olefin group. The 4/2 ratio is 0.3, indicating a slight suppression of the nitration at the C-4 position as compared with that of the parent fluorene (ratio 0.5).

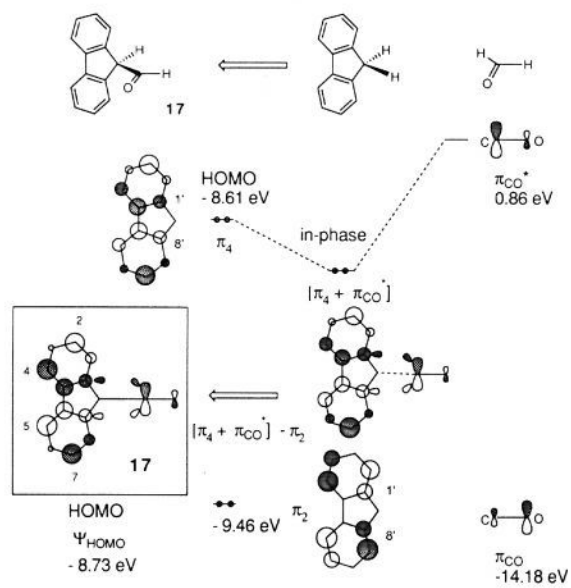
Epoxidation of the Olefin. Epoxidation of substituted spiro-[cyclopent-2-ene-1,9′-fluorene] **13**, **14**, **15**, and **16** with a peroxidic reagent was investigated. The spiro olefins react with *m*-chloroperoxybenzonic acid (MCPBA) in chloroform at 3 °C to give a mixture of the epoxides (Figure 4). The conversion yields and ratios (anti/syn epoxides) are shown in Table III. In all cases the syn epoxides, i.e., the syn addition of the peroxidic reagent with respect to the substituent, are favored (Table III). In the cases of two nitro substituents, the epoxides were isolated and the configurations elucidated on the basis of the characteristic lower-field shifts of the aromatic proton (H-1 or H-8) nearest to the

(16) The ring charge is a sum of π and σ electron populations. π electron populations of benzene, fluorobenzene, phenol, and nitrobenzene are 0, −0.080, −0.102, and +0.031, respectively. Judging from these values, possible intervention of a charge-transfer complex did not rationalize these biased reactions. Pross, A.; Radom, L. *Prog. Phys. Org. Chem.* **1981**, *13*, 1.

Scheme III. A Principle Orbital Interaction



Scheme IV. Orbital Interactions in Fluorene Substituted with a Spiro Carbonyl Group

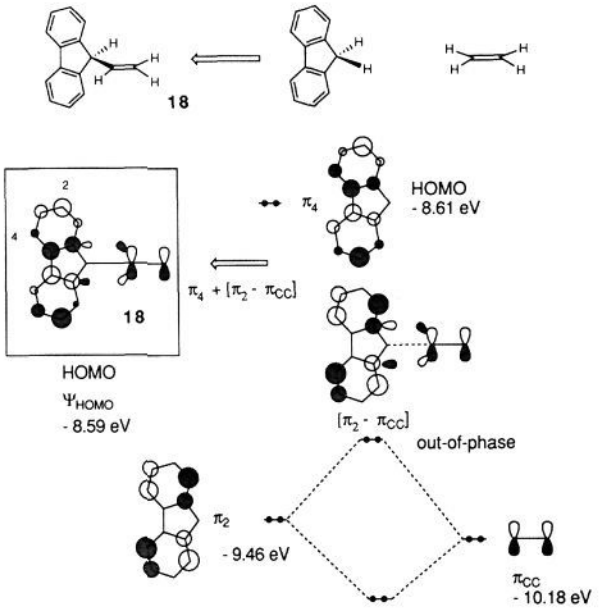


oxygen atom of the epoxide.[17] Although a similar bias is observed in both the reduction of the derivatives of **1** and the epoxidation of the derivatives of **2**, orbitals contributing predominantly to the reactions are different: an unoccupied (vacant) orbital of the ketone predominates in the former reaction, but an occupied orbital of the olefin group contributes the most in the latter.[18] Based on the electron delocalization theory, the attack of the peracid opposite the side of the electron-poor aromatic ring (or the positively charged aromatic ring) (e.g., the unsubstituted ring of the

(17) Low-field shifts of the aromatic proton owing to anisotropy of the oxygen atom of the epoxide correspond well to those observed in the case of the alcohols of **9**–**12**. The chemical shifts of the aromatic protons (the $H_{5,6,7,8}$ protons of the unsubstituted ring), both of the syn epoxides and of the starting olefins, are unperturbed, in good accordance with those of the aromatic protons of the parent spiro[cyclopent-2-ene-1,9′-fluorene] (**2**). In addition, these chemical shifts also correspond well to those of the aromatic protons of the ketone **1**. This indicates that the assignments of the configurations and the structures of all the spiro compounds are consistent throughout. See Experimental Section.

(18) Fukui, K. *Science* **1982**, *218*, 747 and references cited therein. Fleming, I. *Frontier Orbitals and Organic Chemical Reactions*; John Wiley & Sons: London, 1976

Scheme V. Orbital Interactions in Fluorene Substituted with a Spiro Olefin Group

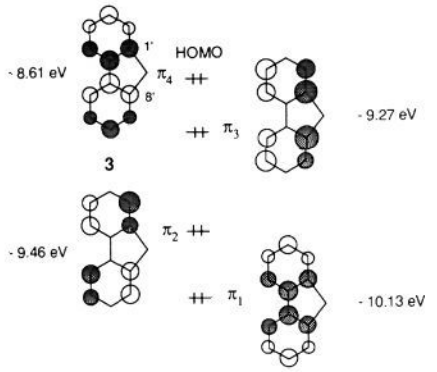


2-nitrofluorene derivative) would be favored,[16] but this is not the experimental reality. These results can also be interpreted in terms of the perturbation of the olefinic π orbital arising from the substituted fluorene.

Orbital Interaction of π Frameworks of Fluorenes Bearing a Spiro Carbonyl Group and a Spiro Olefin Group. In the systems of fluorenes bearing a spiro carbonyl group and a spiro olefin group, π orbitals of fluorenes and those of the carbonyl group or of the olefin group can interact predominantly through the ipso (C-1′ and C-8′) positions of the fluorene ring (see Schemes IV and V). This type of interaction involves σ-type overlaps of the π orbitals in spiro geometry, in a manner similar to spiro conjugation.[19] To reveal the perturbations arising from the spiro interaction, the molecular orbitals of the spiro ketone and the spiro olefin are considered to be constructed from orbitals of the composite subsystems, a fluorene and a carbonyl group or an olefin group.[18]

For the discussion of the orbital interactions of the present systems, we employ the following well-defined principles of orbital interaction.[18,20] In a possible interaction of two orbitals (A and B) (Scheme III), the higher-lying orbital (A) raises its energy by mixing out-of-phase the lower-lying orbital (B), resulting in depletion of electron density from the region between A and B (*orbital interaction rule 1*), while the lower-lying orbital (B) lowers its energy by mixing in-phase the higher-lying orbital (A), resulting in the buildup of the electron density in the region between A and B (*orbital interaction rule 2*).[21] In order to emphasize electron density distribution of the internuclear region in addition to the phase relation of the interacting orbitals, we adopted the diagram depicted in Scheme III. The removal of a bonding electron from the internuclear region can be regarded as diffusion of the electron of each fragment into each *antibonding region* along the internuclear axis; the buildup of a bonding electron is equivalent to

Chart I. Occupied π Orbitals of Fluorene **3**



diffusion of the electron into each *bonding region* along the bond axis.[21] The *bonding* or *antibonding diffusion* depends on energy difference and on overlap: interactions of orbitals with a smaller energy gap or with a larger set of orbital coefficients perturbed more significantly the electron density distribution in the interacting region. Furthermore, out-of-phase combination of HOMO (A) and HOMO (B) results in a hybridized HOMO, activated energetically, while in-phase combination of LUMO (A) and LUMO (B) results in a hybridized LUMO, activated energetically.[18]

Perturbation of the Fluorene Ring. Nitration reaction of fluorene derivatives can be regarded as involving interaction between the HOMO of the fluorene and the LUMO of the nitrating reagent. MNDO calculations[22] showed that the parent fluorene bears a larger coefficient at C-2 (0.390) than at C-4 (0.278) in its HOMO. This rationalizes the preferred nitration at C-2. Spiro substituents would perturb the HOMO of the fluorene ring. Among the occupied π orbitals of the fluorene (Chart I), the HOMO (π_4) and the π_2 of the fluorene are in the same category with respect to the orbital phase at C-1′ and C-8′, antisymmetric with respect to reflection in the mirror plane perpendicular to the aromatic plane. They interact with π orbitals of the carbonyl and the olefin group in spiro geometry, which are also antisymmetric with respect to the same plane. The HOMO (π_4) of the isolated fluorene is modified by orbital mixing of the lower-lying π orbital (π_2) through interaction with the π orbital of the spiro carbonyl group (**17**, Scheme IV) or of the spiro olefin group (**18**, Scheme V).[23]

(I) Fluorene Substituted with a Carbonyl Group in Spiro Geometry. The interaction of the HOMO (π_4) of the fluorene with the occupied π orbital of the carbonyl group (π_{CO}) is not effective, judging from the small contribution of the π orbital of the carbon atom. Instead, the antibonding π orbital of the carbonyl group (π^*_{CO}) can effectively overlap with the HOMO (π_4) of the fluorene at the ipso (C-1′ and C-8′) positions (Scheme IV) because it has a large contribution of the carbon orbital. Since the energy gap between π_4 and π^*_{CO} is smaller than that between π_2 and π^*_{CO}, the former interaction is favored. The in-phase combination ($\pi_4 + \pi^*_{CO}$) contributes predominantly to the HOMO of the combined fluorene **17**. This involves the bonding region between the nuclei (orbital interaction rule 2) (Scheme IV). At the same time, the HOMO (π_4) lowered its energy to reduce the energy separation from π_2. Thus the ($\pi_4 + \pi^*_{CO}$) orbital would mix the lower-lying π_2 orbital so as to diminish the bonding region between the nuclei: π_2 mixes in the ($\pi_4 + \pi^*_{CO}$) orbital in an antibonding manner with respect to the π^*_{CO} fragment (orbital interaction rule 1). This interaction diagram, with emphasis on the electron density dis-

(19) Simmons, H. E.; Fukunaga, T. *J. Am. Chem. Soc.* **1967**, *89*, 5208. Hoffmann, R.; Imamura, A.; Zeiss, G. D. *J. Am. Chem. Soc.* **1967**, *89*, 5215. Gordon, M. D.; Fukunaga, T.; Simmons, H. E. *J. Am. Chem. Soc.* **1976**, *98*, 8401.

