Cycloaddition Reactions of α-Keto Imines. Regio- and Stereoselectivities in the Dienic and Dienophilic Additions to Conjugated Dienes

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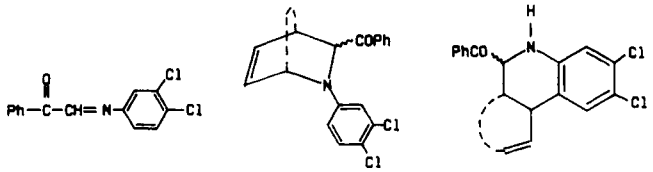
The α-keto imines **4** or their methanol adducts **5** (**a**, R = NO_2; **b**, R = Cl; **c**, R = CH_3; **d**, R = OCH_3) add at room temperature under Lewis acid catalysis to 1,3-butadiene, 2-methyl-1,3-butadiene, 2,3-dimethyl-1,3-butadiene, cyclopentadiene, and 1,3-cyclohexadiene as dienophilic or dienic reagents. **4b** and **5a,b** yield substituted 1,2,5,6-tetrahydropyridines **6**, **8**, and **12** (with all butadienes), 1,2,3,4-tetrahydroquinoline **7** with cis-oriented benzoyl and vinyl groups (with 1,3-butadiene), and 3-*exo*-benzoyl-2-azabicyclo[2.2.1]hept-5-ene **15a** and 3a,4,5,9b-tetrahydro-3*H*-cyclopenta[*c*]quinolines **14** with cis-oriented benzoyl groups (with cyclopentadiene). With 1,3-cyclohexadiene, **4b–d** and **5a–c** give 3-*exo*-benzoyl-2-azabicyclo[2.2.2]oct-5-ene derivatives **16**, the 3-*endo*-benzoyl isomers **17**, and 5,6,6a,7,8,10a-hexahydrophenanthridine derivatives **18** with a cis-oriented benzoyl group. Under stronger conditions (Lewis acid catalysis in refluxing benzene or toluene) **8** and **12** give cyclodehydration rearrangement to 6,7-dihydropyrido[1,2-*a*]indoles **11** and 6,9-dihydropyrido[1,2-*a*]indoles **13**, respectively, **16** gives totally stereoselective amino-Claisen conversion to **18**, while the analogue conversion of **17** yields nonspecifically **18** and isomer **19** with a trans-oriented benzoyl group. The stereochemistry of addition and rearrangement products was firmly ascertained by means of NOE ^1H NMR differential spectroscopy. The observed regio- and stereoselectivities of additions and amino-Claisen rearrangements are discussed within the framework of concertedness as well as under the hypothesis of zwitterionic intermediacy.

Aromatic Schiff bases react in the presence of a Lewis acid with double bonds activated by electron-donating groups (EDG) to give products of dienic Diels–Alder addition with inverse electronic demand.[1,2] On the other hand, Schiff bases possessing electron-withdrawing groups (EWG) are expected to behave preferentially as dienophiles, giving a normal Diels–Alder addition.[3] In line with this latter statement, α-keto imine (phenylglyoxal anil) **1** was reported[4] to give adducts of type **2** by reaction with cyclopolyenes under $BF_3{\cdot}Et_2O$ catalysis. In preliminary research[5] we have found, however, that **1** gives with the same cyclopolyenes, under the same conditions, adducts of type **3**. In order to settle this point, we have investigated the reactivity of a series of phenylglyoxal anils with some conjugated dienes and their stereo- and regiochemical outcome.



1 **2** **3**

Results

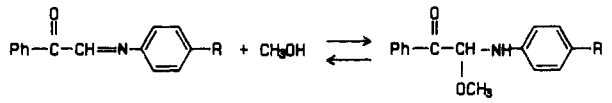
Configurational Analyses. The relative configurations of reagents and products were determined by means of NOE (Nuclear Overhauser Effect) ^1H NMR spectroscopy[6] in the differential mode. The analyses are detailed in the supplementary material (see paragraph at the end of paper).

Preparation and Characterization of the Reagent. The reaction of phenylglyoxal hydrate with a series of anilines in methanol or toluene gives the corresponding anils **4**.[7] Their purification by distillation or chromatography is however accompanied by extended decomposition. The compounds that could be isolated are also highly hygroscopic. A convenient alternative is the utilization of methanol adducts **5**, directly obtained as precipitates when the reaction is carried out in methanol.[7] In solution an equilibrium can be observed between the methanol adduct **5** and the free anil **4**, so that the former

Table I. Product Distribution in the Addition of 4 or 5 to 1,3-Cyclohexadiene in the Presence of $BF_3 \bullet Et_2O$[a]

substr	substit	16, %	17, %	18, %	(16 + 18):17[b]
5a	NO_2	56	15	29	85:15
4b	Cl	45	10	45	90:10
5b	Cl	42	12	46	88:12
4c	CH_3	26	12	62	88:12
5c	CH_3	29	10	61	90:10
4d	OCH_3	19	8	73	92:8

[a] Substrate and $BF_3{\cdot}Et_2O$ were in equimolar ratio. [b] Ratio between $endo_1$ and $endo_2$ transition states (see Discussion).



4 **5**

a, R = NO_2; **b**, R = Cl; **c**, R = CH_3; **d**, R = OCH_3

can be directly utilized for synthetic purposes. The free anils **4b,c** could be recovered after azeotropic removal of

† Dipartimento di Scienze Ambientali.
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(1) (a) Povarov, L. S. *Russ. Chem. Rev., Engl. Transl.* **1967**, *36*, 656. (b) Perricone, S. C.; Elslager, E. F.; Worth, D. F. *J. Heterocycl. Chem.* **1970**, *7*, 135. (c) Worth, D. F.; Perricone, S. C.; Elslager, E. F. *J. Heterocycl. Chem.* **1970**, *7*, 1353. (d) Nomura, Y.; Kimura, M.; Takeuki, Y.; Tomoda, S. *Chem. Lett.* **1978**, 267.

(2) For a recent review on Diels–Alder reactions of azadienes, see: Boger, D. L. *Tetrahedron* **1983**, *39*, 2869.

(3) For recent reviews on Diels–Alder reactions of heterodienophiles, see: (a) Weinreb, S. M.; Levin, J. I. *Heterocycles* **1979**, *12*, 949. (b) Weinreb, S. M.; Staib, R. R. *Tetrahedron* **1982**, *38*, 3087.

(4) McKay, W. R.; Proctor, G. R. *J. Chem. Soc., Perkin Trans. 1* **1981**, 2443.

(5) Lucchini, V.; Prato, M.; Quintily, U.; Scorrano, G. *J. Chem. Soc., Chem. Commun.* **1984**, 48.

(6) Noggle, J. H.; Schirmer, R. E. *The Nuclear Overhauser Effect*; Academic Press: New York, 1971.

(7) Prato, M.; Quintily, U.; Scorrano, G. *Gazz. Chim. Ital.* **1984**, *114*, 405.

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Table II. Lewis Acid Effect on the Product Distribution in the Addition of 5a (R = NO_2) to 1,3-Cyclohexadiene[a]

Lewis acid	16a, %	17a, %	18a, %	(16a + 18a): 17a[b]
BF_3·Et_2O	56	15	29	85:15
$TiCl_4$	59	18	23	82:18
$SnCl_4$	44	31	25	69:31
$AlCl_3$	52	20	28	80:20
$AlCl_2OMenth$[c]	56	17	27	83:17
SO_2[d]	47	26	27	74:26

[a] In $CDCl_3$, unless otherwise stated; Lewis acid and substrate were in equimolar ratio. [b] See footnote *b* in Table I. [c] Menthoxyaluminum dichloride. [d] Used also as solvent in a sealed vessel.

methanol in toluene. In both cases the compound obtained in this manner and the anil liberated in solution from the methanol adduct show the same NMR spectral pattern. No free anil could be recovered from **5a**, while the adduct **5d** loses methanol spontaneously.[7]

Substituted Schiff bases show a preference for the *E* configuration.[8] This is also the case for free anils **4**, as confirmed by the NOE analysis. The energy barriers for rotation around the C–N double bond or for inversion around nitrogen in Schiff bases are relatively high,[8] thus excluding the possibility of a fast equilibrium between the *E* and *Z* isomers of **4**. Since no signals were detected in the NMR spectrum of methanol adducts **5** that could be attributed to the *Z* isomer of **4**, we can concude that adducts **5** in solution liberate exclusively isomers **4** in the *E* configuration.

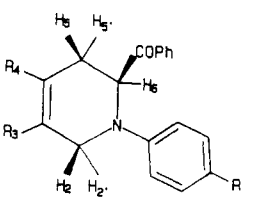
The reactivity of the free anils **4b,c** in the addition to 1,3-cyclohexadiene was tested against that of the methanol adducts **5b,c**. The same products, in the same ratios, were obtained (see Table I). This behavior has a precedent in the case of 5-methoxyhydantoins: the imino derivatives could not be isolated, but the methoxy adducts lose methanol at high temperature or under Lewis acid catalysis to give Diels–Alder adducts with conjugated dienes.[9]

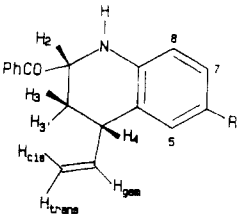
Catalyst. The additions occur only under Lewis acid catalysis. Often stoichiometric amounts of the catalyst were required. We have found that liquid SO_2, acting also as solvent, can be a convenient alternative to the more often utilized BF_3·Et_2O. When the reactions had to be carried out under milder conditions (see below), then CuCl or menthoxyaluminum dichloride were convenient choices. A comparative investigation of the effect of the Lewis acid nature on cycloadduct distribution was undertaken in the case of the additions of **5a** to cyclohexadiene (see Table II).

