

Photocyclizations of *N*-Chloroacetyltyramines. II. Flash Photolysis and Substituent Effect Studies on the Formation of Dimeric Cage Compounds, and Novel Acid-Catalyzed Reversion

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Abstract: Irradiation of *N*-chloroacetyl derivatives of *ar*-dimethyltyramines (**1**) gave dimeric cage compounds (**2**). The presence of cyclohexa-2,4-dienones **3** as transient species and their thermal dimerization was proved by flash photolyses and by trapping with *N*-ethylmaleimide as Diels-Alder adducts. The steric effects of methyl substituents on the dimerization process are discussed. Cyclohexa-2,4-dienone dimers **7**, model compounds for similar intermediates (**5**), yielded the corresponding cage compounds (**8**) in high yield. On treatment with trifluoroacetic acid, the cage dimers in groups **2** and **8** easily reverted to **5** and **7**, respectively, by a novel acid-catalyzed reversion process whose mechanism is discussed.

In the foregoing paper,¹ we proposed that the mechanism for the formation of novel cage dimers from *N*-chloroacetyltyramine probably consists of a series of photocyclizations, [$\pi 4 + \pi 2$] thermal dimerizations, [$\pi 2 + \pi 2$] cycloadditions, and, in the end, bond switching processes.

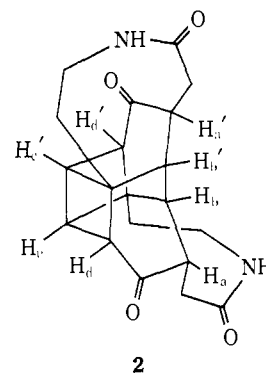
We report here on the presence of cyclohexa-2,4-dienone **3** and its thermal dimerization as evidenced by flash photolysis and chemical reactions, on the steric effect that methyl groups have on the dimerization process, on the cycloaddition of Diels-Alder dimers of cyclohexa-2,4-dienone **7**, and finally on a novel acid-catalyzed reversion of cage dimers (**2** and **8**).

Results

Cage Formation from Methyl-Substituted Tyramine Derivatives. When a 10% aqueous ethanol solution of *N*-chloroacetyl-3,5-dimethyltyramine (**1c**) was irradiated for 3 hr, the cage dimer **2c** was isolated in 65% yield as the single product. On the basis of mass spectrum and elemental analysis, compound **2c** has the composition $C_{24}H_{30}N_2O_4$. The complete structure of **2c** was established by comparing its ir, uv, and especially nmr spectra (Table I) with those of the corresponding dimer from **1a**, whose structure had been determined by X-ray analysis.² Comparable irradiation of *N*-chloroacetyl-2,5-dimethyltyramine (**1d**) gave a similar result. The yield of dimer **2d** was nearly 71%. On the other hand, *N*-chloroacetyl-2,6-dimethyltyramine (**1e**) gave tarry unidentifiable products.

N-Chloroacetyl-2,3-dimethyltyramine (**1f**), surprisingly, gave a *mixed dimeric cage 2f* which was isolated in 34.5% yield as the single identifiable product. The structure of **2f** is supported by spectral data, especially by the nmr spectrum at 94°, which displays the signals of four methyl groups as distinct singlets. Further support for this structure is provided by an interesting reversion reaction.

The nmr data of **2c**, **2d**, and **2f** with those of **2a** are summarized in Table I. The signals of methine groups



in the central cage system are quite simple, though the arrangement of hydrogens in dimer **2** is quite complex.

Flash Photolysis. When a nondegassed 0.1 mM solution of **1a** in 10% aqueous ethanol was flash photolyzed at room temperature, a new absorption spectrum of a transient species appeared as shown by the solid curve in Figure 1. The spectrum is almost identical with that of the transient species from *N*-chloroacetyl-*m*-tyramine,³ and consists of two groups, a strong peak at 325 nm and weak peaks at 370–400 nm. The weak bands must be assigned to the corresponding phenoxy radical.^{4,5} The strong band, which appears also under alkaline conditions, is attributed to the ground state of the cyclohexa-2,4-dienone **3a** for the reasons mentioned earlier.³ Compounds **1b–d** on flash photolysis gave similar results summarized in Figure 1 and Table II.

The kinetics of the fading of these transient species followed second-order decay with rate constants k of 5.3×10^3 , 2.0×10^3 , and $1.1 \times 10^3 M^{-1} \text{sec}^{-1}$ for **3a**, **3c**, and **3d**, respectively.

Photolysis of 1c in the Presence of *N*-Ethylmaleimide. When a 20% aqueous ethanol solution of **1c** in the presence of a twofold molar excess of *N*-ethylmaleimide was irradiated with 2537-Å light (10-W low-pressure

(3) S. Naruto, O. Yonemitsu, N. Kanamaru, and K. Kimura, *J. Amer. Chem. Soc.*, **93**, 4053 (1971).

(4) Cf. E. T. Land, G. Porter, and E. Strachan, *Trans. Faraday Soc.*, **57**, 1885 (1960).

(5) H.-I. Joschek and L. I. Grossweiner, *J. Amer. Chem. Soc.*, **88**, 3261 (1966).

(1) T. Iwakuma, H. Nakai, O. Yonemitsu, and B. Witkop, *J. Amer. Chem. Soc.*, **96**, 2564 (1974).

(2) T. Iwakuma, H. Nakai, O. Yonemitsu, D. S. Jones, I. L. Karle, and B. Witkop, *J. Amer. Chem. Soc.*, **94**, 5136 (1972).

