benzyl ester hydrochloride, $[\alpha]^{22}_D$ -43.8 (c 1, methanol) (lit.[6] $[\alpha]^{22}_D$ -43.3 (c 1, methanol).

***N*-((1*R*,2*R*,4*R*)-Bicyclo[2.2.1]heptan-2-ylcarbonyl)-(*S*)-proline (6).** To a solution of 1 g (3 mmol) of Diels-Alder adduct **4a** in 50 mL of methanol was added 400 mg of Pd on charcoal. The mixture was stirred vigorously under 1 atm of hydrogen for 24 h, filtered, and concentrated in vacuo. The remaining residue was triturated with ether to give 720 mg (99%) of the carboxylic acid **6** as a colorless solid: mp 122 °C; $[\alpha]^{22}_D$ -131° (c 0.4, CH_2Cl_2); IR (KBr) 1710 (COOH), 1650 (amide) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.8 (broad, 1 H, COOH), 4.56 (m, 1 H, α-CH), 3.64-3.59 (m, 1 H, NCH_{2a}), 3.57-3.50 (m, 1 H, NCH_{2b}), 2.87-2.83 (m, 1 H, H5), 2.49 (m, 1 H, H4), 2.42-2.38 (m, 1 H, $H3_a$), 2.26 (m, 1 H, H1), 2.06-1.92 (m, 3 H), 1.82-1.78 (m, 1 H), 1.62-1.34 (m, 7 H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 176.8, 172.1, 60.3 (α-C), 47.6 (NCH_2), 45.6, 40.9, 39.2, 37.0, 32.2, 28.9, 27.1, 24.8, 24.5. Anal. Calcd for $C_{13}H_{19}NO_3$: C, 65.80; H, 8.07; N, 5.90. Found: C, 65.81; H, 7.91; N, 5.90.

(1*R*,2*R*,4*R*)-Bicyclo[2.2.1]heptane-2-carboxylic Acid (7). A mixture of 430 mg (1.82 mmol) of the proline derivative **6** and 12 mL of 9 N aqueous hydrochloric acid was heated to 80 °C for 12 h and then extracted three times with 10 mL of ether. The combined organic layers were dried with magnesium sulfate, filtered, and concentrated in vacuo to afford 230 mg (90%) of the title compound as a colorless solid: $[\alpha]^{22}_D$ 33.3° (c 1, ethanol) (lit.[2] $[\alpha]^{22}_D$ 33.9° (c 1.06, ethanol)); ^1H NMR (400 MHz, $CDCl_3$) δ 10.99 (broad, 1 H, COOH), 2.80 (m, 1 H, H5), 2.57 (m, 1 H, H4), 2.53 (m, 1 H, H1), 1.69-1.22 (m, 8 H); HRMS calcd for $C_8H_{12}O_2$ 140.083, found 140.083.

Acknowledgment. This research was supported by the Degussa AG and the Fonds der Chemischen Industrie (Liebig-Stipendium).

Thermally Irreversible Photochromic Systems. A Theoretical Study

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Received May 31, 1988

A guiding principle for molecular design of thermally irreversible diarylethene-type photochromic compounds has been proposed on the basis of calculations of state correlation diagrams.

Photochromic organic compounds have attracted a significant amount of attention, because of their potential ability for various applications. Among them the most promising one is to use the photochromic compounds for optical memory media.[2] Despite the recent development of laser technology, however, few applications of the compounds have been realized in optical information storage. One reason for this is the lack of thermal stability of the colored forms.

We have recently reported on a new type of thermally stable photochromic system, diarylethene derivatives having heterocyclic rings (**1a**, **1b**).[3] The colored ring-closed forms (**2a**, **2b**) remain stable for more than 12 h at 80 °C. The colored forms revert to the open ring forms (**1a**, **1b**) only when they are exposed to visible light. On the other hand, the thermal stability was not observed for 2,3-dimesityl-2-butene (**3a**), which has phenyl rings instead of the heterocyclic rings. The photogenerated colored form (**4a**) returns to the open-ring form (**3a**) in the dark with a half-life of 1.5 min at 30 °C.

