and 10.50–10.65 (broad, 1 H, NH); mass spectrum (70 eV) *m/e* 385 (M^+), 246, 215, and 172.

Anal. Calcd for $C_{22}H_{27}NO_3S$: C, 68.55; H, 7.06; N, 3.63. Found: C, 68.58; H, 6.69; N, 3.52.

The second fraction afforded 0.82 g (12%) of **3-anilino-5,5-dimethyl-2-cyclohexen-1-one** (**8**), mp 184–185 °C (benzene–hexane), as yellowish needles: ir (Nujol) 3200 (NH), 1590 (C=O), and 1560 cm^{-1} (C=C); NMR ($CDCl_3$) δ 1.00 (s, 6 H, methyl protons), 2.05 (s, 2 H, $-CH_2C=C$), 2.35 (s, 2 H, $COCH_2-$), 5.30 (s, 1 H, CH=C<), 7.05–7.40 (m, 5 H, phenyl protons), and 8.70–8.80 (broad, 1 H, NH); mass spectrum (70 eV) *m/e* 215 (M^+).

Anal. Calcd for $C_{14}H_{17}NO$: C, 78.10; H, 7.96; N, 6.51. Found: C, 77.76; H, 7.82; N, 6.28.

Reaction of 3-Anilino-5,5-dimethyl-2-cyclohexen-1-one (8) with Sulfur. A solution of 1.08 g (5 mmol) of **8** and 0.32 g (10 mmol) of sulfur in 15 ml of mesitylene containing copper shavings (1.0 g) was refluxed for 3 h. After the reaction mixture was allowed to stand at ambient temperature overnight, the resulting solid was filtered and recrystallized from benzene to give 0.85 g (74%) of **bis(1-oxo-3-anilino-5,5-dimethyl-2-cyclohexen-2-yl) sulfide,** mp 265–266 °C, which was consistent with **6** obtained in the above reaction.

Reaction of a Mixture of 3-Anilino-5,5-dimethyl-2-cyclohexen-1-one and 5,5-Dimethyl-1,3-cyclohexanedione with Sulfur. The reaction was similarly carried out as described above using **8** (1.08 g, 5 mmol), **2c** (0.70 g, 5 mmol), sulfur (0.64 g, 20 mmol), and copper shavings (1.0 g). After removal of the resulting 0.45 g (40%) of the sulfide **6**, the filtrate was concentrated in vacuo and the residue was chromatographed on silica gel to give 0.82 g (43%) of **(1-oxo-3-anilino-5,5-dimethyl-2-cyclohexen-2-yl)(1,3-dioxo-5,5-dimethylcyclohexan-2-yl) sulfide,** mp 208–210 °C, which was consistent with **7** obtained in the above reaction.

Reaction of *N*-Sulfinylaniline (1a) with Diethyl Malonate (2d). The reaction was carried out at 140 °C for 6 h using the procedure described above with **1a** (4.20 g, 0.03 mol), **2d** (4.80 g, 0.03 mol), and copper shavings (3 g) in *m*-xylene (30 ml). After removal of solvent containing formed diethyl sulfite, of which structure was determined by comparison of the retention time with that of an authentic sample, the residue was similarly treated to give 2.65 g (43%) of **malonanilic acid ethyl ester** (**9**): mp 38–40 °C (lit.[11] mp 38–39 °C); ir (Nujol) 3300 (NH), 1730 (C=O), and 1660 cm^{-1} (C=O); NMR ($CDCl_3$) δ 0.85 (t, 3 H, CH_2CH_3), 3.20 (s, 2 H, $COCH_2CO$), 3.85 (q, 2 H, CH_2CH_3), 6.85–7.75 (m, 5 H, phenyl protons), and 9.10–9.30 (broad, 1 H, NH).

Reactions of *N*-Sulfinylaniline (1a) with Ketones 2e,f. The reactions were carried out in a similar manner. After similar workup, **1-phenyl-2,5-dimethylpyrrole** (**10**) and **(β-anilino-β-phenyl)ethyl phenyl ketone** (**11**) were obtained in 65 and 58% yields, respectively.

10 had mp 50–51 °C (lit.[12] mp 49–51 °C); white plates; ir (Nujol) 1590 cm^{-1} (C=C); NMR ($CDCl_3$) δ 2.05 (s, 6 H, methyl protons), 5.90 (s, 2 H, CH=C), and 7.00–7.50 (m, 5 H, phenyl protons); mass spectrum (70 eV) *m/e* 171 (M^+).

11 had mp 171–172 °C; pale yellow needles; ir (Nujol) 3350 (NH) and 1655 cm^{-1} (C=O); NMR ($CDCl_3$) δ 3.40 (d, J = 7 Hz, 2 H, $COCH_2-$), 3.85–4.15 (broad, 1 H, NH), 4.98 (t, J = 7 Hz, 1 H, CH_2-**CH**<), and 6.40–7.15 (m, 15 H, phenyl protons); mass spectrum (70 eV) *m/e* 301 (M^+) and 209 ($M^+ - NHPh$).

Anal. Calcd for $C_{21}H_{19}NO$: C, 83.69; H, 6.35; N, 4.65. Found: C, 83.52; H, 6.14; N, 4.69.

Reaction of *N*-Sulfinyl-*p*-toluidine (1b) with Phenylacetonitrile (12). The reaction was carried out at 140 °C for 6 h using the procedure described above with **1b** (3.06 g, 0.02 ml), **12** (4.68 g, 0.04 mol), and copper shavings (2 g) in 20 ml of *m*-xylene. After similar treatment, the residue was chromatographed on silica gel to give 0.60 g (26%) of ***trans*-α,β-dicyanostilbene** (**13**): mp 161–162 °C (lit.[13] mp 161 °C); ir (Nujol) 2250 cm^{-1} (CN); NMR ($CDCl_3$) δ 7.10–7.95 (m, phenyl protons).

Registry No.—**1a,** 1122-83-4; **1b,** 15795-42-3; **2a,** 123-54-6; **2b,** 504-02-9; **2c,** 126-81-8; **2d,** 105-53-3; **2e,** 110-13-4; **2f,** 94-41-7; **3,** 26567-78-2; **4,** 60224-19-3; **5,** 24706-50-1; **6,** 60224-20-6; **7,** 60224-21-7; **8,** 18940-21-1; **9,** 53341-66-5; **10,** 83-24-9; **11,** 742-43-8; **12,** 140-29-4; **13,** 2450-55-7; copper, 7440-50-8; diphenylketene, 525-06-4.