Table I. Nmr Spectra of 2a, 2c, 2d, and 2f in D₂O

Proton ^a	Chemical Shift (δ) and Splittings			
	2a	2c	2d	2f ^b
H _a	3.00 (q, <i>J</i> = 3.5, 8.5 Hz)			^c
H _{a'}	3.00 (q, <i>J</i> = 3.5, 8.5 Hz)			
H _b	2.34 (d, <i>J</i> = 3.5 Hz)	2.34 (s)	2.26 (s)	2.38 (d, <i>J</i> = 3.5 Hz)
H _{b'}	2.34 (d, <i>J</i> = 3.5 Hz)	2.34 (s)	2.26 (s)	
H _c	3.12 (d, <i>J</i> = 4.0 Hz)	3.00 (s)		
H _{c'}	3.12 (d, <i>J</i> = 4.0 Hz)	3.00 (s)		3.00 (d, <i>J</i> = 5.0 Hz)
H _d	2.84 (d, <i>J</i> = 4.0 Hz)		2.56 (s)	
H _{d'}	2.84 (d, <i>J</i> = 4.0 Hz)		2.56 (s)	2.86 (d, <i>J</i> = 5.0 Hz)
Methyl		1.25 (6 H, s)	1.32 (6 H, s)	1.10 (3 H, s)
		1.43 (6 H, s)	1.42 (6 H, s)	1.24 (3 H, s)
				1.30 (3 H, s)
				1.44 (3 H, s)

^a See structure 2. ^b Measured at 94°. ^c Concealed in the signals for α-methylenes of carbonyl groups.

Table II. Transient Uv Spectra of Cyclohexa-2,4-dienone 3 and Phenoxy Radicals in the Flash Photolysis of Substituted Tyramines 1a-d. Woodward's Rules Were Used for the Calculation of the Homoannular Conjugated Cyclohexadienones

Compd	λ _{max} , nm		Calcd for dienone
	Dienone	Phenoxy radical	
1a	325	370, 391	320
1b	318	371, 384	320
1c	339	369, 389	330
1d	333	370, 384	332

lamp), about half of the incident light was absorbed by 1c and a Diels-Alder adduct 4 was isolated in 29% yield, accompanied by dimer 2c (16.8%) (Scheme I).

The composition C₁₈H₂₂N₂O₄ of compound 4 agrees with the mass spectrum and with the ir spectrum which contains four carbonyl groups at 1768 and 1720 (imide), 1700 (ketone), and 1660 cm⁻¹ (lactam). A vinyl proton at 5.52 ppm, two methyl groups (1.33 and 1.48 ppm), and ethyl group (1.04 and 3.40 ppm) are characteristic of the nmr spectrum. Since the bridgehead proton is concealed in the signals for the lactam ring, the stereochemistry of 4, either endo or exo configuration, is undecided, though the endo adduct is usually preferred.⁶

Model Cage Compounds.⁷ When the cyclohexa-2,4-dienone 6a,¹² synthesized from durene, was heated in a sealed tube at 165° for 40 hr, the Diels-Alder dimer 7a was obtained in 87% yield.

Irradiation of an ethyl acetate solution of 7a in a Pyrex tube with a 100-W high-pressure mercury lamp gave the cage compound 8a in quantitative yield. The composition of 8a was determined by mass spectrometry and elemental analysis as C₂₀H₂₈O₂, isomeric with the starting material 7a. The original enone chromophore of 7a had disappeared completely in 8a, and the carbonyl

(6) K. Alder and G. Stein, *Angew. Chem.*, **50**, 510 (1937); P. Hoffman and R. B. Woodward, *J. Amer. Chem. Soc.*, **87**, 4388 (1965).

(7) Numerous reports on inter- or intramolecular cycloadditions of [π₂ + π₂] systems have been published.⁸ Among them, cyclopentadiene⁹ and cyclopentadienone dimers¹⁰ have been converted photochemically to the corresponding cage compounds by intramolecular cycloaddition; the corresponding transformations of six-membered analogs, cyclohexa-1,3-diene dimers to cage compounds are not known.¹¹

(8) For reviews, see W. L. Dilling, *Chem. Rev.*, **66**, 373 (1966); D. Seebach, "Methoden der Organischen Chemie" (Houben-Weyl), Vol. IV/4, Georg Thieme, Stuttgart, 1971, p 383.

(9) G. O. Schenck and R. Steinmetz, *Chem. Ber.*, **96**, 520 (1963).

(10) E. Baggiolini, E. G. Herzog, S. Iwasaki, R. Schorta, and K. Schaffner, *Helv. Chim. Acta*, **50**, 297 (1967).

(11) D. Valentine, N. J. Turro, Jr., and G. S. Hammond, *J. Amer. Chem. Soc.*, **86**, 5202 (1964).

(12) H. Hart and R. M. Lange, *J. Org. Chem.*, **31**, 3776 (1966).

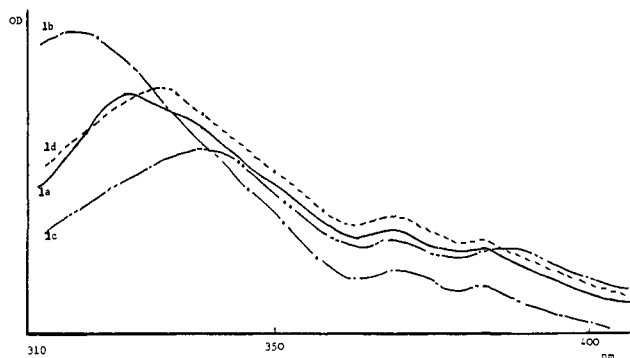


Figure 1. Transient absorption spectra of *N*-chloroacetyltyramine (1a) (—), 1b (---), 1c (·····), and 1d (-·-·-·).

peak in the ir spectrum had shifted from 1665 (enone) to 1700 cm⁻¹ (saturated ketone). The nmr spectrum of 8a lacks vinyl protons indicative of a symmetrical dimer, an observation supported by the signals of methyl and methine groups which appear as if 8a were a monomer. The above data suggest that in the photolysis of 7a the cage product 8a was formed through intramolecular cycloaddition.

The related Diels-Alder dimer 7b¹³ gave the cage compound 8b in quantitative yield under the conditions described above.

Diels-Alder dimers 7c,¹⁴ 7d,¹⁵ 7e,¹⁶ and 7f¹⁶ with 3,5-dihydroxy groups each gave the same type of cage compounds 8c, 8d, 8e, and 8f, respectively. Recently, similar results on irradiation of 7d, 7e, 7f, and other dienone dimers have been reported.¹⁷

Acid-Catalyzed Ring Reversion of Cage Compounds.¹⁴ During the course of an investigation of the chemical properties of 2 and the model cage compounds 8, it was observed that some representatives of groups 2 and 8 reverted easily to Diels-Alder dimers 5 and 7 through a novel acid-catalyzed reversion reaction.