Reaction Conditions. The cycloaddition reactions were performed at room temperature. To a solution of the substrate in anhydrous methylene chloride were added the Lewis acid and the diene in that order. The reactions in liquid SO_2 were run by dissolving substrate and diene in the solvent at −78 °C. The reaction vessel was sealed and the solution was allowed to reach room temperature.

Addition to Noncyclic Dienes: (a) 1,3-Butadiene. From the reaction of methanol adduct **5a** (R = NO_2) under BF_3 catalysis, dienophilic adduct **6a** and dienic adduct **7a** were obtained in the rough ratio of 1:3 (from integrated areas of selected resonances in the NMR spectrum of the crude reaction mixture) and could be isolated by flash chromatography. The adduct **7b** (R = Cl) was formed almost quantitatively from the analogous reaction of **5b**.

The tetrahydroquinoline derivatives **7** might be derived from the tetrahydropyridine adducts **6** through an amino-Claisen rearrangement.[10] We have in fact observed this conversion from the adducts of dienophilic addition of **4** or **5** to cyclic dienes (see below). However, when **6a** was refluxed in toluene for 5 h with stoichiometric BF_3, only slow decomposition was observed, and no signals attributable to **7a** could be identified.





6, $R_3 = R_4 = H$
8, $R_3 = H$; $R_4 = CH_3$
12, $R_3 = R_4 = CH_3$

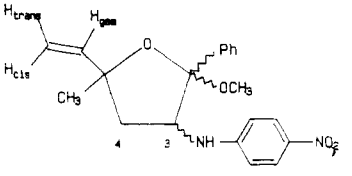
7

The configurational structure of the tetrahydroquinoline derivatives **7** could be determined by simple decoupling experiments. The multiplet of methylenic $H_{3'}$ resonating at high field is in the form of a quartet, with constants $J_{2,3'}$ and $J_{3',4}$ both equal to 12.2 Hz (**7a**) or 11.9 Hz (**7b**). Therefore, the Karplus rule would suggest that $H_{3'}$ is antiperiplanar to H_2 and H_4, so that the benzoyl group and the vinyl group are cis-oriented. Since signals that may pertain to the trans isomer could not be observed in the spectra of the reaction mixture, we conclude that the formal dienic additions of **5a,b** to butadiene are totally stereoselective.

(b) 2-Methyl-1,3-butadiene. From the reaction of **5a,b** (BF_3·Et_2O catalysis) the 4-methyl-*N*-aryltetrahydropyridine derivatives **8a,b** could be observed or isolated.

In the case of **5a** two sets of signals were detected that could be reasonably attributed to tetrahydrofuran derivatives **9** and **10**. These isomes could be isolated by chromatography. Examples of the formation of tetrahydrofurans from cycloaddition of α,β-unsaturated carbonyl derivatives are known.[11]

Tetrahydrofurans **9** and **10** could be slowly converted quantitatively into **8a** under BF_3 catalysis at room temperature. It should be noted that the 4-methylpyridine derivatives **8a,b** were formed regiospecifically, either as primary or as secondary products, while no evidence was found for the 3-methyl isomer.

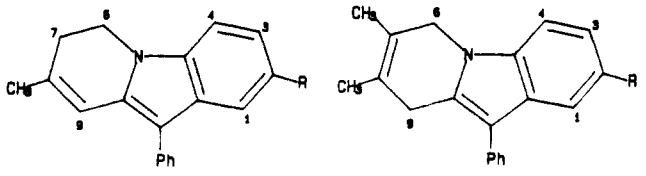


9 and 10

Heating **8a,b** in refluxing toluene for 8 h with stoichiometric BF_3 led to pyrido[1,2-*a*]indole derivatives **11a,b** whose structure and unsaturation pattern were unambigously determined by means of a NOE investigation. This cyclodehydration reaction is accompanied by a [1,3] shift of one methylenic hydrogen from position 7 to position 9.

(c) 2,3-Dimethylbutadiene. Only the tetrahydropyridine derivatives **12a,b** could be quantitatively isolated from the reaction of **5a,b** or observed in the crude reaction

(8) (a) McCarty, C. G. In *The Chemistry of Carbon-Nitrogen Double Bond*; Patai, S., Ed.; Wiley-Interscience: New York, 1970; p 363. (b) Merényi, G.; Wettermark, G.; Roos, B. *Chem. Phys.* **1973**, *1*, 340.
(9) Ben-Ishai, D.; Goldstein, E. *Tetrahedron* **1971**, *27*, 3119.
(10) (a) Jolidon, S.; Hansen, H.-J. *Helv. Chim. Acta* **1977**, *60*, 978. (b) Lutz, R. P. *Chem. Rev.* **1984**, *84*, 205.
(11) De Simoni, G.; Tacconi, G. *Chem. Rev.* **1975**, *75*, 651.

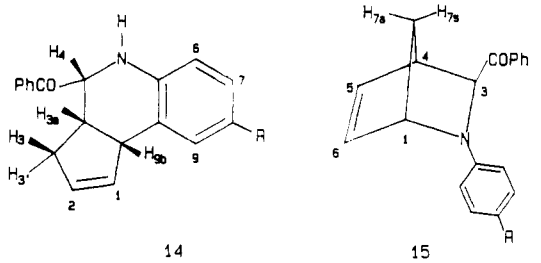


11 13

spectra. The prolonged action of BF_3 on **12a,b** in refluxing toluene led to the formation of pyrido[1,2-*a*]indoles **13a,b**. In this instance the cyclodehydration reaction was not accompanied by hydrogen shift, probably because of the steric hindrance opposed by the methyl in position 7 or because of the double-bond stabilization induced by multiple methyl substitutions.

Addition to Cyclic Dienes: (a) Cyclopentadiene. When catalyzed by BF_3 or SO_2, the reaction of **5a,b** is instantaneous at room temperature, affording quantitatively the tetrahydrocyclopenta[*c*]quinolines **14a,b**. The structure of these adducts was defined through NOE analysis. It should be noted that the additions are regiospecific (only 3*H* isomers are formed) and stereospecific (the orientation of the benzoyl group is cis with respect to cyclopentene ring).

With the milder catalysts menthoxyaluminum dichloride or CuCl the reaction is slower, and the products of dienophilic addition **15a,b** are also formed. Under Lewis acid catalysis the azanorbornenes **15a,b** are converted to quinoline derivatives **14a,b**. The conversion is slow with the latter catalysts and instantaneous with BF_3. With longer reaction times the rearrangement also occurs thermally (at 70 °C in toluene 80% conversion of **15a** was observed in 30 days; 5 min were required for quantitative conversion at 150 °C in the absence of solvent). The nitro derivative **15a** is stable enough to allow its isolation and complete characterization through NOE analysis. The less stable chloro derivative **15b** could only be identified in the NMR spectrum of the crude reaction mixture.



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(b) 1,3-Cyclohexadiene. Under BF_3 or SO_2 catalysis the anils **5a–d** behave as dienophiles, yielding the isomers **16a–d** and **17a–d**, and as dienes, with formation of the adducts **18a–d**. These latter were produced regio- and stereospecifically (cis orientation of the benzoyl group with respect to the cyclohexene ring). The three adducts were formed in different ratios depending on the nature of the substituent in the aniline ring and the catalyst (see Tables I and II). The nitro and chloro derivatives were isolated by flash chromatography and characterized through NOE analyses.

The three products are stable under the reaction conditions. Rearrangements of isomeric azabicyclooctenes **16** and **17** were only induced by stoichiometric amounts of BF_3 at the temperature of refluxing benzene. The rearrangements were thoroughly investigated in the case of the nitro and chloro derivatives **16a,b** and **17a,b**. The behavior of the two isomers differs in one important point. The rearrangement of *exo*-benzoylazabicyclooctenes **16a,b** yields stereospecifically the *cis*-phenanthridine derivatives **18a,b**; the analogous rearrangement of the *endo*-benzoyl

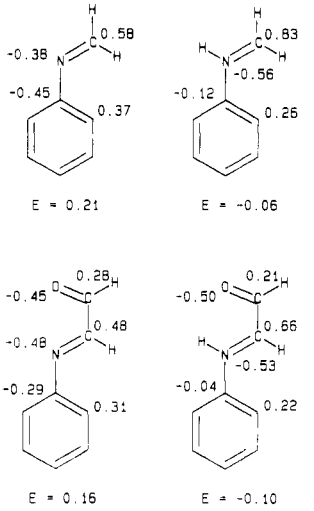
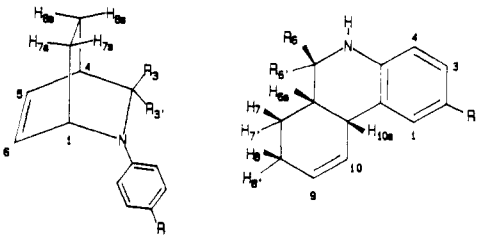


Figure 1. LUMO energies for free and N-protonated *N*-phenylimine and *N*-phenylimino aldehyde and corresponding p AO coefficients.

isomers **17a,b** is not stereospecific, yielding both *cis*- (**18a**, 13%; **18b**, 5%) and *trans*- (**19a**, 83%; **19b**, 94%) phenanthridines.



