The role of potassium hydroxide in the reaction is believed to be the deprotonation of the substrate, while potassium carbonate may serve as a dehydrating agent. The solubilization of both potassium salts may be promoted by PEG-400. In the previously described rhenium carbonyl catalyzed homogeneous oxidation of cyclic ketones, it was proposed that the metal complex is involved in hydroperoxide decomposition by a homolytic process. Under the basic phase-transfer conditions utilized in this investigation, rhenium carbonyl may alternatively promote the reaction of the carbanion with oxygen or the cleavage of the hydroperoxide anion. Irrespective of the mechanistic details, the oxidation of monocyclic ketones to diacids and of bicyclic ketones to keto diacids or hydroxyquinones occurs in high yield, and under remarkably mild conditions (room temperature, 1 atm) using rhenium carbonyl and PEG-400.

Experimental Section

Melting point determinations were made by using a Fisher-Johns apparatus. Proton magnetic resonance spectra were recorded on a Varian XL-300 spectrometer, while an FT-80 instrument was used for carbon-13 spectral determinations. Infrared spectra were recorded on a Perkin-Elmer 783 spectrometer, and a VG-7070E spectrometer was used for mass spectral determinations. Elemental analyses were done by M-H-W Laboratories, Phoenix, AZ. Gas chromatographic determinations were made on a Varian Vista 6000 gas chromatograph (FID detector) equipped with a 2-m 5% Carbowax 20M (or OV-17) on Chromosorb W column.

All of the necessary chemicals were purchased from commercial sources. Solvents were purified by standard methods.

General Procedure for the $Re_2(CO)_{10}$-Catalyzed Oxidation of Ketones Using PEG-400, KOH, and K_2CO_3. The ketone (10 mmol) was added to a stirred mixture of ground potassium hydroxide (40 mmol), ground potassium carbonate (40 mmol), rhenium carbonyl (0.1 mmol), and PEG-400 (3 drops) in 1,2-dimethoxyethane (20 mL). Oxygen was bubbled through the stirred reaction mixture until the ketone was consumed (see Tables I and II for reaction times). The progress of the reaction was monitored by gas chromatography. The reaction mixture was acidified (ice bath) to pH 4 by using 10 N hydrochloric acid and then extracted with ether. The ether extract was dried ($MgSO_4$) and concentrated by rotary evaporation to give the product. Further purification, when necessary, was effected by recrystallization or by silica gel column chromatography.

The same procedure was used with other phase-transfer agents, with the following quantities used: TDA-1, 1.0 mmol; $PhCH_2N(C_2H_5)_3^+Cl^-$ or $(C_4H_9)_4N^+Br^-$, 0.3 mmol.

Except for 5-ketodecane-1,10-dioic acid, all of the products are known compounds and were identified by comparison of melting points and spectral data with literature results and with authentic samples in most instances. Spectral data for **3** ($HOOCCH_2CH_2CH_2CH_2COCH_2CH_2CH_2COOH$): ^1H NMR (DMSO-d_6) δ 1.40 (m, 4 H, protons on C-7, C-8), 1.62 (quintet, 2 H, protons on C-3), 2.14 (2 overlapping triplets, 4 H, protons on C-4, C-6), 2.33–2.43 (2 overlapping triplets, 4 H, protons on C-2, C-9); ^{13}C NMR (DMSO-d_6) δ 18.7, 22.7, 24.0, 32.8, 33.5, 40.9, 41.5 (methylene carbons), 174.1, 174.3 (acid carbonyls), 209.9 (ketone carbon); assignments for both ^1H and ^{13}C NMR were confirmed by appropriate decoupling experiments; chemical-ionization mass spectrum, m/e 217 (M + 1), 199 (M + 1 - H_2O), 181 (M + 1 - $2H_2O$); mp 108–110 °C.

Anal. Calcd for $C_{10}H_{16}O_5$: C, 55.54; H, 7.46. Found: C, 55.71; H, 7.71.

Acknowledgment. We are grateful to British Petroleum, and to the Natural Sciences and Engineering Research Council, for support of this research.

Registry No. Cyclohexanone, 108-94-1; cycloheptanone, 502-42-1; cyclooctanone, 502-49-8; cyclononanone, 3350-30-9; cyclododecanone, 830-13-7; 4-*tert*-butylcyclohexanone, 98-53-3; 1-decalone, 4832-16-0; 1-tetralone, 529-34-0; 2-tetralone, 530-93-8; 1,3-diphenyl-2-propanone, 102-04-5; 1-phenyl-2-butanone, 1007-32-5; adipic acid, 124-04-9; heptanedioic acid, 111-16-0; octanedioic acid, 505-48-6; nonanedioic acid, 123-99-9; dodecanedioic acid, 693-23-2; 3-(1,1-dimethylethyl)hexanedioic acid, 10347-88-3; 5-oxodecanedioic acid, 1468-33-3; 2-hydroxy-1,4-naphthoquinone, 83-72-7; benzoic acid, 65-85-0.

Intramolecular Hetero-Diels–Alder Reaction of Alkylidene- and Benzylidenepyrazolones and Benzylideneisoxazolones. Investigations toward the Conformation of the Transition State[1]

Lutz F. Tietze,* Thomas Brumby,† Martina Pretor, and Gerd Remberg

Institut für Organische Chemie der Universität Göttingen, Tammannstrasse 2, D-3400 Göttingen, FRG

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Stereochemical aspects of the intramolecular hetero-Diels–Alder reaction of hetero dienes are studied. Knoevenagel condensation of aromatic aldehydes **1**, **12**, **15**, and **21** with pyrazolones **8a–h** and isoxazolone **17** gave the corresponding hetero dienes, e.g., **9a–h**, which cyclized to the adducts **10a–h**, **11a–h**, **13**, **14**, **16**, **19**, **20**, **23a–d**, and **24a–d**, respectively. Both *E* and *Z* hetero dienes gave mixtures of cis- and trans-annulated cycloadducts, with the cis-annulated compounds formed preferentially. This suggests an *E*/*Z* isomerization preceding the cycloaddition, which has been proved by UV–vis spectroscopy and HPLC. The tandem-Knoevenagel–Diels–Alder reaction of **1** and **8a** and **8b** was carried out with and without irradiation, yielding the same ratio of cis and trans adducts **10a,b** and **11a,b**. Since it has been shown that the ratio of *E* and *Z* hetero dienes is different in the two sets of experiments, it can be assumed that the cycloadducts are formed only via the *E* hetero diene. Reaction of the aliphatic aldehyde **25** with pyrazolones **8a–d** gave the cycloadducts **28–30** with preferential formation of cis-annulated compounds **28a–d** and **29a–d**, whereas the reaction of **31** and **32** yielded the trans adduct **36** as main product.

The intermolecular Diels–Alder reaction[2] of α,β-unsaturated carbonyls with electron-donor-substituted alkenes such as enol ethers or ketene acetals is a well-established method for the synthesis of dihydropyrans,[2g] whereas alkyl-substituted alkenes do not act as dienophiles. Contrary to this observation, the intramolecular reaction of hetero

† Part of T.B.'s Ph.D. Thesis, Göttingen, 1987.

(1) Intra- and Intermolecular Hetero-Diels–Alder Reactions. 17. Part 16, see ref 12.

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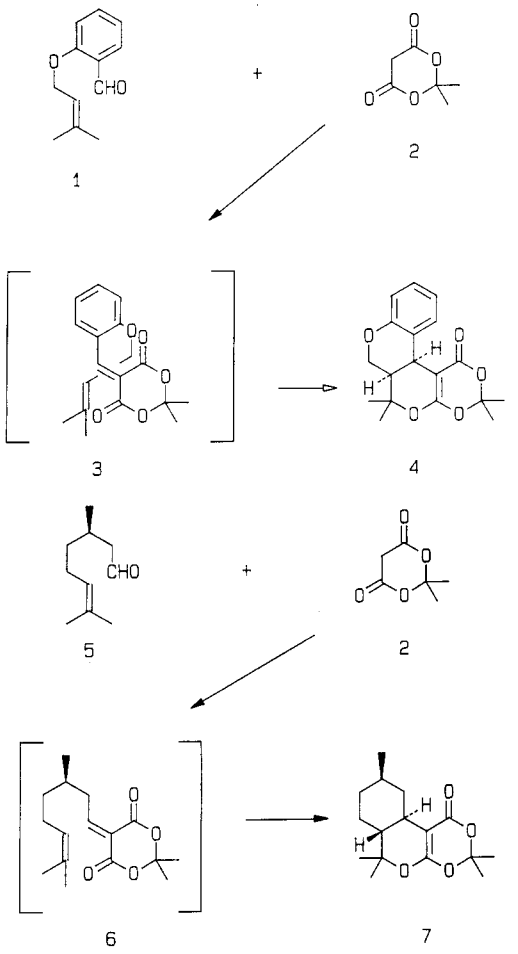
dienes **3** and **6**, which are activated by an electron-acceptor substituent in the α-position, gives excellent yields of the corresponding cycloadducts.[3] Enol ethers were also employed successfully in the cycloaddition of oxa dienes of



this type.[4] The simple preparation of the hetero dienes and the high stereoselectivity of the cycloaddition are the main advantages of this reaction; e.g., the hetero dienes **3** or **6** can easily be obtained by Knoevenagel condensation of aldehydes **1** or **5** with a 1,3-dicarbonyl compound **2** at room temperature with ethylenediammonium diacetate (EDDA) as catalyst.[5] As the result of their high reactivity,

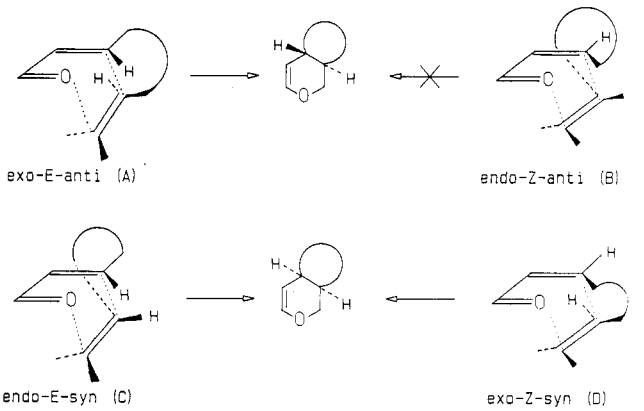


Figure 1. Transition states in the intramolecular hetero-Diels–Alder reaction of oxa dienes.

the hetero dienes are usually formed in situ only. The cycloaddition of **3** yields almost exclusively in a noninduced diastereoselective fashion[6] the cis-annulated polycyclic compound **4**, whereas **6** gives the trans system **7**. Asymmetric induction can be effected by a stereogenic center in the chain[3a–c] or in the dicarbonyl compound,[7] with induced diastereoselectivity, i-de > 90%.

In order to explain the selectivity of this tandem-Knoevenagel–hetero-Diels–Alder reaction and to predict the influence of changes in the system, information about the conformation of the transition state and their controlling factors is needed. In the hetero-Diels–Alder reaction, we have to distinguish between four different transition states (Figure 1): (1) *exo-E-anti* (A), (2) *endo-E-syn* (C), (3) *endo-Z-anti* (B), and (4) *exo-Z-syn* (D). In the formation of trans-annulated products only the *exo-E-anti* transition state (A) can be operative since the *endo-Z-anti* form (B) is not possible for geometrical reasons. However, both the *endo-E-syn* (C) and the *exo-Z-syn* (D) orientations are possible in the transition state leading to the cis-annulated cycloadducts.

Since there is only a formal distinction between *E* and *Z* hetero dienes in **3** and **6**, no information on the conformations of the transition states can be obtained from these systems. We therefore investigated the intramolecular hetero-Diels–Alder reaction of benzylidenepyrazolones[8] and -isoxazolones as well as of alkylidenepyrazolones, although steric and electronic differences surely exist compared to **3** and **6**. In addition, some of the cycloadducts are powerful pesticides.