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Intramolecular Diels–Alder Reactions. 12. Competitive [4 + 2] and [2 + 2] Cycloadditions of *N*-(Phenylpropargyl)-*cis*-cinnamamide[1a]

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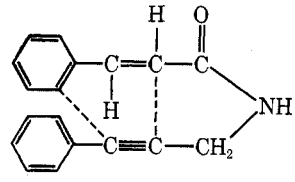
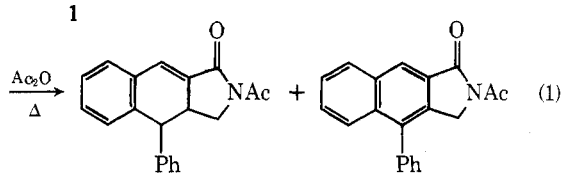
Refluxing *N*-(phenylpropargyl)-*cis*-cinnamamide in Ac_2O gave competitive [4 + 2] and [2 + 2] intramolecular cycloadditions in mode 2 to form (a) a mixture of benz[*f*]isoindole (**2b**) and its dihydro derivative **2a** and (b) substituted 3-pyrrolin-2-one **12** (following spontaneous cycloreversion), respectively. Structural studies on **12** and its bromo and dideuterio derivatives are reported. Modal selectivity in the cyclizations is interpreted in terms of relative frontier molecular orbital energy levels, while regiospecificity is interpreted in terms of stereochemical relationships. Action of the C≡C in an electron acceptor role in these cycloadditions is discussed.

In a preceding paper in this series[2] we described the syntheses of the nine possible unsaturated amides of the type $Ph(C_2)CH_2NHC(=O)(C_2)'Ph$, where (C_2) and $(C_2)'$ are variously *cis*-CH=CH–, *trans*-CH=CH–, and –C≡C– units. Six of these amides were investigated for possible intramolecular cyclization in refluxing acetic anhydride. Of these six, one [$(C_2) = (C_2)' =$ *trans*-CH=CH–] failed to undergo cyclization, while the other five underwent [4 + 2] cycloadditions either in mode 1 ("normal" Diels–Alder reaction) or mode 2 "abnormal" Diels–Alder reaction), or in a combination of both modes.[2] In particular, *N*-(phenylpropargyl)-*trans*-cinnamamide (**1**) cyclized in mode 2 to yield an unresolved mixture (**2**) (ca. 4:1) of *N*-acetyl lactams **2a** and **2b** in 75% yield (eq 1). The present paper concerns the cyclization of a seventh one of these am-



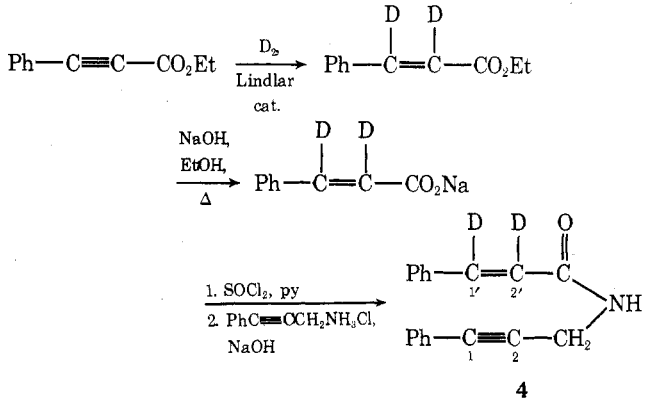
1



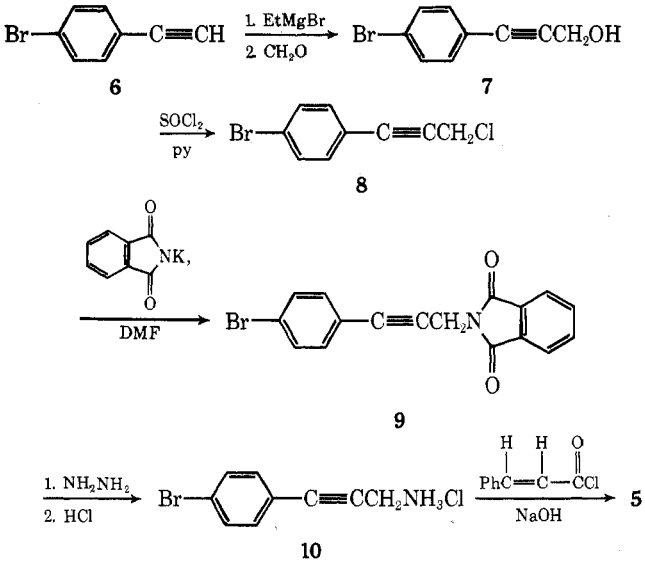
2a 2b (1)

ides, vis., *N*-(phenylpropargyl)-*cis*-cinnamamide (**3**), as well as its dideuterio derivative **4** and its *p*-bromo derivative **5**. Synthetic routes to **4** and **5** are shown in Schemes I and II. The overall yield of intermediate amine hydrochloride **10** from *p*-bromophenylacetylene (**6**) is 45%.

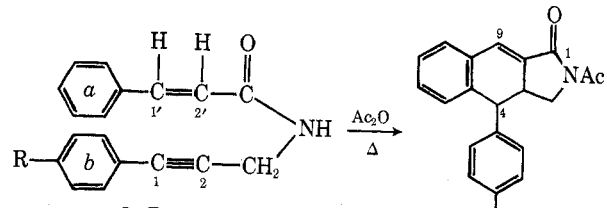
Scheme I



Scheme II

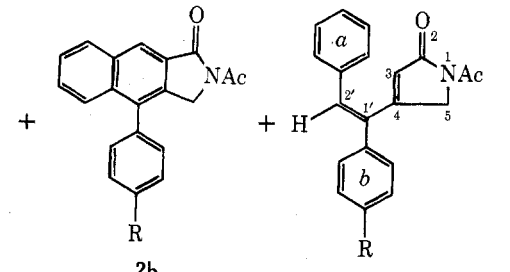


Cyclization of **3** or **5** in refluxing acetic anhydride yields two crystalline products (eq 2). For **3**, these are the same unresolved mixture **2** (mp 270 °C, 23%, isolated from concentrated solution) as formed from **1**, plus a new *N*-acetyl lactam **12** ($C_{20}H_{17}NO_2$, mp 132 °C, 37%, obtained on evaporation of the mother liquor from crystallization of **2**). For **5**, they are the mixture **11** (of **11a** and **11b**, mp 286 °C, 27%, isolated as for **2**) and the *N*-acetyl lactam **13** (mp 113 °C, 28%, isolated as for **12**). Compounds **12** and **13** were assigned the same carbon skeletal structures on the basis of closely similar ^{1}H NMR