16, R_3 = COPh; $R_{3'}$ = H **18**, R_6 = H; $R_{6'}$ = COPh
17, R_3 = H; $R_{3'}$ = COPh **19**, R_6 = COPh; $R_{6'}$ = H

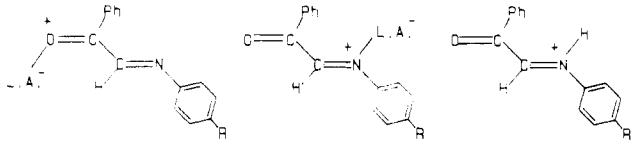
Ab Initio Quantum Mechanical Computations on Model Molecules. For the purposes of the following discussion, the LUMO nodal properties of Diels–Alder reagents **4** have been estimated by ab initio MO calculations (program package MONSTERGAUSS,[12] STO-3G level) on the model molecules *N*-phenylimine and *N*-phenylimino aldehyde (respectively lacking and possessing an EWG). The effect of Lewis acid catalysis was checked on the corresponding N-protonated compounds. The geometries of the computational models have been taken from literature sources;[13] only in the case of protonated species were the C–N bond lengths subjected to parabolic optimization. Results are reported in Figure 1. The signs and relative magnitudes of the p AO contributions to LUMOs are not expected to change in the fully optimized structures. The FMO properties of isoprene are taken from literature,[14] while those of cyclopentadiene and cyclohexadiene are well-known.[15a]

Discussion

The α-keto imines add to conjugated dienes under Lewis acid catalysis only. Either **4** or **5** can be used with similar results, as in the case of the addition of **4b,c** and **5b,c** to

(12) Csizmadia, I. G.; Peterson, M. R.; Poirier, R. A. Program MONSTERGAUSS; University of Toronto: Toronto, 1981.
(13) Bernstein, J.; Schmidt, G. M. J. *J. Chem. Soc., Perkin Trans. 2* **1972**, 951.
(14) (a) Alston, P. V.; Ottenbrite, R. M. *J. Org. Chem.* **1975**, *40*, 1111. (b) Houk, K. N. *Acc. Chem. Res.* **1975**, *8*, 361.
(15) Fleming, I. *Frontier Orbitals and Organic Chemical Reactions*; Wiley: London, 1976, (a) p 123; (b) p 125; (c) p 121; (d) p 150.

cyclohexadiene, where the same products in the same distribution were obtained (see Table I). This would suggest that the active substrate is the free anil **4** complexed by Lewis acid. The site of coordination may be carbonyl oxygen (**20**) or imine nitrogen (**21**). Coordination



20 **21** **22**

in the Lewis acid catalyzed addition of iminourethanes was suggested to occur at carbonyl oxygen,[16] where the positive charge can be most dispersed by resonance. However, in cases where the conjugated acids are not stabilized by mesomeric effects, imines are much stronger bases than carbonyl compounds.[17] This would suggest that free anils **4** are preferentially coordinated at imine nitrogen.

On the other hand the protonated iminium ion **22** can be generated directly from methanol adduct **5** through removal of the methoxy group by the Lewis acid. The product distribution in the reaction of **5a** with 1,3-cyclohexadiene is influenced by the nature of the Lewis acid (see Table II). The changes however are too small for recognizing a significative trend, thus making difficult to rule out the intervention of protonated iminium intermediates of type **22**.

For the purposes of the present discussion, knowledge of the configuration of anils **4** is essential. By means of NOE analysis we have shown that the configuration is *E*. Reasonably, the configuration is not altered by coordination of the Lewis acid at carbonyl oxygen (structure **20**). As the rotation around the C–N bond is energetically unfavored in protonated Schiff bases,[8b] we can assume that the *E* configuration is maintained also in the nitrogen coordinate Lewis acid complex **21** as well as in the protonated iminium ion **22**.

As in other Lewis acid catalyzed cycloadditions of imines,[16,18] it is difficult to assess whether the reaction occurs through a concerted mechanism or through zwitterionic intermediacy. We will examine the consistency of both hypotheses with respect to the regio and stereo outcomes of these addition reactions.

Concerted Mechanism. Unsaturated heterosystems such as anils **4** are characterized by low-lying LUMOs.[19] Lewis acid complexation or protonation brings about a further energy lowering of LUMO (confirmed by our ab initio estimates), so that the dienophilic addition of **4** is a case of normal Diels–Alder reaction, while the dienic addition is a Diels–Alder reaction with reverse electronic demand. In any case the relevant FMO interaction is between the LUMO of the anil and the HOMO of the reaction partner.

1. Regioselectivity. The additions of **4** or **5** to conjugated dienes are always regiospecific, whether the anils behave as dienophiles or as dienes.

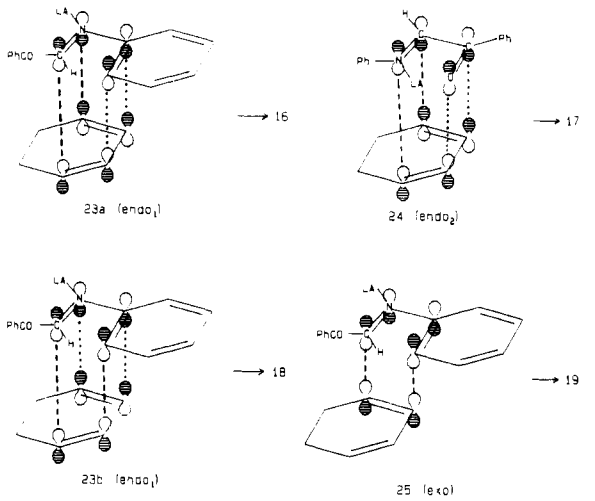


Figure 2. Endo and exo configurational complexes for concerted addition of anil **4** to cyclohexadiene: (- - -) primary and (···) secondary orbital interactions.

When the concerted mechanism is considered, the regioselectivity in the dienic additions of anils **4** is governed by the p AO contributions at the terminal carbon atoms in the formal dienic system constituted by the C–N double bond and the cis-conjugated double bond of Kekulé type in the aniline ring. A terminal EWG lowers the AO contribution to the LUMO at the bound carbon atom,[15b] and indeed this is confirmed by our computational results. Nevertheless, and for all tested structures, a greater p AO coefficient is steadily associated with an iminic carbon atom than with a cis ortho atom in the aniline ring (Figure 1). Therefore the large–large/small–small selection rule[15c] would dictate that the terminal carbon atom in the conjugated system of the reaction partner would rather bind with an iminic carbon than with the aniline ortho carbon. The same considerations may also explain the regiospecific formation of 4-alkoxy-substituted tetrahydroquinolines from the addition of other *N*-phenyl-substituted Schiff bases to vinyl ethers.[1]

As for the regiospecific dienophilic addition to isoprene, the HOMO of the diene is reported[14] to display the greatest p AO contribution at the terminal carbon geminal to methyl group. As the LUMO of protonated Schiff bases (Figure 1) is polarized toward the carbon end of the C–N double bond, the same selection rule offers the rationale for the experimentally observed orientation.

2. Stereoselectivity. The additions of anils **4** are totally stereoselective when they add as dienes or to cyclopentadiene as dienophiles. The dienophilic addition to 1,3-cyclohexadiene gives **16** (*exo*-benzoyl):**17** (*endo*-benzoyl) ratios varying from 5:1 to 2:1 depending on substituent and catalyst. This parallels the preference for exo orientation in aldimine cycloaddition.[20]

Cyclic transition states have been considered in the addition of iminourethanes to cyclic conjugated olefins.[16] The stereochemical outcomes were rationalized in terms of steric or coulombic interactions within the supermolecular complex. In our case, considerations based on secondary orbital interactions appear more suited.

The inspection of LUMO nodal properties of model molecules, free and N-protonated N-phenylimino aldehydes (Figure 1), reveals that both the cis-conjugated double bond in the aniline ring and the carbonyl π system can interact in a stabilizing manner with a conjugated π bond system. Therefore, in the concerted addition to

(16) (a) Krow, G.; Rodebaugh, R.; Carmosin, R.; Figures, W.; Pannella, H.; DeVicaris, G.; Grippi, M. *J. Am. Chem. Soc.* **1973**, *95*, 5273. (b) Krow, G. R.; Rodebaugh, R.; Grippi, M.; DeVicaris, G.; Hyndman, C.; Marakowski, J. *J. Org. Chem.* **1973**, *38*, 3094.

(17) pK_{BH^+} of imine of benzophenone, 7.2: Culbertson, J. B. *J. Am. Chem. Soc.* **1951**, *73*, 4818. pK_{BH^+} of benzophenone, −4.97: Edward, J. T.; Wong, S. C. *J. Am. Chem. Soc.* **1977**, *99*, 4229. Cited in Stewart, R. *The Proton: Applications to Organic Chemistry*; Academic Press: Orlando, FL 1985.

(18) Cheng, Y.-S.; Ho, E.; Mariano, P. S.; Ammon, H. L. *J. Org. Chem.* **1985**, *50*, 5678.