When the octamethyl model cage compound 8a was allowed to stand in trifluoroacetic acid at room tempera-

(13) T. L. Brown, D. Y. Curtin, and R. P. Fraser, *J. Amer. Chem. Soc.*, **80**, 4439 (1958).

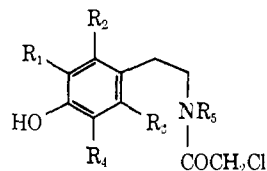
(14) T. Iwakuma, O. Yonemitsu, N. Kanamaru, K. Kimura, and B. Witkop, *Angew. Chem.*, **85**, 84 (1973); *Angew. Chem., Int. Ed. Engl.*, **12**, 72 (1973).

(15) E. Adler, L. Junghahn, U. Lindberg, B. Berggren, and G. Westin, *Acta Chem. Scand.*, **14**, 1261 (1960).

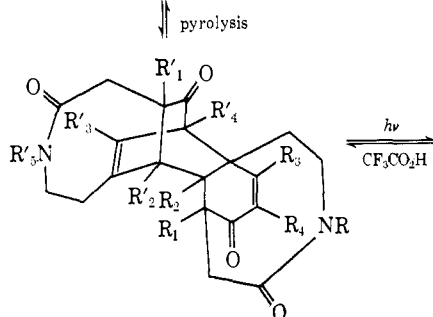
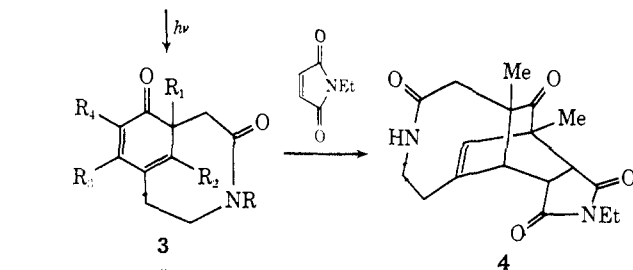
(16) E. Adler, T. Dahlen, and G. Westin, *Acta Chem. Scand.*, **14**, 1580 (1960).

(17) H.-D. Becker and A. Konar, *Tetrahedron Lett.*, 5177 (1972); H.-D. Becker, *Justus Liebigs Ann. Chem.*, 1675 (1973).

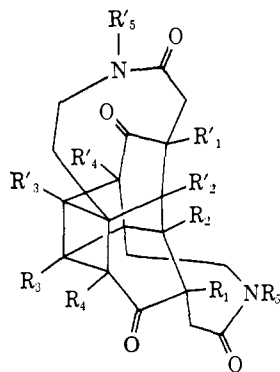
Scheme I



- 1a, $R_1-R_5 = H$
 b, $R_1-R_4 = H$; $R_5 = CH_2C_6H_5$
 c, $R_1, R_4 = Me$; $R_2, R_3, R_5 = H$
 d, $R_1, R_3 = Me$; $R_2, R_4, R_5 = H$
 e, $R_2, R_3 = Me$; $R_1, R_4, R_5 = H$
 f, $R_1, R_2 = Me$; $R_3-R_5 = H$



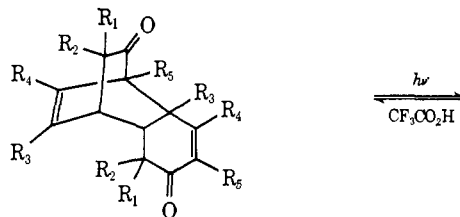
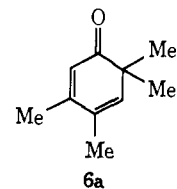
- 5a, mp $>300^\circ$
 b, mp $292-295^\circ$
 d, mp $>320^\circ$
 f, mp $315-317^\circ$



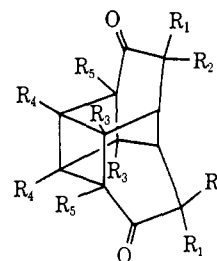
- 2a, b¹
 c, mp $270-275^\circ$ dec
 d, mp $>300^\circ$
 e (very low yield)
 f, $R'_1, R'_2, R_3, R_4 = Me$; $R_1, R_2, R_3', R_4', R_5, R_5' = H$; mp $296-298^\circ$ dec

ture for 1.5 hr, **8a** disappeared completely and reverted to the cyclohexa-2,4-dienone dimer **7a**. The hexamethyl compound **8b** did not revert to the corresponding cyclohexadienone dimer **7b** under the same conditions, but rearranged to an undefined product on heating in trifluoroacetic acid.

The model cage compounds **8c-f** with 4,11-dihydroxy groups gave similar results. When **8f** was dissolved in



- 7a, $R_1-R_4 = Me$; $R_5 = H$
 b, $R_1, R_2, R_5 = Me$; $R_3, R_4 = H$
 c, $R_1 = CH_2Cl$; $R_2 = OH$; $R_3-R_5 = H$
 d, $R_1, R_3 = Me$; $R_2 = OH$; $R_4, R_5 = H$
 e, $R_1, R_5 = Me$; $R_2 = OH$; $R_3, R_4 = H$
 f, $R_1, R_3, R_5 = Me$; $R_2 = OH$; $R_4 = H$



- 8a, mp $156-158^\circ$
 b, mp $188-190^\circ$
 c, mp $228-229^\circ$
 d, mp $226-227^\circ$
 e, mp $>300^\circ$
 f, mp $246-248^\circ$

trifluoroacetic acid, it disappeared immediately and reverted quantitatively to **7f**. The tetramethyl compound **8d**, though less reactive than **8f**, was converted to **7d** within 30 min, while the isomeric tetramethyl compound **8e** underwent side reactions in analogy to **8b**. The bischloromethyl compound **8c** remained unchanged even after heating under reflux for 17 hr.