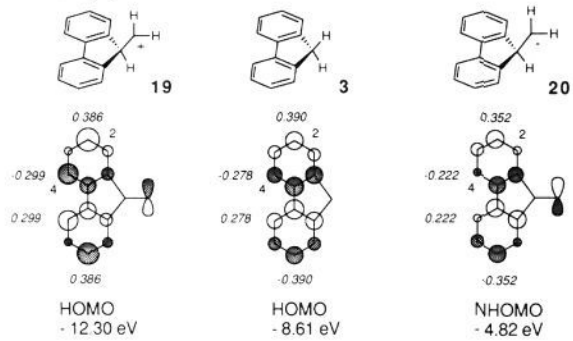
(20) Walsh, A. D. *J. Chem. Soc.* **1953**, 2266. Albright, T. A.; Burdett, J. K.; Whangbo, M.-H. *Orbital Interactions in Chemistry*; John Wiley & Sons, Inc.: New York, 1985.

(21) In the case of orbital interactions of two vacant orbitals, the depletion and buildup of the orbital electron density (or the diffusion of orbital into the internuclear region) are notional because there is no electron present. However, we are interested in the interpretation of the reaction in terms of frontier orbital theory. We thus consider the virtual electron density (and virtual orbital diffusion region) which is to be attacked by electrons of an occupied orbital (e.g., the HOMO) of a reagent.

(22) Dewar, M. J. S.; Thiel, W. *J. Am. Chem. Soc.* **1977**, *99*, 4899.

(23) Such intramolecular orbital mixing through the intermolecular interactions of two subsystems has been proposed for the first time as orbital mixing rules in refs 9a and 24b and the following paper: Ishida, M.; Beniya, Y.; Inagaki, S.; Kato, S. *J. Am. Chem. Soc.* **1990**, *112*, 8980. An example of the application of this orbital mixing rule to benzene derivatives has been reported in Santiago, C.; Houk, K. N.; Snow, R. A.; Paquette, L. A. *J. Am. Chem. Soc.* **1976**, *98*, 7443.

Chart II. (N)HOMOs of Fluorene and Its Ionized Derivatives



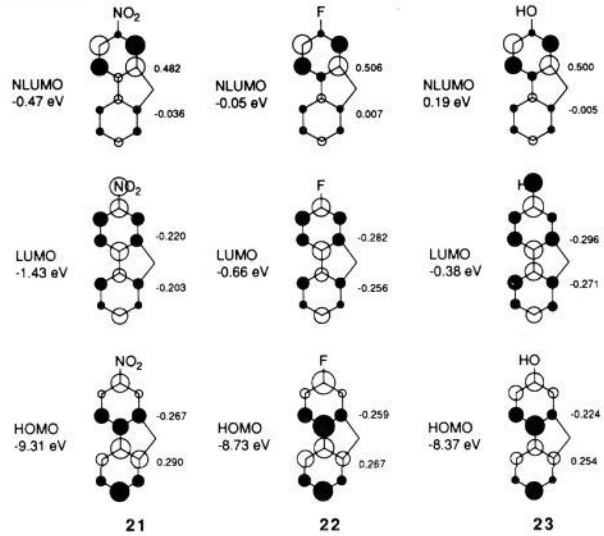
tribution between the nuclei, agrees completely with the application of the orbital mixing rules proposed by Inagaki and Fukui[23] and by Hoffmann[24b] on the basis of the theoretical formulation of perturbation theory. This orbital mixing predicts that the perturbed HOMO (Ψ_{HOMO}) of the fluorene bearing the spiro carbonyl group would have increased coefficients at C-4 (C-5) and rather unperturbed C-2 (C-7) coefficients, which should favor the nitration at C-4 (Scheme IV).

(II) Fluorene Substituted with an Olefin Group in Spiro Geometry. The occupied orbitals of the fluorene (π_4 and π_2) interact with the bonding π orbital of ethylene (π_{CC}) (Scheme V). The interaction of π_2 with π_{CC} is favored because the energy gap is smaller as compared with that between π_4 (HOMO) and π_{CC}. The out-of-phase combination ($\pi_2 - \pi_{CC}$) raises its energy to close to the energy of the HOMO (π_4), involving the antibonding region between nuclei (orbital interaction rule 1). The HOMO of the fluorene (π_4) mixes this resultant lower-lying ($\pi_2 - \pi_{CC}$) orbital so as to enhance the antibonding nature of the internuclear region: π_4 (HOMO) takes in the ($\pi_2 - \pi_{CC}$) orbital in an antibonding manner with respect to the π_{CC} fragment (orbital interaction rule 1). This orbital mixing predicts contraction of the coefficient at C-4 (C-5) and rather unperturbed C-2 (C-7), which would depress the nitration at C-4.[23]

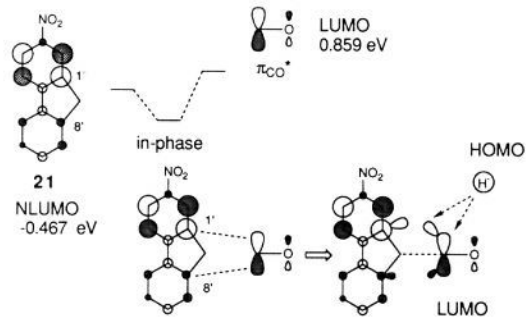
Calculations of Perturbed Fluorene Rings. Calculations based on MNDO methods were carried out on models of the experimental systems: a fluorene substituted with a formyl group in a perpendicular geometry (**17**, Scheme IV) and a fluorene substituted with an ethylene group in a perpendicular geometry (**18**, Scheme V). Although neither apparent enlargement nor contraction of the orbital coefficient of C-4 is observed in these neutral models, changes in energy level of the π orbital (HOMO) of the fluorene indicated intrinsic intervention of the orbital mixing perturbation discussed above. The HOMO of the spiro ketone **17** lowered its energy (−8.73 eV), and the HOMO of the spiro olefin **18** raised its energy (−8.59 eV) both as compared with the energy of the fluorene itself (HOMO, −8.61 eV).[24]

The effects of conjugative spiro substituents can be detected in the cases of ionized models which involve fluorenes bearing a carbenium ionic center or a carbanion center (both fixed as a planar sp^2-hybridized carbon atom) in place of the carbonyl group and the olefin group, respectively (Chart II). In the fluorene cation **19**, the substitution of the carbenium center (i.e., a vacant p orbital, $\pi^*_{CH_2}$) in perpendicular geometry increased the coefficient of C-4 (0.299) as compared with that of C-2 (0.386). The ratio of C-2/C-4 coefficients of the HOMO is decreased to 1.29, whereas that of fluorene (**3**) is 1.40. The energy level of the HOMO of the cation **19** is greatly lowered to −12.30 eV, far below that of the HOMO of fluorene (**3**) (−8.61 eV), indicating the in-phase combination of the HOMO of the fluorene with the vacant $\pi^*_{CH_2}$ orbital. This perturbation did increase the coefficient of C-4, although the coefficient of C-2 remains larger than that of C-4. This orbital perturbation therefore accounts, at least in part, for the observed nitration of the fluorene bearing the spiro ketone.

Chart III. Frontier Orbitals and their Vicinities of Substituted Fluorenes



Scheme VI. Distortion of the Carbonyl π^* Orbital



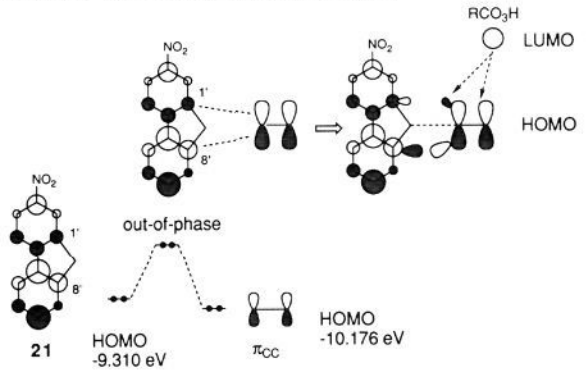
A substituent effect arising from the carbanion center was also evaluated (Chart I). The HOMO of the fluorene anion (**20**) predominantly involves the methylene carbon. The next-HOMO (NHOMO) involves π orbitals of the fluorene moiety. Coefficients of C-2 (0.352) and C-4 (0.222) in the NHOMO were perturbed. The ratio (C-2/C-4 coefficients) is increased to 1.59, indicating a decrease of the coefficient of C-4. This contraction of the π orbital at C-4 provided a reasonable interpretation for the retarded nitration of the fluorene bearing an olefin group. The energy level of the NHOMO is also raised to −4.82 eV, as compared with that of the fluorene itself (−8.61 eV, HOMO). This change is also in agreement with the out-of-phase combination of the HOMO of the fluorene with the occupied π orbital of the methylene carbon atom (π_{CH_2}).[25]

Orbital Distortion of the π Orbital of the Carbonyl Group Arising from Substituted Fluorenes. The reduction of a carbonyl group with a reducing reagent involves interaction of the vacant π orbital of the carbonyl group (π^*_{CO}, LUMO) with the occupied orbital (e.g., HOMO) of the reagent.[18] The orbitals of the substituted spiro ketone (such as **9**) are also assumed to be constructed from orbitals of subsystems, the substituted fluorene and the carbonyl

(24) A protonated carbonyl group can participate in the nitration reaction of spiro[cyclopentane-1,9′-fluoren]-2-one, judging from the acidity of the reaction media. Protonation of a carbonyl oxygen atom lowers the energy of the vacant π_{CO}* orbital (LUMO), accompanied with significant localization of the coefficient on the carbon atom, which results in a stronger interaction with the occupied π orbitals of the fluorene. This type of orbital perturbation has been theoretically formulated in (a) Fukui, K. *Tetrahedron Lett.* **1965**, *2427*. (b) Libit, L.; Hoffmann, R. *J. Am. Chem. Soc.* **1974**, *96*, 1370. (c) Imamura, A.; Hirano, T. *J. Am. Chem. Soc.* **1975**, *97*, 4192.

(25) In the nitrations of saturated fluorene derivatives such as spiro[cyclopentane-1,9′-fluorene] (**5**), an occupied π-type group orbital of the methylene group (π_{CH_2}) would be involved in the interaction of the π orbitals of the fluorene. Clark, T. *A Handbook of Computational Chemistry. A Practical Guide to Chemical Structure and Energy Calculations*; John Wiley & Sons, Inc.: New York, 1985; Chapter 3. See also ref 27.