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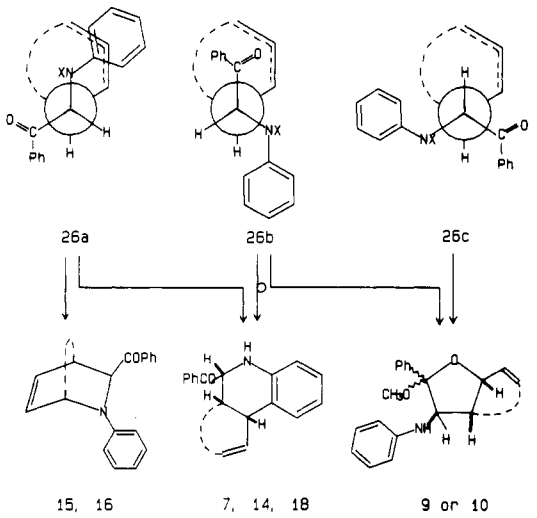

Figure 3. Rotameric conformations of zwitterionic intermediate **26** deriving from attack of **21** or **22** (in *E* configuration) to the *si* face of the dienic reaction partner. X = H or Lewis acid. Arrows give the ring closure reaction paths. Eyelet arrows indicate rotation of the C–N bond.

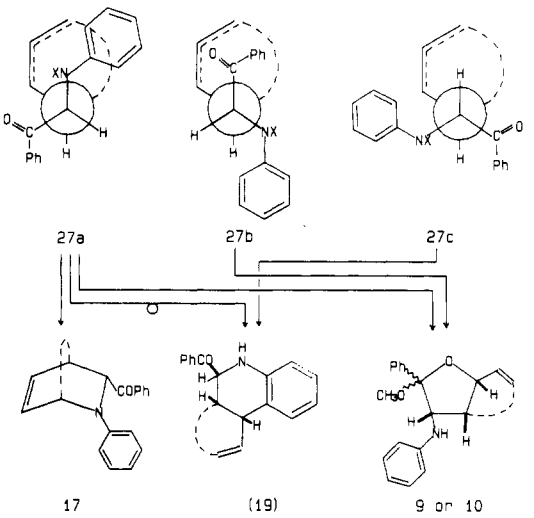

Figure 4. Rotameric conformations of zwitterionic intermediate **27** deriving from attack of **21** or **22** (in *E* configuration) to the *re* face of the dienic reaction partner. X = H or Lewis acid. Arrows give the ring closure reaction paths. Eyelet arrows indicate rotation of the C–N bond.

cyclohexadiene, we can envisage two different endo molecular complexes (Figure 2), which can be named $endo_1$ (**23**) and $endo_2$ (**24**), besides the exo molecular complex **25**. The $endo_1$ configuration provides two different types of secondary orbital interactions, depicted as **23a** and **23b**. These lead to the formation of *exo*-benzoylazabicyclooctenes **16** and *cis*-benzoylphenanthridines **18**, respectively. Thus, within the same configuration of the molecular complex, different primary and secondary orbital interactions may lead to either dienic or dienophilic addition product.

The $endo_2$ configuration **24** leads to the *endo*-benzoylazabicyclooctene **17** only, while the exo configuration **25**, which would have yielded the *trans*-benzoylphenanthridine **19**, is apparently not accessible.

We have found (Tables I and II) that the ratio between adducts **16a,d** and **18a,d**, considered together, and azabicyclooctenes **17a,d** varies between 92:8 and 69:31, depending on the substituent in the aniline ring and on the catalyst; this suggests the following stability order for the configurational complexes: $endo_1 > endo_2 >$ exo.

An interaction diagram of type $endo_1$ can also explain the total stereoselectivities of the dienic and dienophilic additions to cyclopentadiene, which yielded **14** and **15**, respectively, and of the dienic addition to butadiene, giving **7**. No other adducts were recovered from these reactions, so that the configurational complexes of type $endo_2$ and exo do not seem accessible.

The greater stability of $endo_1$ complexes **23** is easily explained by considering secondary orbital interactions between sp_2 carbon atoms. The relative stability of $endo_2$ configuration **24** can be similarly attributed to secondary interactions with the carbonyl π system. In N-protonated *N*-phenylimino aldehyde (Figure 1) the carbonyl π system contributes to the LUMO with greater p AO coefficients than the ipso and cis-ortho carbon atoms in the aniline ring; however the β resonance integral for σ overlap between two carbon p AOs is significantly greater than that between carbon and oxygen p AOs.[15d] Therefore the secondary orbital interaction should be considerably more relevant in the configurational complex **23** than in the other complex **24**.

Zwitterionic Mechanism. In Figures 3 and 4 a general scheme based on the hypothesis of zwitterionic intermediacy is proposed. The iminic species **21** or **22**, supposedly in the *E* configuration, can add to either face of the conjugated π system of the reaction partner, giving rise to diastereomeric zwitterions **26** and **27**, stabilized by allylic resonance. The actual rotameric configurations **26a–c** and **27a–c** of these intermediates can give ring closure to the connected structures. Numbers refer to the compounds actually observed. The structures referenced by a number within parentheses have only been recovered as rearrangement products. The reaction paths marked by an eyelet arrow either require the rotation of the C–N bond in **26** or **27** or originate from the addition of **21** or **22** in the *Z* configuration. Similar configurations can be envisaged for the oxygen-coordinated complex **20**.

Only in the addition of **5a** to isoprene have we been able to isolate products that incorporate methanol (**9** and **10**). The formation of these tetrahydrofuran derivatives can only be accounted for by a zwitterionic mechanism, which foresees ring closure in configurations **26b,c** or **27a,b**, followed by quench with methanol.

As for the formation of the other primary adducts, the two mechanistic hypotheses seem to be equally plausible.

1. Regioselectivity. Within the hypothesis of a stepwise mechanism, the iminic species **21** or **22** give rise to intermediates **26** and **27** stabilized by allylic resonance only by adding to one end of the π-conjugated system of the reaction partner. The addition to isoprene occurs at the terminal carbon atom geminal to the methyl group, with formation of a zwitterionic intermediate further stabilized by methyl substitution. Ring closures within these intermediates necessarily lead to the observed regiospecific adducts.

2. Stereoselectivity. The zwitterionic mechanism can account for the observed stereoselectivities only by consideration of the following assumptions: (a) the iminic species **21** or **22** add in the *E* configuration; (b) rotamers **26a,b** and **27a,b** are formed preferentially to rotamers **26c** and **27c**, or are the only productive rotamers; (c) the barriers for the interconversion between the different rotamers of **26** or **27** or for the rotation around the C–N bond are large relative to the recombination barrier.[21]

A stepwise mechanism was proposed for the addition of iminourethanes to cyclic polyenes,[16] which however could

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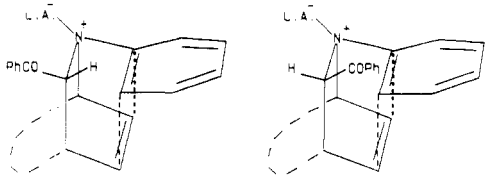
rationalize the observed stereochemistry by assuming a relevant role of steric hindrance and the possibility of rotameric interconversion.

Rearrangements. The amino-Claisen rearrangements of azanorbornenes **15a,b** and azabicycloctenes **16a,b** and **17a,b** are examples of [3,3] sigmatropic reactions for which concerted or nonsynchronous (either radical or zwitterionic) mechanisms have been proposed.[10,22]

In a concerted sigmatropic rearrangement the termini of the π-conjugated system along which the bond migrates must come sufficiently close. The rearrangements of **16** and **17** therefore can only operate from those invertomers with endo-oriented aniline ring.

The corresponding transition states **28a** and **28b** are forced into the boat configuration by the benzoylmethano bridge. This configuration is topologically very similar



28a 28b

to endo$_1$ complex **23**. While however in this latter secondary orbital interactions are stabilizing, they are considered destabilizing in the boat (as opposed to the chair) transition state of Cope or Claisen rearrangements.[23] This fact should have only trivial energy consequences, as Cope conversions, sterically obliged to a boat transition state, occur easily[24] and the boat form is operative to some extent in Claisen rearrangements also in the absence of steric strain.[25]

While these considerations do actually account for the stereospecific rearrangements of *exo*-benzoyl adducts **15** and **16**, the nonstereospecific rearrangement of *endo*-benzoylazabicyclooctenes **17** is more intriguing. The production of some *cis*-benzoylphenanthridine **18** besides a larger amount of the trans isomer **19** is not even explained by the hypothesis of a nonconcerted process. It is easy to verify on a molecular model that the correct rotamer of zwitterion **27**, with proper orientation of the aniline group, ring closes stereospecifically to isomer **19** only, while no rotameric conformation nor any rotation of the C–N bond can lead to isomer **18**. It may be speculated that the strong conditions necessary for the interconversion could induce some inversion at the benzoylic carbon in **17**, through an acid-catalyzed keto–enolic mechanism.

Conclusions

The formation of the tetrahydrofuranic species **9** and **10** can be only explained by the zwitterionic hypothesis. These compounds however have been observed as minor products in one instance only. For the formation of the other adducts both concerted and zwitterionic mechanistic hypotheses should be considered.

While in cycloaddition reactions the regioselectivity degree is not regarded to be significant for a choice between the two hypotheses, a high degree of stereoselectivity is generally considered indicative of a concerted mechanism.