Results and Discussion

The condensation of **1** with **8a–h** was accomplished in acetonitrile at room temperature by using ethylenediammonium diacetate as catalyst. The benzylidene compounds **9** are thermally stable at room temperature; cyclization, however, to the adducts **10/11** is easily caused by heating to 80 °C or by traces of acid or contact with silica already at room temperature. Therefore, crystallization at low temperature is the only way to obtain pure samples of **9a–g**, usually in moderate yields. Only **9h**,

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Table I. Yields and Diastereomeric Ratios of the Diels–Alder Adducts 10a–h and 11a–h

educts	cycloadducts (yield, %)	cis:trans ratio[a] determined by HPLC	cis:trans ratio[a] determined by ^{13}C NMR	de[b]
1 + 8a	**10a/11a** (94)	4.62 (0.04):1	4.62 (0.90):1	64.4
1 + 8b	**10b/11b** (90)	16.8 (0.9):1	18.0 (2.7):1	88.7
1 + 8c	**10c/11c** (86)	4.49 (0.14):1	4.38 (0.21):1	63.6
1 + 8d	**10d/11d** (80)	44.5 (2.5):1	–	95.6
1 + 8e	**10e/11e** (90)	5.45 (0.20):1	5.42 (0.70):1	69.0
1 + 8f	**10f/11f** (85)	17.0 (1.6):1	18.2 (2.4):1	88.9
1 + 8g	**10g/11g** (83)	3.91 (0.12):1	3.83 (0.69):1	59.3
9h	**10h/11h** (90)[c]	49.0 (0.9):1	–	96.0
	(79)[d]	50.2 (1.1):1	–	96.1

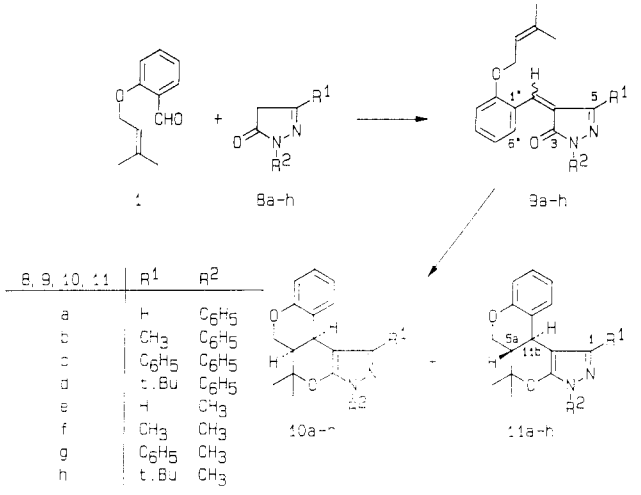
[a] Standard deviation in parentheses, calculated from HPLC data. [b] (10 – 11)/(10 + 11) × 100%. [c] Decalin, 180 °C. [d] Toluene, 110 °C.

Table II. Yields of Hetero Dienes and Cycloadducts in the Reactions of 1, 12, 15, and 21 with 8 and 17

educts	hetero diene (yield, %)	cycloadducts (yield, %)	cis:trans ratio[a]	de
21 + 8a	**22a** (85)	**23a/24a** (74)	3.16 (0.04):1	51.9
21 + 8b	**22b** (79)	**23b/24b** (75)	23.2 (0.1):1	91.7
21 + 8c	**22c** (73)	**23c/24c** (89)	10.2 (0.2):1	82.1
21 + 8d	**22d** (92)	**23d/24d** (78)	10.3 (0.3):1	82.2
12 + 8b	–	**13/14** (89)	24.4 (1.3):1	91.2
15 + 8b	–	**16** (85)	>99:1	>98
1 + 17	**18** (92)	**19/20** (87)	5.20 (0.16)	67.7

[a] Determined by HPLC; standard deviation in parentheses.

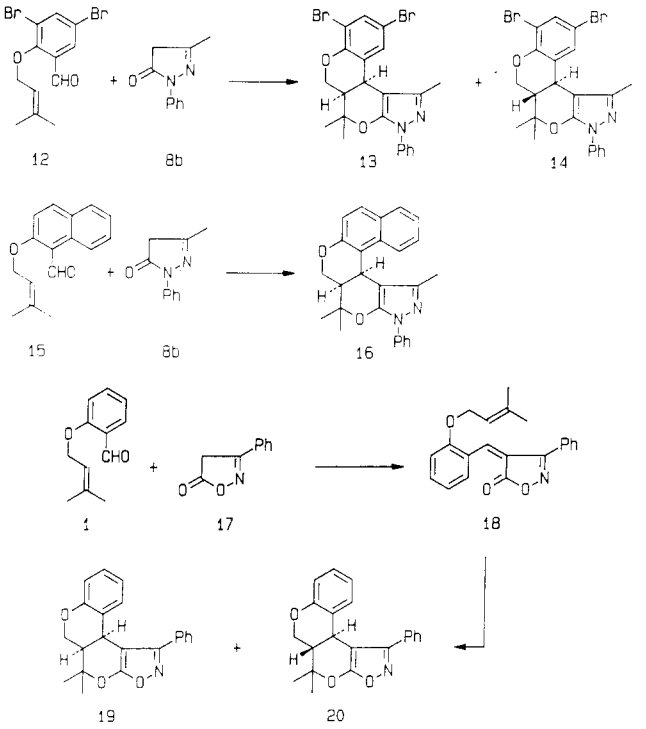
which failed to cyclize under usual conditions, could be purified by flash chromatography.



Because of the low stability of the benzylidenepyrazolones **9**, the compounds were usually formed in situ and converted to the Diels–Alder adducts without isolation by subsequent refluxing of the reaction mixtures for 16–24 h. In contrast to the cycloaddition of **3**, a mixture of cis and trans isomers was usually found in these reactions, the former always predominating. The ratio of **10/11** was determined by ^{13}C NMR spectroscopy and HPLC (Table I).

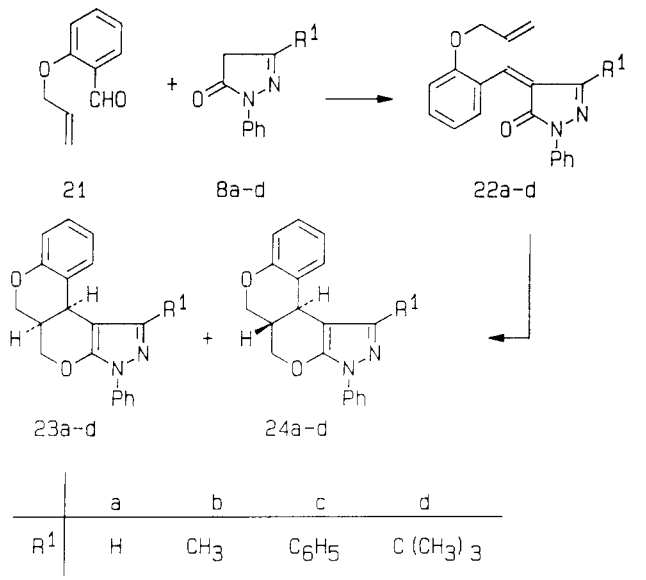
In addition, more highly substituted aldehydes **12** and **15** were also used, giving the cycloadducts **13/14** and **16** in 89% and 85% yield, respectively. With **15**, no transannulated cycloadduct was found. In a similar way, condensation of the phenylisoxazolone **17** with **1** gave **18**, which was cyclized in toluene at 110 °C. The cis-fused adduct **19** was the main product (Table II).

The stability of the benzylidenepyrazolones could be increased by using benzaldehydes **21** without methyl



groups at the olefinic double bond. By this means the HOMO energy of the dienophile is lowered. Since the separation of $HOMO_{dienophile}$ and $LUMO_{diene}$ is most important in these Diels–Alder reactions which belong to the inverse electron demand type, the rate of the cycloaddition is much lower.

The hetero dienes **22** were isolated without difficulty after the usual condensation reaction in high yields. The cycloaddition to give **23a–d** and **24a–d** had to be carried out at 180 °C in decalin. These severe conditions caused a slight decrease in yields compared to the reaction of pyrazolones **8** with **1** (Table II).



The structures of the isolated benzylidene compounds **9**, **18**, and **22** and of the cycloadducts **10**, **11**, **13**, **16**, **19**, and **23** were established by ^1H NMR and ^{13}C NMR spectroscopy. The anisotropic effect of the C=O bond causes a characteristic downfield shift for 6″-H in the *Z* isomer, i.e., in **9**, **18**, and **22**. The signal appears at δ 8, well separated from other absorptions, and is a very convenient indicator of the *Z* geometry of the double bond. For unequivocal proof, an X-ray structure of **9f** was taken.[9] In accord with

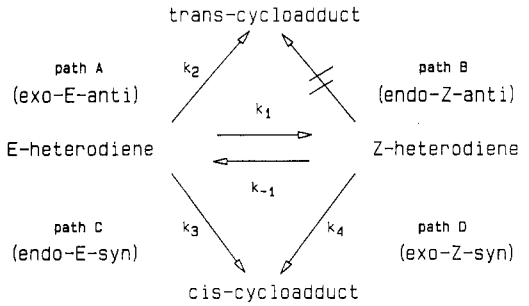


Figure 2. Kinetic scheme for the intramolecular hetero-Diels–Alder reaction of oxa dienes.

previous investigations[10] it was found that the benzylidenepyrazolones **9a,e** and **22a** with hydrogen at C-5 are more stable in the *E* configuration, whereas **9b–d,f–h**, **18**, and **22b–d** show a *Z* configuration in the ground state.

In the cis-fused cycloadducts **10a–h**, **13**, **16**, **19**, and **23a–d**, the signal of 11b–H appears as a broad doublet ($J_{11b,5a}$ = 5–6 Hz) with the couplings to 11-H and sometimes to 6-H_{eq} not being resolved. The latter ($J_{11b,6eq}$ = 1.3–1.5 Hz) is found for **10a,b,e,f**, **13**, and **16**, i.e., for all compounds with hydrogen or methyl at C-1, indicating that 11b-H displays a pseudoequatorial orientation, whereas the coupling for the cycloadducts **10c,d,g,h** and **19** with phenyl or *tert*-butyl at C-1 is not observed. Here a pseudoaxial orientation of 11b-H can be assumed. In addition, these compounds exhibit a pronounced shift difference for the methyl groups at C-5 both in ^{1}H and ^{13}C NMR ($\delta_{eq} - \delta_{ax}$ = 0.29–0.43 and 3.4–5.0 respectively). In the isolated trans-fused adducts, a large coupling between 11b-H and 5a-H is observed, e.g., 11.2 Hz for **11b** and 10.5 Hz for **24b**.

The signal of C-5a in **10a–h** can also serve as indicator of the stereochemistry of the ring junction. In all cis-fused compounds, the resonance is found in the range of δ 37–41, whereas the corresponding signals of the trans isomers appear in the range of δ 44–47.[11]

Configuration and Conformation of the Transition State. Both (*E*)- and (*Z*)-benzylidene compounds yield mixtures of trans- and cis-fused cycloadducts. Since we can assume that the products are obtained via a concerted mechanism,[12] the trans adduct has to be formed via an *exo-E-anti* transition state. The *endo-Z-anti* geometry can be excluded on grounds of unfavorable steric interactions and severe angle strain.[2a,b,e] This means that an interconversion of the (*E*/*Z*)-benzylidene compounds must take place during the reaction. Such an isomerization can be caused by light (light was not excluded from the reaction vessel) or by acid catalysis (EDDA, which was used as catalyst for the condensation, contains small amounts of acetic acid). For the investigations we used **22a** and **22b**, since they do not undergo cycloaddition at room temperature. Irradiation of a solution of pure (*Z*)-**22a** and (*Z*)-**22b** respectively in different solvents like ether, acetonitrile, heptane, or mixtures of heptane and ether with daylight caused isomerization within a few minutes to reach a photostationary state, which is solvent dependent (photostationary state in heptane/ether (3:1): **22a**, *E*/*Z* = 1.1:1; **22b**, *E*/*Z* = 0.7:1). A fast reisomerization occurs after addition of catalytic amounts of ethylenediammonium diacetate in the dark. Without the catalyst

(9) Data of the X-ray analysis will be published elsewhere.
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(12) Tietze, L. F.; Bratz, M.; Machinek, R. *J. Org. Chem.* **1987**, *52*, 1638.

Table III. Ratio of Diastereomers 10a/11a Derived from the Hetero-Diels–Alder Reaction of 9a in Different Solvents and with Different Reaction Temperatures

solvent	rctn temp 80 °C	rctn temp 98 °C	polarity of the solvent
heptane	3.40 (0.02)[b]	3.18 (0.09)	0.00
carbon tetrachloride	4.00 (0.02)		0.18
dibutyl ether	3.94 (0.01)	3.39 (0,04)	0.25
benzene	4.03 (0.03)		0.32
1,2-dichloroethane	4.15 (0.01)		0.49
dioxane	4.41 (0.01)		0.56
acetonitrile	4.91 (0.01)		0.65
acetonitrile/EDDA	5.06 (0.01)		–
isopropyl alcohol	4.82 (0.01)		0.82
acetic acid	4.92 (0.02)		high

[a] Plotting the ratio against the polarity of the solvent[13] gives an approximately linear correlation. [b] Standard deviation in parentheses.