3, R = H
5, R = Br

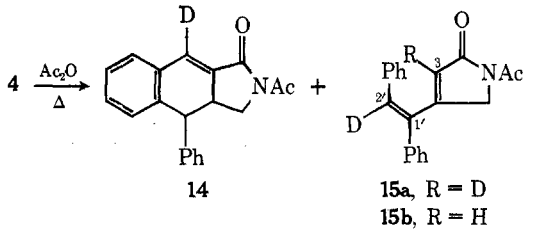
2a 11a



2b 11b 12, R = H 13, R = Br (2)

spectra. The only significant difference between these spectra was the occurrence of a four-proton A_2B_2 multiplet centered at δ 7.38 for **13**, in place of a five-proton singlet for a phenyl group at δ 7.34 for **12**. Analogously, the ^{1}H NMR spectral patterns of **2** and **11** were very similar to one another, though markedly different from those of **12** and **13**. The composition of **11**, as a mixture of **11a** and **11b** (10–15% of the latter), was based on ^{1}H NMR integrations and the earlier structural studies on **2**.[2]

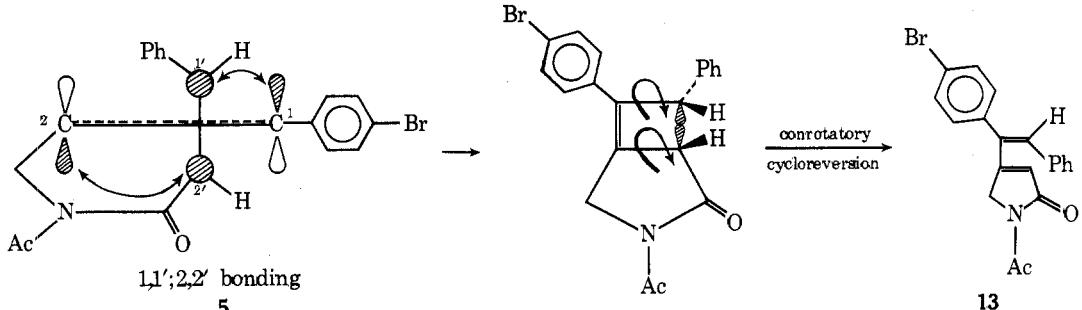
Assignment of the structure of (*Z*)-1-acetyl-4-(1,2-diphenyl)vinyl-3-pyrrolin-2-one to **12** is consistent with the following observations made on this substance. Ozonolysis produces benzaldehyde. The infrared spectrum in $CHCl_3$ shows imide bands at 1730 and 1700 cm^{-1}, while in KBr the spectrum has absorptions at 845 (trisubstituted alkene), 755, and 695 cm^{-1} (5 vicinal aromatic H).[3] The ^{1}H NMR spectrum consists of four singlets which correlate with the presence of two different phenyl groups, H-2′, and Ac, respectively, a triplet at δ 6.00 (J_{allyl} = 1.5 Hz) for H-3, and a doublet at δ 4.32 for two H at C-5. The mass spectrum contains prominent peaks at *m/e* 218 (100%) and 202 (29%) that correspond to the respective losses of AcN=C=O and [CH_2N(Ac)=C=O + 2 H] from the molecular ion. An ion fragment at *m/e* 178 for $C_{14}H_{10}^+$ implies that the phenyl groups are located on adjacent carbon atoms. Indicative of a more extensive conjugated system in **12** than in its open-chain precursor **3** is a bathochromic shift of the longest wavelength maximum ($\Delta\lambda$ = 60 nm) in the ultraviolet absorption spectrum after cyclization. Corroborating this change is an increase in the ease of polarographic reduction ($\Delta E_{1/2}$ = 0.45 V vs. SCE) after cyclization. A definitive structural assignment for **12**, however, was obtained only from an x-ray crystallographic study of **13**,[4] which established the locations of the double bonds, clarified the stereochemistries at C-1′ and C-2′, and correlated rings a and b in the open-chain amides **3** and **5** with those in cyclization products **12** and **13**.



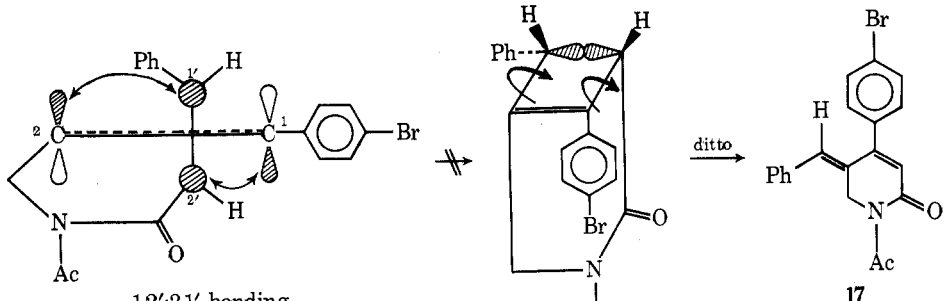
14 15a, R = D 15b, R = H (3)

To help elucidate mechanistic details of the molecular rearrangement involved in the transformation **3** → **12**, deuterated compound **4** (96% isotopically pure) was refluxed in acetic anhydride in the previous manner to yield **14** (18%, mp 270 °C, ostensibly free of any aromatized component, as based on ^{1}H NMR and mass spectra), plus a mixture (32%) of dideuterio compound **15a** and monodeuterio compound **15b** (ratio of 1.22:1) (eq 3). On the basis of the cyclizations of **4** and **5** it is

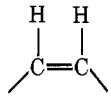
Scheme III

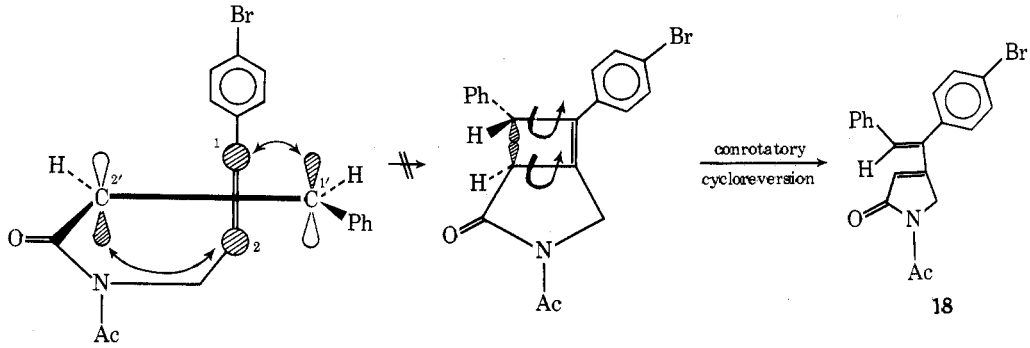


1,1′;2,2′ bonding
5 **16** **13** (a)