Scheme VII. Distortion of the Olefin π Orbital



group. Coefficients for substituted fluorenes, 2-nitrofluorene (**21**), 2-fluorofluorene (**22**), and 2-hydroxyfluorene (**23**) (in place of 2-methoxyfluorene, for the sake of simplicity in calculation) are calculated on the basis of MNDO methods, and coefficients of frontier orbitals and their vicinities are shown in Chart III. In accordance with the orbital phase agreement and similar energy, the π^*_{CO} orbital interacts preferentially with the next-LUMO (NLUMO) of the fluorene derivative, not with the LUMO. The LUMOs bear the orbitals at the ipso (C-1′ and C-8′) positions, symmetric in sign with respect to the plane passing through C-9 and the carbonyl group; the NLUMOs and π^*_{CO} are antisymmetric in sign (Scheme VI). The NLUMOs have coefficients largely localized on the benzene ring bearing a nitro, fluoro, or methoxy substituent (for example, at C-1′ rather than at C-8′). In addition, there are small energy separations between the NLUMO (**21**, −0.47 eV; **22**, −0.05 eV; **23**, 0.19 eV) and π^*_{CO} (0.86 eV). In-phase combination of the NLUMO of the fluorene (for example, 2-nitrofluorene (**21**)) and π^*_{CO} orbital lowered the energy of the π^*_{CO} fragment, activating it for attack of a nucleophile (Scheme VI). At the points of interaction (at C-1′ and C-8′), different amplitudes of the wave functions of the NLUMO of the fluorene result in different buildup of the *virtual bonding region* between nuclei (orbital interaction rule 2).[21] A larger vacant bonding region captures the incoming electrons of a nucleophile more efficiently. Therefore the π^*_{CO} fragment favors the interaction with the HOMO of the hydride ion on the side of the substituent, resulting in a biased reduction product.

Perturbation of the Olefin Group Arising from Substituted Fluorenes. In the epoxidation of an olefin with a peracid, the occupied π orbital of the olefin group (π_{CC}, HOMO) interacts with the vacant orbital (LUMO) of the peracid.[18,26] The HOMOs of the substituted fluorenes can interact with the π_{CC} orbital (Scheme VII) because of the orbital phase agreement (Chart III). Owing to their similar energies (HOMO **21**, −9.31 eV; HOMO **22**, −8.73 eV; HOMO **23**, −8.37 eV; π_{CC}, −10.18 eV), this interaction is significantly favored. The case of 2-nitrofluorene (**21**) is considered here as an example (Scheme VII). Out-of-phase combination of π_{CC} with the HOMO of the substituted fluorene raises the energy so as to activate the π_{CC} fragment of the olefin to the attack of an electrophile. Those HOMOs of substituted fluorenes have biased orbital coefficients at the points of interaction: the coefficient of C-8′ is larger than that of C-1′. These different overlaps result in divergent amplitudes of the *antibonding region* between nuclei (orbital interaction rule 2). The antibonding diffusion, arising from the orbital bearing a larger coefficient, greatly reduces the electron-donating ability toward the attack of the electron-deficient orbital of an electrophile. Thus the π_{CC} fragment favors the attack of an electrophile on the side of the substituent, providing a reasonable interpretation of the observed biased epoxidation of the olefin.

Orbital Distortion of the Olefinic π Orbital. In order to shed light on how the orbitals are distorted, changes in the three-dimensional shape of olefinic π orbitals on the introduction of a spiro

(26) Fukui, K. *Bull. Chem. Soc. Jpn.* **1966**, *39*, 498.

Scheme VIII

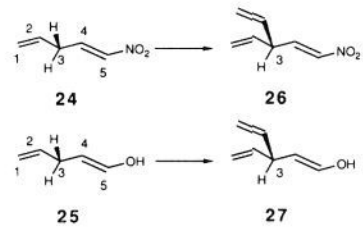
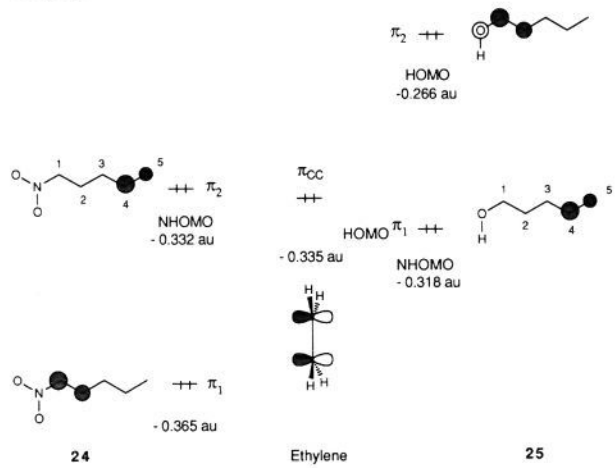


Chart IV. Occupied π Orbitals of Substituted 1,4-Pentadienes and Ethylene



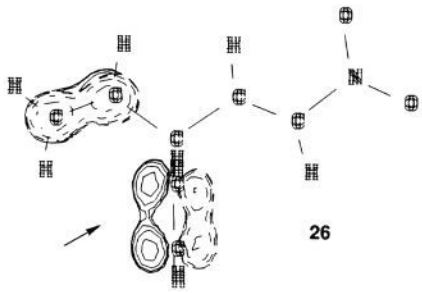
conjugative π system were investigated. For simplicity in calculation, 1,4-pentadienes **24** and **25** were taken as spiro conjugative π systems in place of the fluorene. The ethylene in perpendicular geometry substituted at the 3 position of the 1,4-pentadiene in **26** and **27** represents the spiro olefins of the fluorene systems (Scheme VIII). Geometries were optimized on the basis of ab initio STO-3G basis sets, and the three-dimensional pictures of orbitals were obtained with the PSI77 program.[27] Orbital coefficients and orbital energy levels of π orbitals of 1,4-pentadienes are modified by a sterically distant substituent at C-1. Substitution of an electron-withdrawing group such as a nitro group lowers the energy levels of occupied π orbitals (π_1 and π_2):[18] the NHOMO orbital (π_2), −0.332 au; the lower-lying π orbital (π_1), −0.365 au (Chart IV).[28] Substitution of an electron-donating group such as a hydroxy group, on the other hand, raises the energy of the HOMO (π_2) of the dienes (−0.266 au), whereas the lower-lying π orbital (the NHOMO, π_1) is relatively unperturbed (Chart IV). Because of the similar energy to the π orbital (HOMO) of the ethylene (π_{CC}, −0.335 au), both substitutions favor the interactions between the NHOMOs and π_{CC}. Both NHOMOs bear coefficients localized on the side of the unsubstituted olefin fragment (C-4–C-5). Such an interaction is revealed in the trienes **26** and **27**. The occupied π orbital of the ethylene moiety of the trienes (NHOMOs) is shown in Chart V, which depicts out-of-phase combination of these two fragments and a significant distortion of the occupied π rbital of the ethylene on the side opposite the substituent. The bonding nature of the π orbital is weaker on this side. This unsymmetrical π orbital is the cause of the unsymmetrical π face of the olefin group and probably of the carbonyl group.

Orbital Interactions Involving Orbitals of Reagents. In the reduction of the spiro ketones **1** and the epoxidation of the spiro olefins **2**, consideration of the orbital of the approaching reagent leads to a problem of three-body interactions between the fluorene, the carbonyl (or the olefin), and the reagent. The case of 2-

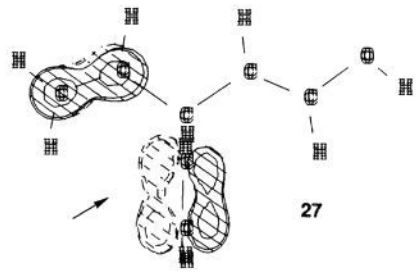
(27) Jorgensen, W. L.; Salem, L. *The Organic Chemist's Book of Orbitals*; Academic Press: New York, 1973.

(28) The unsubstituted 1,4-pentadiene has the HOMO (−0.304 au) and the NHOMO (−0.330 au). The HOMO of the diene **24** (−0.266 au) is localized on the nitro moiety.

Chart V. Orbital Contour Plots of the NHOMOs of Trienes **26** (the 36th orbital) and **27** (the 29th orbital) and the Distortion (arrow) of the Bonding Ethylenic π Lobe Arising from Out-of-phase Mixing

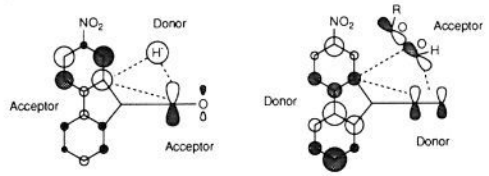


26



27

Scheme IX



nitrofluorene is considered as an example (Scheme IX). In the reduction reaction, cyclic interactions will take place as shown in Scheme IXA, wherein the hydride is represented by an s-type orbital. This cyclic interaction involves the interactions among the nitrobenzene moiety of the fluorene (the NLUMO of the acceptor), the carbonyl group (the LUMO of the acceptor), and the hydride ion (the HOMO of the donor). This system satisfies the orbital phase continuity requirement, showing in-phase overlap between the HOMO of the donor and the (N)LUMO of the acceptor with in-phase overlap between the (N)LUMOs of the acceptors, indicating cyclic electron delocalization.[29] In the epoxidation reaction, a similar cyclic orbital interaction also takes place as shown in Scheme IXB, wherein the antibonding σ orbital of the O–O bond (σ^*_{O-O}) represents the LUMO of the peracid (acceptor).[30] This cyclic interaction involves the interactions between the nitrobenzene moiety of the fluorene (the HOMO of the donor) and the olefin group (the HOMO of the donor) and the peracid (the LUMO of the acceptor). This arrangement of the donor–acceptor systems also satisfies the orbital phase continuity, with in-phase overlap between the HOMO of the donor and the LUMO of the acceptor and out-of-phase overlap between the HOMOs of the donors, indicating cyclic electron delocalization.[29] The continuous cyclic electron delocalization amplifies the interaction between the spiro substituents.

In summary, we have described examples of biased reactions of spiro[cyclopentane-1,9′-fluoren]-2-ones and spiro[cyclopent-2-ene-1,9′-fluorenes]. These substrates exhibit orbital interactions which stem from the σ-type overlap of the π frameworks of the carbonyl group and the fluorene ring and the π frameworks of the olefin group and the fluorene ring. π-Facial selectivities of the carbonyl and olefin group are also discussed on the basis of the transition states which involve all the reagents.[31] Here we also propose an orbital interaction motif which can describe the reciprocal perturbations of interacting π frameworks. We also recognized the intrinsic perturbation of the reaction centers arising from the asymmetric substituents.