Table IV. Hetero-Diels–Alder Reaction of 9a and 9b in Heptane at 98 °C

educts	ratio 10/11 (std deviation) with irradn	ratio 10/11 (std deviation) without irradn	photostationary state, *E*:*Z*	thermodynamic equilibrium, *E*:*Z*
9a	3.15 (0.04):1	3.18 (0.09):1	2:1	10:1
9b	26.4 (1.4):1	27.2 (1.3):1	1:2	1:5

the isomerization occurs much more slowly (thermodynamic equilibrium in heptane/ether (3:1): **22a**, *E*/*Z* = 10.5:1; **22b**, *E*/*Z* = 1:5). However, the question remains whether path C or path D or both are employed in the formation of the cis-annulated cycloadducts (Figure 2). According to the kinetic scheme, the ratio of cis and trans cycloadducts should depend on the concentration of *E* and *Z* hetero diene, if the rate constant k_3 is small compared to k_2 and k_4 and also if k_2, k_3, and k_4 are of similar magnitude. However, if k_4 is small, the ratio of cis and trans cycloadducts should not be influenced by the amount of *E* and *Z* hetero diene in the reaction mixture.

In two different sets of experiments, solutions of **9a** and **9b** in heptane were irradiated with a mercury high-pressure lamp at 20 °C until the photostationary state was reached and then heated to 98 °C with continued irradiation. At intervals the ratio of the formed cis/trans cycloadducts **10a/11a** and **10b/11b** respectively as well as of the starting material (*E*/*Z*)-**9a** and (*E*/*Z*)-**9b** respectively was determined by HPLC in samples taken from the reaction vessel.

In the second set of similar experiments, solutions of **9a** and **9b** in heptane were heated to 98 °C without irradiation. It shall be noted that not only does the rate of the reaction depend on the solvent used and the reaction temperature but also the ratio of the diastereomers (Table III). Therefore, both sets of experiments—with and without irradiation—were carried out in the same solvent and at the same temperature.

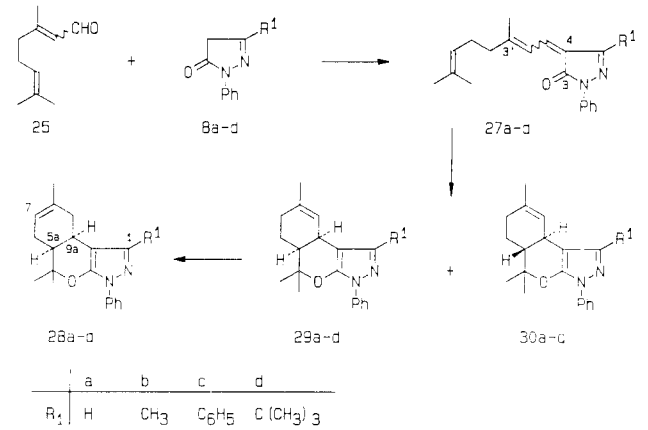
The ratio of *E* and *Z* hetero dienes in the two sets of experiments—with and without irradiation—was found to be different; however, it remained constant for a given experiment, since k_1 and $k_{-1} \gg k_2$, k_3, and k_4. On the other hand, the ratio of the cis and trans cycloadducts **10a/11a** and **10b/11b** respectively was identical in both sets of experiments within experimental error (Table IV). Thus, a measurable participation of path D can be excluded; this means that an *endo-E-syn* transition state has a lower energy than an *exo-Z-syn* transition state in the hetero-Diels–Alder reaction of hetero dienes of type **9** and presumably also of types **3** and **6**.

The conclusions drawn from these experiments are only valid if the hetero-Diels–Alder reactions of **9a** and **9b**

proceed under kinetic control. Therefore, the pure cycloadducts **10a** and **10b** were kept under reaction conditions for 24 h. No isomerization was observed. A further proof for the *E* hetero diene being the intermediate in the cycloaddition of (*Z*)-benzylidenepyrazolones (*Z*)-**9b–h** is the reaction of **9d** with and without irradiation. With irradiation, the reaction goes to completion within 30 min at 98 °C whereas in the dark, the cycloaddition requires 4 h at 110 °C. This result can only be explained by an isomerization of the *Z* to the *E* double bond prior to the cycloaddition, which is fast with irradiation and slow with thermal conditions.

Factors Controlling the Diastereoselectivity. The hitherto described experiments have shown that the intramolecular hetero-Diels–Alder reactions of benzylidenepyrazolones **9** are cis selective due to the lower energy of the *endo-E-syn* transition state. However, it is not understood whether this depends on the aromatic ring system or only on the existence of sp^2 hybrids in the chain and whether their position has an essential effect on the selectivity. We therefore synthesized the alkylidenepyrazolone **27** and the alkylidenedimethylbarbituric acid **33** and investigated the selectivity in the cycloaddition of these compounds.

The condensation of **25** (*E*/*Z* = 2:1 by GLC) with **8a–d** in acetonitrile at 20 °C with ethylenediammonium acetate as catalyst gave **27a–d** in high yields. Compounds **27b–d** were obtained as mixtures of two isomers. Although the



spectral data did not allow an unambiguous assignment of the stereochemistry of the 4,1′ double bond, we assume that it has the *Z* configuration since in benzylidenepyrazolones this geometry is always preferred if $R^1 \neq H$. This view is supported by the fact that **27a** (R^1 = H) was a mixture of three or four isomers (^{13}C NMR). The configuration of the 2′,3′ double bond in **27** was determined from the chemical shifts of C-4′ and the 3′-methyl group. Thus the signals for these carbons are found at δ 41.1–42.0 and 17.7–18.4 respectively in the *E* compounds and at δ 32.9–33.5 and 25.6–25.9 respectively in the *Z* compounds. The observed shift difference of the allylic carbons in the *E*/*Z* isomers is in accord with the known value of 7–9 ppm for analogous alkenes.[14]

In contrast to the benzylidenepyrazolones **9**, the alkylidenepyrazolones **27** are quite stable and had to be heated in refluxing decalin for 1–2.5 h to provide the diastereomeric cycloadducts **29a–d** and **30a–d**. In addition, an isomeric cis-annulated cycloadduct **28** was found, which could arise from **29** via isomerization of the double bond.[15]

(13) Snyder, L. R. *Principles of Adsorption Chromatography*; M. Dekker: New York, 1976; Chapter 8.
(14) Lange, G. L.; Lee, M. *Magn. Reson. Chem.* **1986**, *24*, 656 and references cited therein.

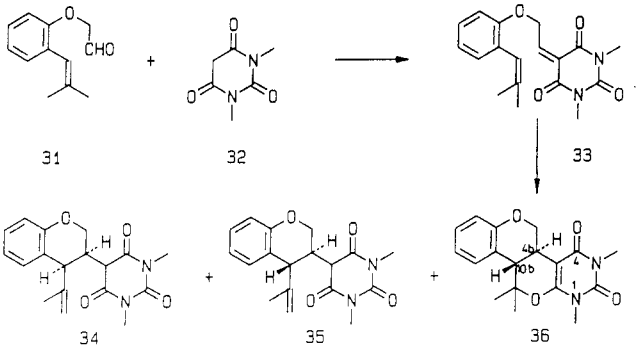
Table V. Yields and Ratios of Cycloadducts 28–30

educt	yield,[a] %	29	30	28	de,[b] %
27a	86	59.9	29.3	10.8[c]	34.4
27b	75	85.79 (0.07)[d]	10.09 (0.07)	4.12 (0.06)	79.8
27c	80	55.89 (0.07)	23.75 (0.07)	20.36 (0.04)	52.5
27d	61	87.20 (0.12)	12.80 (0.13)		74.4

[a] Yields refer to mixtures of **28–30**. [b] For the calculation the sum of **29** and **28** was used. [c] In addition small amounts of four unknown compounds were observed in the chromatogram. [d] Values in parentheses give standard deviations.

The corresponding pyrans which may be formed via an electrocyclic ring closure were not detected.[16]

The ratio of the products **28–30** was determined by HPLC, and the main product **29** was always isolated by crystallization. In the case of **27c**, all compounds were separated by preparative HPLC and their structures determined by spectroscopy. In all other cases, the structure determination of the minor products was done from the product mixtures and their chromatographic behavior. Always the cis-annulated compound **29** was obtained preferentially although the reaction is not as selective as the Diels–Alder reaction of **9** (Table V). Compounds **29** and **30** are obtained under kinetic control, since **29** does not isomerize to **30** under reaction conditions.



In the reaction of **32** and **31**, which was prepared from the known 2-(2-methyl-1-propenyl)phenol[17] in three steps, the alkylidene compound **33** could not be isolated since a fast transformation to 44% of the trans Diels–Alder product **36** and 22% of a 5.2:1 mixture of the diastereomeric ene products **34** and **35** took place already at room temperature. According to the ^{13}C NMR spectra, the amount of the cis-annulated Diels–Alder product is far below 5%.

Again, also **36** is formed in a kinetically controlled fashion, since pure **36** does not isomerize under reaction conditions. The trans-annulated adducts **30** and **36** show a large coupling constant for the hydrogens at the ring junction (e.g., **30a**, $J_{5a,9a}$ = 12 Hz; **36**, $J_{4b,10b}$ = 11 Hz) and an absorption of C-5a and C-4b respectively around δ 45 (e.g., **30c**, δ 46.4; **36**, δ 45.7) whereas in the cis-annulated compounds **28** and **29** the large coupling constant is absent and the absorption of C-5a is found in the range of δ 39.5–40.2.

The experiments show that in the intramolecular hetero-Diels–Alder reaction of 1-oxa 1,3-dienes forming annulated six membered ring systems the hybridization of the atoms in the chain has a significant influence on the selectivity. In compounds with a double bond conjugated

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(16) Tietze, L. F.; v.Kiedrowski, G.; Berger, B. *Synthesis* **1982**, *683* and references cited therein.
(17) (a) Oki, M.; Iwamur, H. *Bull. Chem. Soc. Jpn.* **1966**, *39*, 470. (b) Shulgin, A. T.; Baker, A. W. *J. Am. Chem. Soc.* **1959**, *81*, 4524.

to the hetero diene as in **9a–h** and **27a–d**, the cis-annulated adducts are formed preferentially, whereas in hetero dienes with double bonds at other positions like **33**, the selectivity does not differ from the results with aldehydes, which have only sp^3 hybrids in the chain. In the latter case, the trans adduct is formed nearly exclusively.[2h] These results can be explained nicely if one assumes that the reactions are goverened first by stereoelectronic and secondly by steric effects.[18] Thus the dienophile should approach the diene along a trajectory with an angle of approximately 109°.[19] Taking this premise into account, Dreiding models show that in an *endo-E-syn* transition state the planes of the pyrazolone and the aryl group or the double bond in hetero dienes **9** and **27** respectively are perpendicular to each other. In an *exo-E-anti* transition state, an angle of 50–60° would result. Thus, in the latter case a strong steric interaction between substituents at C-5 (R^1) and the phenyl group or substituents at C-2′ in **9** and **27** respectively would exist, causing a cis selectivity of the Diels–Alder reaction via an *endo-E-syn* transition state. This is in agreement with the high selectivity in the transformations of **9d** as well as **15** and **8b**.

Dreiding models of **33** show that there is no severe steric hindrance in the *exo-E-anti* and the *endo-E-syn* transition states leading to **36**; however, in the *endo-E-syn* transition state a favorable approach of the dienophile from the front side along a 109° trajectory is not possible for geometrical reasons.

Experimental Section

Instrumentation. Proton NMR spectra were recorded with Varian XL-200, XL-100, HA-100, and EM-360A spectrometers and ^{13}C NMR spectra with Varian XL-200 and FT-80A spectrometers. Multiplicities were determined with the APT pulse sequence. Chemical shifts are given in δ units relative to internal TMS with the following abbreviations: s = singlet, d = doublet, t = triplet, q = quartet, mc = multiplet centered, br = broad, ax. = axial, eq = equatorial.[20] Mass spectra were measured on a Varian MAT 311A instrument (70 eV), with high resolution of the molecular ion routinely determined on a Varian MAT 731 instrument (70 eV). Infrared spectra (KBr, cm^{-1}) were recorded with a Perkin-Elmer 297 instrument. UV–vis spectra (MeCN, λ_{max}, nm, (log ϵ)) were taken with a Varian Cary 219 spectrometer. Melting points were determined on a Kofler hot stage and are corrected. HPLC analysis was accomplished with a Varian LC 5000 instrument (Vista CDS 401 data system) and a Knauer HPLC system (Merck-Hitachi integrator D 2000) using 25 × 0.4 cm stainless steel columns. Elemental analyses were carried out in the analytical laboratory of the university. Photoreactions were run in a cylindrical vessel of Duran, using a Heraeus TQ 150 high-pressure mercury lamp.

Materials. All solvents were distilled prior to use. Acetonitrile, decalin, and heptane used for the Diels–Alder reactions were filtered through basic alumina (Alumina Woelm B super I, Fa. Woelm Pharma, Eschwege) before use. Products were generally isolated by flash chromatography on SiO_2 (Silica Woelm 32–63 active, Fa. Woelm Pharma, Eschwege). Pyrazolones were prepared according to literature.[8] Hexane, heptane, and acetonitrile for HPLC were purchased from J. T. Baker Chemical Co.; water was bidistilled in quartz vessels. Ether was distilled from KOH, filtered through basic alumina, and passed through a membrane filter (0.2 μm). All HPLC solvents were degassed by application of ultrasound prior to use.