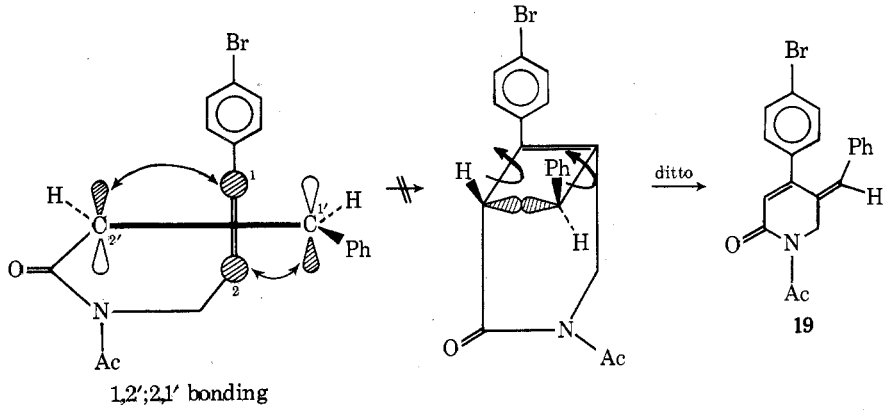


1,2′;2,1′ bonding
5 **17** (b)

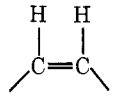
Mode 2:  HOMO + —C≡C— LUMO cases



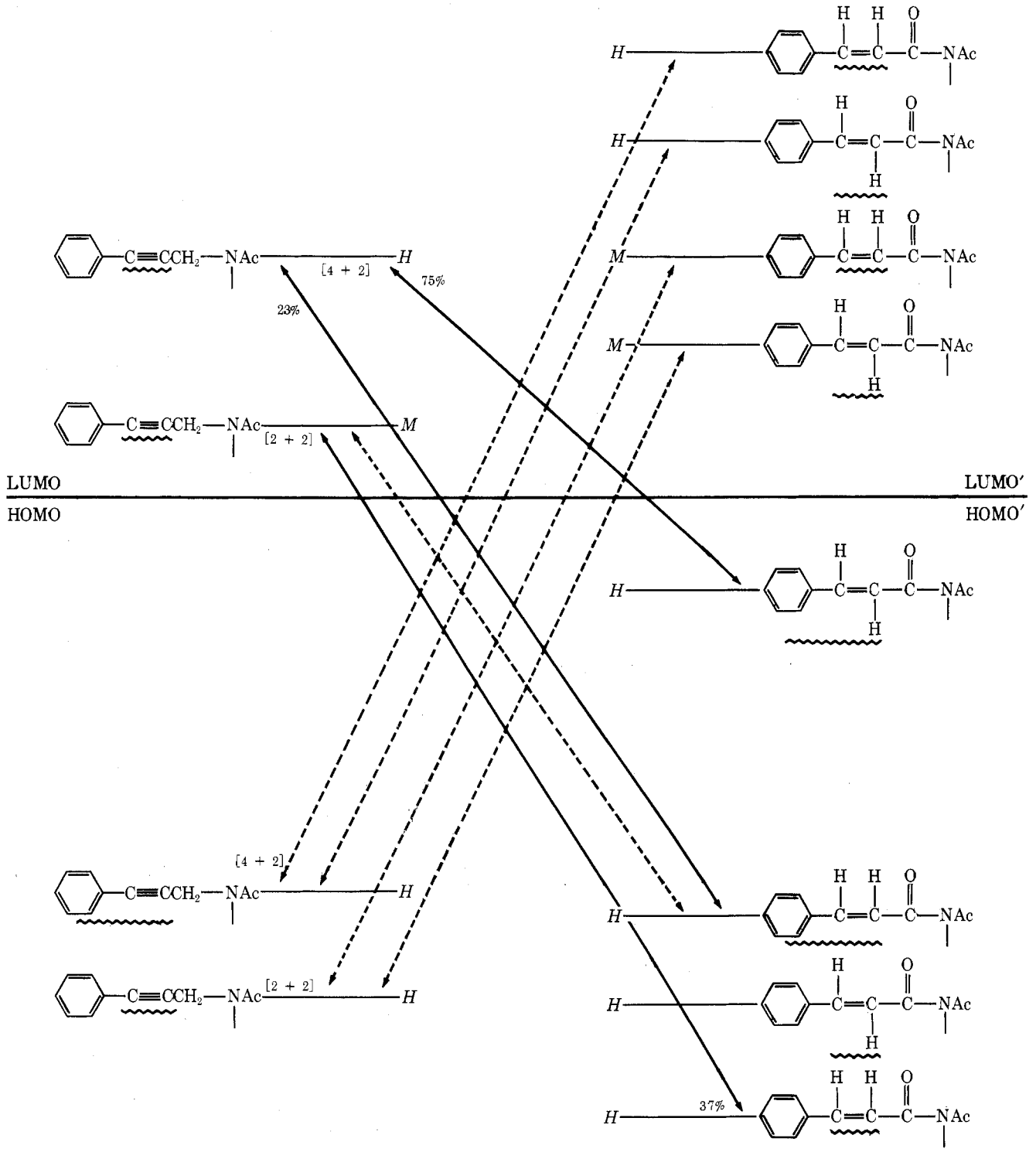
1,1′;2,2′ bonding
5 **18** (c)



1,2′;2,1′ bonding
5 **19** (d)

Mode 1:  LUMO + —C≡C— HOMO cases

Scheme IV. LUMO Control in Mode 2 [4 + 2] and [2 + 2] Cycloadditions of *N*-(Phenylpropargyl)cinnamamides[a]



[a] *H* and *M* denote Hückel-type and Möbius-type molecular orbital energy levels, respectively.[11]

apparent that in the transformation of **3** into **12** C-1 becomes C-1′, C-2 becomes C-4, C-1′ becomes C-2′, and C-2′ becomes C-3. Hence, during this transformation the bond between C-1′ and C-2′ is broken, while new bonds between C-1 and C-1′ and between C-2 and C-2′ are formed. As noted in the following paragraphs, these are the characteristics which are expected for an intramolecular, thermally induced, concerted $[_\pi 2_s + _\pi 2_a]$ cycloaddition reaction to form a strained cyclobutene intermediate, plus the thermally induced, concerted conrotatory cycloreversion of the intermediate ($[_\sigma 2_a + _\pi 2_s]$ or $[_\sigma 2_s + _\pi 2_a]$) to a butadiene structure.