Experimental Section

General Methods. All the melting points were measured with a Yanagimoto hot-stage melting point apparatus (MP-500) and are uncorrected. Proton NMR spectra were measured on a JEOL GX 400-MHz NMR spectrometer with TMS as an internal reference in $CDCl_3$ as the solvent unless otherwise specified. All J values are given in hertz, and chemical shifts are reported in ppm. ^{13}C NMR spectra were recorded on a JEOL GX-400 (at 100 MHz) in $CDCl_3$, and chemical shifts are reported in ppm, referenced by assignment of the middle resonance of deuteriochloroform as 77.0 ppm from TMS. Flash column chromatography was performed on silica gel (Merck, kieselgel 60, 230–400 mesh) with a specified solvent.[32] Low-resolution mass spectra (MS) and high-resolution mass spectra (HRMS) were recorded on a JEOL DX303 instrument. Combustion analyses were carried out in the microanalytical laboratory of this faculty.

Synthesis of Spiro[cyclopentane-1,9′-fluoren]-2-one. (A) Preparation of 9-(Ethoxycarbonyl)fluorene. A solution of fluorene-9-carboxylic acid (10.5 g) in 80 mL of ethanol was treated with 1 mL of concentrated H_2SO_4 (98% w/w) at ambient temperature. The solution was heated to reflux at 110 °C (external temperature) for 8.5 h. Evaporation of ethanol followed by addition of ice encouraged crystallization of the crude ester. The product was extracted with CH_2Cl_2 (300 mL). The extract was washed with saturated aqueous Na_2CO_2 and brine, dried over Na_2SO_4, and concentrated under reduced pressure to give 11.12 g (93% yield) of the ethyl ester of fluorene-9-carboxylic acid, mp 44.5–45 °C (recrystallized from n-hexane). ^1H NMR: 7.76 (2 H, d, J = 7.7), 7.67 (2 H, d, d, d, J = 1.1, 1.1, 7.3), 7.42 (2 H, t, t, J = 1.1, 7.33), 7.34 (2 H, t, d, J = 7.33, 1.1), 4.86 (s, 1 H), 4.23 (2 H, q, J = 7.0), 1.28 (3 H, t, J = 7.0). Anal. $C_{16}H_{14}O_2$.

(B) Preparation of 9-(Ethoxycarbonyl)-9-(3-(ethoxycarbonyl)-propyl)fluorene by Alkylation of 9-(Ethoxycarbonyl)fluorene. At ambient temperature, sodium hydride (441 mg, 60%, 1.1 equiv with respect to the ester) was added to 12 mL of degassed DMSO in one portion with stirring. The flask was flushed with argon, and an argon atmosphere was maintained throughout the reaction. The flask was cooled to 17 °C (water temperature). A solution of 9-(ethoxycarbonyl)fluorene (2.38 g) in 4 mL of DMSO was added dropwise via a syringe over 3 min with stirring. After the addition was complete, the resultant yellow solution was stirred at 17 °C for 10 min. To this solution was added ethyl 4-bromobutyrate (1.99 g, Aldrich) dropwise over 2 min, and the mixture was stirred at 17 °C for 1.5 h. The mixture was poured into 200 mL of ice and water, extracted with CH_2Cl_2 (700 mL), and dried over Na_2SO_4. The organic layer was concentrated under reduced pressure to give a liquid residue, which was flash-chromatographed with AcOEt/n-hexane (1:15) as the eluent to give 2.87 g (81%) of the desired diester, mp 76–77 °C (colorless cubes, recrystallized from n-hexane). ^1H NMR: 7.72 (2 H, d, d, J = 0.7, 6.6), 7.54 (2 H, d, d, J = 0.7, 6.6), 7.39 (2 H, d, t, J = 1.1, 7.4), 7.32 (2 H, d, t, J = 1.1, 7.4), 4.07 (2 H, q, J = 7.3), 4.03 (2 H, q, J = 7.3), 2.37 (2 H, q, J = 4.2), 2.10 (2 H, t, J = 7.3), 1.18 (3 H, t, J = 7.3), 1.12 (3 H, t, J = 7.0), 1.05 (2 H, m). Anal. $C_{22}H_{24}O_4$.

(C) The Dieckmann Condensation and Decarboxylation. The Dieckmann Condensation. Sodium ethoxide (1.8 equiv, 123 mg) was added all at once to a solution of the diester (353 mg) in 5 mL of toluene (degassed with argon), the flask was immediately flushed with argon, and an argon atmosphere was maintained throughout the reaction.[12] The mixture was heated at 135 °C (external temperature) for 2.5 h. After cooling, the reaction mixture was poured into 30 mL of 4 N aqueous HCl, and the whole was extracted with AcOEt (300 mL). The organic layer was dried over Na_2SO_4 and concentrated under reduced pressure to give an oily residue (201.3 mg, 66%). The residue was subjected to decarboxylation reaction without further purification.

Decarboxylation. The keto ester (201.3 mg), obtained in the above way, was dissolved in 1 mL of acetic acid, followed by addition of 1 mL of concentrated HCl.[12] The resultant heterogeneous mixture was heated

(29) Inagaki, S.; Fujimoto, H.; Fukui, K. *J. Am. Chem. Soc.* **1976**, *98*, 4693. Inagaki, S.; Hirabayashi, Y. *J. Am. Chem. Soc.* **1977**, *99*, 7418.

(30) In the addition of carbene to an ethylene, the carbene (methylene) approaches slightly off-center and with its plane approximately parallel to the ethylene plane. The approach of the peracid to olefins is likely to begin with an interaction of an unoccupied orbital with the olefin π system. Hoffmann, R.; Hayes, D. M.; Skell, P. *J. Phys. Chem.* **1972**, *76*, 664.

(31) Wu, Y.-D.; Tucker, J. A.; Houk, K. N. *J. Am. Chem. Soc.* **1991**, *113*, 5018.

(32) Still, W. C.; Kanh, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.

to 100 °C (external temperature) for 2 h. During the heating, the mixture became homogeneous. The reaction mixture was poured into 300 mL of ice and water, and a white powder precipitated. The crude product was extracted with ethyl acetate (300 mL), washed with brine, and dried over Na_2SO_4. Evaporation of the solvent gave 114 mg (74% yield) of the spiro ketone **1**. Spiro[cyclopentane-1,9′-fluoren]-2-one (**1**): mp 181–182 °C (recrystallized from *n*-hexane, colorless cubes). ^{1}H NMR: 7.75 (2 H, $H_{4,5}$, d, t, J = 7.9, 1.1), 7.38 (2 H, $H_{3,6}$, d, t, J = 1.5, 7.3), 7.35 (2 H, $H_{1,8}$, d, J = 7.0), 7.30 (2 H, $H_{2,7}$, d, t, J = 1.5, 7.7), 2.73 (2 H, t, J = 7.7), 2.63 (2 H, t, J = 7.7), 2.59 (2 H, quint, J = 7.7). Anal. Calcd for $C_{17}H_{14}O$: C, 87.15; H, 6.02; N, 0.0. Found: C, 87.16; H, 6.08; N, 0.0.

Preparation of Spiro[cyclohexane-1,9′-fluoren]-2-one. Spiro[cyclohexane-1,9′-fluoren]-2-one (**4**) was prepared from 9-(ethoxycarbonyl)-fluorene and ethyl 5-bromovalerate in the same manner as **1**. Spiro-[cyclohexane-1,9′-fluoren]-2-one (**4**): mp 173.5–174 °C. ^{1}H NMR: 7.75 (2 H, d, J = 7.0), 7.61 (2 H, d, J = 7.7), 7.40 (2 H, d, t, J = 1.1, 7.5), 7.33 (2 H, d, t, J = 1.1, 7.5), 2.88 (2 H, t, J = 6.6), 2.23–2.16 (6 H, m). Anal. Calcd for $C_{18}H_{16}O$: C, 87.06; H, 6.50; N, 0.0. Found: C, 86.80; H, 6.62; N, 0.0.

Preparation of Spiro[cyclopentane-1,9′-fluorene]. Spiro[cyclopentane-1,9′-fluorene] (**5**) was prepared by the cyclization of 9-(4-chlorobutyl)fluorene in the presence of a lithium base as described below.

(A) Preparation of 9-(4-Chlorobutyl)fluorene. Under an argon atmosphere, a solution of *n*-butyllithium in hexane (1.5 M, 4 mL, 1.2 equiv) was added dropwise over 6 min to a solution of fluorene (834 mg) in THF (7 mL) at −75 °C. The mixture was stirred at −74 °C for 1 h, and to the resultant red solution was added a solution of 4-bromo-1-chlorobutane (872 mg, 1.01 equiv) in 1 mL of THF over 5 min. After the mixture was stirred at −74 °C for 3.5 h, the reaction was quenched by the addition of 5 mL of brine. The whole was extracted with CH_2Cl_2 (150 mL), washed with brine (30 mL), and dried over Na_2SO_4. The residue after evaporation of the solvent was flash-chromatographed to give 616 mg (48%) of 9-(4-chlorobutyl)fluorene as a colorless oil.

(B) Cyclization of 9-(4-Chlorobutyl)fluorene to 5. Under an argon atmosphere, a solution of 9-(4-chlorobutyl)fluorene (403 mg) in THF (5 mL) was added to a solution of *n*-butyllithium in hexane (1.5 M, 3.2 mL, 2.4 equiv) over 20 min at −70 °C. The mixture was stirred at −68 °C for 1 h, followed by the addition of brine (5 mL). The whole was extracted with CH_2Cl_2 (150 mL), washed with brine, and dried over Na_2SO_4. Evaporation of the solvent gave 344 mg (100%) of **5** as a colorless solid. Spiro[cyclopentane-1,9′-fluorene] (**5**): mp 90–91.5 °C (sublimation 85 °C (ext)/0.4 mmHg, colorless powder). ^{1}H NMR: 7.70 (2 H, d, d, J = 7.0, 1.5), 7.43 (2 H, d, d, J = 7.3, 1.5), 7.31 (2 H, t, d, J = 7.3, 1.5), 7.29 (2 H, t, d, J = 7.5, 1.6), 2.13 (4 H, m), 2.09 (4 H, m). Anal. Calcd for $C_{17}H_{16}$: C, 92.68; H, 7.32. Found: C, 92.59; H, 7.37.

Preparation of Spiro[cyclohexane-1,9′-fluorene]. Spiro[cyclohexane-1,9′-fluorene] (**6**) was prepared from fluorene and 5-bromo-1-chloropentane in the same manner as **5**. Spiro[cyclohexane-1,9′-fluorene] (**6**): mp 97.5–98 °C (recrystallized from *n*-hexane). ^{1}H NMR: 7.74 (2 H, d, d, J = 0.7, 7.7), 7.66 (2 H, d, J = 7.3), 7.35 (2 H, d, t, J = 1.1, 7.3), 7.30 (2 H, d, t, J = 1.5, 7.3), 1.93 (4 H, m), 1.75 (6 H, m). Anal. Calcd for $C_{18}H_{18}$: C, 92.26; H, 7.74. Found: C, 91.96; H, 7.87.