Preparation of 2,4-Dihydro-2-methyl-3*H*-pyrazol-3-one (8e). 4,5-Dihydro-1-methyl-5-oxo-1*H*-pyrazole-4-carboxylic Acid Methyl Ester. A solution of 6.90 g (150 mmol) of methylhydrazine in 10 mL of dry methanol was added dropwise to 23.8 g (140 mmol) of dimethyl (methoxymethylene)malonate in 90 mL of methanol. The initial reaction was exothermic, and the rate of addition was controlled to achieve gentle reflux. Refluxing was continued by heating for an additional 4 h. After cooling to room temperature, the solvent was removed under reduced pressure and the resulting crystalline material thoroughly washed with ether. The yield after drying was 17.3 g (81%). The compound was used for the following transformations without further purification. An analytically pure sample was obtained by crystallization from ethanol: mp 125–126 °C; ^1H NMR (60 MHz, CD_3OD) δ 3.55 (s, 3 H, NCH_3), 3.73 (s, 3 H, OCH_3), 5.18 (s, 1 H, 4-H), 7.57 (s, 1 H, 5-H); ^{13}C NMR (20 MHz, CD_3OD) δ 33.23 (NCH_3), 51.39 (OCH_3), 96.28 (C-4), 139.81 (C-5), 156.48 (C-3), 165.27 ($COOCH_3$). Anal. Calcd for $C_6H_8N_2O_3$: C, 46.15; H, 5.16; N, 17.94. Found: C, 46.32; H, 5.08; N, 17.98.

2-Methyl-2,4-dihydro-3*H*-pyrazol-3-one. KOH (10.0 g) was dissolved in a mixture of 20 mL of water, 20 mL of ethanol, and 10.1 g (65 mmol) of 4,5-dihydro-1-methyl-5-oxo-1*H*-pyrazole-4-carboxylic acid methyl ester. The resulting deep red solution was heated at 100 °C for 2 h. Concentrated hydrochloric acid was added dropwise (CO_2 evolution) with cooling in an ice bath. The resulting acidic mixture (pH 1–2) was heated at 100 °C for 10 h to complete the decarboxylation. The solvent was evaporated to dryness at reduced pressure, and the KCl/product mixture was extracted with ether in a Soxhlet apparatus for 2 days. The pyrazolone crystallized from the ethereal solution. The yield was 5.14 g (81%). An analytically pure sample was obtained by crystallization from an ethyl acetate/methanol mixture: mp 110–111.5 °C; R_f 0.26 (methanol/ethyl acetate, 1:10); ^1H NMR (60 MHz, CD_3OD) δ 3.50 (s, 3 H, NCH_3), 5.46 (s, 2 H, 4-H), 7.27 (s, 1 H, 5-H); ^{13}C NMR (20 MHz, $CDCl_3$) δ 31.96 (NCH_3), 88.51 (C-4, enol), 136.19 (C-5), 157.11 (C-3). Anal. Calcd for $C_4H_6N_2O$: C, 48.97; H, 6.16; N, 28.55. Found: C, 49.12; H, 6.11; N, 28.53.

Synthesis of 5-*tert*-Butyl-2-methyl-2,4-dihydro-3*H*-pyrazol-3-one (8h). Ethyl 4,4-dimethyl-3-oxopentanoate (14.2 g, 83 mmol) was dissolved in 60 mL of dry methanol, and 3.9 g (85 mmol) of methylhydrazine in 30 mL of methanol was added. The mixture was refluxed for 17 h. After cooling to room temperature, the solvent was removed under reduced pressure. The remaining product was thoroughly washed with *tert*-butyl methyl ether and dried in vacuo. The yield was 9.5 g (76%). An analytically pure sample was obtained by crystallization from methanol: mp 148–149 °C; R_f 0.21 (ethyl acetate); ^1H NMR (100 MHz, $CDCl_3$) δ 1.22 (s, 9 H, $C(CH_3)_3$), 3.20 (s, 2 H, 4-H), 3.29 (s, 3 H, NCH_3); ^{13}C NMR (20 MHz, $CDCl_3$) δ 27.91 ($C(CH_3)_3$), 30.73 (NCH_3), 34.35 ($C(CH_3)_3$), 36.88 (C-4), 165.87 (C-5), 172.13 (C-3). Anal. Calcd for $C_8H_{14}N_2O$: C, 62.31; H, 9.15; N, 18.17. Found: C, 62.49; H, 9.08; N, 18.23.

General Procedure I. Diels–Alder Reaction of Aldehydes 1, 12, and 15 with Pyrazolones 8a–h. Pyrazolone (1.00 mmol) and 0.02–0.05 mmol of ethylenediammonium diacetate (EDDA) are suspended in 25 mL of dry acetonitrile, and 1.02–1.30 mmol of aldehyde in 5 mL of acetonitrile is added. Stirring at room temperature for 30 min is followed by refluxing of the mixture for 16–24 h. After removal of the solvent under reduced pressure, the residue is flash chromatographed in the solvent mixture stated (35–40 g of SiO_2). Yields refer to the isolated mixtures of diastereoisomers, which are not separable by this method. A sample is analyzed by HPLC; the main component is obtained as a single isomer by crystallization.

Reaction of 1 with 8a. The diastereomeric mixture, which was obtained after flash chromatography in 90% yield, was separated (SiO_2, 0.063–0.200 mm, ethyl acetate/petroleum ether, 1:10). The purity of the fractions was checked with HPLC.

Fraction 1. (5a*RS*,11b*RS*)-3,5a,6,11b-Tetrahydro-5,5-dimethyl-3-phenyl-5*H*-[1]benzopyrano[4′,3′:4,5]pyrano[2,3-*c*]pyrazole (10a): R_f 0.09 (ethyl acetate/petroleum ether, 1:10);

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(19) Asynchronous transition states have already been proposed for the inter- and intramolecular Diels–Alder reaction in terms of steric hindrance of unsymmetrical addends. (a) Roush, W. R.; Essenfeld, A. P.; Warmus, J. S. *Tetrahedron Lett.* **1987**, *28*, 2447. (b) Brown, F. K.; Houk, K. N. *Tetrahedron Lett.* **1985**, *26*, 2297. (c) Wu, T. C.; Houk, K. N. *Tetrahedron Lett.* **1985**, *26*, 2293. (d) Lin, Y. T.; Houk, K. N. *Tetrahedron Lett.* **1985**, *26*, 2269. (e) Boeckman, R. K., Jr.; Ko, S. S. *J. Am. Chem. Soc.* **1982**, *104*, 1033. (f) Roush, W. R.; Peseckis, S. M. *J. Am. Chem. Soc.* **1981**, *103*, 6696. (g) White, J. D.; Sheldon, B. G. *J. Org. Chem.* **1981**, *46*, 2273. (h) Taber, D. F.; Campbell, C. C.; Grinn, B. P.; Chin, I. C. *Tetrahedron Lett.* **1981**, *22*, 5141.

(20) Additional NMR and HPLC data are available from the thesis of Thomas Brumby, Göttingen 1987, FRG.

mp 128.5–130 °C (*tert*-butyl methyl ether); UV 227 (4.20), 246 (4.22), 272 (sh), 281 (3.65); IR 1600, 1585, 1515, 1260; ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.53 (s, 3 H, 5-CH_3 ax.), 1.63 (s, 3 H, 5-CH_3 eq), 2.22 (ddd, J = 11.1 Hz, J = 5.4 Hz, J = 3.6 Hz, 1 H, 5a-H), 3.83 (t, J = 11.1 Hz, 1 H, 6-H ax.), 4.14 (d, br, J = 5.4 Hz, 1 H, 11b-H), 4.43 (ddd, J = 11.1 Hz, J = 3.6 Hz, J = 1.5 Hz, 1 H, 6-H eq), 6.88 (dd, J = 8.0 Hz, J = 1.3 Hz, 1 H, 8-H), 7.04 (td, J = 7.5 Hz, J = 1.5 Hz, 1 H, 10-H), 7.16–7.34 (m, 2 H, 9-H, 11-H), 7.39–7.56 (m, 4 H, *m*-Ph, *p*-Ph, 1-H), 7.74–7.86 (m, 2 H, *o*-Ph); MS, *m/z* 332 (13, M^+), 289 (3, M – C_3H_7), 264 (31, M – C_5H_8), 263 (14, M – C_5H_9), 247 (2, M – C_5H_9O), 73 (100); exact mass calcd for $C_{21}H_{20}N_2O_2$ 332.1525, found 332.1525.

Fraction 2. (5a*RS*,11b*SR*)-3,5a,6,11b-Tetrahydro-5,5-dimethyl-3-phenyl-5*H*-[1]benzopyrano[4′,3′:4,5]pyrano[2,3-*c*]pyrazole (11a): R_f 0.08 (ethyl acetate/petroleum ether, 1:10); mp 173–175 °C (*tert*-butyl methyl ether); UV 233 (sh), 245 (4.24), 272 (sh), 281 (3.54); IR 1605, 1595, 1515, 1230; ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.32 (s, 3 H, 5-CH_3 ax.), 1.63 (s, 3 H, 5-CH_3 eq), 2.28 (td, J = 11.5 Hz, J = 3.8 Hz, 1 H, 5a-H), 3.96 (d, J = 11.2 Hz, 1 H, 11b-H), 4.03 (dd, J = 10.2 Hz, J = 11.3 Hz, 1 H, 6-H ax.), 4.47 (dd, J = 10.2 Hz, J = 3.9 Hz, 1 H, 6-H eq), 6.89 (dd, J = 8.0 Hz, J = 1.5 Hz, 1 H, 8-H), 7.01 (td, J = 7.5 Hz, J = 1.2 Hz, 1 H, 10-H), 7.16–7.36 (m, 2 H, *p*-Ph, 9-H), 7.40–7.52 (m, 2 H, *m*-Ph), 7.60–7.70 (m, 1 H, 11-H), 7.78–7.84 (m, 2 H, *o*-Ph), 8.29 (s, 1 H, 1-H); MS, *m/z* 332 (76, M^+), 317 (8, M – CH_3), 289 (13, 317 – CO), 264 (100, M – C_5H_8), 263 (76, M – C_5H_9), 247 (9, M – C_5H_9O); exact mass calcd for $C_{21}H_{20}N_2O_2$ 332.1525, found 332.1525.

Elemental analysis of the diastereomeric mixture calcd for $C_{21}H_{20}N_2O_2$: C, 75.88; H, 6.06; N, 8.43. Found: C, 76.17; H, 6.08; N, 8.46.

Reaction of 1 with 8b. (5a*RS*,11b*RS*)-3,5a,6,11b-Tetrahydro-1,5,5-trimethyl-3-phenyl-5*H*-[1]benzopyrano[3′,4′:4,5]pyrano[2,3-*c*]pyrazole (10b): R_f 0.31 (ethyl acetate/petroleum ether, 1:5); reaction time, 18 h; yield, 90%; mp 154–156 °C (*tert*-butyl methyl ether/hexane); UV 229 (4.15), 255.5 (4.29), 264.5 (sh), 275 (sh), 283 (3.73); IR 1595, 1575, 1265, 1130; ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.54 (s, 3 H, 5-CH_3 ax.), 1.57 (s, 3 H, 5-CH_3 eq), 2.17 (s, 4 H, 1-CH_3), 2.18 (ddd, J = 11.0 Hz, J = 4.0 Hz, J = 5.0 Hz, 1 H, 5a-H), 4.10 (t, J = 11.0 Hz, 1 H, 6-H ax.), 4.18 (d, br, J = 5.0 Hz, 1 H, 11b-H), 4.46 (ddd, J = 11.0 Hz, J = 4.0 Hz, J = 1.5 Hz, 1 H, 6-H eq), 6.84 (dd, J = 8.1 Hz, J = 1.1 Hz, 1 H, 8-H), 6.94 (td, J = 7.4 Hz, J = 1.3 Hz, 1 H, 10-H), 7.16–7.50 (m, 5 H, 9-H, 11-H, *p*-Ph and *m*-Ph), 7.70–7.80 (m, 2 H, *o*-Ph); MS, *m/z* 346 (82, M^+), 331 (2, M – CH_3), 303 (12, 331 – CO), 278 (100, M – C_5H_8), 277 (47, M – C_5H_9), 261 (25, M – C_5H_9O), 214 (18, M – $C_8H_8N_2$), 77 (85, $C_6H_5^+$). Anal. Calcd for $C_{22}H_{22}N_2O_2$: C, 76.28; H, 6.40; N, 8.09. Found: C, 76.01; H, 6.66; N, 8.09.