One of the four cage compounds derived from tyramine derivatives **2c** easily reverted to **5c** in 80% yield with trifluoroacetic acid at room temperature for 1 hr. The composition $C_{24}H_{30}N_2O_4$ of **5c**, determined by mass spectrometry and elemental analysis, is identical with that of the starting material **2c**. In the ir spectrum a broad peak at 1660 cm^{-1} is assigned to amide and α,β -unsaturated ketone groups. The $\pi-\pi^*$ absorption peak of the α,β -unsaturated ketone appears at 252 nm (ϵ 5100) in the uv spectrum. The signals of two vinyl protons at room temperature appear as two doublets (4.94 and 5.20; 5.84 and 6.10 ppm), probably due to hindered inversion of the eight-membered lactam ring.¹⁸ This hindrance is overcome at elevated temperature and at 120° the two vinyl protons at 5.14 and 5.94 ppm become distinct singlets.

The structure of **5c** was further confirmed by the following two experiments. On irradiation in solution **5c** reverted to the starting cage compound **2c** in 87% yield. When the thermolysis of **5c** was carried out in the presence of excess *N*-ethylmaleimide, the monomeric

(18) Cf. K. Hemmi, H. Nakai, S. Naruto, and O. Yonemitsu, *J. Chem. Soc., Perkin Trans. 2*, 2252 (1972).

cyclohexa-2,4-dienone **3c** was trapped as the Diels-Alder adduct **4**.

The unsymmetric dimeric cage compound **2f** also underwent ring reversion to yield **5f** in 85% yield under the conditions described above. The spectral data supported structure **5f**, especially the observation of only one vinyl proton at 5.46 ppm as a doublet in the nmr spectrum at 100°.

Although **2d** remained unchanged in trifluoroacetic acid after standing at room temperature for 16 hr, on heating under reflux for 21 hr, **5d** was isolated in 70% yield, while prolonged heating of **2a** caused progressive decomposition; therefore heating was stopped after 6 hr to give **5a** in 37% yield in addition to unreacted **2a**.

All dimers **5a**, **5c**, **5d**, and **5f** as well as model dimers **7a**, **7d**, and **7f** were converted to the corresponding cage compounds, respectively, easily and in high yields when they were irradiated with a 100-W high-pressure lamp.

Discussion

Flash Photolysis and Trapping of 3c with N-Ethylmaleimide. The appearance of strong absorption bands near 330 nm in the flash photolyses of **1a-d** provides unequivocal proof for the presence of the cyclohexa-2,4-dienone **3** as transient precursor of the cage dimer from *N*-chloroacetyltyramine. While the dienone derived from *N*-chloroacetyl-*m*-tyramine decayed (or enolized) rapidly to the phenol following first-order kinetics,³ **3** is unable to decay by the same type of enolization.

Although cyclohexa-2,4-dienones are well known to rearrange photochemically¹⁹ and to undergo ring opening by the addition of solvents,²⁰ we failed to detect **3** as an intermediate by these reactions, indicative of rapid thermal decay of **3**. In fact, the relatively large second-order rate constants of decay clearly indicate that rapid thermal dimerization even under steady-state irradiation has precedence over the photolysis of dienone. Since thermal dimerization of unstable cyclohexa-2,4-dienones usually occurs in Diels-Alder fashion,²¹ the product of such a process must be **5**.

The presence of the cyclohexa-2,4-dienone **3** was shown by a trapping experiment of **3c** with *N*-ethylmaleimide. On irradiation, even in the presence of excess *N*-ethylmaleimide, dimerization of **3c** proceeded too fast to prevent completely the formation of **3c**; however, we were able to isolate the adduct **4** in fair yield. Assuming that this Diels-Alder addition, though in the presence of light, proceeded by combination of the reactants, **3c** and *N*-ethylmaleimide, in the ground state, we conclude that the adduct **4** must have endo rather than exo configuration.⁶

Effects of Methyl Substituents. Next we examined the steric effects of methyl substituents on the reactivity of the aromatic nucleus. Compound **1d**, substituted asymmetrically in relation to the phenolic hydroxyl, and compound **1c**, substituted symmetrically (*ceteris paribus*), gave single products **2d** and **2c** in good yield.

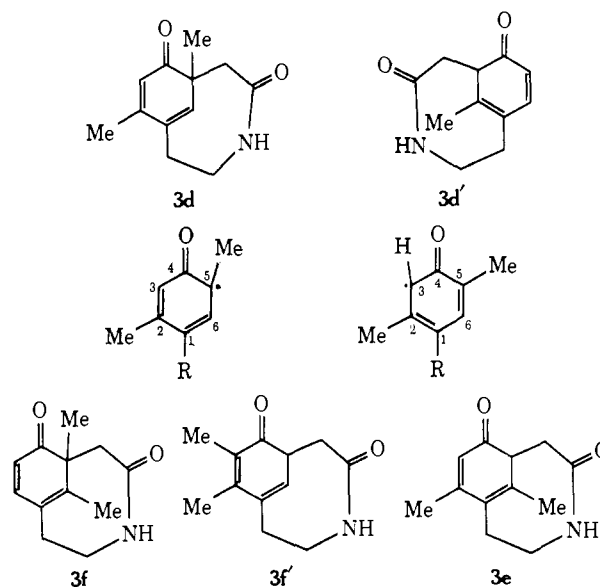
(19) H. Hart, P. M. Collins, and A. J. Waring, *J. Amer. Chem. Soc.*, **88**, 1005 (1966); J. D. Hobson, M. M. AlHolly, and J. R. Malpass, *Chem. Commun.*, 764 (1968).

(20) D. H. R. Barton and G. Quinkert, *J. Chem. Soc.*, 1 (1960); O. L. Chapman and J. D. Lassila, *J. Amer. Chem. Soc.*, **90**, 2449 (1968); J. Griffiths and H. Hart, *ibid.*, **90**, 3297 (1968).

(21) A. J. Waring, *Advan. Alicycl. Chem.*, **1**, 226 (1966).

Although two transient cyclohexa-2,4-dienones **3d** and **3d'** are possible, the reaction proceeds only *via* **3d**, because the radical formed at position 5 is more stable than at position 3. In addition the methyl group at position 3 may exercise steric hindrance on the formation of **3d'**. In support of this assumption the 2,6-dimethylated tyramine **1e** did not give detectable amounts of **2e**.