Nitration of Spiro[cyclopentane-1,9′-fluoren]-2-one. Acetic anhydride (0.8 mL) was added in one portion to a 30-mL Erienmeyer flask charged with a weighed amount of fuming HNO_3 (79 mg, 2.4 equiv with respect to **1**), at −70 °C.[12] The mixture was stirred at −70 °C for 5 min, and then 1 mL of methylene chloride was added to dilute the nitrating reagent. At −75 °C (acetone–dry ice, external temperature), spiro[cyclopentane-1,9′-fluoren]-2-one (**1**) (114 mg) was added in one portion. After being stirred at −75 °C for 5 h, the whole mixture was added to 200 mL of ice and water and extracted with methylene chloride (300 mL). The extract was washed with brine and dried over Na_2SO_4. Evaporation of the solvent gave a residue (383 mg), which was flash-chromatographed to give 105 mg (77%) of the 4-nitro isomer and 14 mg (11%) of the 2-nitro isomer. 2′-Nitrospiro[cyclopentane-1,9′-fluoren]-2-one (**9**): mp 204.5–206 °C (recrystallized from *n*-hexane, pale yellow needles). ^{1}H NMR: 8.31 (1 H, H_3, d, d, J = 8.4, 2.2), 8.20 (1 H, H_1, d, J = 1.8), 7.84 (1 H, H_4, d, J = 8.4), 7.83 (1 H, H_5, d, t, J = 7.7, 1.1), 7.48–7.44 (1 H, H_6, m), 7.43–7.41 (2 H, $H_{7,8}$, m), 2.78 (2 H, t, J = 7.7), 2.69 (2 H, m), 2.52 (2 H, m). 4′-Nitrospiro[cyclopentane-1,9′-fluoren]-2-one (**10**): mp 112.5–114 °C (recrystallized from *n*-hexane, pale yellow cubes). ^{1}H NMR: 8.04 (1 H, H_5, m), 7.86 (1 H, H_3, d, d, J = 8.1, 1.1), 7.54 (1 H, H_1, d, d, J = 7.5, 1.1), 7.41 (1 H, H_2, t, J = 8.1), 7.43–7.37 (3 H, $H_{6,7,8}$, m), 2.75 (2 H, m), 2.67 (2 H, m), 2.49 (2 H, m). ^{13}C NMR: 216.1 (s), 150.9 (s), 148.8 (s), 145.1 (s), 136.4 (s), 134.1 (s), 129.6 (d), 128.3 (d), 127.7 (d), 127.4 (d), 125.0 (d), 123.8 (d), 122.7 (d), 64.2 (s), 38.7 (t), 36.0 (t), 20.3 (t). Anal. Calcd for $C_{17}H_{13}NO_2$: C, 73.11; H, 4.69; N, 5.02. Found: C, 73.07; H, 4.67; N, 5.27.

Nitration of Spiro[cyclohexane-1,9′-fluoren]-2-one. Spiro[cyclohexane-1,9′-fluoren]-2-one (**4**) (81 mg) was nitrated with the reagent prepared from fuming HNO_3 (43 mg, 2.4 equiv) and acetic anhydride (0.7 mL) in methylene chloride (0.9 mL) for 9 h at −43 °C. The residue was flash-chromatographed (AcOEt:*n*-hexane 1:10) to give 25 mg (26%) of the 4-nitro isomer, 50 mg (52%) of the 4-nitro isomer, and 11 mg (14%) of recovered starting material. 2-Nitrospiro[cyclohexane-1,9′-fluoren]-2-one: mp 134.5–136.5 °C (recrystallized from *n*-hexane, pale yellow cubes). ^{1}H NMR: 8.42 (1 H, d, J = 1.8), 8.32 (1 H, d, d, J = 8.5, 1.8), 7.84 (1 H, d, J = 8.4), 7.83 (1 H, d, d, J = 7.2, 1.8), 7.74 (1 H, d, d, J = 7.5, 1.8), 7.47 (2 H, m), 2.95 (1 H, m), 2.87 (1 H, m), 2.30–2.16 (6 H, m). Anal. Calcd for $C_{18}H_{15}NO_3$: C, 73.70; H, 5.15; N, 4.78. Found: C, 73.63; H, 5.18; N, 4.74. 4-Nitrospiro[cyclohexane-1,9′-fluoren]-2-one: mp 211–211.5 °C (recrystallized from *n*-hexane, pale yellow cubes). ^{1}H NMR ($CDCl_3$): 7.97 (1 H, m), 7.82 (1 H, d, d, J = 8.1, 1.1), 7.76 (1 H, m), 7.72 (1 H, d, d, J = 7.5, 1.1), 7.44 (1 H, t, J = 8.1), 7.46–7.41 (2 H, m), 2.98 (1 H, m), 2.79 (1 H, m), 2.38–2.05 (6 H, m). Anal. Calcd for $C_{18}H_{15}NO_3$: C, 73.70; H, 5.15; N, 4.78. Found: C, 73.45; H, 5.12; N, 4.80.

Nitration of Spiro[cyclopentane-1,9′-fluorene]. Spiro[cyclopentane-1,9′-fluorene] (**5**) (53 mg) was nitrated with the reagent prepared from fuming HNO_3 (39 mg, 94%, 2.4 equiv) and acetic anhydride (0.6 mL) in 0.6 mL of methylene chloride at −43 °C for 8 h. The residue obtained was flash-chromatographed ($CHCl_3$:*n*-hexane 1:20) to give 52 mg (81%) of the 2-nitro isomer and 9 mg (14%) of the 4-nitro isomer. 2′-Nitrospiro[cyclopentane-1,9′-fluorene]: mp 92.5–93 °C (recrystallized from *n*-hexane, pale yellow needles). ^{1}H NMR: 8.27 (1 H, d, J = 1.5), 8.24 (1 H, d, d, J = 8.4, 2.2), 7.78 (1 H, d, J = 8.1), 7.49 (1 H, d, J = 7.3), 7.42 (1 H, d, t, J = 1.5, 7.3), 7.39 (1 H, d, t, J = 1.5, 7.3), 2.18 (4 H, m), 2.12 (4 H, m). Anal. Calcd for $C_{17}H_{15}NO_2$: C, 76.96; H, 5.70; N, 5.28. Found: C, 77.24; H, 5.78; N, 5.36. 4′-Nitrospiro[cyclopentane-1,9′-fluorene]: mp 158–159 °C (recrystallized from *n*-hexane, pale yellow cubes). ^{1}H NMR: 7.94 (1 H, d, J = 8.1), 7.76 (1 H, d, d, J = 8.1, 1.1), 7.66 (1 H, d, d, J = 7.5, 1.1), 7.47 (1 H, d, J = 7.0), 7.41 (1 H, t, d, J = 7.7, 1.1), 7.39 (1 H, t, J = 8.1), 7.35 (1 H, t, d, J = 7.7, 1.5), 2.16 (4 H, t, J = 5.1), 2.14 (4 H, m). Anal. Calcd for $C_{17}H_{15}NO_2$: C, 76.96; H, 5.70; N, 5.28. Found: C, 76.68; H, 5.72; N, 5.08.

Nitration of Spiro[cyclohexane-1,9′-fluorene]. Spiro[cyclohexane-1,9′-fluorene] (**6**) (105 mg) was nitrated at −43 °C with the reagent prepared from fuming HNO_3 (2.4 equiv) and acetic anhydride to give 74% of the 2-nitro isomer and 26% of the 4-nitro isomer. The ratio was determined from NMR spectra before isolation. 2′-Nitrospiro[cyclohexane-1,9′-fluorene]: mp 127.5–128.5 °C (recrystallized from *n*-hexane, pale yellow cubes). ^{1}H NMR: 8.52 (1 H, d, J = 2.2), 8.28 (1 H, d, d, J = 8.3, 2.2), 7.82 (1 H, d, J = 8.4), 7.82 (1 H, m), 7.42 (2 H, m), 1.97–1.76 (10 H, m). Anal. Calcd for $C_{18}H_{17}NO_2$: C, 77.39; H, 6.13; N, 5.01. Found: C, 77.31; H, 6.22; N, 4.99. 4′-Nitrospiro[cyclohexane-1,9′-fluorene]. ^{1}H NMR: 7.91 (1 H, d, d, J = 7.5, 1.1), 7.88 (1 H, d, d, J = 7.7, 0.7), 7.74 (2 H, d-like, J = 7.0), 7.41–7.35 (3 H, m), 1.99–1.72 (10 H, m).

Nitration of the Parent Fluorene. Fluorene **3** was nitrated at −43 °C with the reagent prepared from fuming HNO_3 (2.4 equiv) and acetic anhydride to give 56% of the 2-nitro isomer and 28% of the 4-nitro isomer after isolation. Their IR and NMR spectra were in good accordance with those of authentic samples.[14]

Nitration of 9-(Ethoxycarbonyl)fluorene. 9-(Ethoxycarbonyl)fluorene (**8**) was nitrated at −76 °C with the nitrating reagent prepared from fuming HNO_3 (2.4 equiv) and acetic anhydride) to give a 48% yield of the 2-nitro isomer and at 24% yield of the 4-nitro isomer. 2-Nitro-9-(ethoxycarbonyl)fluorene: mp 127.5 °C (recrystallized from *n*-hexane). ^{1}H NMR: 8.55 (1 H, d, J = 1.8), 8.35 (1 H, d, d, J = 8.4, 1.5), 7.86 (1 H, d, J = 8.4), 7.84 (1 H, m), 7.78 (1 H, d-like), 7.49 (2 H, m), 4.91 (1 H, s), 4.28 (2 H, q, J = 7.0), 1.33 (3 H, t, J = 7.0). Anal. Calcd for $C_{16}H_{13}NO_4$: C, 67.84; H, 4.63; N, 4.95. Found: C, 67.62; H, 4.62; N, 4.82. 4-Nitro-9-(ethoxycarbonyl)fluorene: mp 63.5–64 °C (recrystallized from *n*-hexane). ^{1}H NMR: 8.04 (1 H, m), 7.90 (2 H, t, J = 7.3), 7.73 (1 H, m), 7.45 (3 H, m), 4.91 (1 H, s), 4.24 (2 H, q, J = 7.0), 1.28 (3 H, t, J = 7.0). Anal. Calcd for $C_{16}H_{13}NO_4$: C, 67.84; H, 4.63; N, 4.95. Found: C, 67.57; H, 4.63; N, 4.89.