Reaction of 1 with 8c. (5a*RS*,11b*RS*)-3,5a,6,11b-Tetrahydro-5,5-dimethyl-1,3-diphenyl-5*H*-[1]benzopyrano[4′,3′:4,5]pyrano[2,3-*c*]pyrazole (10c): R_f 0.31 (chloroform/ether/petroleum ether, 2:1:8); reaction time, 22 h; yield, 86%; mp 182–183 °C (chloroform); UV 218 (sh), 228 (sh), 274 (4.39), 283 (sh), 328 (3.07); IR 1600, 1570, 1510; ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.29 (s, 3 H, CH_3 ax.), 1.65 (s, 3 H, CH_3 eq), 2.38–2.41 (m, 1 H, 5a-H), 4.20–4.60 (AB part of an ABX system, 2 H, 6-H, δ_A 4.42,δ_B 4.54, J_{AB} = 12 Hz, J_{AX} = 4.2 Hz, J_{BX} = 4.0 Hz), 4.61 (d, J = 6.0 Hz, 1 H, 11b-H), 6.51–6.59 (m, 1 H, 10-H), 6.70–6.75 (m, 1 H, 8-H), 6.86–6.90 (m, 1 H, 11-H), 6.98–7.07 (m, 1 H, 9-H), 7.20–7.50 (m, 6 H, *m*-1-Ph, *m*-3-Ph, *p*-1-Ph, *p*-3-Ph), 7.73–7.89 (m, 4 H, *o*-1-Ph, *o*-3-Ph); MS, *m/e* 408 (31, M^+), 393 (1, M – CH_3), 365 (5, 393 – CO), 340 (77, M – C_5H_8), 339 (72, M – C_5H_9), 323 (4, M – C_5H_9O), 276 (6, M – C_8H_9O), 77 (32, $C_6H_5^+$), 43 (100). Anal. Calcd for $C_{27}H_{24}N_2O_2$: C, 79.39; H, 5.92; N, 6.86. Found: C, 79.57; H, 5.94; N, 6.90.

Reaction of 1 with 8d. (5a*RS*,11b*RS*)-1-*tert*-Butyl-3,5a,6,11b-tetrahydro-5,5-dimethyl-3-phenyl-5*H*-[1]benzopyrano[4′,3′:4,5]pyrano[2,3-*c*]pyrazole (10d): R_f 0.24 (ether/petroleum ether, 1:10); reaction time, 15 h; yield, 80%; mp 149–151 °C (*tert*-butyl methyl ether); UV 235 (sh), 254 (4.25), 274 (sh), 283 (3.37); IR 1600, 1590, 1575, 1515; ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.09 (s, 3 H, 5-CH_3 ax.), 1.37 (s, 9 H, 1-*t*-Bu), 1.51 (s, 3 H, 5-CH_3 eq), 2.40 (td, $J_{11b,5a}$ = $J_{6ax.,5a}$ = 5.0 Hz, $J_{6eq,5a}$ = 6.5 Hz, 1 H, 5a-H), 4.29 (dd, $J_{5a,6ax.}$ = 5.0 Hz, $J_{6eq,6ax.}$ = 12.0 Hz, 1 H, 6-H ax.), 4.34 (d, br, $J_{5a,11b}$ = 5.0 Hz, 1 H, 11b-H), 4.56 (dd, $J_{5a,6eq}$ = 6.5 Hz, $J_{6ax.,6eq}$ = 12.0 Hz, 1 H, 6-H eq), 6.82 (dd, J = 8.0 Hz, J = 1.2 Hz, 1 H, 8-H), 6.93 (td, J = 7.5 Hz, J = 1.5 Hz, 1 H, 10-H), 7.12–7.27 (m, 2 H, 9-H and 11-H), 7.32–7.48 (m, 3 H, *m*- and *p*-Ph), 7.79–7.88 (m, 2 H, *o*-Ph); MS, *m/z* 388 (91, M^+), 373 (3, M – CH_3), 345 (9, 373 – CO), 320 (100, M – C_5H_8), 319 (46, M – C_5H_9), 305 (13, 320 – CH_3), 303 (12, M – C_5H_9O). Anal. Calcd for $C_{25}H_{28}N_2O_2$: C, 77.29; H, 7.26; N, 7.21. Found: C, 77.26; H, 7.21; N, 7.21.

Reaction of 1 with 8e. (5a*RS*,11b*RS*)-3,5a,6,11b-Tetrahydro-3,5,5-trimethyl-5*H*-[1]benzopyrano[4′,3′:4,5]pyrano[2,3-*c*]pyrazole (10e): R_f 0.29 (ether); reaction time, 14 h; yield, 90%; mp 139.5–141.5 °C (ethyl acetate); UV 218 (4.08), 267 (sh), 276 (3.41), 283 (3.14); IR 1592, 1540, 1495, 1260; ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.46 (s, 3 H, 5-CH_3 ax.), 1.58 (s, 3 H, 5-CH_3 eq), 2.17 (ddd, J = 11.0 Hz, J = 3.6 Hz, J = 5.4 Hz, 1 H, 5a-H), 3.62 (s, 3 H, 3-CH_3), 3.74 (t, J = 11.0 Hz, 1 H, 6-H ax.), 4.08 (d, br, J = 5.4 Hz, 1 H, 11b-H), 4.39 (ddd, J = 11.0 Hz, J = 3.6 Hz, J = 1.5 Hz, 1 H, 6-H eq), 6.84 (dd, J = 8.1 Hz, J = 1.4 Hz, 1 H, 8-H), 6.99 (td, J = 7.4 Hz, J = 1.4 Hz, 1 H, 10-H), 7.17 (ddd, J = 8.1 Hz, J = 7.4 Hz, J = 1.7 Hz, 1 H, 9-H), 7.27 (s, 1 H, 1-H), 7.41 (dd, J = 7.4 Hz, J = 1.7 Hz, 1 H, 11-H); MS, *m/z* 270 (60, M^+), 255 (2, M – CH_3), 253 (3, M – OH), 227 (17, 255 – N_2 or CO), 202 (100, M – C_5H_8), 201 (35, M – C_5H_9), 185 (22), 172 (11), 69 (27, $C_5H_9^+$). Anal. Calcd for $C_{16}H_{18}N_2O_2$: C, 71.09; H, 6.71; N, 10.36. Found: C, 70.86; H, 7.01; N, 10.40.

Reaction of 1 with 8f. (5a*RS*,11b*RS*)-3,5a,6,11b-Tetrahydro-1,3,5,5-tetramethyl-5*H*-[1]benzopyrano[4′,3′:4,5]pyrano[2,3-*c*]pyrazole (10f): R_f 0.30 (ether); reaction time, 21 h; yield, 86%; mp 139–140 °C (chloroform/hexane); UV 218 (4.04), 224 (sh), 268 (sh), 284 (3.43); IR 1585, 1575, 1500, 1265, 1230; ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.37 (s, 3 H, 5-CH_3 ax.), 1.42 (s, 3 H, 5-CH_3 eq), 1.96–2.07 (m, 1 H, 5a-H), 2.01 (s, 3 H, 1-CH_3), 3.49 (s, 3 H, 3-CH_3), 3.87 (t, $J_{5a,6ax.}$ = $J_{6eq,6ax.}$ = 11.0 Hz, 1 H, 6-H ax.), 4.02 (d, br, $J_{5a,11b}$ = 5.0 Hz, 1 H, 11b-H), 4.23 (ddd, $J_{6ax.,6eq}$ = 11.0 Hz, $J_{5a,6eq}$ = 4.0 Hz, $J_{11b,6eq}$ = 1.4 Hz, 1 H, 6-H eq), 6.77–6.96 (m, 2 H, 8-H and 10-H), 7.10–7.22 (m, 1 H, 9-H), 7.34–7.42 (m, 1 H, 11-H); MS, *m/z* 284 (54, M^+), 269 (1, M – CH_3), 241 (15, 269 – CO), 216 (100, M – C_5H_8), 215 (81, M – C_5H_9), 199 (39, M – C_5H_9O), 187 (5, 215 – CO), 91 (20, $C_7H_7^+$), 69 (21, $C_5H_9^+$). Anal. Calcd for $C_{17}H_{20}N_2O_2$: C, 71.81; H, 7.09; N, 9.85. Found: C, 71.71; H, 7.17; N, 9.85.

Reaction of 1 with 8g. (5a*RS*,11b*RS*)-3,5a,6,11b-Tetrahydro-3,5,5-trimethyl-1-phenyl-5*H*-[1]benzopyrano[4′,3′:4,5]pyrano[2,3-*c*]pyrazole (10g): R_f 0.30 (*tert*-butyl methyl ether/petroleum ether, 1:1); reaction time, 16 h; yield, 83%; mp 151–152 °C (ethyl acetate); UV 226 (sh), 232 (sh), 254 (4.20), 284 (3.82); IR 1590, 1570, 1540, 1260; ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.21 (s, 3 H, 5-CH_3 ax.), 1.59 (s, 3 H, 5-CH_3 eq), 2.28 (td, J = 6 Hz, J = 4 Hz, 1 H, 5a-H), 3.69 (s, 3 H, NCH_3), 4.34–4.60 (m, 3 H, 11b-H, 6-H), 6.50–6.60 (m, 1 H, 10-H), 6.70–6.78 (m, 1 H, 8-H), 6.84–6.92 (m, 1 H, 11-H), 6.96–7.10 (m, 1 H, 9-H), 7.30–7.46 (m, 3 H, *m*-Ph, *p*-Ph), 7.64–7.78 (m, 2 H, *o*-Ph); MS, *m/z* 346 (28, M^+), 331 (2, M – CH_3), 303 (6, M – CH_3 – CO), 278 (55, M – C_5H_8), 277 (100, M – C_5H_9), 261 (11, M – C_5H_9O). Anal. Calcd for $C_{22}H_{22}N_2O_2$: C, 76.28; H, 6.40; N, 8.09. Found: C, 76.40; H, 6.34; N, 8.15.

Reaction of 12 with 8b. (5a*RS*,11b*RS*)-8,10-Dibromo-3,5a,6,11b-tetrahydro-1,5,5-trimethyl-3-phenyl-5*H*-[1]benzopyrano[4′,3′:4,5]pyrano[2,3-*c*]pyrazole (13): R_f 0.32 (ethyl acetate/petroleum ether, 1:5); reaction time, 3 h; yield, 89%; mp 202–204 °C (ethyl acetate); UV 238 (4.27), 251 (4.26), 288.5 (3.58), 297 (3.56); IR 1600, 1570, 1515; ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.53 (s, 3 H, 5-CH_3), 1.55 (s, 3 H, 5-CH_3), 2.18 (s, 1 H, 1-CH_3), 2.10–2.24 (m, 1 H, 5a-H), 4.12 (t, J = 11.0 Hz, 1 H, 6-H ax.), 4.17 (d, br, J = 4.0 Hz, 1 H, 11b-H), 4.61 (ddd, J = 11.0 Hz, J = 4.0 Hz, J = 1.5 Hz, 1 H, 6-H eq), 7.20–7.30 (m, 1 H, *p*-Ph), 7.26–7.45 (m, 2 H, *m*-Ph), 7.51 (dd, J = 2.2 Hz, J = 0.6 Hz, 1 H, 11-H), 7.59 (d, J = 2.2 Hz, 1 H, 9-H), 7.67–7.74 (m, 2 H, *o*-Ph); MS, *m/z* 502 (19, M^+), 434 (45, M – C_5H_8), 433 (12, M – C_5H_9), 417 (10, M – C_5H_9O), 44 (100). Anal. Calcd for $C_{22}H_{20}N_2O_2Br_2$: C, 52.41; H, 4.00; N, 5.56; Br, 31.70. Found: C, 52.27; H, 4.00; N, 5.52; Br, 31.75.

Reaction of 15 with 8b. (5a*RS*,13c*RS*)-3,5a,6,11b-Tetrahydro-1,5,5-trimethyl-3-phenyl-5*H*-naphtho[1″,2″:5′,6′]pyrano[4′,3′:4,5]pyrano[2,3-*c*]pyrazole (16): R_f 0.25 (ether/petroleum ether, 1:3); reaction time, 18 h; yield, 85%; mp 189–190 °C (ethyl acetate); UV 209 (sh), 234 (4.80), 255 (4.34), 265 (sh), 276 (sh), 289 (3.69), 322 (3.43), 336 (3.51); IR 1625, 1600, 1570,

1515; ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.50 (s, 3 H, 1-CH_3), 1.62 (s, 3 H, 5-CH_3), 1.65 (s, 3 H, 5-CH_3), 2.18 (dt, J = 12.0 Hz, J = 4.0 Hz, 1 H, 5a-H), 4.09 (dd, J = 12.0 Hz, J = 11.0 Hz, 1 H, 6-H, ax.), 4.28 (ddd, J = 11.0 Hz, J = 4.0 Hz, J = 1.5 Hz, 1 H, 6-H eq), 4.77 (d, br, J = 4.0 Hz, 1 H, 13c-H), 7.07 (d, J = 9.0 Hz, 1 H, 8-H), 7.14–7.88 (m, 9 H, Ar H), 8.12 (d, br, J = 8.5 Hz, 1 H, 13-H); MS, m/z 396 (55, M^+), 353 (11, M – C_3H_7), 328 (100, M – C_5H_8), 311 (42, M – C_5H_9O). Anal. Calcd for $C_{26}H_{24}N_2O_2$: C, 78.76; H, 6.10; N, 7.07. Found: C, 78.75; H, 6.19; N, 7.07.