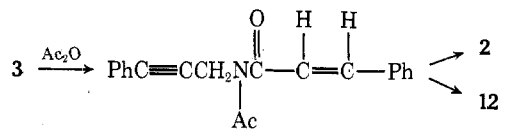
A priori, there are four distinguishable ways in which $[_\pi 2_s + _\pi 2_a]$ cycloaddition of **3**, **4**, or **5** can be envisioned (see Scheme III). In the formality of Scheme III the (C_2) and $(C_2)'$ units of **5** are shown in the orthogonal conformation for which thermal cycloaddition is symmetry allowed.[5] In case a the plane of the vinylene unit is taken to be that of the paper and the (C_2) (i.e., C≡C) linear unit stretches across the double bond. This geometry allows the (C_2) and $(C_2)'$ units to approach closely in a sterically least hindered manner. Consistent with the studies on the deuterated amide **4**, new bonds form between the pair C-1 and C-1′ and the pair C-2 and C-2′. The process involves suprafacial addition to the cis double bond and antarafacial addition to the triple bond to form the hypothetical inter-

mediate **16** (a fused 4,5-bicyclic ring system with a bridgehead carbon–carbon double bond). Strained intermediate **16** then undergoes conrotatory cycloreversion of the four-membered ring to yield the observed product **13.** Suprafacial addition to the $(C_2)'$ unit and antarafacial addition to the (C_2) unit implies an interaction between HOMO′, the highest occupied molecular orbital energy level of the $(C_2)'$ unit, and LUMO, the lowest unoccupied molecular orbital energy level of the (C_2) unit. In other words, the $(C_2)'$ unit is serving as an electron donor and the (C_2) unit is serving as an electron acceptor. We shall designate this manner of [2 + 2] cycloaddition as mode 2, where mode 1 will involve interaction between LUMO′ and HOMO, i.e., with $(C_2)'$ in the role of electron acceptor and (C_2) in that of electron donor. It might be noted that **3** undergoes both [4 + 2] and [2 + 2] cycloadditions in mode 2, i.e., where the C≡C unit is an electron acceptor.[2,6]

Case b (Scheme III) illustrates an alternative possibility for cyclization in mode 2, but with a change in regiospecificity. Cases c and d represent mode 1 cyclization, with the same two alternatives for regiospecificity. In mode 1 the C=C would be oriented edgewise to the linear C≡C, with, perhaps, some increased steric crowding of substituents on these units in the transition state. Addition would occur suprafacially to (C_2) and antarafacially to $(C_2)'$.

No evidence for the formation of compounds **17–19** was found. Hence, it is clear that intramolecular [2 + 2] cycloaddition of **3** occurs with both modal selectivity and regiospecificity. As indicated previously,[2] the same considerations apply to the intramolecular [4 + 2] cycloadditions of **1** and **3**. Subsequent paragraphs will be concerned with the rationalizations of these observations.

Since conversion of *cis*-cinnamic acid (and its derivatives) into *trans*-cinnamic acid (and derivatives) is a well-known isomerization, one might anticipate that the [4 + 2] cycloaddition of **3** occurs by means of the pathway **3** → **1** (or *N*-acetyl-**1**) → **2**. Experimental evidence, however, indicates that isomerization of **3** prior to Diels–Alder cycloaddition is unlikely. As noted previously,[2] spectral examination of the reaction mixture of **3** in acetic anhydride showed no detectable concentration of a trans intermediate after 1 h of refluxing. Likewise, neither *cis*-cinnamylamine[2] nor phenylpropargyl *cis*-cinnamate[7] is isomerized on extended refluxing in acetic anhydride. Most likely the routes from **3** to **2** and to **12** involve competitive cyclizations of the acetylated intermediate **20,** as



(4)

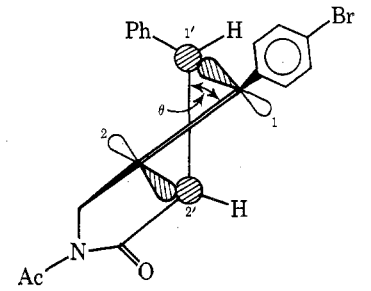
20

indicated in eq 4. We assume that this pathway is the correct one in the arguments which follow.

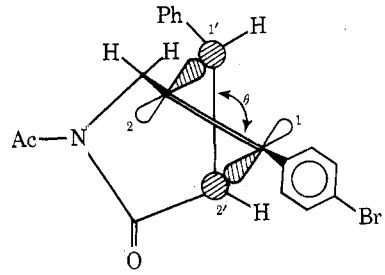
We ascribe the preference for mode 2 cyclization of both **1** and **3** (as their *N*-acetyl derivatives) primarily to a combination of the high electron affinity and the low electron-donating capacity of the C≡C bond.[2,8,9] This leads to LUMO control of the cyclizations as illustrated in the hypothetical MO energy level diagram (Scheme IV). In this scheme[10] cycloadditions which are observed experimentally are represented by solid double-headed arrows. Those which are theoretically possible, but are not observed experimentally, are represented by broken arrows. Yields observed are also shown. Scheme IV is constructed on the basis of the following postulated relationships. (1) Interaction between addendum units increases as the vertical separation of energy levels decreases, and vice versa. (2) For either end of the open-chain starting amide, a 4-π-electronic system is a better electron donor (higher MO energy level) than is the corresponding 2-π system. (3) Of $(C_2)'$ units the trans isomer is both a stronger electron donor and an electron acceptor than is its cis counterpart. (4) For [4 + 2] thermal cycloadditions, only Hückel-type MO energy levels are considered for the addenda. Contrariwise, for [2 + 2] thermal cycloadditions a Möbius-type unoccupied MO energy level (i.e., a lower energy level than corresponds to the Hückel one)[11] is used for the (C_2) or $(C_2)'$ unit which adds antarafacially.[12] (5) Mode 2 selectivity is shown by arrows which connect the LUMO quadrant to the HOMO′ quadrant (negative slope), while mode 1 selectivity connects LUMO′ and HOMO quadrants (positive slope).