Surprisingly, the 2,3-dimethylated tyramine **1f** formed the two dienones **3f** and **3f'** which acted both as dienone



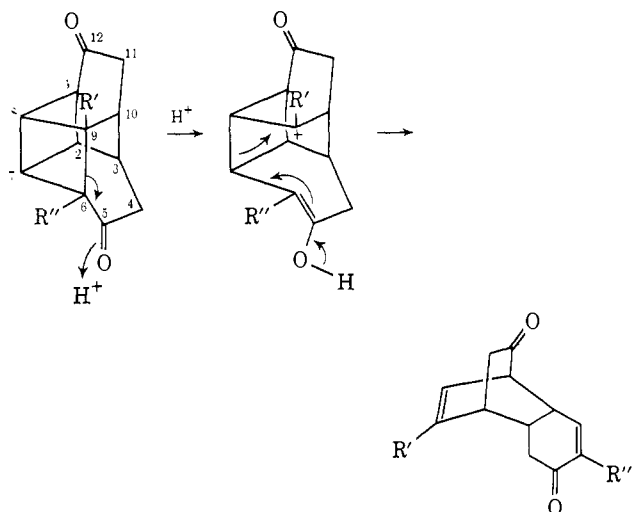
and dienophile, respectively, to yield a mixed dimer **2f**. The presence of **3f** and the fact that **3f** could not act as dienophile indicate that steric hindrance due to the methyl group at position 2 manifests itself mainly in the Diels-Alder dimerization rather than in the dienone formation process. In the case of **1e** a transient absorption spectrum with λ_{\max} 340 nm of dienone **3e** was observed by flash photolysis though dimerization of **3e** was a minor reaction.

Model Cage Compounds and Ring Reversion. Although the formation of **8** from **7** is only an additional example for numerous cycloadditions of $[\pi 2 + \pi 2]$ systems, this example serves as an important model for the transformation of **5** to **2**. It is well known that a cycloaddition reaction between an enone and an isolated double bond proceeds *via* the triplet state of the enone.²² Preliminary mechanistic studies indicate that the cyclization from **7** to **8** is sensitized by singlet as well as by triplet sensitizers. Detailed results on sensitization, quenching, and emission spectra will be reported soon.

Because of large differences in reactivities for the acid-catalyzed reversion reactions of the various cage compounds, the accurate kinetic treatment is still incomplete; however, a relative order of reactivity, derived from the above data, can be expressed as **8f** > **8d** ~ **2c** ~ **2f** ~ **8a** > **2a** ~ **2d** > **8c** ~ **8c** ~ **8e** ~ **8b**. This order clearly indicates that the stabilization of a carbonium cation at C-9 by an alkyl substituent, especially by a methyl group, is the most important requirement for acid-catalyzed reversion. A substituent at C-6 assists the reaction probably because of steric repulsion between both substituents.

(22) P. de Mayo, *Accounts Chem. Res.*, **4**, 41 (1971).

On the basis of the above data, the mechanism of the acid-catalyzed reversion reaction of such cage compounds can be described by



Experimental Section

***N*-Chloroacetyltyramines (1c–f).** A 10-mmol solution of the respective starting compounds, such as 3,5-dimethyl-*O*-methyltyramine,²³ 2,5-dimethyl-*O*-methyltyramine,²³ 2,6-dimethyl-*O*-methyltyramine,²³ or 2,3-dimethyl-*O*-methyltyramine,²³ respectively, in 15 ml of 48% hydrobromic acid was heated under reflux for 3–5 hr. After evaporation *in vacuo*, the residue was dissolved in 24 ml of 10% sodium hydroxide, and to the stirred solution was added dropwise chloroacetyl chloride (15 mmol) over 5 min at 5–10°. The reaction mixture was stirred for 30 min at the same temperature, washed with benzene, and acidified by the addition of hydrochloric acid. The acidified solution was extracted with ethyl acetate; the extract was washed with water and dried over sodium sulfate. Evaporation of the solvent left the *N*-chloroacetyltyramine 1c, 1d, 1e, or 1f in 40–50% yield (Table III).

Table III. Properties of *N*-Chloroacetyltyramines 1c–f

Compd	Mp, °C	Appearance (solvent of recrystn)	Uv $\lambda_{\max}^{\text{EtOH}}$, nm	Ir ν^{Nujol} , cm ⁻¹	Mass <i>m/e</i> M ⁺
1c	131–134	Needles (EtOAc–benzene)	279 (1670)	3260 1652	241
1d	111–113	Prisms (benzene)	278 (1608)	3420 1645	241
1e	150–151	Prisms (EtOAc–benzene)	281 ^a (1575)	3330 1647	241
1f	113–114	Needles (EtOAc–benzene)	280 (1744)	3260 1660	241

^a Solvent, 10% aqueous ethanol.

Photodimerization of *N*-Chloroacetyl-3,5-dimethyltyramine (1c). A solution of 723 mg (3 mmol) of 1c in 300 ml of 10% aqueous ethanol was irradiated with a 100-W high-pressure mercury lamp for 3 hr. After removal of chloride ion with silver carbonate, the solution was evaporated to dryness. The residue was chromatographed on silica gel (50 g) and eluted with ethyl acetate–methanol to give 400 mg (65%) of the cage dimer 2c. Recrystallization from water afforded colorless needles; mp 270–275° dec; uv λ_{\max} (H₂O) 302 nm (ϵ 203); ir (Nujol) ν 1702 and 1660 cm⁻¹; mass spectrum *m/e* 410 (M⁺), 381, 366, 338, 205, and 190; nmr (D₂O) δ 1.24 (s, 6 H), 1.44 (s, 6 H), 2.34 (s, 2 H), 3.00 (s, 2 H), 2.28 (d, 2 H, J = 13 Hz), 2.78 (d, 2 H, J = 13 Hz), and 3.28–3.60 (m, 4 H).