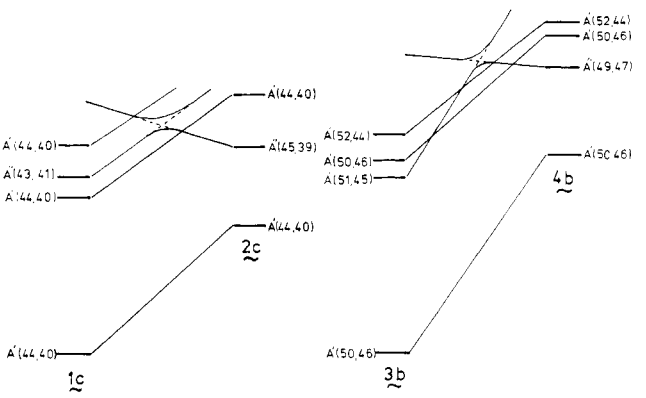
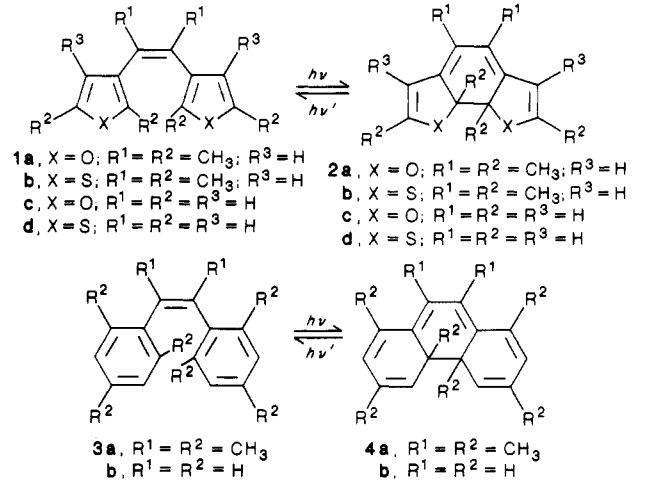
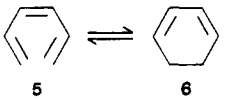


Figure 1. State correlation diagrams in disrotatory mode for the reactions from **1c** to **2c** and from **3b** to **4b**.



In order to get a guiding principle for molecular design of thermally irreversible photochromic compounds, we have carried out a theoretical study to elucidate the different thermal behavior between the diarylethene derivatives having heterocyclic rings and those having phenyl rings.

According to the Woodward-Hoffman rule based on the π orbital symmetries[4] for 1,3,5-hexatriene (**5**), which is the simplest molecular frame work of the above-mentioned compounds, a conrotatory cyclization reaction to cyclohexadiene (**6**) is brought about by light and disrotatory cyclization by heat.



5 **6**

The cycloreversion reaction is allowed both photochemically in the conrotatory mode and thermally in the disrotatory mode. From the simple symmetry consideration of the hexatriene framework, we might not expect the thermal irreversibility of the cycloreversion reaction. A state energy calculation is indispensable to discuss the thermal stability.

Semiempirical MNDO calculations[5] were carried out for 1,2-di(3-furyl)ethene (**1c**), 1,2-di(3-thienyl)ethene (**1d**),

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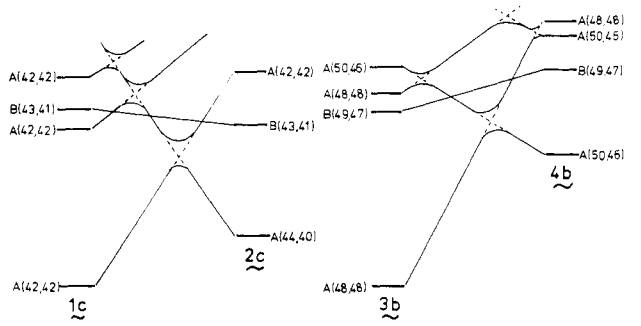

Figure 2. State correlation diagrams in conrotatory mode for the reactions from **1c** to **2c** and from **3b** to **4b**.