General Procedure II. Cyclization of 9h and 18. The hetero diene and a few crystals of hydroquinone were dissolved in dry toluene. The solution was purged with argon and heated to reflux for the time given below. Workup followed procedure I.

Cyclization of 9h. (5a*RS*,11b*RS*)-1-*tert*-Butyl-3,5a,6,11b-tetrahydro-3,5,5-trimethyl-5*H*-[1]benzopyrano-[4′,3′:4,5]pyrano[2,3-*c*]pyrazole (10h): R_f 0.29 (ether/petroleum ether, 2:1); reaction time, 4 h; yield, 79%; mp 157–158 °C (*tert*-butyl methyl ether); UV 216 (sh), 270 (sh), 276 (3.34), 283 (3.23); IR 1605, 1585, 1565, 1535, 1250; ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.02 (s, 3 H, 5-CH_3 ax.), 1.31 (s, 9 H, $C(CH_3)_3$), 1.45 (s, 3 H, 5-CH_3 eq), 2.31 (dt, J = 6 Hz, J = 5 Hz, 1 H, 5a-H), 3.59 (s, 3 H, 3-CH_3), 4.20–4.30 (m, 2 H, 11b-H, 6-H ax.), 4.52 (dd, J = 12 Hz, J = 6 Hz, 1 H, 6-H eq), 6.78 (dd, J = 8 Hz, J = 1.3 Hz, 1 H, 8-H), 6.90 (td, J = 7.5 Hz, J = 1.3 Hz, 1 H, 10-H), 7.14 (mc, 1 H, 9-H), 7.32 (d, br, J = 7.5 Hz, 1 H, 11-H); MS, m/z 326 (48, M^+), 311 (3, M – CH_3), 283 (9, M – C_3H_7), 258 (100, M – C_5H_8), 257 (61, M – C_5H_9), 243 (26, M – C_5H_9N), 241 (48, M – C_5H_9O). Anal. Calcd for $C_{20}H_{26}N_2O_2$: C, 73.59; H, 8.03; N, 8.58. Found: C, 73.65; H, 7.99; N, 8.66.

Compound **10h** was obtained within 30 min in 90% yield, when the reaction mixture in heptane was irradiated with a mercury high-pressure lamp (Hanau, TQ 150) at 98 °C.

Cyclization of 18. (5a*RS*,11b*RS*)-5a,11b-Dihydro-5,5-dimethyl-1-phenyl-5*H*,6*H*-[1]benzopyrano[4′,3′:4,5]pyrano-[3,2-*d*]isoxazole (19): R_f 0.35 (ether/petroleum ether, 1:1); reaction time, 12 h; yield, 87%; mp 189–191 °C (methanol); UV 218 (4.20), 238 (sh), 275 (3.49), 283 (3.38); IR 1625; ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.37 (s, 3 H, 5-CH_3 ax.), 1.66 (s, 3 H, 5-CH_3 eq), 2.32 (td, J = 5.6 Hz, J = 4.0 Hz, 1 H, 5a-H), 4.29 (dd, J = 12.0 Hz, J = 5.6 Hz, 1 H, 6-H ax.), 4.41 (d, br, J = 5.6 Hz, 1 H, 11b-H), 4.51 (dd, J = 12.0 Hz, J = 4.0 Hz, 1 H, 6-H eq), 6.46– 6.82 (m, 3 H, 8-H, 10-H, 11-H), 7.06 (mc, 1 H, 9-H), 7.36–7.70 (m, 5 H, Ph); MS, m/z 333 (55, M^+), 318(2, M – CH_3), 290 (7, 318 – CO), 265 (51, M – C_5H_8), 264 (4, M – C_5H_9), 248 (3, M – C_5H_9O), 105 (100, $C_7H_5O^+$). Anal. Calcd for $C_{21}H_{19}NO_3$: C, 75.66; H, 5.74; N, 4.20. Found: C, 75.67; H, 5.77; N, 4.24.

General Procedure III. Synthesis of the Benzylidenepyrazolones. Pyrazolone (3.00 mmol) and 0.06–0.15 mmol of ethylenediammonium diacetate (EDDA) are suspended in 25 mL of dry acetonitrile, and 3.15–3.60 mmol of aldehyde in 5 mL of acetonitrile is added. The pyrazolone dissolves quickly, and the solution becomes red. Stirring at room temperature is continued until no pyrazolone is detected by TLC. The solvent is removed under reduced pressure, the residue is purified by flash chromatography in the solvent stated, and the resulting oil is crystallized. Yields refer to crystalline materials. Compounds **9a,b,f** and **18** are not stable to silica. These benzylidenepyrazolones were isolated by crystallization in the solvent given after removal of the acetonitrile under reduced pressure.

Reaction of 21 with 8a. 2,4-Dihydro-2-phenyl-4-[[2-(2-propenyloxy)phenyl]methylene]-3*H*-pyrazol-3-one (22a): R_f 0.23 (ether/petroleum ether, 1:3); reaction time, 60 min; yield, 85%; mp 86–88 °C (*tert*-butyl methyl ether); UV 208 (sh), 249 (4.28), 253 (sh), 314 (4.19), 372 (4.15), 412 (3.71); IR 1705, 1625, 1600, 1504, 1250; ^{1}H NMR (100 MHz, $CDCl_3$) δ 4.58–4.70 (m, 2 H, CH_2), 5.22–5.55 (m, 2 H, =CH_2), 5.86–6.27 (m, 1 H, CH_2CH=), 6.86–7.70 (m, 7 H, 3″-H to 6″-H, *m*-Ph, *p*-Ph), 7.90–8.06 (m, 3 H, 5-H and *o*-Ph), 8.23 (s, 1 H, 1′-H); MS, m/z 304 (100, M^+), 289 (19, M – CH_3), 263 (10, M – C_3H_5), 247 (40, M – C_3H_5O), 77 (64, $C_6H_5^+$). Anal. Calcd for $C_{19}H_{16}N_2O_2$: C, 74.98; H, 5.30; N, 9.20. Found: C, 75.01; H, 5.31; N, 9.30.

Reaction of 21 with 8b. 2,4-Dihydro-5-methyl-2-phenyl-4-[[2-(2-propenyloxy)phenyl]methylene]-3*H*-pyrazol-3-one (22b): R_f 0.22 (ether/petroleum ether, 1:4); reaction time, 120 min; yield, 79%; mp 108–112 °C (methanol); UV 249 (4.34), 256 (sh), 312 (4.20), 325 (sh), 363 (4.17), 440 (sh); IR 1685, 1615, 1590, 1495, 1260; ^{1}H NMR (200 MHz, $CDCl_3$) δ 2.34 (s, 3 H, 5-CH_3), 4.62–4.70 (m, 2 H, CH_2), 5.30–5.54 (m, 2 H, =CH_2), 5.59–6.20 (m, 1 H, CH_2CH=), 6.90–6.98 (m, 1 H, 3″-H), 7.02–7.24 (m, 2 H, 4″-H, 5″-H), 7.36–7.56 (m, 3 H, *m*-Ph, *p*-Ph), 7.94–8.04 (m, 2 H, *o*-Ph), 8.07 (s, 1 H, =C*H*), 9.18 (dd, J = 8.0 Hz, J = 2.0 Hz, 1 H, 6″-H); MS, m/z 318 (100 M^+), 303 (22, M – CH_3), 277 (15, M – C_3H_5), 261 (70, M – C_3H_5O), 77 (80, $C_6H_5^+$). Anal. Calcd for $C_{20}H_{18}N_2O_2$: C, 75.45; H, 5.70; N, 8.80. Found: C, 75.35; H, 5.78; N, 8.84.

Reaction of 21 with 8c. 2,4-Dihydro-2,5-diphenyl-4-[[2-(2-propenyloxy)phenyl]methylene]-3*H*-pyrazol-3-one (22c): R_f 0.26 (ether/petroleum ether, 1:3); reaction time, 90 min; yield, 73%; mp 123–125 °C (ethyl acetate); UV 267 (4.32), 319 (4.07), 328 (sh), 379 (4.13), 438 (3.33); IR 1675, 1590, 1495, 1255; ^{1}H NMR (200 MHz, $CDCl_3$) δ 4.56 (dt, J = 5.0 Hz, J = 1.5 Hz, 2 H, CH_2), 5.18–5.36 (m, 2 H, =CH_2), 5.86–6.10 (m, 1 H, CH=CH_2), 6.80–7.30 (m, 3 H, 3″-H, 4″-H, 5″-H), 7.38–7.63 (m, 6 H, *m*-2-Ph, *p*-2-Ph, *m*-5-Ph, *p*-5-Ph), 7.68–7.82 (m, 2 H, *o*-5-Ph), 8.02–8.16 (m, 2 H, *o*-2-Ph), 8.37 (s, 1 H, 1′-H), 9.19 (dd, J = 8.0 Hz, J = 2.0 Hz, 1 H, 6″-H); MS, m/z 380 (89, M^+), 365 (17, M – CH_3), 339 (10, M – C_3H_5), 323 (53, M – C_3H_5O), 77 (100, $C_6H_5^+$). Anal. Calcd for $C_{25}H_{20}N_2O_2$: C, 78.93; H, 5.30; N, 7.36. Found: C, 78.91; H, 5.20; N, 7.32.

Reaction of 21 with 8d. 5-*tert*-Butyl-2,4-dihydro-2-phenyl-4-[[2-(2-propenyloxy)phenyl]methylene]-3*H*-pyrazol-3-one (22d): R_f 0.35 (ether/petroleum ether, 1:4); reaction time, 170 min; yield, 92%; mp 126–128 °C (*tert*-butyl methyl ether); UV 249 (4.35), 310 (4.12), 377 (4.11), 415 (sh); IR 1680, 1600, 1595, 1502, 1255; ^{1}H NMR (100 MHz, $CDCl_3$) δ 1.48 (s, 9 H, $C(CH_3)_3$), 4.52–4.64 (m, 2 H, =CH_2), 5.84–6.28 (m, 1 H, CH_2CH=), 6.80–7.52 (m, 6 H, 3″-H, 4″-H, 5″-H, *m*-Ph, *p*-Ph), 7.92–8.06 (m, 2 H, *o*-Ph), 8.37 (d, J = 0.5 Hz, 1 H, 1′-H), 8.84 (dd, J = 8 Hz, J = 2 Hz, 1 H, 6″-H); MS, m/z 360 (58, M^+), 345 (13, M – CH_3), 303 (100, M – C_3H_5O), 91 (17, $C_7H_7^+$), 77 (45, $C_6H_5^+$), 57 (38). Anal. Calcd for $C_{23}H_{24}N_2O_2$: C, 76.64; H, 6.71; N, 7.77. Found: C, 76.62; H, 6.79; N, 7.83.

Reaction of 1 with 8a. 2,4-Dihydro-4-[[2-[(3-methyl-2-butenyl)oxy]phenyl]methylene]-2-phenyl-3*H*-pyrazol-3-one (9a): R_f 0.38 (ether/petroleum ether, 1:2); reaction time, 30 min, yield, 83%; mp 86–87 °C (ether/hexane); UV 248 (4.32), 314 (4.18), 375 (4.14), 412 (sh); IR 1715, 1625, 1605, 1505, 1255; ^{1}H NMR (60 MHz, $CDCl_3$) δ 1.75 (s, br, 6 H, CH_3), 4.60 (d, br, J = 7 Hz, 2 H, CH_2), 5.47 (m, 1 H, CH_2CH=), 6.80–7.80 (m, 7 H, 2″-H, 3″-H, 4″-H, 5″-H, *m*-Ph, *p*-Ph), 7.80–8.15 (m, 3 H, *o*-Ph, 5-H), 8.21 (s, 1 H, 1′-H); MS, m/z 332 (37, M^+), 317 (2, M – CH_3), 289 (8, 317 – CO), 264 (100, M – C_5H_8), 263 (46, M – C_5H_9), 247 (6, M – C_5H_9O). Anal. Calcd for $C_{21}H_{20}N_2O_2$: C, 75.88; H, 6.06; N, 8.43. Found: C, 75.96; H, 6.20; N, 8.43.