Diels–Alder Adduct 4. A 20% aqueous ethanol solution (50 ml) of 120.5 mg (0.5 mmol) of 1c in the presence of 125 mg (1.0 mmol) of *N*-ethylmaleimide was irradiated with a 10-W low-pressure

mercury lamp for 8 hr. After work-up, as described above, the evaporated ethanol solution was chromatographed on alumina tlc (ethyl acetate–methanol = 7:1) to give 16.7 mg of 2c and 48.7 mg (29.1%) of 4. Recrystallization from ethyl acetate–ether afforded colorless prisms: mp 161–163°; ir (Nujol) ν 3200, 1768, 1720, 1700, and 1666 cm⁻¹; mass spectrum *m/e* 330 (M⁺), 301, 219, 218, 206, and 125; nmr (CDCl₃) δ at 60° 1.48 (s, 3 H), 1.33 (s, 3 H), 1.04 (t, 3 H, J = 7.5 Hz), and 5.52 (s, 1 H).

Photodimerization of *N*-Chloroacetyl-2,5-dimethyltyramine (1d). A solution of 72.3 mg (0.3 mmol) of 1d in 30 ml of 10% aqueous ethanol was irradiated with a 10-W lamp for 2 hr. After evaporation of the solvent *in vacuo* below 40°, the residue was triturated with 5 ml of ethanol to give 43.5 mg (70.8%) of 2d as colorless crystals. Recrystallization from water afforded colorless prisms: mp > 300°; uv λ_{\max} (H₂O) 302 nm (ϵ 152); ir (Nujol) ν 3460, 3240, 1704, and 1668 cm⁻¹; mass spectrum *m/e* 410 (M⁺), 395, 382, 366, 353, 348, and 325; nmr (D₂O) δ 1.32 (s, 6 H) and 1.42 (s, 6 H).

Photolysis of *N*-Chloroacetyl-2,6-dimethyltyramine (1e). An aqueous ethanol solution of 72.3 mg (0.3 mmol) of 1e was irradiated as described above. The solution was concentrated to a volume of 5 ml and extracted with ethyl acetate. The aqueous layer was concentrated *in vacuo* to dryness, and the residue was purified by silica gel tlc (ethyl acetate–methanol = 1:1) to give 1.6 mg (2.6%) of colorless crystals of a dimer, probably 2e: ir (Nujol) ν 1695 and 1658 cm⁻¹; mass spectrum *m/e* 410 (M⁺).

Photodimerization of *N*-Chloroacetyl-2,3-dimethyltyramine (1f). A solution of 96.4 mg (0.4 mmol) of 1f in 40 ml of 10% aqueous ethanol containing 34 mg (0.41 mmol) of sodium bicarbonate was irradiated with a 100-W lamp. After evaporation of the solvent *in vacuo*, the residue was digested with 10 ml of ethanol, and insoluble inorganic salts were filtered off. The filtrate was concentrated *in vacuo*, chromatographed on an alumina tlc, and developed with ethyl acetate–methanol (1:1) to give 28.3 mg (34.5%) of dimer 2f. Recrystallization from 95% aqueous ethanol afforded colorless prisms: mp 296–298° dec; ir (Nujol) ν 3370, 3300, 3200, 1690, 1675, and 1640 cm⁻¹; mass spectrum *m/e* 410 (M⁺); nmr (D₂O) δ at 94° 1.10 (s, 3 H), 1.24 (s, 3 H), 1.30 (s, 3 H), and 1.44 (s, 3 H).

Flash Photolysis. A flash photolysis apparatus provided by Nakano Electric Co. was used. Two photolysis lamps placed parallel to a quartz cell were operated at 300–600 J input. A spectroflash lamp was operated at 20–30 J. The half-width of both lamps was less than 5 μ sec. The transient absorption spectra were obtained by the photographic method, followed by recording with a Nakami microphotometer NLM-8.

The decay curves at the peak of transient absorption were recorded on a memory scope. The apparatus and the procedure have been described in more detail elsewhere.²⁴

Model Cage Compounds. 1,3,4,4a,5,8a-Hexahydro-3,3,4,5,5,8,8a,9-octamethyl-1,4-ethenonaphthalene-2,6-dione (7a). 3,4,6-Tetramethylcyclohexa-2,4-dienone¹² (6a, 179.2 mg) was heated in a sealed tube at 165° for 40 hr. After cooling, the brown viscous oil was purified by preparative tlc on silica gel (benzene–ethyl acetate 20:1) to give 157 mg (87.7%) of 7a as colorless needles: mp 168–171° (from *n*-pentane) or 168–170.5° (from methanol–water); uv λ_{\max} (MeOH) 236 and 300 nm; ir (Nujol) ν 1705, 1665, and 1625 cm⁻¹; mass spectrum *m/e* 300 (M⁺); nmr (CCl₄) δ 0.95 (s, 3 H), 1.08 (s, 6 H), 1.12 (s, 3 H), 1.29 (s, 3 H), 1.50 (s, 3 H), 1.60 (s, 3 H), 1.89 (s, 3 H), 2.03 (d, 1 H, J = 1.5 Hz), 2.25 (d, 1 H, J = 1.5 Hz), 2.68 (s, 1 H), and 5.70 (s, 1 H).

1,3,4,4a,5,8a-Hexahydro-3,5-bis(chloromethyl)-3,5-dihydroxy-1,4-ethenonaphthalene-2,6-dione (7c). To a solution of 122 mg (0.5 mmol) of 1,3,4,4a,5,8a-hexahydro-1,4-ethenonaphthalene-3,5-bis(spirooxirane)-2,6-dione²⁵ in 15 ml of dioxane was added 3 ml of 36% hydrochloric acid and the solution was allowed to stand at room temperature overnight. After removal of the solvents *in vacuo* at 40°, the residue was triturated in 5 ml of benzene to give 149 mg (94.3%) of 7c. Recrystallization from ethyl acetate afforded colorless prisms: mp 175–176° dec; ir (Nujol) ν 3475, 3340, 1722, and 1698 cm⁻¹; mass spectrum *m/e* 316 (M⁺), 221, and 158.