Scheme V depicts a stereochemical rationale for the regioselectivity of [2 + 2] cycloaddition of **3** by means of 1,1′;2,2′

Scheme V



a
1,1′;2,2′ bonding

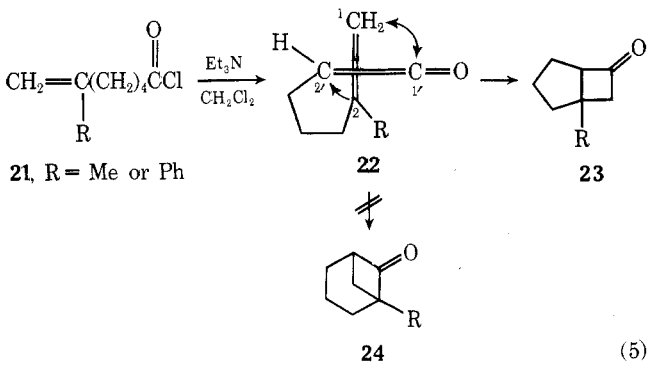


b
1,2′;2,1′ bonding

bonding, in preference to 1,2′;2,1′ bonding. In order to attain a crossed conformation of the C=C and C≡C bonds the molecule must coil with the aryl ends passing over one another. In the formal representations of Scheme III, the dihedral angle (θ) shown for the C_1–C_2 and $C_{1'}$–$C_{2'}$ bonds is 90°. However, as shown in Scheme V, maximum p-lobe overlap in the transition state will occur for $\theta \simeq 45°$ or 135°. The former conformation (case a) is easily attained without undue strain in bond angles elsewhere in the molecule. The latter conformation (case b), on the other hand, will be more difficult to attain because of the requisite stretching of bond lengths and/or alteration of bond angles in the –C–N–C– system. Only if this system contained a longer chain of atoms would one expect case b to offer energetic competition or preference to case a.

It might be noted that a precedent exists for the same regiospecificity in an analogous N-free system. Thus, Baldwin and Page[13] reported the conversion of 6-substituted 6-heptenoyl chlorides **21** into bicyclo[3.2.0]heptanones **23** (rather than into bicyclo[3.1.1]heptanones **24**), presumably via the intermediate unsaturated ketene **22** (eq 5). It is apparent that the symmetry relationships between the crossed C=C units in **22** are similar to those between the crossed C=C and C≡C units in **3,** but the mode of cyclization of **22** cannot be ascertained from the product formed.

Under simplistic conditions one would expect Scheme IV to reflect approximately the relative yields of products from competitive [4 + 2] and [2 + 2] cycloaddition processes. Ob-



21, R = Me or Ph (5)

servation of exclusive [4 + 2] cyclization from **1** is consistent with a higher HOMO′ for the $(C_2)'$–C=C_{Ar} unit than for the $(C_2)'$ unit in the substrate. Inclusion of the Möbius-type LUMO energy level for the yne (C_2) unit in the scheme permits a rationalization for the larger yield of **12** (via [2 + 2] cycloaddition) than of **2** ([4 + 2] adduct) from amide **3**.

Experimental Section[14]

***p*-Bromophenylpropargyl Alcohol (7).** To a stirred solution of ethylmagnesium bromide (prepared from 4.5 g of Mg and 15 ml of EtBr) in 120 ml of ether at room temperature in an atmosphere of nitrogen was added (all at once) a solution of 30 g of *p*-bromophenylacetylene[15] (**6**) [ir ($CHCl_3$) 3300, 2120, 830 cm^{-1}; NMR ($CDCl_3$) δ 7.32 (center of A_2B_2 m, J_{AB} = 8.5 Hz, 4 aromatic H) and 3.07 (s, 1 H, C≡CH)]. After evolution of ethane ceased (2.5 h), a stream of anhydrous formaldehyde (from thermal depolymerization of paraformaldehyde) in nitrogen carrier gas was introduced until a test for residual Grignard reagent[16] was negative. The mixture was treated with ice and then with excess 10% H_2SO_4 and extracted with ether. Evaporation of the dried (K_2CO_3) organic layer and sublimation of the residue at 70 °C (0.7 mm) gave 23.6 g (67%) of needles: mp 80.5–81.5 °C; ir ($CHCl_3$) 3630, 3430 (OH), 2240 cm^{-1} (w, C≡C); NMR ($CDCl_3$) δ 7.33 (center of A_2B_2 m, J_{AB} = 8.5 Hz, 4 aromatic H), 4.47 (s, 2 H, CH_2OH), 2.37 (broad, 1 H, OH).

Anal. Calcd for C_9H_7BrO: C, 51.21; H, 3.34; Br, 37.86. Found: C, 51.61; H, 3.02; Br, 37.89.

***p*-Bromophenylpropargyl Chloride (8).** The conversion of **7** into **8** followed the procedure used to prepare phenylpropargyl chloride.[17] The product was obtained as a crude solid (86%), converted to plates on evaporative distillation at 65 °C (0.7 mm): mp 41–42 °C; ir ($CHCl_3$) 2270, 2220 cm^{-1}; NMR ($CDCl_3$) δ 7.31 (center of A_2B_2 m, J_{AB} = 8.5 Hz, 4 aromatic H), 4.31 (s, 2 H, CH_2Cl); MS *m/e* (rel intensity)[18a] 232 (12), 230 (44), and 228 (36) (M^+), 195 (97) and 193 (100) (M − Cl), 144 (33, M − [Cl + Br]).

Anal. Calcd for C_9H_6BrCl: C, 47.09; H, 2.63; total halogen (as Cl), 30.90; relative isotopic abundances of molecular ions, 0.32/1.3/1.0. Found: C, 46.92; H, 2.51; total halogen (as Cl), 31.19; relative intensities of molecular ions, 0.33/1.2/1.0.

***N*-(*p*-Bromophenylpropargyl)phthalimide (9).** A mixture of 31.2 g (0.136 mol) of **8**, 28 g (0.15 mol) of potassium phthalimide, and 700 ml of dimethylformamide was stirred at 50 °C for 10 h, cooled, and poured into water. The precipitate was collected by filtration and combined with product from $CHCl_3$ extraction of the filtrate to give 41 g (89%) of **9** (mp 213–217 °C), purified by recrystallization from MeCN and sublimation (160 °C, 0.8 mm) to give prisms: mp 214–215.5 °C; MS *m/e* 339 (100, M^+).

Anal. Calcd for $C_{17}H_{10}BrNO_2$: N, 4.12. Found: N, 3.85.

***p*-Bromophenylpropargylammonium Chloride (10).** A mixture of 31.5 g of imide **9**, 3.14 g of hydrazine (97%), and 1.4 l. of methanol was stirred and refluxed for 2 h. Then 65 ml of concentrated hydrochloric acid was added and refluxing was continued for 30 min longer. The cooled mixture was filtered (to remove phthalhydrazide). The filtrate was concentrated to 30 ml and filtered to collect crude solid **10** (20 g, 87%), obtained as plates from absolute EtOH: mp 255–259 °C dec; NMR (Me_2SO-d_6) δ 7.61 (center of A_2B_2 m, J_{AB} = 8.5 Hz, 4 aromatic H), 4.72 (broad signal, 2 H, CH_2NH_2·HCl, exchanged in D_2O–DCl), 3.92 (broad signal, 2, CH_2N); MS *m/e* (rel intensity)[18b] 210 (97) and 208 (100) (M − [H + HCl]), 130 (58, M − [HCl + Br]).