Reaction of 1 with 8b. 2,4-Dihydro-5-methyl-4-[[2-[(3-methyl-2-butenyl)oxy]phenyl]methylene]-2-phenyl-3*H*-pyrazol-3-one (9b): R_f 0.27 (chloroform/hexane, 3:2); reaction time, 18 h; yield, 24%; mp 102–104 °C (ether/hexane); UV 249 (4.26), 310 (4.07), 338 (sh), 370 (4.13), 418 (sh); IR 1680, 1610, 1595, 1250; ^{1}H NMR (60 MHz, $CDCl_3$) δ 1.70–1.80 (m, 6 H, =$C(CH_3)_2$), 2.32 (s, 3 H, 5-CH_3), 4.60 (d, br, J = 7 Hz, 2 H, CH_2), 5.53 (mc, 1 H, CH_2CH), 6.80–7.70 (m, 5 H), 7.90–8.13 (m, 3 H), 9.17 (dd, J = 8 Hz, J = 2 Hz, 1 H, 6″-H); MS, m/z 346 (31, M^+), 331 (2, M – CH_3), 303 (7, 303 – CO), 278 (100, M – C_5H_8), 277 (61, M – C_5H_9), 261 (57, M – C_5H_9O). Anal. Calcd for $C_{22}H_{22}N_2O_2$: C, 76.28; H, 6.40; N, 8.09. Found: C, 76.17; H, 6.46; N, 8.17.

Reaction of 1 with 8f. 2,4-Dihydro-2,5-dimethyl-4-[[2-[(3-methyl-2-butenyl)oxy]phenyl]methylene]-3*H*-pyrazol-3-one (9f): R_f 0.27 (ether/pentane, 1:1); reaction time, 45 min; yield, 54%; mp 74–76 °C (ether/hexane); UV 244 (3.83), 304 (4.10), 312 (sh), 363 (3.99), 402 (sh); IR 1670, 1610, 1600, 1490, 1260; ^{1}H NMR (80 MHz, $CDCl_3$) δ 1.60–1.85 (m, 6 H, =$C(CH_3)_2$), 2.20 (s, 3 H, 5-CH_3), 3.34 (s, 3 H, 2-CH_3), 4.57 (d, J = 7 Hz, 2 H, CH_2), 5.43 (mc, 1 H, CH_2CH=), 6.75–7.50 (m, 3 H, 3″-H, 4″-H, 5″-H), 7.88 (s, 1 H, 1′-H), 9.15 (dd, J = 8 Hz, J = 2 Hz, 1 H, 6″-H); MS, m/z 284 (10, M^+), 269 (1, M – CH_3), 241 (2, 269 – CO), 216 (68, M – C_5H_8), 215 (93, M – C_5H_9), 199 (48, M – C_5H_9O), 187 (5, 215 – CO), 123 (14, 199 – C_6H_4), 69 (84, $C_5H_9^+$), 41 (100). Anal. Calcd for $C_{17}H_{20}N_2O_2$: C, 71.81; H, 7.09; N, 9.85. Found: C, 71.84; H, 7.10; N, 9.93.

Reaction of 1 with 8h. 5-*tert*-Butyl-2,4-dihydro-2-methyl-4-[[2-[(3-methyl-2-butenyl)oxy]phenyl]-methylene]-3*H*-pyrazol-3-one (9h): R_f 0.40 (ethyl acetate/

petroleum ether, 1:5); reaction time, 240 min; yield, 86%; mp 46–49 °C (hexane); UV 245 (3.76), 304 (4.03), 310 (sh), 3.62 (3.93), 404 (sh); IR 1675, 1610, 1595, 1490, 1250; ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.41 (s, 9 H, $C(CH_3)_3$), 1.74 (s, br, 3 H, $=CCH_3$), 1.80 (s, br, 3 H, $=CCH_3$), 3.37 (s, 3 H, NCH_3), 4.61 (d, br, J = 7 Hz, 2 H, CH_2), 5.51 (mc, 1 H, $CH_2CH=$), 6.90–7.10 (m, 2 H, 5″-H, 3″-H), 7.48 (ddd, J = 8.5 Hz, J = 7.5 Hz, J = 2.0 Hz, 1 H, 4″-H) 8.37 (s, 1 H, 1′-H), 8.99 (dd, J = 8.0 Hz, J = 2.0 Hz, 1 H, 6″-H); MS, m/z 326 (23, M^+), 311 (9, M – CH_3), 283 (10, 311 – CO), 258 (93, M – C_5H_8), 257 (100, M – C_5H_9), 241 (75, M – C_5H_9O), 201 (31, 258 – C_4H_9), 69 ($C_5H_9^+$), 57 (43, $C_4H_9^+$). Anal. Calcd for $C_{20}H_{26}N_2O_2$: C, 73.59; H, 8.03; N, 8.58. Found: C, 73.74; H, 8.00; N, 8.68.

Reaction of 1a with 17. 4-[[2-[(3-Methyl-2-butenyl)oxy]-phenyl]methylene]-3-phenylisoxazol-5[4*H*]-one (18): R_f 0.43 (ether/pentane, 1:1); reaction time, 60 min; yield, 92%; mp 117–119 °C (methanol); UV 215 (sh), 241 (sh), 308 (3.90), 395 (4.06); IR 1756, 1615, 1600, 1260; ^{1}H NMR (100 MHz, $CDCl_3$) δ 1.71 (s, 3 H, CH_3 cis), 1.81 (s, 3 H, CH_3 trans), 4.58 (d, J = 7 Hz, 2 H, CH_2), 5.40 (mc, 1 H, $CH_2CH=$), 6.98 (d, J = 8 Hz, 1 H, 3″-H), 7.10 (t, J = 8 Hz, 1 H, 5″-H), 7.40–7.80 (m, 6 H, 4″-H, Ph-H), 8.38 (s, 1 H, 1′-H), 9.03 (dd, J = 8 Hz, J = 2 Hz, 1 H, 6″-H); MS, m/z 333 (15, M^+), 318 (1, M – CH_3), 290 (2, 318 – CO), 265 (37, M – C_5H_8), 264 (6, M – C_5H_9), 221 (23, 265 – CO_2), 220 (100, 248 – CO). Anal. Calcd for $C_{21}H_{19}NO_3$: C, 75.66; H, 5.74; N, 4.20. Found: C, 75.31; H, 5.66; N, 4.07.

General Procedure IV. Cyclization of the Benzylidenepyrazolones 22. A few crystals of hydroquinone and 0.5–2.3 mmol of benzylidenepyrazolone are suspended in 30 mL of dry decalin. The apparatus is purged with argon, and the mixture is refluxed for the time stated. After cooling to room temperature, the resulting orange to brown solution is filtered through basic alumina. The absorbent is washed with ca. 200 mL of petroleum ether. The product is then eluted with ethyl acetate; 200–300 mL is used to ensure complete recovery. A sample of this solution is analyzed by HPLC. Often the Diels–Alder adduct is obtained analytically pure by simple crystallization. Otherwise the product is purified by flash chromatography in the solvent given, followed by crystallization. Yields refer to crystalline materials.

Reaction of 22a. (5a*RS*,11b*SR*)-3,5a,6,11b-Tetrahydro-3-phenyl-5*H*-[1]benzopyrano[4′,3′:4,5]pyrano[2,3-*c*]pyrazole (23a): R_f 0.27 (ether/petroleum ether, 1:2); reaction time, 3 h; yield, 74%; mp 122.5–125 °C (ethyl acetate/hexane); UV 229 (4.13), 246 (4.17), 265 (sh), 272 (sh), 282 (3.51); IR 1602, 1582, 1517, 1495, 1415; ^{1}H NMR (200 MHz, $CDCl_3$) δ 2.57 (mc, 1 H, 5a-H), 4.14–4.60 (m, 5 H, 5-H, 6-H, 11b-H), 6.85 (dd, J = 8 Hz, J = 1.5 Hz, 1 H, 8-H), 6.99 (td, J = 7 Hz, J = 1.5 Hz, 1 H, 10-H), 7.10–7.34 (m, 2 H, 9-H, 11-H), 7.36–7.54 (m, 3 H, *m*-Ph, *p*-Ph), 7.62 (s, 1 H, 1-H), 7.70–7.80 (m, 2 H, *o*-Ph); MS, m/z 304 (100, M^+), 289 (6, M – CH_3), 274 (8, M – CH_2O), 247 (5, M – C_3H_5O), 145 (58, $C_9H_9N_2^+$). Anal. Calcd for $C_{19}H_{16}N_2O_2$: C, 74.98; H, 5.30; N, 9.20. Found: C, 75.05; H, 5.18; N, 9.30.

Reaction of 22b. (5a*RS*,11b*SR*)-3,5a,6,11b-Tetrahydro-1-methyl-3-phenyl-5*H*-[1]benzopyrano[4′,3′:4,5]pyrano[2,3-*c*]pyrazole (23b): R_f 0.30 (ethyl acetate/hexane, 1:3); reaction time, 3 h; yield, 75%; mp 152–154 °C (*tert*-butyl methyl ether/hexane); UV 222 (4.15), 253 (4.27), 272 (sh), 282 (3.60); IR 1595, 1580, 1520, 1495, 1450; ^{1}H NMR (200 MHz, $CDCl_3$) δ 2.45 (s, 3 H, 1-CH_3), 2.40–2.56 (m, 1 H, 5a-H), 4.14 (d, br, J = 5.0 Hz, 1 H, 11b-H), 4.32 (dd, J = 11.0 Hz, J = 10.0 Hz, 1 H, 6-H ax.), 4.32–4.46 (AB part of an ABX system, 2 H, 5-H, δ_A 4.37, δ_B 4.41, J_{AX} = J_{BX} = 3.5 Hz, J_{AB} = 11.5 Hz), 4.51 (ddd, J = 11.0 Hz, J = 3.5 Hz, J = 1.0 Hz, 1 H, 6-H eq), 6.81 (dd, J = 8.0 Hz, J = 1.0 Hz, 1 H, 8-H), 6.92 (td, J = 7.5 Hz, J = 1.3 Hz, 1 H, 10-H), 7.08–7.46 (m, 5 H, 9-H, 11-H, *m*-Ph, *p*-Ph), 7.68–7.77 (m, 2 H, *o*-Ph); MS, m/z 318 (74, M^+), 303 (8, M – CH_3), 261 (6, M – C_3H_5O), 145 (100). Anal. Calcd for $C_{20}H_{18}N_2O_2$: C, 75.45; H, 5.70; N, 8.80. Found: C, 75.32; H, 5.75; N, 8.71.

Fifty-five milligrams of the diastereomeric mixture was chromatographed on silica gel (0.063–0.200 mm; ethyl acetate/petroleum ether, 1:6).

Fraction 1. (5a*RS*,11b*RS*)-3,5a,6,11b-Tetrahydro-1-methyl-3-phenyl-5*H*-[1]benzopyrano[4′,3′:4,5]pyrano[2,3-*c*]pyrazole (24b): R_f 0.21 (ethyl acetate/petroleum ether, 1:6); yield, 4.3 mg; ^{1}H NMR (200 MHz, $CDCl_3$) δ 2.48 (s, 3 H, 1-CH_3), 2.30–2.54 (m, 1 H, 5a-H), 3.81 (d, br, J = 10.5 Hz, 1 H, 11b-H), 3.98 (dd, J = 11.1 Hz, J = 10.2 Hz, 1 H, 6-H ax.*), 4.09 (dd, J = 12.2 Hz, J = 10.0 Hz, 1 H, 5-H ax.*), 4.46 (dd, J = 10.0 Hz, J = 6.3 Hz, 1 H, 5-H eq*), 4.50 (dd, J = 10.2 Hz, J = 3.2 Hz, 1 H, 6-H eq*), 6.92–7.02 (m, 2 H, 8-H, 10-H), 7.16–7.50 (m, 5 H, 9-H, 11-H, *m*-Ph, *p*-Ph), 7.70–7.80 (m, 2 H, *o*-Ph).

Fraction 2: R_f 0.18 (ethyl acetate/petroleum ether, 1:6); identical with the main product **23b** obtained by crystallization.

Reaction of 22c. (5a*RS*,11b*SR*)-3,5a,6,11b-Tetrahydro-1,3-diphenyl-5*H*-[1]benzopyrano[4′,3′:4,5]pyrano[2,3-*c*]-pyrazole (23c): R_f 0.27 (ether/petroleum ether, 1:3); reaction time, 90 min; yield, 89%; mp 192–194 °C (*tert*-butyl methyl ether); UV 214 (sh), 232 (sh), 265 (sh), 274 (4.35), 282 (sh); IR 1595, 1568, 1520, 1495, 1455; ^{1}H NMR (200 MHz, $CDCl_3$) δ 2.60–2.74 (m, 1 H, 5a-H), 4.35 (t, J = 11.5 Hz, 1 H, 6-H ax.), 4.28 (mc, 2 H, 5-H), 4.58 (ddd, J = 11.5 Hz, J = 4.0 Hz, J = 1.0 Hz, 1 H, 6-H eq), 4.70 (d, br, J = 5.0 Hz, 1 H, 11b-H), 6.66–6.86 (m, 2 H, 8-H, 10-H), 7.01–7.16 (m, 2 H, 9-H, 11-H), 7.20–7.56 (m, 6 H, *m*-1-Ph, *m*-3-Ph, *p*-1-Ph, *p*-3-Ph), 7.80–7.92 (m, 2 H, *o*-3-Ph), 7.98–8.08 (m, 2 H, *o*-1-Ph); MS, m/z 380 (64, M^+), 365 (1, M – CH_3), 350 (1, M – CH_2O), 323 (3, M – C_3H_5O), 43 (100). Anal. Calcd for $C_{25}H_{20}N_2O_2$: C, 78.93; H, 5.30; N, 7.36. Found: C, 78.94; H, 5.41; N, 7.29.