2,4,4,7,8,9,11,11-Octamethylpentacyclo[6.4.0.0.2⁷.0^{3,10}.0^{8,9}]dodeca-5,12-dione (8a). An ethyl acetate solution (5 ml) of 45 mg of the Diels–Alder dimer 7a was irradiated externally in a Pyrex tube with a 100-W high-pressure lamp for 2 hr. Evaporation of the solvent gave 45 mg (100%) of 8a as colorless prisms, which after

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recrystallization from methanol showed mp 156–158°; uv λ_{\max} (EtOH) 300 nm; ir (Nujol) ν 1700 cm^{-1} ; mass spectrum m/e 300 (M^+); nmr (CCl_4) δ 10.4 (s, 6 H), 1.12 (s, 12 H), 1.25 (s, 6 H), 1.75 (s, 2 H), and 2.15 (s, 2 H).

1,4,4,6,11,11-Hexamethylpentacyclo[6.4.0.0^{2,7}.0^{3,10}.0^{6,9}]dodeca-5,12-dione (8b). An ethyl acetate solution (40 ml) of 305 mg of **7b** was irradiated for 3 hr under the conditions described above. Evaporation of the solvent gave **8b** quantitatively. Recrystallization from ethyl acetate gave colorless needles: mp 188–190°; uv λ_{\max} (MeOH) 302 nm; ir (Nujol) ν 1695 cm^{-1} ; mass spectrum m/e 272 (M^+); nmr (CCl_4) δ 0.98 (s, 6 H), 1.13 (s, 6 H), 1.23 (s, 6 H), 2.06 (2 H), 2.66 (2 H), and 2.90 (2 H).

Photocycloadditions of 7c–f. A 10 mM solution of **7** in ethyl acetate was irradiated with a 100-W high-pressure lamp (Eikosha) for 1.5 hr. After evaporation of the solvent, recrystallization from an appropriate solvent gave **8**.

4,11-Bis(chloromethyl)-4,11-dihydroxypentacyclo[6.4.0.0^{2,7}.0^{3,10}.0^{6,9}]dodeca-5,12-dione (8c). Compound **7c** (15.8 mg, 0.05 mmol) was irradiated and the product recrystallized from ethyl acetate to give 6.0 mg (38%) of colorless needles: mp 228–229°; ir (Nujol) ν 3445 and 1709 cm^{-1} ; nmr (CDCl_3) δ 3.05 (broad s, 2 H), 3.44 (broad s, 6 H), and 3.60 (s, 4 H).

4,11-Dihydroxy-2,4,9,11-tetramethylpentacyclo[6.4.0.0^{2,7}.0^{3,10}.0^{6,9}]dodeca-5,12-dione (8d). Photocyclization of 110.4 mg of **7d** yielded 90 mg (81.9%) of **8d**, after recrystallization from ethyl acetate–methanol, as colorless prisms: mp 226–227°; ir (Nujol) ν 3480, 3455, and 1705 cm^{-1} ; mass spectrum m/e 276 (M^+), 230, 215, 138, 122, and 121; nmr (CDCl_3) δ 1.28 (s, 6 H), 1.39 (s, 6 H), 2.41 (s, 2 H), 2.56 (s, 2 H), 2.65 (d, 2 H, $J = 4.0$ Hz), and 2.90 (d, 2 H, $J = 4.0$ Hz).

4,11-Dihydroxy-1,4,6,11-tetramethylpentacyclo[6.4.0.0^{2,7}.0^{3,10}.0^{6,9}]dodeca-5,12-dione (8e). Irradiation of 27.3 mg (0.1 mmol) of **7e** yielded 17.5 mg (64.1%) of **8e**, after recrystallization from methanol, as colorless prisms: mp >300°; ir (Nujol) ν 3440 and 1700 cm^{-1} ; mass spectrum m/e 276 (M^+), 258, 248, 230, 215, 187, 159, and 138.

4,11-Dihydroxy-1,2,4,6,9,11-hexamethylpentacyclo[6.4.0.0^{2,7}.0^{3,10}.0^{6,9}]dodeca-5,12-dione (8f). Irradiation of 91.3 mg (0.3 mmol) of **7f** gave 66.9 mg (73.1%) of **8f**, after recrystallization from ethyl acetate, as colorless prisms: mp 246–248° dec; ir (Nujol) ν 3340 and 1700 cm^{-1} ; mass spectrum m/e 304 (M^+); nmr (pyridine- d_5) δ 1.10 (s, 6 H), 1.22 (s, 6 H), 1.43 (s, 6 H), 2.50 (s, 2 H), and 2.98 (d, 2 H).

Diacetate of 8e. A solution of 10 mg (0.036 mmol) of **8e** in 1 ml of acetic anhydride was heated under reflux for 30 min. After removal of the acetic anhydride, the residue was triturated in 5 ml of ether to give 10 mg (77%) of **8e**-diacetate. Recrystallization from methanol afforded colorless prisms: mp 228–229°; ir (Nujol) ν 1715 cm^{-1} ; mass spectrum m/e 360 (M^+); nmr (CDCl_3) δ 1.31 (s, 6 H), 1.48 (s, 6 H), 2.03 (s, 6 H), 2.50–2.90 (m, 4 H), and 3.58 (d, 2 H, $J = 4.0$ Hz).

Ring Reversion of Cage Compounds. 1,3,4,4a,5,8a-Hexahydro-3,3,4,5,5,8,8a,9-octamethyl-1,4-ethenonaphthalene-2,6-dione (7a). A solution of 30.7 mg of **8a** in 2 ml of trifluoroacetic acid was allowed to stand at room temperature for 1.5 hr. The acid was evaporated *in vacuo* to leave a quantitative yield of **7a** in an almost pure state. Recrystallization from methanol with a trace of water gave 22.5 mg (73.3%) of colorless needles, which were identical with the authentic sample described above.

1,3,4,4a,5,8a-Hexahydro-3,5-dihydroxy-1,3,5,7,8a,9-hexamethyl-1,4-ethenonaphthalene-2,6-dione (7f). **8f** (15 mg, 0.049 mmol) was dissolved in 1 ml of trifluoroacetic acid at room temperature. After 10 min, the acid was evaporated *in vacuo* to leave a colorless solid, which was recrystallized from ether to give **7f** in quantitative yield, identical with an authentic sample¹⁴ with regard to mixture melting point, tlc, ir, and nmr spectra.