Table I. Relative Ground-State Energy Difference between the Open-Ring Form and the Ring-Closed One

compound	disrotatory, kcal/mol	conrotatory, kcal/mol	half-life
1,2-diphenylethene	41.8[a]	27.3[a]	1.5 min[h]
1,2-di(3-pyrrolyl)ethene	32.3[b]	15.5[c]	32 min[i]
1,2-di(3-furyl)ethene	27.0[d]	9.2[e]	>12 h[j]
1,2-di(3-thienyl)ethene	12.1[f]	-3.3[g]	>12 h[k]

[a-g] The calculated energies of the open-ring forms are (*a*) -1958.1159 eV, (*b*) -1832.3101 eV, (*c*) -1832.3174 eV, (*d*) -2033.5359 eV, (*e*) -2033.5386 eV, (*f*) -1865.8387 eV, and (*g*) -1865.8398 eV. [h-k] Half-lives of the ring-closed forms of (*h*) 2,3-dimesityl-2-butene, at 20 °C, (*i*) 2,3-bis(5-cyano-2-methyl-3-pyrrolyl)-2-butene at 20 °C, (*j*) 2,3-bis(2,5-dimethyl-3-furyl)-2-butene at 80 °C, (*k*) 2,3-bis(2,5-dimethyl-3-thienyl)-2-butene at 80 °C.

1,2-diphenylethene (**3b**), and 1,2-di(3-pyrrolyl)ethene together with their closed forms. In the calculations, methyl groups were substituted by hydrogens for the sake of convenience. Geometrical optimizations were fully performed, except that the aromatic rings were assumed to be planar.

Figures 1 and 2 show the state correlation diagrams[6] for the reactions from **1c** to **2c** and from **3b** to **4b** in disrotatory and conrotatory modes, respectively. The relative ground-state energies of the ring-closed forms are given in Table I. The two heterocyclic rings were assumed to be in the parallel orientation for the disrotatory reaction and in the antiparallel orientation for the conrotatory reaction. According to the correlation diagrams of Figure 1, orbital symmetry allows the disrotatory cyclizations in the ground state, in both cases under C_s symmetry, from **1c** to **2c** and from **3b** to **4b**. The relative ground-state energies of the products are, however, 27.0 and 41.8 kcal/mol higher than the respective energies of the reactants. This indicates that thermal cyclization does not take place practically in both cases. The energy is expected to increase further by the steric repulsion when hydrogens are replaced by methyl groups. This result is consistent with the experimental fact that the ring closure reaction is not brought about by heat even at a high temperature (~300 °C).

On the contrary, orbital symmetry forbids the conrotatory cyclizations in the ground state from **1c** to **2c** and from **3b** to **4b**, which proceeds under C_2 symmetry, because each S_0 open-ring form correlates with a highly excited state of the ring-closed form, as shown by dotted lines in Figure 2. Because of a non-crossing rule, the actual correlations are those given by the solid lines. Even in this case, the large barrier prohibits the conrotatory cyclization in the ground state. On the other hand, no such large barrier exists in the S_2 state for **1c** and S_1 states for **3b**. This indicates that the cyclizations of both 1,2-di(3-furyl)ethene and 1,2-diphenylethene are allowed in the photochemically excited states. This prediction agrees with the experimental fact that compounds **1a** and **3a** convert to the ring-closed forms **2a** and **4a** upon visible or UV irradiation.