As a matter of fact, the order of stability of the supermolecular complexes **23–25**, as deduced from consideration of the observed stereoselectivities, can be fairly well accounted for by nonempirical estimates of the strength of secondary orbital interactions. The zwitterionic rotamers **26** and **27** can justify the experimental findings only if a series of ad hoc restrictions are considered.

Experimental Section

General Data. NMR spectra were recorded with a Bruker WP200SY spectrometer operating at 200 MHz. Chemical shifts are in ppm relative to Me_4Si, coupling constants are in hertz. In all cases the solvent was $CDCl_3$. Multiplicities are abbreviated as follows: m, multiplet; s, singlet; d, doublet; t, triplet; q, quartet. The variable frequencies of N–H resonances are not reported. Melting points, obtained with a Buchi apparatus, are uncorrected. The organic solutions from workup of reaction mixtures were dried over Na_2SO_4. Low pressure column chromatography was performed with Merck 15111 silica gel (15–40 mesh). Lewis acids were purified with standard methods. Menthoxyaluminum dichloride was prepared according to a published procedure.[26]

Nuclear Overhauser Effect Measurements. The samples (in $CDCl_3$) were freed from oxygen through sonication under nitrogen flow. The usual procedure for gated irradiation experiments was modified[27] and the selected nucleus was saturated by an 8-s cyclic perturbation of all multiplet lines with a 45-dB attenuation of a nominal 0.2-W decoupling power. The % enhancements are obtained from the multiplier of the reference spectrum which brings the observed multiplet to exact matching with the corresponding multiplet in the perturbed spectrum. Errors are estimated at about 0.3%.

General Procedure. To a stirred solution of **4** (1 g) and 1 equiv of Lewis acid in 30 mL of anhydrous CH_2Cl_2 was added 1.5 equiv of the reaction partner at room temperature. With $BF_3{\cdot}Et_2O$ or SO_2 (used as solvent) the reaction was complete in a few minutes. The reaction mixture was then poured into 50 mL of 5% aqueous $NaHCO_3$. The organic layer was washed with water, dried, and concentrated in vacuo. The residue was crystallized or chromatographed under low pressure (4–6 atm) on silica gel.

Reaction of 2-[(4-Nitrophenyl)amino]-2-methoxy-1-phenylethanone (5a) with 1,3-Butadiene. Chromatographic separation (toluene/ethyl acetate 99:1 as eluant) of the reaction mixture afforded 16% of 6-benzoyl-1,2,5,6-tetrahydro-1-(4-nitrophenyl)pyridine (**6a**) and 40% of (2α,4α)-2-benzoyl-4-ethenyl-1,2,3,4-tetrahydro-6-nitroquinoline (**7a**).

6a: mp 121–122 °C (EtOH); ^{1}H NMR δ 2.73 (ddq, $H_{5'}$, $J_{5,5'}$ = 17.4, $J_{4,5'} = J_{5',6} = J_{2',5'}$ = 1.7), 2.91 (ddq, H_5, $J_{5,6}$ = 7.3, $J_{2',5} = J_{4,5} = J_{3,5}$ = 2.8), 4.15 (br m, H_2 and $H_{2'}$), 5.73 (dd, H_6), 5.75 (ddq, H_4, $J_{3,4}$ = 10.1, $J_{2,4} = J_{2',4}$ = 2.0), 5.92 (dq, H_3, $J_{2,3} = J_{2',3}$ = 3.0), 6.78 (m, *p*-$NO_2C_6H_4$, H_o), 7.51 (m, COPh, H_m), 7.63 (m, COPh, H_p), 7.94 (m, COPh, H_o), 8.10 (m, *p*-$NO_2C_6H_4$, H_m). Anal. Calcd for $C_{18}H_{16}N_2O_3$: C, 70.06; H, 5.23; N, 9.09. Found: C, 69.95; H, 5.18; N, 9.02.

7a: mp 160–161 °C (EtOH); ^{1}H NMR δ 1.68 (dt, $H_{3'}$, $J_{3,3'}$ = 12.8, $J_{2,3'} = J_{3',4}$ = 12.2), 2.45 (ddd, H_3, $J_{3,4}$ = 4.7, $J_{2,3}$ = 3.2), 3.70 (br ddd, H_4, $J_{H,gem}$ = 8.5), 5.12 (dd, H_2), 5.35 (dd, vinylic H_{trans}, $J_{trans,gem}$ = 9.7, $J_{trans,cis}$ = 1.7), 5.38 (dd, vinylic H_{cis}, $J_{cis,gem}$ = 17.1), 5.69 (ddd, vinylic H_{gem}), 6.65 (dd, H_8, $J_{7,8}$ = 9.2, $J_{5,8}$ = 2.0), 7.54 (m, COPh, H_m), 7.66 (m, COPh, H_p), 7.96 (m, H_5, H_7, and COPh, H_o). Anal. Found: C, 70.15; H, 5.19, N, 9.08.

Reaction of 2-[(4-Chlorophenyl)amino]-2-methoxy-1-phenylethanone (5b) with 1,3-Butadiene. Crystallization from EtOH of the reaction mixture gave 77% of (2α,4α)-2-benzoyl-6-chloro-4-ethenyl-1,2,3,4-tetrahydroquinoline (**7b**): mp 115–116 °C; ^{1}H NMR δ 1.54 (dt, $H_{3'}$, $J_{3,3'}$ = 12.8, $J_{2,3'} = J_{3',4}$ = 11.9), 2.33 (ddd, H_3, $J_{3,4}$ = 4.9, $J_{2,3}$ = 2.9), 3.65 (br ddd, H_4, $J_{4,gem}$ = 8.8), 5.02 (dd, H_2), 5.25 (dd, vinylic H_{trans}, $J_{trans,gem}$ = 9.8, $J_{trans,cis}$ = 1.8), 5.29 (ddd, vinylic H_{cis}, $J_{cis,gem}$ = 17.1, $J_{4,cis}$ = 0.6), 5.66 (ddd, vinylic H_{gem}), 6.64 (H_8, $J_{7,8}$ = 7.9, $J_{5,8}$ = 1.1), 7.02 (ddd, H_7, $J_{5,7}$ = 2.4, $J_{4,7}$ = 0.8), 7.04 (d, H_5), 7.51 (m, COPh, H_m), 7.63 (m, COPh, H_o),

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7.94 (m, COPh, H_p). Anal. Calcd for $C_{18}H_{16}ClNO$: C, 72.26; H, 5.42; Cl, 11.91; N, 4.70. Found: C, 72.85; H, 5.52; Cl, 11.68; N, 4.65.

Reaction of 5a with 2-Methyl-1,3-butadiene. Chromatographic separation (toluene as eluant) of the reaction mixture afforded in order 2% of 3-[(4-nitrophenyl)amino]-5-ethenyltetrahydro-2-methoxy-5-methyl-2-phenylfuran (**9**), 5% of stereoisomer **10**, and 65% of 6-benzoyl-1,2,5,6-tetrahydro-4-methyl-1-(4-nitrophenyl)pyridine (**8a**).

8a: mp 156–157 °C (EtOH); ^{1}H NMR δ 1.68 (br s, Me), 2.53 (dq when {Me}, $H_{5'}$, $J_{5,5'}$ = 17.1, $J_{5',6}$ = $J_{2,5'}$ = $J_{2',5'}$ = 1.5), 2.86 (ddq when {Me}, H_5, $J_{5,6}$ = 7.6, $J_{3,5}$ = $J_{2,5}$ = $J_{2',5}$ = 2.9), 4.06 and 4.14 (AB system, split in td when {Me}, H_2 and $H_{2'}$, $J_{2,2'}$ = 16.5, $J_{2,3}$ = 2.9, $J_{2',3}$ = 2.9), 5.59 (q when {Me}, H_3), 5.72 (dd, H_6), 6.77 (m, p-$NO_2C_6H_4$, H_o), 7.51 (m, COPh, H_m), 7.63 (m, COPh, H_p), 7.83 (m, COPh, H_o), 8.10 (m, p-$NO_2C_6H_4$, H_m). Anal. Calcd for $C_{19}H_{18}N_2O_3$: C, 70.79; H, 5.63; N, 8.69. Found: C, 70.56; H, 5.64; N, 8.43.

9: mp 185–186 °C (EtOH); ^{1}H NMR δ 1.52 (s, Me), 2.10 (dd, H_4 or $H_{4'}$, $J_{4,4'}$ = 12.2, $J_{3,4}$ = 11.0), 2.38 (dd, $H_{4'}$ or H_4, $J_{3,4'}$ = 7.3), 3.12 (s, OMe), 3.96 (dd, H_3), 5.05 (dd, H_{trans}, $J_{trans,gem}$ = 10.7, $J_{cis,trans}$ = 0.9), 5.20 (dd, H_{cis}, $J_{cis,gem}$ = 17.4), 6.05 (dd, H_{gem}), 6.32 (m, p-$NO_2C_6H_4$, H_o), 7.24 (m, COPh, H_m and H_p), 7.41 (m, COPh, H_o), 7.92 (m, p-$NO_2C_6H_4$, H_m). Anal. Calcd for $C_{20}H_{22}N_2O_4$: C, 67.78; H, 6.26; N, 7.90. Found: C, 67.52; H, 6.24; N, 7.86.