1,3,4,4a,5,8a-Hexahydro-3,5-dihydroxy-3,5,8a,9-tetramethyl-1,4-ethenonaphthalene-2,6-dione (7d). A solution of **8d** (27.6 mg, 0.1 mmol) in 2 ml of trifluoroacetic acid was allowed to stand at room temperature for 30 min. After work-up as described above, **7d** was isolated in 80% yield, which was identical with an authentic sample¹⁵ by mixture melting point tlc, ir, and nmr spectra.

Attempted Acid-Catalyzed Ring Reversion of 8b, 8c, and 8e. A trifluoroacetic acid solution of **8c** was heated under reflux for 17 hr. After evaporation of the solvent, the starting material was recovered quantitatively. Compound **8e** was also treated under the same conditions; however, no trace of a ring-reversion product was detected. Compound **8b** in trifluoroacetic acid was heated under reflux for 2 hr to give an undefined product (87%), mp 182–184°.

Diels–Alder Dimer 5c. **2c** (40 mg, 0.097 mmol) was dissolved in 3 ml of trifluoroacetic acid at room temperature. After 1 hr, the solvent was evaporated *in vacuo* to leave a colorless solid, which was chromatographed on alumina. Elution with ethyl acetate–methanol (6:1) gave 32.1 mg (80.2%) of **5c**, which was recrystallized from ethyl acetate–methanol to give colorless needles: mp 292–295° dec; uv λ_{\max} (MeOH) 250 nm (ϵ 5100); ir (Nujol) ν 3300, 1710, and 1660 cm^{-1} ; mass spectrum m/e 410 (M^+); nmr ($\text{DMSO}-d_6$) δ at 120° 5.94 (s, 1 H) and 5.14 (s, 1 H).

Diels–Alder Dimer 5f. **2f** (50 mg, 0.12 mmol) was treated with trifluoroacetic acid under the conditions described in the preceding experiment. After chromatography on alumina, 42.6 mg (85.2%) of **5f** was obtained and recrystallized from ethyl acetate–methanol to give colorless prisms: mp 315–317° dec; uv λ_{\max} 3.44 (broad s, 6 H) and 3.60 (s, 4 H); uv λ_{\max} (EtOH) 255 nm (ϵ 7400); ir (Nujol) ν 3410, 3360, 1715, 1658, and 1642 (sh) cm^{-1} ; mass spectrum m/e 410 (M^+), 382, 381, 366, 252, 232, and 206; nmr (CDCl_3 - $\text{CF}_3\text{CO}_2\text{H}$) δ at 100° 1.10 (s, 3 H), 1.29 (s, 3 H), 1.70 (s, 3 H), 1.73 (s, 3 H), and 5.46 (d, 1 H, $J = 6.0$ Hz).

Diels–Alder Dimer 5d. A trifluoroacetic acid solution (3 ml) of 35 mg of **2d** was heated under reflux for 21 hr. After evaporation of the solvent, the residue was chromatographed on an alumina column (10 g). Elution with ethyl acetate–methanol (4:1) gave 24.2 mg (70.0%) of **5d**, which was recrystallized from ethyl acetate–methanol to give a colorless crystalline powder: mp >320°; uv λ_{\max} (MeOH) 242 nm (ϵ 7590); ir (Nujol) ν 1704 and 1650 cm^{-1} ; mass spectrum m/e 410 (M^+), 366, 205, and 186; nmr (CDCl_3 - $\text{DMSO}-d_6$) an olefinic proton appears at δ 5.74 and 5.92 (total 1 H); δ at 118° 5.88 (s, 1 H).

Diels–Alder Dimer 5a. A trifluoroacetic acid solution (3 ml) of 100 mg of **2a** was heated under reflux for 6 hr. After evaporation of the solvent, the residue was recrystallized from ethanol to give 37 mg (37%) of **5a** as a colorless crystalline powder: mp >300°; uv λ_{\max} (H_2O) 235 nm (ϵ 5860); ir (Nujol) ν 1713 and 1665 cm^{-1} ; mass spectrum m/e 354 (M^+), 325, 211, 178, and 147; nmr ($\text{DMSO}-d_6$ - $\text{CF}_3\text{CO}_2\text{H}$) δ 5.57 (d, 1 H, $J = 6.1$ Hz), 5.84 (d, 1 H, $J = 10$ Hz), and 6.14 (d, 1 H, $J = 10$ Hz).

Photocycloaddition of Diels–Alder Dimers. A 10 mM solution of Diels–Alder dimer **5** was irradiated with a 100-W high-pressure mercury lamp in the usual way. After evaporation of the solvent, the residue was recrystallized to yield the cage compound **2**, which was identical with the respective authentic sample,² with regard to mixture melting point, tlc, ir, and mass spectra. The results are summarized in Table IV.

Table IV. Photocycloadditions of Diels–Alder Dimers^a

Compd	Solvent	Irradiation time, hr	Product	Yield, %
5a (5 mg)	EtOAc–MeOH– H_2O (7:2:1)	1	2a	71.7
5c (123 mg)	EtOAc–MeOH (1:1)	3	2c	87
5d (5 mg)	EtOAc–MeOH– H_2O (20:2.5:1)	50 min	2d	84
5f (10 mg)	EtOAc–MeOH (1:1)	2	2f	77

^a External irradiation with a 100-W high-pressure mercury lamp.

Thermolysis of 5c in the Presence of *N*-Ethylmaleimide to Diels–Alder Adduct 4. A mixture of 10 mg (0.024 mmol) of **5c** and 30 mg (0.24 mmol) of *N*-ethylmaleimide was gently heated over an open flame for 10 min until it became tan and viscous. After cooling to room temperature, the reaction mixture was purified by preparative tlc on silica gel. Development with ethyl acetate–methanol, followed by recrystallization from ethyl acetate–ether gave 1 mg (12.5%) of **4** as colorless prisms, identical with an authentic sample with regard to mixture melting point, tlc, and mass spectrum.

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