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Table II. Aromatic Stabilization Energy

group	energy, kcal/mol
phenyl	27.7
pyrrolyl	13.8
furyl	9.1

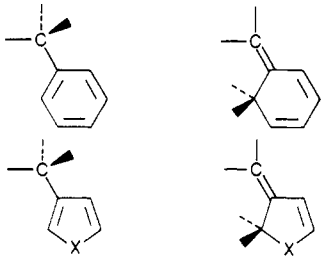
The remarkable difference between diarylethene derivatives having heterocyclic rings and those having phenyl rings is the thermal stability of the ring-closed forms. According to the state energy calculation given in Table I, the ground-state energy difference between the open-ring form and ring-closed one strongly depends on the aryl groups. The large energy difference, 27.3 kcal/mol, of 1,2-diphenylethene decreases to 9.2 kcal/mol when the phenyl rings are replaced by furyl groups. When the phenyl rings are replaced by thienyl groups, the energy difference further decreases and the ring-closed form becomes more stable than the open-ring form. The energy difference is considered to play an important role in the thermal cycloreversion reaction. Solid lines of Figure 2 suggest that the energy barrier of the cycloreversion reaction correlates with the ground-state energy difference. When the energy difference is large, as in the case of 1,2-diphenylethene, the reaction energy barrier becomes small and the cycloreversion reaction is expected to take place readily. On the other hand, the reaction barrier becomes large when the energy difference becomes small as shown for 1,2-di(3-furyl)ethene. In this case, the reaction is expected hardly to occur. The energy barrier, which correlates with the ground-state energy difference between the open-ring form and the ring-closed one, controls the thermal stability of the colored form.

The expectation was further confirmed by examining the state energies of 1,2-di(3-pyrrolyl)ethene and the lifetime of the colored form. The groung-state energy difference was calculated to be 15.5 kcal/mol. The lifetime of 2,3-bis(5-cyano-2-methyl-3-pyrrolyl)-2-butene was measured instead of that of 1,2-bis(2,5-dimethyl-3-pyrrolyl)-2-butene. The half-life of 32 min was observed at 20 °C. These values lie in between the values of 1,2-diphenylethene and 1,2-di(3-furyl)ethene. Thus, the lifetime of the colored species measured experimentally qualitatively correlates well with the energy difference calculated for the conrotatory cycloreversion reaction. The relation between the lifetime and the energy difference is summarized in Table I.

The next question is what makes the difference in the ground-state energy of the two isomers. First, we compared the strain energy of the six-membered rings formed by the conrotatory reaction. The optimized geometries of 1,2-di(3-furyl)ethene and 1,2-diphenylethene, however, show almost identical molecular framework of the six-membered ring. Ring strain cannot explain the energy difference.

Next, we examined the aromaticity change from the open-ring form to the ring-closed one. The difference in the energy between the following right- and left-side groups was calculated, as shown in Table II. The energy difference is considered to correspond to the difference in aromaticity as a result of the conjugated electron migration.

The highest energy difference was calculated for the phenyl group and the lowest one for the furyl group.



Destabilization due to the destruction of the aromatic rings during the course of cyclization increases the ground-state energy of the ring-closed form. The aromaticity explains well the trend of the relative stability.

We can conclude that the thermal stability of both isomers of the diarylethene-type photochromic compounds can be improved by introducing aryl groups that have low aromatic stabilization energy.

Registry No. **1a**, 108028-41-7; **1b**, 108028-40-6; **1c**, 117439-52-8; **1d**, 117439-53-9; **3a**, 108028-39-3; **3b**, 588-59-0; 1,2-di(3-pyrrolyl)ethene, 117439-51-7; 2,3-bis(2-cyano-5-methyl-3-pyrrolyl)-2-butene, 117439-54-0.

Facile Synthesis of L-Kynurenine

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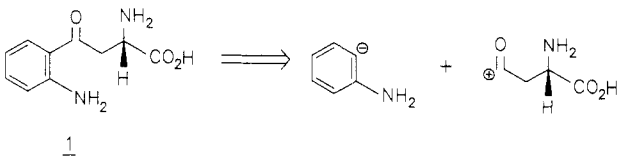
Received June 15, 1988

The aromatic amino acid L-kynurenine (**1**) is a key intermediate in the metabolism of L-tryptophan to nicotinic acid ribonucleotide via the commonly referred to kynurenine pathway. Quinolinic acid, a potent neurotoxic amino acid, is a late-stage intermediate in this pathway and has been implicated in brain diseases such as epilepsy and Huntington's chorea.[1] Lowering levels of quinolinic acid, therefore, may be an attractive means of treatment for these central nervous system disorders.