Preparation of Spiro[cyclopent-2-ene-1,9′-fluorene]. (A) Mesylate of Spiro[cyclopentane-1,9′-fluoren]-2-ol. Methanesulfonyl chloride (mesyl chloride) (1.42 g, 1.5 equiv) was added to a solution of spiro[cyclopentane-1,9′-fluoren]-2-ol (2.48 g) in 20 mL of pyridine at 3 °C. The mixture was stirred at 17 °C (ambient temperature), and then distillation of the solvent gave a residue, which was dissolved in methylene chloride, washed with 1 N aqueous HCl and brine, and dried over Na_2SO_4. Evaporation of the solvent gave 3.1 g (96%) of the mesylate. ^{1}H NMR: 7.72 (2 H, d, J = 7.7), 7.59 (1 H, d, J = 7.7), 7.42–7.31 (5 H, m), 5.00 (1 H, d, J = 5.9), 2.46–2.18 (6 H, m), 2.16 (3 H, s).

(B) Elimination of the Mesylate to 2. A solution of the mesylate (3.1 g) in 18 mL of DMSO was added to a solution of potassium *tert*-butoxide

(1.46 g) in 20 mL of DMSO (degassed) over 15 min under an argon atmosphere at 15 °C.[13] After being stirred at 15 °C for 6.5 h, the red-colored solution was poured into ice and water and extracted with *n*-hexane. The extract was dried over Na_2SO_4. Evaporation of the solvent gave a residue, which was flash chromatographed (*n*-hexane) to give 1.3 g (60%) of the olefin **2**. Spiro[cyclopent-2-ene-1,9′-fluorene] (**2**): mp 48.5–49.5 °C (colorless needles). ^{1}H NMR: 7.71 (2 H, $H_{4,5}$, d, J = 7.7), 7.36 (2 H, $H_{3,6}$, d, J = 7.7), 7.34 (2 H, $H_{1,8}$, t, d, J = 7.0, 1.8), 7.29 (2 H, $H_{2,7}$, t, d, J = 7.3, 1.5), 6.17 (1 H, m), 5.48 (1 H, m), 2.81 (2 H, t-like m), 2.38 (2 H, t-like m). Anal. Calcd for $C_{17}H_{14}$: C, 93.53; H, 6.47. Found: C, 93.43; H, 6.43.

Nitration of Spiro[cyclopent-2-ene-1,9′-fluorene]. Spiro[cyclopent-2-ene-1,9′-fluorene] (**2**) (109 mg, 0.5 mmol) was nitrated at −43 °C in the presence of fuming nitric acid and acetic anhydride in methylene chloride for 8 h. The residue was flash chromatographed to give 11 mg (8%) of the 4-nitro isomer and 40 mg (30%) of the 2-nitro isomer, accompanied with 60 mg (55%) of the recovered starting material. 2′-Nitrospiro[cyclopent-2-ene-1,9′-fluorene] (**13**): mp 151.5–152.0 °C (recrystallized from *n*-hexane, pale yellow cubes). ^{1}H NMR: 8.26 (1 H, H_3, d, d, J = 8.4, 2.2), 8.19 (1 H, H_1, d, J = 1.8), 7.79 (1 H, H_4, d, J = 7.7), 7.79 (1 H, H_5, m), 7.42 (3 H, $H_{6,7,8}$, m), 6.27 (1 H, m), 5.44 (1 H, m), 2.87 (2 H, m), 2.41 (2 H, t, J = 7.0). Anal. Calcd for $C_{17}H_{13}NO_2$: C, 77.55; H, 4.98; N, 5.32. Found: C, 77.69; H, 4.93; N, 5.49. 4′-Nitrospiro[cyclopent-2-ene-1,9′-fluorene] (**14**): mp 71–71.5 °C (recrystallized from *n*-hexane, pale yellow cubes). ^{1}H NMR: 8.00 (1 H, H_5, d, J = 7.0), 7.82 (1 H, H_3, d, d, J = 1.1, 8.1), 7.57 (1 H, H_1, d, d, J = 1.1, 7.3), 7.41–7.35 (4 H, $H_{2,6,7,8}$, m), 6.25 (1 H, m), 5.44 (1 H, m), 2.84 (2 H, m), 2.39 (2 H, m). Anal. Calcd for $C_{17}H_{13}NO_2$: C, 77.55; H, 4.98; N, 5.32. Found: C, 77.26; H, 4.69; N, 5.59.

Preparation of Substituted Spiro[cyclopentane-1,9′-fluoren]-2-ones. 2′-Fluorospiro[cyclopentane-1,9′-fluoren]-2-one and 2′-methoxyspiro[cyclopentane-1,9′-fluoren]-2-one were prepared from 2-fluorofluorene-9-carboxylic acid and 2-methoxyfluorene-9-carboxylic acid, respectively, in a manner similar to the parent (**1**). 2′-Fluorospiro[cyclopentane-1,9′-fluoren]-2-one (**11**): mp 145–145.5 °C (recrystallized from *n*-hexane, colorless needles). ^{1}H NMR: 7.69 (1 H, H_5, d, J = 8.1), 7.68 (1 H, H_4, d, d, J = 8.1, 5.1), 7.38 (1 H, H_6, d, t, J = 1.1, 7.3), 7.33 (1 H, H_8, d, d, J = 1.1, 7.9), 7.28 (1 H, H_7, d, t, J = 1.1, 7.3), 7.09 (1 H, H_3, d, t, J = 2.6, 8.7), 7.03 (1 H, d, d, H_1, J = 2.2, 8.8), 2.73 (2 H, m), 2.62 (2 H, m) 2.46 (2 H, m). Anal. Calcd for $C_{17}H_{13}OF$: C, 80.93; H, 5.19; N, 0.0. Found: C, 81.01; H, 5.12; N, 0.0. 2′-Methoxyspiro[cyclopentane-1,9′-fluoren]-2-one (**12**): mp 180–183 °C (recrystallized from *n*-hexane, colorless plates). ^{1}H NMR: 7.64 (2 H, $H_{4,5}$, d, J = 8.4), 7.34 (1 H, H_6, d, t, J = 1.1, 7.3), 7.30 (1 H, H_8, d, J = 7.3), 7.22 (1 H, H_7, d, t, J = 1.1, 7.3), 6.92 (1 H, H_3, d, d, J = 8.4, 2.6), 6.87 (1 H, H_1, d, J = 2.2), 3.85 (3 H, s) 2.72 (2 H, m) 2.61 (2 H, m) 2.44 (4 H, m). Anal. Calcd for $C_{18}H_{16}O_2$: C, 81.79; H, 6.10; N, 0.0. Found: C, 81.52; H, 6.20; N, 0.0.

Reduction of Substituted Spiro[cyclopentane-1,9′-fluoren]-2-ones. Substituted spiro[cyclopentane-1,9′-fluoren]-2-ones (typically 10 mg) were reduced with sodium borohydride (3.6 equiv) in ethanol (2 mL) at −43 °C for a specified time (Table II). Both yields and ratios of the diastereomers were determined from ^{1}H NMR spectra after separation of the products (as a mixture) by flash column chromatography (ethyl acetate/*n*-hexane or methylene chloride/*n*-hexane). Diastereomers were isolated or concentrated by flash column chromatography and/or preparative thin-layer chromatography on TLC plates precoated with silica gel $60F_{254}$ (layer thickness 1 mm, Merck) with specified solvents. Purely isolated diastereomers were analyzed by thin-layer chromatography on TLC plates precoated with silica gel $60F_{254}$ (layer thickness 0.25 mm, Merck), on HPTLC plates precoated with silica gel $60F_{254}$ (Merck), and on glass plates coated with silica gel $60GF_{245}$ (Merck), and by ^{1}H NMR spectroscopy. The assignments of the ^{1}H NMR spectra (in particular, of aromatic protons) are based on the INDOR (internuclear double resonance) and 2D-COSY measurements.

2′-Nitrospiro[cyclopentane-1,9′-fluoren]-2-ols. The diastereomers were separated by flash column chromatography (ethyl acetate/*n*-hexane 1:6). Anti alcohol of **9**: mp 193–196 °C (recrystallized from *n*-hexane/methylene chloride, yellow powder). ^{1}H NMR: 8.28 (1 H, H_3, d, d, J = 2.2, 8.06), 8.26 (1 H, H_1, d, J = 1.46), 7.84 (1 H, H_5, m), 7.81 (1 H, H_4, d, J = 8.43), 7.65 (1 H, H_8, m), 7.47 (2 H, $H_{6,7}$, m), 4.33 (1 H, t, J = 6.23), 2.54 (1 H, m), 2.49–2.12 (5 H, m). Anal. Calcd for $C_{17}H_{15}NO_3$: C, 72.58; H, 5.38; N, 4.98. Found: C, 72.53; H, 5.38; N, 4.96. Syn alcohol of **9**: mp 147–149 °C (recrystallized from *n*-hexane/methylene chloride, yellow needles). ^{1}H NMR: 8.44 (1 H, H_1, d, J = 2.2), 8.31 (1 H, H_3, d, d, J = 2.2, 8.25), 7.83 (1 H, H_4, d, J = 8.43), 7.81 (1 H, H_5, m), 7.44 (3 H, $H_{6,7,8}$, m), 4.35 (1 H, t, J = 6.23), 2.55 (1 H, m), 2.36 (2 H, m), 2.19 (3 H, m). Anal. Calcd for $C_{17}H_{15}NO_3$: C, 72.58; H, 5.38; N, 4.98. Found: C, 72.32; H, 5.33; N, 5.15.

4′-Nitrospiro[cyclopentane-1,9′-fluoren]-2-ols. A mixture of the diastereomers (mp 123–130 °C, yellow powder, recrystallized from *n*-hexane/methylene chloride), obtained by flash column chromatography (methylene chloride:*n*-hexane 2:1), was subjected to combustion analysis. Anal. Calcd for $C_{17}H_{15}NO_3$: C, 72.58; H, 5.38; N, 4.98. Found: C, 72.34; H, 5.38; N, 4.94. Although complete isolation of each diastereomer could not be attained, the concentration of the diastereomers was accomplished by preparative thin-layer chromatography (ethyl acetate:*n*-hexane 1:6, 10 developments). Anti alcohol of **10**. ^{1}H NMR: 7.99 (1 H, H_5, d, d, J = 6.97, 1.47), 7.79 (1 H, H_3, d, d, J = 8.06, 1.1), 7.63 (1 H, H_1, d, d, J = 1.1, 8.06), 7.61 (1 H, H_8, br d, J = 8.06), 7.46 (1 H, H_7, d, t, J = 1.46, 7.60), 7.44–7.39 (2 H, $H_{6,2}$, m), 4.30 (1 H, t, J = 6.23), 2.48 (1 H, m), 2.35–2.10 (5 H, m). Syn alcohol of **10**. ^{1}H NMR: 7.93 (1 H, H_5, d, J = 8.06), 7.81 (2 H, $H_{1,3}$, d, J = 8.06), 7.44–7.42 (3 H, $H_{2,7,8}$, m), 7.36 (1 H, H_6, m), 4.31 (1 H, t, J = 5.86), 2.51 (1 H, m), 2.37–2.20 (5 H, m).