10: mp 118–119 °C (EtOH); ^{1}H NMR δ 1.56 (s, Me), 2.07 (dd, H_4 or $H_{4'}$, $J_{4,4'}$ = 12.2, $J_{3,4}$ = 11.0), 2.60 (dd, $H_{4'}$ or H_4, $J_{3,4'}$ = 7.3), 3.20 (s, OMe), 3.93 (dd, H_3), 5.16 (dd, H_{trans}, $J_{trans,gem}$ = 10.7, $J_{cis,trans}$ = 1.2), 5.42 (dd, H_{cis}, $J_{cis,gem}$ = 17.1), 6.10 (dd, H_{gem}), 6.38 (m, p-$NO_2C_6H_4$, H_o), 7.31 (m, COPh, H_m and H_p), 7.52 (m, COPh, H_o), 7.98 (m, p-$NO_2C_6H_4$, H_m). Anal. Found: C, 67.70; H, 6.31; N, 7.68.

Reaction of 5b with 2-Methyl-1,3-butadiene. Chromatographic separation ($CHCl_3$ as eluant) of the reaction mixture afforded 72% of 6-benzoyl-1,2,5,6-tetrahydro-4-methyl-1-(4-chlorophenyl)pyridine (**8b**): mp 115–116 °C; ^{1}H NMR δ 1.68 (s, Me), 2.44 (dq when {Me} $H_{5'}$, $J_{5,5'}$ = 17.1, $J_{5',6}$ = $J_{2,5'}$ = $J_{2',5'}$ = 1.5), 2.79 (ddq when {Me}, H_5, $J_{5,6}$ = 7.7, $J_{3,5}$ = $J_{2,5}$ = $J_{2',5}$ = 2.8), 3.97 (complex m, H_2 and $H_{2'}$), 5.51 (dd, H_6), 5.57 (q when {Me}, H_3, $J_{2,3}$ = $J_{2',3}$ = 2.9), 6.76 (m, p-ClC_6H_4, H_m), 7.15 (m, p-ClC_6H_4, H_o), 7.47 (m, COPh, H_m), 7.59 (m, COPh, H_p), 7.92 (m, COPh, H_o). Anal. Calcd for $C_{19}H_{18}ClNO$: C, 73.19; H, 5.82; Cl, 11.37; N, 4.49. Found: C, 72.93; H, 5.89; Cl, 11.43; N, 4.51.

Reaction of 5a with 2,3-Dimethyl-1,3-butadiene. Crystallization from EtOH of the reaction mixture afforded 75% of 6-benzoyl-1,2,5,6-tetrahydro-3,4-dimethyl-1-(4-nitrophenyl)-pyridine (**12a**): mp 165–166 °C; ^{1}H NMR δ 1.61 (br s, Me_3), 1.74 (br s, Me_4), 2.51 (br d, dq when {Me_4}, $H_{5'}$, $J_{5,5'}$ = 17.1, $J_{5',6}$ = $J_{2,5'}$ = $J_{2',5'}$ = 1.6), 2.89 (complex m, dtq when {Me_4}, H_5, $J_{5,6}$ = 7.6, $J_{2,5}$ = $J_{2',5}$ = 2.5, $J_{3,5}$ = 1.2), 3.95 (br s, H_2 and $H_{2'}$), 5.65 (dd, H_6), 6.78 (m, p-$NO_2C_6H_4$, H_m), 7.51 (m, COPh, H_m), 7.63 (m, COPh, H_p), 7.93 (m, COPh, H_o), 8.11 (m, p-$NO_2C_6H_4$, H_o). Anal. Calcd for $C_{20}H_{20}N_2O_3$: C, 71.41; H, 5.99; N, 8.32. Found: C, 71.38; H, 6.04; N, 8.40.

Reaction of 5b with 2,3-Dimethyl-1,3-butadiene. Chromatographic separation ($CHCl_3$ as eluant) of the reaction mixture afforded 88% of 6-benzoyl-1,2,5,6-tetrahydro-3,4-dimethyl-1-(4-chlorophenyl)pyridine (**12b**): mp 102–103 °C; ^{1}H NMR δ 1.61 (br s, Me_3), 1.70 (br s, Me_4), 2.43 (br d, dq when {Me_4}, $H_{5'}$, $J_{5,5'}$ = 17.1, $J_{5',6}$ = $J_{2,5'}$ = $J_{2',5'}$ = 1.6), 2.82 (complex d, dtq when {Me_4}, H_5, $J_{5,6}$ = 7.6, $J_{2,5}$ = $J_{2',5}$ = 2.6, $J_{3,5}$ = 1.1), 3.78 and 3.90 (AB system split in t when {Me_3}, H_2 and $H_{2'}$, $J_{2,2'}$ = 15.9), 5.46 (dd, H_6), 6.76 (m, p-ClC_6H_4, H_m), 7.15 (m, p-ClC_6H_4, H_o), 7.47 (m, COPh, H_m), 7.58 (m, COPh, H_p), 7.92 (m, COPh, H_o). Anal. Calcd for $C_{20}H_{20}ClNO$: C, 73.72; H, 6.19; Cl, 10.88; N, 4.30. Found: C, 73.53; H, 6.14; Cl, 11.08; N, 4.28.

Reaction of 5a with Cyclopentadiene. The title reaction afforded, after crystallization from EtOH of the reaction mixture, 88% of (3aα,4β,9bβ)-4-benzoyl-3a,4,5,9b-tetrahydro-8-nitro-3*H*-cyclopenta[*c*]quinoline (**14a**): mp 189–192 °C; ^{1}H NMR δ 1.90 (dddd, $H_{3'}$, $J_{3,3'}$ = 16.2 $J_{3',3a}$ = 8.9, $J_{2,3'}$ = 2.5, $J_{1,3'}$ = 1.6), 2.30 (ddq, H_3, $J_{3,3a}$ = 8.9, $J_{1,3}$ = $J_{2,3}$ = $J_{3,9b}$ = 2.5), 3.38 (qd, H_{3a}, $J_{3a,9b}$ = 9.0, $J_{3a,4}$ = 3.7), 4.23 (complex d, H_{9b}), 5.20 (d, H_4), 5.59 (complex d, H_2, $J_{1,2}$ = 5.8), 5.82 (dtd, H_1, $J_{1,9b}$ = 2.8), 6.65 (dd, H_6, $J_{6,7}$ = 9.2, $J_{6,9}$ = 1.2), 7.54 (m, COPh, H_m), 7.66 (m, COPh, H_p), 7.88 (m, H_7, H_9, and COPh, H_o). Anal. Calcd for $C_{19}H_{16}N_2O_3$: C, 71.24; H, 5.03; N, 8.74. Found: C, 71.31; H, 4.94; N, 8.76.

When the reaction was carried out at −20 °C for 8 h with menthoxyaluminum dichloride as catalyst, it was possible to isolate from unreacted **5a** after usual workup and chromatography (toluene as eluant) 8% of 3-*exo*-benzoyl-2-(4-nitrophenyl)-2-azabicylo[2.2.1]hept-5-ene (**15a**): mp 148–150 °C; ^{1}H NMR δ 1.66 (br dt, H_{7a}, $J_{7s,7a}$ = 8.8, $J_{1,7a}$ = $J_{4,7a}$ = 1.6) 2.17 (dt, H_{7s}, $J_{1,7s}$ = $J_{4,7s}$ = 1.8), 3.49 (complex m, H_4), 4.28 (s, H_3), 4.99 (complex m, H_1), 6.48 (m, p-$NO_2C_6H_4$, H_m), 6.60 and 6.63 (br AB system, H_5 and H_6, $J_{5,6}$ = 5.1), 7.58 (m, COPh, H_m), 7.70 (m, COPh, H_p), 8.03 (m, p-$NO_2C_6H_4$, H_o), 8.13 (m, COPh, H_o). Anal. Found: C, 71.04; H, 5.07; N, 8.71.

Reaction of 5b with Cyclopentadiene. The title reaction afforded, after crystallization from EtOH of the reaction mixture, 87% of (3aα,4β,9bβ)-4-benzoyl-8-chloro-3a,4,5,9b-tetrahydro-3*H*-cyclopenta[*c*]quinoline (**14b**): mp 178–179 °C; ^{1}H NMR δ 1.89 (dddd, $H_{3'}$, $J_{3,3'}$ = 16.2, $J_{3',3a}$ = 8.8, $J_{2,3'}$ = 2.8, $J_{1,3'}$ = 1.8), 2.37 (ddq, H_3, $J_{3,3a}$ = 8.9, $J_{1,3}$ = $J_{2,3}$ = $J_{3,9b}$ = 2.7), 3.30 (qd, H_{3a}, $J_{3a,9b}$ = 9.0, $J_{3a,4}$ = 3.4), 4.14 (complex d, H_{9b}), 5.02 (d, H_4), 5.57 (complex d, H_2, $J_{1,2}$ = 5.6), 5.69 (dtd, H_1, $J_{1,9b}$ = 2.7), 6.61 (d, H_6, $J_{6,7}$ = 8.5), 6.95 (dd, H_7, $J_{7,9}$ = 2.5), 7.00 (dd, H_9, $J_{9,9b}$ = 0.9), 7.50 (m, COPh, H_m), 7.62 (m, COPh, H_p), 7.92 (m, COPh, H_o). Anal. Calcd for $C_{19}H_{16}ClNO$: C, 73.69; H, 5.22; Cl, 11.49; N, 4.46. Found: C, 73.16; H, 5.08; Cl, 11.41; N, 4.26.