***N*-(*p*-Bromophenylpropargyl)-*cis*-cinnamamide (5).** Schotten–Baumann reaction between **10** and *cis*-cinnamoyl chloride was conducted in a previously described manner[2] to give crude amide **5** (needles from benzene–petroleum ether, mp 108.5–109.5 °C, 70%), recrystallized fromthe same solvent: mp 110–111 °C; NMR ($CDCl_3$) δ 7.7–7.1 (m, 9 aromatic H), 6.80 (d, J = 12.5 Hz, 1 H, CH=CHCO), 5.98 (d, CH=CHCO) superimposed on 6.2–5.7 (broad signal, 2 H total, NH), 4.24 (d, J = 5.5 Hz, 2 H, CH_2NH); MS *m/e* (rel intensity)[18c] 341 (22) and 339 (24) (M^+), 131 (100, PhCH=CHCO$^+$), 103 (68, PhCH=CH$^+$) 102 (27), 77 (44, Ph^+).

Anal. Calcd for $C_{18}H_{14}BrNO$: C, 63.54; H, 4.15; Br, 23.49; N, 4.12. Found: C, 63.38; H, 4.11; Br, 23.77; N, 4.17.

***N*-(Phenylpropargyl)-α,β-dideuterio-*cis*-cinnamamide (4).** In the manner of Bloomfield and Fuchs[19] ethyl phenylpropiolate was reduced catalytically in the presence of D_2 gas. Hydrolysis of the deuterated ester[2] gave α,β-dideuterio-*cis*-cinnamic acid [NMR (neat) δ 7.7–6.9 (m, aromatic H), 12.32 (s, CO_2H)]. Schotten–Baumann reaction of the acid chloride plus phenylpropargylammonium chloride[2] gave needles of **4**: mp 97–98 °C (from benzene–petroleum ether); ir ($CHCl_3$) 3450 (w), 1660 cm^{-1} (s); NMR ($CDCl_3$) δ 7.8–7.1 (m, aromatic H), 6.1–5.5 (broad, NH), 4.27 (d, J = 5.5 Hz, CH_2NH); MS *m/e* (rel intensity)[18c] 263 (97, M^+), 262 (43), 158 (26, PhC≡CCH_2NHCO^+), 133 (100, PhCD=$CDCO^+$), 115 (25, PhC≡CCH_2^+), 105 (71, PhCD=CD^+), 78 (38), 77 (25).

Anal. Calcd for $C_{18}H_{13}D_2NO$: D, 13.33 atom % excess. Found: D, 12.80 atom % excess.

Cyclization of *N*-(Phenylpropargyl)-*cis*-cinnamamide (3). A solution of 0.5 g of amide **3**[2] in 300 ml of Ac_2O was refluxed for 6 h, concentrated (in vacuo) to 50 ml, cooled, and filtered to give 135 mg (23%) of platelets (mp 269–270 °C), identified as Diels–Alder mixture **2** by direct comparison with the product obtained from analogous cyclization of *N*-(phenylpropargyl)-*trans*-cinnamamide.[2]

Evaporation of the filtrate gave a red-brown gum, converted to faintly yellow prisms on crystallization from ethanol (yield 213 mg, 37%, mp 127–128 °C). Recrystallization gave purified **12**: mp 131–132 °C; ir ($CHCl_3$) 1730, 1700 cm^{-1}; ir (KBr) 1730, 1670, 845, 755, 695 cm^{-1}; uv (absolute EtOH) λ_{max} 237 nm (log ϵ 4.25), 310 (4.08); λ_{min} 222 (4.04), 287 (4.04); NMR ($CDCl_3$) δ 7.34 (s, 5 aromatic H), 7.28 (s, 5 aromatic H), 7.02 (s, 1 H, H at C-2′), 6.00 (t, J = 1.5 Hz, 1 H, H at C-3), 4.32 (d, J = 1.5 Hz, 2 H, methylene at C-5), 2.52 (s, 3 H, Ac); MS *m/e* (rel intensity)[18c] 303 (73, M^+), 261 (28, M − CH_2CO), 260 (38, M − Ac), 218 (100, $C_{17}H_{14}^+$ or M − AcNCO, checked by high resolution), 217 (58), 203 (21), 202 (29), 178 (9, $C_{14}H_{10}^+$, checked by high resolution), 43 (26, Ac^+), 188 (metastable, 217 → 202), 157–159 (metastable, 303 → 219, 303 → 218).

Anal. Calcd for $C_{20}H_{17}NO_2$: C, 79.18; H, 5.65; N, 4.62. Found: C, 79.07; H, 5.36; N, 4.42.

Refluxing a solution of either **2** or **12** in Ac_2O–AcOD gave no exchange, as based on the NMR spectra.

Cyclization of Bromoamide 5. A solution of 4 g of **5** in 2.4 l. of Ac_2O was refluxed in an atmosphere of N_2 for 6 h. Concentration of the solution to 35 ml gave 1.22 g (27%) of crystalline product **11**: mp 284–286 °C dec; NMR ($CDCl_3$) δ 8.1–6.5 (m, 9 H, aromatic H plus H-9), 4.0–3.0 (m, 4 aliphatic H), 2.55 (s, 3 H, Ac) for **11a**, which contains 10–15% of aromatized compound **11b** as based on singlets at δ 4.70 (methylene) and 2.67 (Ac).

Anal. Calcd for $C_{20}H_{16}BrNO_2$: C, 62.84; H, 4.22; N, 3.67. Found: C, 62.44; H, 4.22; N, 3.93.

Evaporation of the filtrate from **11** gave a black gum which was stirred with 30 ml of ethanol at room temperature. The resultant yellow solution was decanted from insoluble black oily residue and cooled to −10 °C to yield 1.25 g (28%) of yellow, crystalline **13**: mp 112–113 °C; NMR ($CDCl_3$) δ 7.31 (s, aromatic H in ring a) which is superimposed on 7.38 (center of A_2B_2 m, J_{AB} = 8.5 Hz, 9 H total, aromatic H in ring b), 7.05 (s, 1 H, H at C-2′), 6.01 (t, J = 1.8 Hz, 1 H, H at C-3), 4.31 (d, J = 1.8 Hz, 2 H, CH_2NAc), 2.53 (s, 3 H, Ac); MS *m/e* (rel intensity)[18d] 383 (48) and 381 (51) (M^+), 340 (31) and 338 (29) (M − Ac), 298 (36) and 296 (41) (M − AcNCO), 284 (50) and 282 (70) (M − CH_2NAcCO), 217 (100, M − [AcNCO + Br]), 216 (36), 215 (46), 203 (27), 202 (64), 86 ($AcNCOH^+$), 43 (97, Ac^+).

Anal. Calcd for $C_{20}H_{16}BrNO_2$: C, 62.84; H, 4.22; N, 3.67. Found: C, 62.55; H, 4.19; N, 3.27.