2′-Fluorospiro[cyclopentane-1,9′-fluoren]-2-ols. The diastereomers were separated by flash column chromatography (ethyl acetate:*n*-hexane 1:12). Anti alcohol of **11**: mp 83–83.5 °C (recrystallized from *n*-hexane, colorless fine needles). ^{1}H NMR: 7.69 (1 H, H_5, d, J = 7.33), 7.64 (1 H, H_4, d, d, J = 8.25, 5.13), 7.56 (1 H, H_8, d, J = 7.32), 7.39 (1 H, H_6, d, t, J = 1.47, 7.52), 7.31 (1 H, H_7, d, t, J = 1.1, 7.33), 7.09 (1 H, H_1, d, d, J = 9.16, 2.2), 7.04 (1 H, H_3, d, t, J = 2.56, 8.79), 4.21 (1 H, t, J = 6.23), 2.48 (1 H, m), 2.31 (2 H, m), 2.13 (3 H, m). HRMS (M^+) calcd for $C_{17}H_{15}FO$: 254.1107. Found: 254.1108. Anal. Calcd for $C_{17}H_{15}FO{\cdot}1/2\ H_2O$: C, 77.54; H, 6.13; N, 0.0. Found: C, 77.82; H, 6.31; N, 0.0. Syn alcohol of **11**: mp 70.5–71.5 °C (recrystallized from *n*-hexane, colorless fine needles). ^{1}H NMR: 7.66 (1 H, H_4, d, d, J = 8.43, 5.13), 7.65 (1 H, H_5, d, J = 8.42), 7.37 (1 H, H_8, d, J = 7.7), 7.34 (1 H, H_6, d, t, J = 1.46, 7.33), 7.28 (1 H, H_1, d, d, J = 9.35, 2.2), 7.28 (1 H, H_7, d, t, J = 1.46, 7.14), 7.08 (1 H, H_3, d, t, J = 2.57, 8.98), 4.25 (1 H, t, J = 6.05), 2.48 (1 H, m), 2.31 (2 H, m), 2.13 (3 H, m). Anal. Calcd for $C_{17}H_{15}FO$: C, 80.29; H, 5.95; N, 0.0. Found: C, 80.51; H, 6.25; N, 0.0.

2′-Methoxyspiro[cyclopentane-1,9′-fluoren]-2-ols. No adequate solvents for separating the mixture of the diastereomers could be found. However, the concentration of the major product (the anti alcohol) could be carried out by repeated (twice at least) fractional recrystallization from *n*-hexane to give the colorless cubes (86:14 anti:syn): mp 123.5–124.5 °C. Anal. Calcd for $C_{18}H_{18}O_2$: C, 81.17; H, 6.81; N, 0.0. Found: C, 80.93; H, 6.84; N, 0.0. Anti alcohol of **12**. ^{1}H NMR: 7.65 (1 H, H_4, d, J = 6.96), 7.61 (1 H, H_5, d, J = 8.06), 7.52 (1 H, H_8, d, J = 7.32), 7.36 (1 H, H_6, d, t, J = 1.1, 7.33), 7.26 (1 H, H_7, d, t, J = 1.1, 7.33), 6.94 (1 H, H_1, d, J = 2.2), 6.89 (1 H, H_3, d, d, J = 8.25, 2.2), 4.22 (1 H, t, J = 6.6), 3.87 (3 H, s), 2.47 (1 H, m), 2.29 (2 H, m), 2.10 (3 H, m). Syn alcohol of **12**. ^{1}H NMR: 7.65 (1 H, H_5, d, J = 8.43), 7.62 (1 H, H_4, d, J = 6.96), 7.35 (1 H, H_8, d, J = 8.43), 7.31 (1 H, H_6, d, t, J = 1.1, 7.33), 7.23 (1 H, H_7, d, t, J = 1.1, 7.33), 7.13 (1 H, H_1, d, J = 2.2), 6.93 (1 H, H_3, d, d, J = 8.43, 2.2), 4.21 (1 H, t, J = 6.6), 3.88 (3 H, s), 2.47 (1 H, m), 2.29 (2 H, m), 2.10 (3 H, m).

The configurations of substituted spiro[cyclopentane-1,9′-fluoren]-2-ols were elucidated on the basis of NOE experiments and the characteristic lower-field shift of H-1 or H-8 owing to the anisotropic effect of the hydroxy group.[15] In the anti alcohol of **9**, NOE enhancement (5%) was seen between the methine H-2 proton and the aromatic H-1 proton (at 8.26 ppm), while no NOE was detected between the methine H-2 proton and the aromatic H-8 proton (7.65 ppm) (see Figure 3). In the syn alcohol of **9**, NOE enhancement (7%) between the methine H-2 proton and the aromatic H-8 proton (at 7.44 ppm) was detected, while no NOE was detected between the methine H-2 proton and the aromatic H-1 proton (at 8.44 ppm). In the anti alcohol of **11**, NOE enhancement (4%) between the methine H-2 proton and the aromatic H-1 proton (at 7.09 ppm) was seen, while no NOE was detected between the methine H-2 proton and the aromatic H-8 proton (7.56 ppm). In the syn alcohol of **11**, NOE enhancement (2%) between the methine H-2 proton and the aromatic H-8 proton (at 7.37 ppm) was detected, while no NOE was detected between the methine H-2 proton and the aromatic H-1 proton (at 7.28 ppm). Analogously, the structure of the anti alcohol of **10** was determined on the basis of the low field shift of H-8 (7.61 ppm) and the unperturbed H-1 proton (at 7.63 ppm). The syn alcohol of **10** was lower-field-shifted H-1 (7.81 ppm) and unperturbed H-8 (7.43 ppm). Similarly, the structure of the anti alcohol of **12** was supported by lower-shifted H-8 (at 7.52 ppm) and unperturbed H-1 (6.94 ppm). The syn alcohol of **12** was lower-field-shifted H-1 (at 7.13 ppm) and unperturbed H-8 (7.35 ppm).

Preparation of Substituted Spiro[cyclopent-2-ene-1,9′-fluorene]. Substituted spiro[cyclopent-2-ene-1,9′-fluorenes] were prepared from the corresponding spiro[cyclopentane-1,9′-fluoren]-2-ones in a manner similar to the parent (**2**). 2′-Fluorospiro[cyclopent-2-ene-1,9′-fluorene] (**15**): mp 44–46 °C. ^{1}H NMR: 7.66–7.61 (2 H, $H_{4,5}$, m), 7.34 (1 H, H_8, d, J = 7.3), 7.33 (1 H, H_6, t, J = 6.6), 7.27 (1 H, H_7, d, t, J = 1.1, 7.3),

7.04 (1 H, H_1, d, d, J = 9.2, 2.2), 7.03 (1 H, H_3, d, t, J = 2.6, 8.4), 6.19 (1 H, m), 5.46 (1 H, m), 2.80 (2 H, m), 2.36 (2 H, m). Mass spectrum: 236 (m/e). Anal. Calcd for $C_{17}H_{13}F$: C, 86.22; H, 5.55. Found: C, 86.41; H, 5.55. 2'-Methoxyspiro[cyclopent-2-ene-1,9'-fluorene] (**16**): mp 111.5–112 °C. ^{1}H NMR: 7.61 (1 H, H_5, d, d, J = 1.1, 7.3), 7.61 (1 H, H_4, d, J = 9.2), 7.32 (1 H, H_8, d, J = 7.3), 7.31 (1 H, H_6, t, J = 7.3), 7.22 (1 H, H_7, d, t, J = 1.1, 7.7), 6.89 (1 H, H_1, d, J = 2.2), 6.89 (1 H, H_3, d, d, J = 2.2, 8.8), 6.17 (1 H, m), 5.48 (1 H, m), 3.85 (3 H, s), 2.80 (2 H, m), 2.37 (2 H, m). Anal. Calcd for $C_{18}H_{16}O$: C, 87.06; H, 6.50. Found: C, 86.85; H, 6.61.

Epoxidation of Spiro[cyclopent-2-ene-1,9'-fluorene] (2). Spiro[cyclopentane-1,9'-fluorene] (**2**) (107 mg) was added in one portion to a solution of MCPBA (190 mg, 70%, 1.5 equiv) in 2 mL of chloroform at 3 °C (in an ice and water bath). The mixture was stirred at 3 °C for 4 h, and then evaporation of the solvent gave a residue, which was flash chromatographed (CH_2Cl_2:*n*-hexane 1:3) to give 105 mg (92%) of the epoxide: mp 92.5–93.0 °C (recrystallized from *n*-hexane). ^{1}H NMR: 7.77 (1 H, d, J = 7.3), 7.74 (1 H, d, d, J = 0.73, 8.8), 7.72 (1 H, d, J = 7.7), 7.40 (1 H, d, t, J = 1.47, 7.3), 7.36 (1 H, d, d, J = 7.33, 1.1), 7.34 (1 H, d, t, J = 1.1, 6.4), 7.30 (1 H, d, t, J = 1.1, 7.3), 3.81 (1 H, d), 3.27 (1 H, d, J = 2.6), 2.44 (1 H, m), 2.20 (1 H, m), 2.18 (1 H, m), 1.80 (1 H, m). Anal. Calcd for $C_{17}H_{14}O$: C, 87.15; H, 6.02. Found: C, 86.89; H, 6.00.

Epoxidation of Substituted Spiro[cyclopent-2-ene-1,9'-fluorenes]. Epoxidation of substituted spiro[cyclopent-2-ene-1,9'-fluorenes] was carried out at 3 °C in the same manner as for **2**. Both yields and ratios of the diastereomers were determined from ^{1}H NMR spectra after separation of the products (as a mixture) by flash column chromatography. The diastereomers of the epoxides were separated by flash column chromatography with a specified solvent. Purely isolated diastereomers were analyzed by thin-layer chromatography on TLC plates precoated with silica gel $60F_{254}$ (layer thickness 0.25 mm, Merck), on HPTLC plates precoated with silica gel $60F_{254}$ (Merck), and on glass plates coated with silica gel $60GF_{254}$ (Merck) and by ^{1}H NMR spectroscopy. The assignments of the ^{1}H NMR spectra are based on the INDOR (internuclear double resonance) measurements.