Reaction of 5a with 1,3-Cyclohexadiene. After chromatography (toluene as eluant) the title reaction gave in order 28% of (6α,6aβ,10aβ)-6-benzoyl-5,6,6a,7,8,10a-hexahydro-2-nitrophenanthridine (**18a**), 57% of 3-*exo*-benzoyl-2-(4-nitrophenyl)-2-azabicyclo[2.2.2]oct-5-ene (**16a**), and 13% of 3-*endo*-benzoyl isomer **17a**.

16a: mp 151–152 °C (EtOH); ^{1}H NMR δ 1.24 (complex m, H_{8s}), 1.52 (complex m, H_{7a}), 1.60 (complex m, H_{8a}), 2.27 (complex m, H_{7s}), 3.20 (dq, H_4, $J_{4,5}$ = 7.9, $J_{3,4}$ = $J_{4,8s}$ = $J_{4,8a}$ = 2.9), 4.80 (dd, H_3, $J_{3,8a}$ = 1.5), 4.86 (dt, H_1, $J_{1,6}$ = 7.1, $J_{1,7s}$ = $J_{1,7a}$ = 2.7), 6.45 (m, p-$NO_2C_6H_4$, H_m), 6.60 and 6.63 (split AB system, H_5 and H_6, $J_{5,6}$ = 7.3), 7.57 (m, COPh, H_m), 7.69 (m, COPh, H_p), 8.02 (m, p-$NO_2C_6H_4$, H_o), 8.10 (m, COPh, H_o). Anal. Calcd for $C_{20}H_{18}N_2O_3$: C, 71.84; H, 5.43; N, 8.38. Found: C, 71.90; H, 5.46; N, 8.24.

17a: mp 210–211 °C (MeOH); ^{1}H NMR δ 1.51 (complex m, H_{7a}), 1.59 (complex m, H_{8a}), 1.90 (complex m, H_{8s}), 2.11 (complex m, H_{7s}), 3.33 (complex m, H_4), 4.90 (dt, H_1, $J_{1,6}$ = 6.6, $J_{1,7s}$ = $J_{1,7a}$ = 1.5), 4.99 (d, H_3, $J_{3,4}$ = 2.4), 6.15 (ddd, H_5, $J_{5,6}$ = 7.8, $J_{4,5}$ = 6.7, $J_{5,8s}$ = 0.9), 6.44 (m, p-$NO_2C_6H_4$, H_m), 6.66 (ddd, H_6, $J_{6,7s}$ = 1.5), 7.55 (m, COPh, H_m), 7.67 (m, COPh, H_p), 8.04 (m, p-$NO_2C_6H_4$, H_o and COPh, H_o). Anal. Found: C, 71.48; H, 5.50; N, 8.27.

18a: mp 165–166 °C (MeOH); ^{1}H NMR δ 1.12 (complex d, H_7, $J_{7,7'}$ = 13.1), 1.29 (dm, $H_{7'}$), 1.85 (complex m, H_8), 1.99 (complex m, $H_{8'}$), 2.57 (ddt, H_{6a}, $J_{6a,7'}$ = 12.5, $J_{6a,10a}$ = 5.2, $J_{6,6a}$ = $J_{6a,7}$ = 3.2), 3.77 (br t, H_{10a}, $J_{10,10a}$ = 5.8), 5.20 (d, H_6), 5.79 (complex d, H_9, $J_{9,10}$ = 10.1, $J_{8,9}$ = $J_{8',9}$ = 3.7), 6.29 (ddt, H_{10}, $J_{8,10}$ = $J_{8',10}$ = 2.1), 6.61 (d, H_4, $J_{3,4}$ = 8.9), 7.54 (m, COPh, H_m), 7.67 (m, COPh, H_p), 7.93 (m, COPh, H_o), 7.94 (dd, H_3, $J_{1,3}$ = 2.5), 8.09 (dd, H_1, $J_{1,10}$a = 1.2). Anal. Found: C, 71.66; H, 5.41; N, 8.23.

Reaction of 5b with 1,3-Cyclohexadiene. After chromatography (toluene as eluant) the title reaction gave in order 34% of (6α,6aβ,10aβ)-6-benzoyl-2-chloro-5,6,6a,7,8,10a-hexahydrophenanthridine (**18b**), 44% of 3-*exo*-benzoyl-2-(4-chlorophenyl)-2-azabicyclo[2.2.2]oct-5-ene (**16b**), and 15% of 3-*endo*-benzoyl isomer **17b**.

16b: mp 144–145 °C (EtOH); ^{1}H NMR δ 1.14 (complex m, H_{8a}), 1.50 (complex m, H_{7a}), 1.57 (complex m, H_{8s}), 2.25 (complex m, H_{7s}), 3.08 (dqd, H_4, $J_{4,5}$ = 6.7, $J_{3,4}$ = $J_{4,8s}$ = $J_{4,8a}$ = 2.8, $J_{4,6}$ = 1.4), 4.49 (dd, H_3, $J_{3,8a}$ = 1.4), 4.62 (dtd, H_1, $J_{1,6}$ = 5.2, $J_{1,7s}$ = $J_{1,7a}$ = 3.0, $J_{1,5}$ = 1.6), 6.49 (m, p-ClC_6H_4, H_m), 6.52 (ddd, H_5, $J_{5,6}$ = 8.1), 6.64 (ddd, H_6), 7.07 (m, p-ClC_6H_4, H_o), 7.54 (m, COPh, H_m), 7.65 (m, COPh, H_p), 8.09 (m, COPh, H_o). Anal. Calcd for $C_{20}H_{18}ClNO$: C, 74.18; H, 5.60; Cl, 10.95; N, 4.33. Found: C, 74.07; H, 5.58; Cl, 10.90; N, 4.29.

17b: mp 154–155 °C (EtOH); ^{1}H NMR δ 1.44 (complex m, H_{7a}), 1.52 (complex m, H_{8a}), 1.82 (complex m, H_{8s}), 2.14 (complex m, H_{7s}), 3.20 (complex m, H_4), 4.69 (br dt, H_1, $J_{1,6}$ = 6.6, $J_{1,7s}$ = $J_{1,7a}$ = 1.5), 4.73 (d, H_3, $J_{3,4}$ = 2.4), 6.11 (ddd, H_5, $J_{5,6}$ = 8.1, $J_{4,5}$ = 6.7, $J_{5,8s}$ = 0.9), 6.43 (m, p-ClC_6H_4, H_m), 6.68 (ddd, H_6, $J_{6,7s}$ = 1.8), 7.09 (m, p-ClC_6H_4, H_o), 7.51 (m, COPh, H_m), 7.63 (m, COPh, H_p), 8.04 (m, COPh, H_o). Anal. Found: C, 74.12; H, 5.54; Cl, 10.88; N, 4.30.

18b: mp 170-171 °C (MeOH); ^{1}H NMR δ 1.12 (dm, H_7, $J_{7,7'}$ = 13.1), 1.34 (dm, $H_{7'}$), 1.81 (complex m, H_8), 1.98 (complex m, $H_{8'}$), 2.43 (ddt, H_{6a}, $J_{6a,7'}$ = 12.5, $J_{6a,10a}$ = 5.4, $J_{6,6a}$ = $J_{6a,7}$ = 3.0), 3.73 (br t, H_{10a}, $J_{10,10a}$ = 5.8), 4.75 (br s, H_5), 5.11 (d, H_6), 5.73 (complex d, H_9, $J_{9,10}$ = 10.1, $J_{8,9}$ = $J_{8',9}$ = 3.6), 6.19 (ddt, H_{10}, $J_{8,10}$ = $J_{8',10}$ = 2.4), 6.61 (d, H_4, $J_{3,4}$ = 8.5), 6.97 (dd, H_3, $J_{1,3}$ = 2.4), 7.11 (dd, H_1, $J_{1,10a}$ = 1.1), 7.51 (m, COPh, H_m), 7.63 (m, COPh, H_p), 7.93 (m, COPh, H_o). Anal. Found: C, 74.11; H, 5.59; Cl, 11.07; N, 4.23.

Cyclodehydration Reactions of Tetrahydropyridines 8a,b and 12a,b. A solution of 0.1 g of the tetrahydropyridine derivative and 1 equiv of BF_3·Et_2O in 10 mL of toluene was heated at reflux for 4 h. One more equivalent of Lewis acid was added to the cold solution, which was further refluxed for 4 h. The solution was then poured in 20 mL of 5% aqueous $NaHCO_3$. The organic layer was washed with water, dried, and concentrated in vacuo. The residue was chromatographed (toluene as eluant).

From **8a**, 21% of 6,7-dihydro-8-methyl-2-nitro-10-phenylpyrido[1,2-*a*]indole (**11a**): mp 195-197 °C (EtOH); ^{1}H NMR δ 2.03 (dt, Me_8, $J_{Me,9}$ = 1.5, $J_{Me,7}$ = 1.1), 2.66 (tdq, H_7, $J_{6,7}$ = 7.1, $J_{7,9}$ = 1.3), 4.23 (t, H_6), 6.54 (sextet, H_9), 7.36 (dd, H_4, $J_{3,4}$ = 9.0, $J_{1,4}$ = 0.5), 7.37 (m, Ph, H_p), 7.52 (m, Ph, H_o and H_m), 8.12 (dd, H_3, $J_{1,3}$ = 2.2), 8.67 (dd, H_1). Anal. Calcd for $C_{19}H_{16}N_2O_2$: C, 74.99; H, 5.30; N, 9.21. Found: C, 74.68; H, 5.28; N, 9.05.