Cyclization of Deuterioamide 4. A solution of 2.35 g of **4** in 1.5 l. of Ac_2O was refluxed for 6 h, concentrated to 200 ml, and allowed to stand at room temperature to deposit 0.5 g (18%) of monodeuterolactim **14**: mp 271–272 °C; NMR ($CDCl_3$) δ 7.5–6.6 (m, 9 aromatic H), 4.1–3.0 (m, 4 aliphatic H), 2.60 (s, 3 H, Ac); MS *m/e* (rel intensity)[18d] 304 (100, M^+), 262 (70, M − CH_2CO), 205 (26, M − CH_2NAcCO), 204 (27), 203 (34), 179 (65), 43 (33, Ac^+). From these spectra one can estimate that **14** contains no more than 8% of aromatized product.

Evaporation of the mother liquor from **14** and cooling the residue to −10 °C gave a yellow solid, recrystallized from EtOH to produce 0.9 g (32%) of mixture **15**: mp 127.5–128.5 °C; ir (CS_2) 1730 (vs), 1700

(s), 840 (w), 780 (m), 750 (m), 690 cm^{-1} (s); NMR ($CDCl_3$) δ 7.33 (s, aromatic H), 7.27 (s, aromatic H), 4.30 (s, methylene), 2.52 (s, Ac) for **15a,** plus a weak triplet at 6.0 for the presence of some **15b;** MS *m/e* (rel intensity)[18d] 305 (60, M^+), 304 (29), 263 (26, M − CH_2CO), 262 (38, M − Ac), 220 (100, M − AcNCO), 219 (90), 218 (45), 217 (29), 205 (26, PhCD=CPhC=CH^+), 204 (39), 203 (29), 43 (53, Ac^+).

Anal. Calcd for $C_{20}H_{15}D_2NO_2$: D, 11.77 atom % excess. Found: D, 9.10 atom % excess (i.e., 55% **15a** and 45% **15b**).

Polarography. Polarographic reduction of **3** and **12** in the solvent–electrolyte CH_3CN–Et_4NBr was conducted by Dr. D. R. Olson in the manner previously described.[20] Half-wave reduction potentials found are presented in the following table.

Compd	$-E_{1/2}$[a] in anhydrous	$-E_{1/2}'$ medium	$-E_{1/2}$ with 3.8% H_2O added	$-E_{1/2}'$ added
3	1.98[b]	Poor	1.88	2.43
	2.19[b]	wave		
12	1.53	2.38	1.47	2.44

[a] In volts vs. a saturated calomel electrode. [b] Two half-waves of equal heights.

Ozonolysis of 12. A solution of 0.74 g of **12** in 25 ml of dry CH_2Cl_2 (containing 1% pyridine) was treated with a stream of ozone until the reaction mixture became green. It was then stirred with a mixture of 1.3 g of powdered Zn and 2.5 ml of glacial HOAc for 2 h, filtered, and evaporated. Treatment of the viscous yellow residue with 5 ml of 2,4-dinitrophenylhydrazine reagent[21] gave 0.1 g (15%) of benzaldehyde 2,4-DNP derivative, mp 230–232 °C, identified (after recrystallization) by direct comparison with an authentic sample.

Registry No.—**2a,** 59015-42-8; **2b,** 59015-46-2; **3,** 59015-39-3; **4,** 60224-30-8; **5,** 60224-31-9; **6,** 766-96-1; **7,** 37614-58-7; **8,** 60224-32-0; **9,** 60224-33-1; **10,** 60224-34-2; **11a,** 60224-35-3; **11b,** 60224-36-4; **12,** 60224-37-5; **13,** 54153-66-1; **14,** 60224-38-6; **15a,** 60224-39-7; **15b,** 60224-40-0; potassium phthalimide, 1074-82-4.

References and Notes

(1) (a) This investigation was supported in part by research grant GM 12730 from the National Institutes of General Medical Sciences, U.S. Public Health Service. For part 11 in this series see ref 7. (b) Teaching and Research Assistant, 1969–1973. (c) Research Assistant, 1965–1968.

(2) L. H. Klemm, T. M. McGuire, and K. W. Gopinath, *J. Org. Chem.,* **41,** 2571 (1976). As defined in this paper, mode 1 involves action of the $(C_2)'$ unit of the acid moiety as a "dienophile" and of the $Ph(C_2)$ unit of the amine moiety as a "diene", whereby cyclization occurs into the phenyl ring of the amine moiety. Mode 2 involves action of the (C_2) unit of the amine moiety as a "dienophile" and of the $Ph(C_2)'$ unit of the acid moiety as a "diene" whereby cyclization occurs into the phenyl ring of the acid moiety. In mode 1 the diene system is electron rich and the dienophile is electron deficient, while in mode 2 the diene system is electron deficient and the dienophile is electron rich.

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(12) The frontier MO energy level exhibited by a specific structural unit, e.g., a –C≡C–, varies with the substituents attached to the unit and with the direction in space from whence the addendum unit, e.g., *cis*-CH=CH–, approaches in order to undergo cycloaddition (i.e., in the extent of orbital overlap which is experienced by the interacting addenda). The effect of substituents on frontier MO energy levels has been considered by many authors [e.g., see K. N. Houk, *J. Am. Chem. Soc.,* **95,** 4092 (1973); K. N. Houk, J. Sims, R. E. Duke, R. W. Strozier, and J. K. George, *ibid.,* **95,** 7287 (1973); N. D. Epiotis, *ibid.,* **95,** 5625 (1973)] and was taken into account in the [4 + 2] cycloaddition processes reported in ref 2. The geometric sense associated with the Hückel MO energy levels in Scheme IV assumes an approach of the π systems in parallel planes with endwise overlap of the p orbitals on the terminal atoms of the two systems in the transition state [M. J. S. Dewar, "The Molecular Orbital Theory of Organic Chemistry", McGraw-Hill, New York, N.Y., 1969, pp 319–320]. The geometric sense associated with the Möbius MO energy levels in Scheme IV assumes an approach of the π systems in edge-to-face, perpendicular planes (crossed bonds) with perpendicular overlap of the p orbitals on the terminal atoms in the transition state (see Scheme V). For simplicity we have arbitrarily assigned the geometric variations in MO energy levels exclusively to the unoccupied orbitals, though one can rationalize that there will be geometric variations in both occupied and unoccupied levels. It might be noted that Hückel and Möbius MO energy levels correspond only to two extreme geometric types of transition states. Intermediate geometric types can be visualized, but they may be energetically unfavorable [K. Fukui, "Theory of Orientation and Stereoselection", Springer-Verlag New York, New York, N.Y., 1975, pp 22–33].

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