Epoxides of 2'-Nitrospiro[cyclopent-2-ene-1,9'-fluorene]. A crude mixture of the epoxides was obtained by flash column chromatography (methylene chloride:*n*-hexane 1:2). Diastereomers were isolated by flash column chromatography (ethyl acetate:*n*-hexane 1:15). Syn epoxide of 2-nitrospiro[cyclopent-2-ene-1,9'-fluorene] (**13**): mp 203.5–204.5 °C (recrystallized from *n*-hexane). ^{1}H NMR: 8.56 (1 H, H_1, d, J = 1.8), 8.31 (1 H, H_3, d, d, J = 8.2, 1.8), 7.85 (1 H, $H_{4/5}$, d, J = 9.2), 7.83 (1 H, $H_{5/4}$, d, J = 8.4), 7.49 (1 H, H_6, d, t, J = 1.5, 7.1), 7.43 (1 H, H_7, d, J = 7.7), 7.40 (1 H, H_8, d, J = 7.7), 3.86 (1 H, br s), 3.28 (1 H, d, J = 2.2), 2.52 (1 H, m), 2.26 (2 H, m), 1.83 (1 H, m). Anal. Calcd for $C_{17}H_{13}NO_3$: C, 73.11; H, 4.69; N, 5.02. Found: C, 73.04; H, 4.71; N, 5.08. Anti epoxide of 2'-nitrospiro[cyclopent-2-ene-1,9'-fluorene] (**13**): mp 239.5–240.0 °C (recrystallized from *n*-hexane). ^{1}H NMR: 8.33 (1 H, H_3, d, d, J = 8.4, 2.2), 8.17 (1 H, H_1, d, J = 1.8), 7.87 (1 H, H_4, d, J = 8.4), 7.82 (1 H, H_5, m), 7.79 (1 H, H_8, m), 7.79 (1 H, H_8, m), 7.48 (2 H, $H_{6,7}$, m), 3.89 (1 H, br s), 3.29 (1 H, d, J = 2.6), 2.51 (1 H, m), 2.35 (1 H, m), 2.21 (1 H, m), 1.85 (1 H, m). Anal. Calcd for $C_{17}H_{13}NO_3$: C, 73.11; H, 4.69; N, 5.02. Found: C, 73.34; H, 4.61; N, 5.31.

Epoxides of 4'-Nitrospiro[cyclopent-2-ene-1,9'-fluorene]. A crude mixture of the epoxides was obtained by flash column chromatography (methylene chloride:*n*-hexane 2:1). Diastereomers were isolated by flash column chromatography (ethyl acetate:*n*-hexane 1:15). Syn epoxide of 4'-nitrospiro[cyclopent-2-ene-1,9'-fluorene] (**14**): mp 118–119 °C (recrystallized from *n*-hexane). ^{1}H NMR: 8.06 (1 H, H_5, d-like, J = 7.3), 7.99 (1 H, H_1, d, d, J = 7.5, 1.1), 7.87 (1 H, H_3, d, d, J = 8.3, 1.1), 7.47–7.36 (4 H, $H_{2,6,7,8}$, m), 3.85 (1 H, br s), 3.28 (1 H, d, J = 2.2), 2.51 (1 H, m), 2.32 (1 H, m), 2.27 (1 H, m), 1.82 (1 H, m). Anal. Calcd for $C_{17}H_{13}NO_3$: C, 73.11; H, 4.69; N, 5.02. Found: C, 72.90; H, 4.65; N, 4.90. Anti epoxide of 4'-nitrospiro[cyclopent-2-ene-1,9'-fluorene] (**14**): mp 125.5–126.5 °C (recrystallized from *n*-hexane). ^{1}H NMR: 7.99 (1 H, H_5, d-like, J = 7.9), 7.86 (1 H, H_3, d, d, J = 8.1, 1.1), 7.78 (1 H, H_8, d-like, J = 7.0), 7.55 (1 H, H_1, d, d, J = 7.3, 1.1), 7.47 (1 H, H_7, d, t, J = 1.5, 7.3), 7.43 (1 H, H_6, d, t, J = 1.8, 7.5), 7.41 (1 H, H_2, d, J = 7.3), 3.84 (1 H, d, J = 2.2), 3.28 (1 H, d, J = 2.2), 2.52 (1 H, m), 2.23 (2 H, m), 1.82 (1 H, m). Anal. Calcd for $C_{17}H_{13}NO_3$: C, 73.11; H, 4.69; N, 5.02. Found: C, 72.90; H, 4.74; N, 4.85.

Epoxides of 2'-Fluorospiro[cyclopentane-1,9'-fluorene]. A crude mixture of the epoxides was obtained by flash column chromatography (ethyl acetate:*n*-hexane 1:50). The minor diastereomer (higher R_f, the anti) was isolated by flash column chromatography (diethyl ether:*n*-hexane 1:30) with the use of a large amount of flash silica gel. The pure major isomer (lower R_f, the syn) could be obtained by triple flash column chromatography (diethyl ether:*n*-hexane 1:30) with the use of a large amount of flash silica gel. Syn epoxide of 2'-fluorospiro[cyclopent-2-ene-1,9'-fluorene] (**15**): mp 76.5–77.5 °C (recrystallized from *n*-hexane, colorless powder). ^{1}H NMR: 7.71 (1 H, H_5, d, J = 7.32), 7.66 (1 H, H_4, d, d, J = 5.13, 8.24), 7.41 (1 H, H_3, d, d, J = 2.56, 7.87), 7.40 (1 H, H_6, d, t, J = 1.1, 7.15), 7.31 (1 H, H_7, br t, J = 6.96), 7.29 (1 H, H_8, d, J = 7.33), 7.08 (1 H, H_1, d, t, J = 2.56, 8.61), 3.81 (1 H, br s), 3.27 (1 H, d, J = 2.57), 2.45 (1 H, m), 2.29–2.05 (2 H, m), 1.80 (1 H, m). HRMS (M^+) calcd for $C_{17}H_{13}FO$, 252.0950, found, 252.0949. Anal. Calcd for $C_{17}H_{13}OF$: C, 80.93; H, 5.19; N, 0.0. Found: C, 80.79; H, 5.24; N, 0.0. Anti epoxide of 2'-fluorospiro[cyclopent-2-ene-1,9'-fluorene] (**15**): mp 80.5–83.0 °C (recrystallized from *n*-hexane, colorless powder). ^{1}H NMR: 7.70 (1 H, H_8, d, J = 6.96), 7.69 (1 H, H_4, d, d, J = 5.13, 8.06), 7.68 (1 H, H_5, d, J = 7.69), 7.39 (1 H, H_6, d, t, J = 1.47, 7.52), 7.33 (1 H, H_7, d, t, J = 1.47, 7.51), 7.10 (1 H, H_3, d, t, J = 2.56, 8.79), 7.03 (1 H, H_1, d, d, J = 2.56, 8.80), 3.81 (1 H, d, J = 2.57), 3.27 (1 H, d, J = 2.57), 2.47 (1 H, m), 2.19 (2 H, m), 1.79 (1 H, m). Anal. Calcd for $C_{17}H_{13}OF$: C, 80.93; H, 5.19; N, 0.0. Found: C, 80.94; H, 5.19; N, 0.0.

Epoxides of 2'-Methoxyspiro[cyclopent-2-ene-1,9'-fluorene]. Diastereomers were isolated by flash column chromatography (methylene chloride:*n*-hexane 1:3) with the use of a large amount of flash silica gel. Syn epoxide of 2'-methoxyspiro[cyclopent-2-ene-1,9'-fluorene] (**16**): mp 138.0–138.5 °C (recrystallized from *n*-hexane, colorless powder). ^{1}H NMR: 7.67 (1 H, H_5, d, J = 7.69), 7.63 (1 H, H_4, d, J = 8.43), 7.37 (1 H, H_6, d, t, J = 1.1, 7.33), 7.30 (1 H, H_8, d, J = 7.33), 7.26 (1 H, H_1, d, J = 2.2), 7.22 (1 H, H_7, d, t, J = 0.73, 7.33), 6.94 (1 H, H_3, d, d, J = 2.2, 8.24), 3.89 (3 H, s), 3.80 (1 H, br s), 3.28 (1 H, d, J = 2.56), 2.46 (1 H, m), 2.24 (1 H, m), 2.13 (1 H, m), 1.79 (1 H, m). Anal. Calcd for $C_{18}H_{16}O_2$: C, 81.79; H, 6.10; N, 0.0. Found: C, 81.62; H, 6.12; N, 0.0. Anti epoxide of 2'-methoxyspiro[cyclopent-2-ene-1,9'-fluorene] (**16**): mp 118.0–119.0 °C (recrystallized from *n*-hexane, colorless needles). ^{1}H NMR: 7.66 (2 H, $H_{4,8}$, br d, J = 8.43), 7.64 (1 H, H_5, br d, J = 8.06), 7.36 (1 H, H_6, d, t, J = 1.1, 7.33), 7.27 (1 H, H_7, d, t, J = 1.1, 7.69), 6.93 (1 H, H_3, d, d, J = 2.2, 8.43), 6.87 (1 H, H_1, d, J = 2.2), 3.87 (3 H, s), 3.80 (1 H, br d, J = 2.2), 3.27 (1 H, d, J = 2.57), 2.46 (1 H, m), 2.25 (1 H, m), 2.14 (1 H, m), 1.79 (1 H, m). Anal. Calcd for $C_{18}H_{16}O_2$: C, 81.79; H, 6.10; N, 0.0. Found: C, 82.08; H, 6.14; N, 0.0.

The configurations of epoxides of substituted spiro[cyclopent-2-ene-1,9'-fluorenes] (in the case of 2-fluoro and 2-methoxy) were elucidated, after separation on TLC (AcOEt:*n*-hexane as developing solvent), on the basis of the characteristic lower-field shift of H-1 (in the case of the syn epoxides) or H-8 (in the case of the anti epoxides) owing to the antisotropic effect of the oxygen atom. In the case of **15**, the anti epoxide has the lower-field-shifted H-8 proton (7.70 ppm) and unperturbed H-1 proton (7.03 ppm), whereas the syn epoxide has the lower-field-shifted H-1 proton (7.41 ppm) and the unperturbed H-8 proton (7.28 ppm). In the case of **16**, the anti epoxide has the lower-field-shifted H-8 proton (7.64 ppm) and unperturbed H-1 proton (6.88 ppm), whereas the syn epoxide has the lower-field-shifted H-1 proton (7.26 ppm) and the unperturbed H-8 proton (7.29 ppm).

Calculational Methods. The calculations were performed at the Computer Center of the University of Tokyo. MNDO calculations were carried out on the MOPAC program systems.[33] Geometry optimizations were performed with the standard Davidon–Fletcher–Powell algorithm incorporated in the program. Structures of fluorene derivatives **3**, **17**, **18**, **19**, **20**, **21**, **22**, and **23** were optimized without the restriction of symmetry except for C_s symmetry of the fluorene rings. The ab initio calculations were carried out by using a modified version of the Gaussian 80 computer programs (Gaussian 80H).[34] Structures of the dienes **24** and **25** and of the trienes **26** and **27** were completely optimized by using Martaugh–Sargent gradient optimization techniques on the basis of minimal STO-3G basis sets[35] with the restriction of C_s symmetry for all species. Three-dimensional pictures of the orbitals were obtained by using the PSI77 program[27] based on the geometries optimized with the STO-3G basis sets.

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