From **8b**, 64% of 2-chloro-6,7-dihydro-8-methyl-10-phenylpyrido[1,2-*a*]indole (**11b**): mp 151 °C (EtOH); ^{1}H NMR δ 1.99 (dt, Me_8, $J_{Me,9}$ = 1.5, $J_{Me,7}$ = 1.2), 2.60 (tdq, H_7, $J_{6,7}$ = 7.2, $J_{7,9}$ = 1.3), 4.12 (t, H_6), 6.49 (sextet, H_9), 7.14 (dd, H_3, $J_{3,4}$ = 8.5, $J_{1,3}$ = 1.8), 7.17 (dd, H_4, $J_{1,4}$ = 0.9), 7.35 (m, Ph, H_p), 7.48 (m, Ph, H_o and H_m), 7.65 (dd, H_1). Anal. Calcd for $C_{19}H_{16}ClN$: C, 77.68; H, 5.49; Cl, 12.07; N, 4.77. Found: C, 77.36; H, 5.42; Cl, 12.05; N, 4.72.

From **12a**, 21% of 6,9-dihydro-7,8-dimethyl-2-nitro-10-phenylpyrido[1,2-*a*]indole (**13a**): mp 197-198 °C (EtOH); ^{1}H NMR δ 1.87 and 1.90, (2 br s, Me_7 and Me_8), 3.63 (br s, t when {Me}, H_9, $J_{6,9}$ = 3.6), 4.58 (br s, t when {Me}, H_6), 7.37 (dd, H_4, $J_{3,4}$ = 9.0, $J_{1,4}$ = 0.4), 7.38 (m, Ph, H_p), 7.51 (m, Ph, H_o and H_m), 8.13 (dd, H_3, $J_{1,3}$ = 2.2), 8.68 (dd, H_1). Anal. Calcd for $C_{20}H_{18}N_2O_2$: C, 75.46; H, 5.70; N, 8.80. Found: C, 75.32; H, 5.58; N, 8.72.

From **12b**, 40% of 2-chloro-6,9-dihydro-7,8-dimethyl-10-phenylpyrido[1,2-*a*]indole (**13b**): mp 135-137 °C (EtOH); ^{1}H NMR δ 1.84 (br s, Me_7 and Me_8), 3.57 (br s, t when {Me}, H_9, $J_{6,9}$ = 3.7), 4.46 (br s, t when {Me}, H_6), 7.14 (dd, H_3, $J_{3,4}$ = 8.5 $J_{1,3}$ = 2.1), 7.23 (d, H_4), 7.28 (m, Ph, H_p), 7.48 (m, Ph, H_o and H_m), 7.70 (d, H_1). Anal. Calcd for $C_{20}H_{18}ClN$: C, 78.04; H, 5.89; Cl, 11.52; N, 4.55. Found: C, 78.12; H, 5.78; Cl, 11.48; N, 4.48.

Rearrangements of Azabicyclooctenes 16a,b and 17a,b. A solution of 0.1 g of the azabicyclooctene and 1 equiv of BF_3·Et_2O in 10 mL benzene was refluxed (2 h for chloro derivatives, 8 h for nitro derivatives) and then poured in 20 mL of 5% aqueous $NaHCO_3$. The organic layer was washed with water, dried, and evaporated to dryness. From **16a,b** only **18a,b** were quantitatively formed and identified by NMR spectra. From the reaction of **17a,b**, chromatograhic separation (toluene as eluant) of the crude led to isolation of phenanthridines **18a,b** and **19a,b**.

From **17a**, 83% of (6α,6aα,10aα)-6-benzoyl-5,6,6a,7,8,10a-hexahydro-2-nitrophenanthridine (**19a**) and 13% of 6α,6aβ,10aβ isomer **18a**.

19a: mp 165-166 °C (MeOH); ^{1}H NMR δ 1.69 (dm, H_7, $J_{7,7'}$ = 13.0), 1.86 (complex d, $H_{7'}$), 2.17 (complex m, H_8 and $H_{8'}$), 2.43 (ddt, H_{6a}, $J_{6a,7'}$ = 11.6, $J_{6a,10a}$ = 5.5, $J_{6,6a}$ = $J_{6a,7}$ = 2.7), 3.19 (br t, H_{10a}, $J_{10,10a}$ = 5.5), 4.88 (d, H_6), 4.97 (br s, H_5), 5.80 (complex d, H_9, $J_{9,10}$ = 10.1, $J_{8,9}$ = $J_{8',9}$ = 3.5), 6.14 (ddt, H_{10}, $J_{8,10}$ = $J_{8',10}$ = 2.1), 6.58 (d, H_4, $J_{3,4}$ = 8.9), 7.52 (m, COPh, H_m), 7.64 (m, COPh, H_p), 7.92 (m, COPh, H_o), 7.94 (dd, H_3, $J_{1,3}$ = 2.5), 8.03 (dd, H_1, $J_{1,10a}$ = 1.2). Anal. Calcd for $C_{20}H_{18}N_2O_3$: C, 71.84; H, 5.43; N, 8.38. Found: C, 71.66; H, 5.41; N, 8.33.

From **17b**, 94% of (6α,6aα,10aα)-6-benzoyl-2-chloro-5,6,6a,7,8,10a-hexahydrophenanthridine (**19b**) and 5% of 6α,6aβ,10aβ isomer **18b**.

19b: mp 176-177 °C (MeOH); ^{1}H NMR δ 1.75 (complex m, H_7), 1.82 (complex m, $H_{7'}$), 2.12 (complex m, H_8 and $H_{8'}$), 2.44 (dddd, H_{6a}, $J_{6a,7'}$ = 10.2, $J_{6a,10a}$ = 5.2, $J_{6,6a}$ = 3.9, $J_{6a,7}$ = 3.4), 3.17 (br t, H_{10a}, $J_{10,10a}$ = 5.1), 4.72 (d, H_6), 5.75 (dtd, H_9, $J_{9,10}$ = 9.9, $J_{8,9}$ = $J_{8',9}$ = 3.7, $J_{9,10a}$ = 1.6), 6.01 (ddt, H_{10}, $J_{8,10}$ = $J_{8',10}$ = 2.1), 6.78 (d, H_4, $J_{3,4}$ = 6.6), 6.98 (ddd, H_3, $J_{1,3}$ = 2.4, $J_{3,10a}$ = 0.8), 7.05 (dd, H_1, $J_{1,10a}$ = 1.1), 7.49 (m, COPh, H_m), 7.61 (m, COPh, H_p), 7.93 (m, COPh, H_o). Anal. Calcd for $C_{20}H_{18}ClNO$: C, 74.18; H, 5.60; Cl, 10.95; N, 4.33. Found: C, 74.32; H, 5.56; Cl, 10.89; N, 4.38.

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Registry No. **4a**, 113628-30-1; **4b**, 113628-31-2; **4c**, 113628-32-3; **4d**, 113628-33-4; **5a**, 91851-06-8; **5b**, 91851-05-7; **5c**, 79866-41-4; **6a**, 113628-34-5; **7a**, 113628-35-6; **7b**, 113628-36-7; **8a**, 113628-38-9; **8b**, 113628-39-0; **9**, 113628-37-8; **11a**, 113628-45-8; **11b**, 113628-46-9; **12a**, 113628-40-3; **12b**, 113628-41-4; **13a**, 113628-47-0; **13b**, 113628-48-1; **14a**, 113667-68-8; **14b**, 113667-69-9; **15a**, 113628-42-5; **16a**, 113628-43-6; **16b**, 113628-44-7; **16c**, 113628-49-2; **16d**, 113628-50-5; **17a**, 113667-70-2; **17b**, 113667-71-3; **17c**, 113667-72-4; **17d**, 113667-73-5; **18a**, 107209-59-6; **18b**, 107297-72-3; **18c**, 107209-61-0; **18d**, 107209-60-9; **19a**, 107297-74-5; **19b**, 107297-73-4; CH_2=CHCH=CH_2, 106-99-0; CH_2=$C(CH_3)$CH=CH_2, 78-79-5; CH_2=$C(CH_3)C(CH_3)$=CH_2, 513-81-5; cyclopentadiene, 542-92-7; 1,3-cyclohexadiene, 592-57-4.

Supplementary Material Available: Detailed description of NOE and structural analyses for compounds **4b**, **8b**, **11a**, **13a**, **14a**, **15a**, **16a**, **17a**, **18a**, and **19a** (4 pages). Ordering information is given on any current masthead page.

Regioselective Synthesis of Isoquinuclidin-6-ones. Synthesis of an Ibogamine Intermediate

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Addition of benzeneselenenyl chloride to 5,6-dehydroisoquinuclidines **8** followed by dehydrohalogenation and hydrolysis of the derived vinyl selenides **11** affords isoquinuclidin-6-ones **7** regioselectively. The method has been applied to the synthesis of 7-*syn*-ethylisoquinuclidin-6-one **16**, an intermediate in the synthesis of ibogamine **2a**.

Isoquinuclidin-6-ones **1** have served as key intermediates in several general approaches to the alkaloids *dl*-ibogamine (**2**) and catharanthine (**3**).[3,4] Depending upon the group R of **1**, the versatile carbonyl group has been utilized either

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