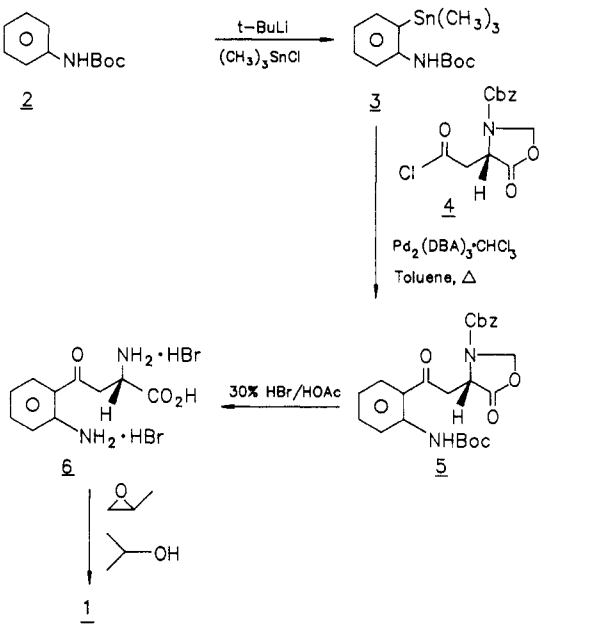
During the course of a research program directed toward the inhibition of various enzymes in this pathway, it became necessary to develop a general synthesis of L-kynurenine which would also allow for the facile preparation of various analogues. While several syntheses of L- and DL-kynurenine have been reported,[2] none were sufficiently versatile to accommodate the preparation of a variety of analogues. For example, tryptophan oxidation or acetamidomalonate addition to phenacyl bromides is impractical due to the difficulties encountered in the preparations of highly functionalized tryptophans and acetophenones, respectively, needed as starting materials.

An attractive route to L-kynurenine would be a convergent synthesis based on the reaction of a suitably protected aniline analogue and an L-aspartic acid synthon (Scheme I). A procedure we felt would be the most synthetically versatile involves a Pd^0-catalyzed cross-coupling[3]

Scheme I



Scheme II



of *N*-(*tert*-butoxycarbonyl)-2-(trimethylstannyl)aniline (**3**) with (*S*)-3-(benzyloxycarbonyl)-5-oxo-4-oxazolidineacetyl chloride (**4**) leading to the desired, fully protected amino acid **5** in one step (Scheme II). Such a procedure should be general, allowing for the utilization of various aniline and aspartic acid analogues, and should proceed with full chiral retention.

Ortho metalation of *N*-(*tert*-butoxycarbonyl)aniline (**2**)[4] followed by quenching with trimethylstannyl chloride afforded **3** in 54% yield after flash chromatography (10% diethyl ether/hexane) as a colorless solid. The protected L-aspartic acid chloride derivative **4** was prepared from the corresponding acid[5] by using an excess of thionyl chloride in toluene. Coupling of **3** and **4** was carried out in the presence of 0.5 mol % of $Pd_2(DBA)_3{\cdot}CHCl_3$[6] in toluene at 70 °C for 3–4 h. Filtration over Celite and concentration in vacuo, followed by flash chromatography (25% EtOAc/hexane), gave **5** as a stiff foam in 79% yield. Complete deprotection of **5** was carried out in one step with 30% HBr/HOAc at room temperature for 15–20 min; addition of diethyl ether then precipitated the bis(hydrobromide salt) as a colorless solid. The supernatant was removed, and the residue was treated several times with more ether and then dried under vacuum to give **6** as a colorless powder in 83% yield.[7] The free amino acid could be prepared by treating **6** with a 6-fold excess of propylene oxide in 2-propanol whereupon L-kynurenine (**1**) was isolated as a light yellow powder in 90% yield. Spectral properties (IR, MS, ^1H NMR) were identical with those of an authentic sample.[8] The high-resolution mass

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(7) Chars at 205–210 °C.

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