Reaction of 22d. (5a*RS*,11b*SR*)-1-*tert*-Butyl-3,5a,6,11b-tetrahydro-3-phenyl-5*H*-[1]benzopyrano[4′,3′:4,5]pyrano-[2,3-*c*]pyrazole (23d): R_f 0.26 (ether/petroleum ether, 1:10); reaction time, 4 h; yield, 78%; mp 215–216 °C (*tert*-butyl methyl ether); UV 224 (4.13), 254 (4.27), 282 (3.54); IR 1595, 1578, 1567, 1517, 1490, 1455; ^{1}H NMR (200 MHz, C_6D_6) δ 1.67 (s, 9 H, $C(CH_3)_3$), 1.60–1.76 (m, 1 H, 5a-H), 3.49 (dd, J = 11.7 Hz, J = 2.1 Hz, 1 H, 6-H ax.), 3.63 (ddd, J = 10.8 Hz, J = 4.2 Hz, J = 1.5 Hz, 1 H, 5-H eq), 3.79 (dd, J = 11.7 Hz, J = 4.1 Hz, 1 H, 6-H eq), 3.90 (dd, J = 12.2 Hz, J = 10.8 Hz, 1 H, 5-H ax.), 4.06 (d, br, J = 4.1 Hz, 1 H, 11b-H), 6.76–7.10 (m, 5 H, Ar H), 7.13–7.26 (m, 1 H, Ar H), 7.50 (mc, 1 H), 8.08 (m, 2 H, *o*-Ph); MS, m/z 360 (100, M^+), 345 (47, M – CH_3), 318 (17, M – C_3H_6), 317 (12, 345 – CO or C_2H_4), 303 (29, M – C_4H_9). Anal. Calcd for $C_{23}H_{24}N_2O_2$: C, 76.64; H, 6.71; N, 7.77. Found: C, 76.70; H, 6.83; N, 7.76.

General Procedure V. Condensation of Citral (25) with Pyrazolones 8a–d. A solution of citral (**25**, 4.9 mmol) in 10 mL of dry acetonitrile is added to a stirred suspension of pyrazolone **8** (5.0 mmol) and ethylenediammonium diacetate (EDDA) (0.1 mmol) in 20 mL of the same solvent. The mixture is stirred at room temperature for 30–90 min (TLC control). After removal of the solvent under reduced pressure, the residue is filtered over a short column with silica gel and the red fractions are recrystallized. Yields refer to crystalline materials.

Reaction of 25 with 8a. 4-(3,7-Dimethyl-2,6-octadienylidene)-2-phenyl-2,4-dihydropyrazol-3-one (27a): eluent, ether/petroleum ether, 1:3; yield, 49% of an oil; ^{13}C NMR showed the presence of at least three isomers; ^{1}H NMR (100 MHz, $CDCl_3$) δ 1.40–2.60 (m, 13 H), 4.95–5.20 (m, 1 H, 6′-H), 6.47 (d, J = 13 Hz, 0.5 H, 2′-H), 7.05–8.05 (m, 7.5 H); MS, m/z 294 (75, M^+), 279 (5, M – CH_3), 251 (11, M – C_3H_7), 238 (5, M – C_4H_8), 226 (19, M – C_5H_8), 221 (36, M – C_6H_{11}), 41 (100). Anal. Calcd for $C_{19}H_{22}N_2O$: C, 77.52; H, 7.53; N, 9.52. Found: C, 77.30; H, 7.42; N, 9.50.

Reaction of 25 with 8b. (4*Z*,2′*E*)-4-(3,7-Dimethyl-2,6-octadienylidene)-5-methyl-2-phenyl-2,4-dihydropyrazol-3-one (27b): eluent, diethyl ether; yield, 86%; mp 86–91 °C (methanol); ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.62 (s, 3 H, 7′-CH_3 cis), 1.69 (s, 3 H, 7′-CH_3 trans), 2.07 (d, J = 1.0 Hz, 3 H, 3′-CH_3), 2.27 (s, 3 H, 5-CH_3), 2.14–2.44 (m, 4 H, 4′-H, 5′-H), 5.12 (mc, 1 H, 6′-H), 7.12–7.24 (m, 1 H, *p*-Ph), 7.35–7.48 (m, 3 H, *m*-Ph, 2′-H), 7.80 (d, br, J = 12 Hz, 1 H, 1′-H), 7.94–8.04 (m, 2 H, *o*-Ph); MS, m/z 308 (31, M^+), 293 (11, M – CH_3), 265 (16, M – C_3H_7), 252 (12, M – C_4H_8), 240 (31, M – C_5H_8), 225 (100, M – C_6H_{11}). Calcd for $C_{20}H_{26}N_2O$: C, 77.89; H, 7.84; N, 9.08. Found: C, 77.83; H, 7.75; N, 9.14.

Reaction of 25 with 8c. (4*Z*,2′*E*)-4-(3,7-Dimethyl-2,6-octadienylidene)-2,5-diphenyl-2,4-dihydropyrazol-3-one (27c): eluent, diethyl ether; yield, 91%; mp 133–135 °C (ethyl acetate); ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.50–1.74 (m, 6 H, 7′-CH_3), 2.00–2.50 (m, 7 H, 3′-CH_3, 4′-H, 5′-H), 5.00–5.20 (m, 1 H, 6′-H), 7.16–8.20 (m, 12 H, Ar H, 2′-H, 1′-H); MS, m/z 370 (100, M^+), 355 (5, M – CH_3), 327 (7, M – C_3H_7), 314 (5, M – C_4H_8), 302 (11, M – C_5H_8), 287 (36, M – C_6H_{11}). Anal. Calcd for $C_{25}H_{26}N_2O$: C, 81.05; H, 7.70; N, 7.56. Found: C, 81.12; H, 7.06; N, 7.65.

Reaction of 25 with 8d. (4*Z*,2′*E*)-5-*tert*-Butyl-4-(3,7-dimethyl-2,6-octadienylidene)-2-phenyl-2,4-dihydropyrazol-

3-one (27d): eluent, ether/petroleum ether, 1:10; yield, 92%; mp 82–84 °C (hexane); ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.41 (s, 9 H, $C(CH_3)_3$), 1.62 (s, br, 3 H, 7′-CH_3 cis), 1.69 (s, br, 3 H, 7′-CH_3 trans), 2.05 (d, J = 1.2 Hz, 3 H, 3′-CH_3), 2.16–2.46 (m, 4 H), 5.13 (mc, 1 H, 6′-H), 7.16 (tt, J = 7.5 Hz, J = 1.0 Hz, 1 H, p-Ph), 7.35–7.47 (m, 2 H, m-Ph), 7.76 (d, J = 12.0 Hz, 1 H, 1′-H), 7.93 (d, br, J = 12.0 Hz, 1 H, 2′-H), 7.98–8.08 (m, 2 H, o-Ph); MS, m/z 350 (32, M^+), 335 (6, M – CH_3), 307 (7, M – C_3H_7), 294 (4, M – C_4H_8), 267 (100, M – C_6H_{11}). Anal. Calcd for $C_{23}H_{30}N_2O$: C, 78.82; H, 8.63; N, 7.87. Found: C, 78.71; H, 8.63; N, 7.99.

General Procedure VI: Diels–Alder Reaction of the Alkylidenepyrazolones 27a–d. A solution of alkylidenepyrazolone **27a–d** (200–400 mg) and a few crystals of hydroquinone in 30 mL of dry decalin is placed in a flask with a reflux condenser. The apparatus is purged with argon and held under inert gas while the solution is heated to reflux for the time given below. After completion of the cycloaddition (TLC control), most of the decalin is distilled off from the mixture under reduced pressure. The residue is filtrated over dry basic alumina (10 g) and the residual decalin eluted with petroleum ether. The cycloadducts are then eluted with ethyl acetate. An aliquot of the solution thus obtained is analyzed by HPLC, and the remainder is flash chromatographed on silica gel if necessary. Otherwise the main products, the data of which are given, are obtained directly by crystallization. Yields refer to the mixtures of diastereomers.

Reaction of 27a. (5a*RS*,9a*SR*)-5,5,8-Trimethyl-3-phenyl-3,5,5a,6,7,9a-hexahydro[2]benzopyrano[3,4-*c*]pyrazole (29a): R_f 0.32 (ether/petroleum ether, 1:3); reaction time, 40 min; yield, 86%; mp 118–121 °C (hexane, sublimates); UV 247 (4.22); IR 1600, 1595, 1510, 1495, 775; ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.20–1.36 (m, 1 H), 1.38 (s, 3 H, 5-CH_3 ax.), 1.54 (s, 3 H, 5-CH_3 eq)8 1.54–1.66 (m, 1 H), 1.70 (s, 3 H, 8-CH_3), 1.78–2.10 (m, 3 H), 3.38–3.48 (m, 1 H, 9a-H), 5.72–5.82 (m, 1 H, 9-H), 7.18–7.28 (m, 1 H, p-Ph), 7.37–7.50 (m, 3 H, m-Ph, 1-H), 7.78–7.88 (m, 2 H, o-Ph); MS, m/z 294 (100, M^+), 279 (25, M – CH_3), 251 (75, M – C_3H_7), 238 (8, M – C_4H_8), 226 (52, M – C_5H_8), 211 (67, M – C_6H_{11}). Anal. Calcd for $C_{19}H_{22}N_2O$: C, 77.52; H, 7.53; N, 9.52. Found: C, 77.59; H, 7.55; N, 9.41.

Reaction of 27b. (5a*RS*,9a*SR*)-1,5,5,8-Tetramethyl-3-phenyl-3,5,5a,6,7,9a-hexahydro[2]benzopyrano[3,4-*c*]pyrazole (29b): R_f 0.25 (*tert*-butyl methyl ether/petroleum ether, 1:6); reaction time, 70 min; yield, 75%; mp 90–95 °C (hexane); UV 256 (4.56); IR 1595, 1580, 1510, 1490, 760; ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.35 (s, 3 H, 5-CH_3 ax.), 1.30–1.48 (m, 1 H), 1.50 (s, 3 H, 5-CH_3 eq), 1.54–1.64 (m, 1 H), 1.70 (s, br, 3 H, 8-CH_3), 1.78–2.10 (m, 3 H), 2.32 (s, 3 H, 1-CH_3), 3.37–3.48 (m, 1 H, 9a-H), 5.82–5.90 (m, 1 H, 9-H), 7.11–7.22 (m, 1 H, p-Ph), 7.32–7.44 (m, 2 H, m-Ph), 7.71–7.80 (m, 2 H, o-Ph); MS, m/z 308 (100, M^+), 293 (19, M – CH_3), 265 (37, M – C_3H_7), 240 (29, M – C_5H_8), 225 (62, M – C_6H_{11}). Anal. Calcd for $C_{20}H_{24}N_2O$: C, 77.89; H, 7.84; N, 9.08. Found: C, 77.75; H, 7.83; N, 9.13.

Reaction of 27c: reaction time, 60 min; yield, 80%; the diastereomeric mixture was separated by preparative HPLC (Nucleosil 5C18 (length = 250 mm, i.d. = 8 mm), acetonitrile/water, 80:20, 1.0 mL/min, 95 atm, automatic injection, c = 2.5 mg/mL in acetonitrile/water, 85:15, 2.5 mg per separation, 40 separations), t_{R1} = 36.2 min (12.4 mg, purity, 95%), t_{R2} = 39.6 min (38.9 mg, purity, 98%), t_{R3} = 47.9 min (18.4 mg, purity, 100%), R_{12} = 0.9, α_{12} = 1.11, R_{23} = 2.1, α_{23} = 1.24.

Fraction 1. (5a*RS*,9a*SR*)-5,5,8-Trimethyl-1,3-diphenyl-3,5,5a,6,9,9a-hexahydro[2]benzopyrano[3,4-*c*]pyrazole (28c): UV 242 (4.14), 267 (4.31); IR 1600, 1595, 1505, 1125, 755, 700; ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.32 (s, br, 3 H, 8-CH_3), 1.48 (s, 3 H, 5-CH_3), 1.50 (s, 3 H, 5-CH_3), 1.87 (dt, J = 6.5 Hz, J = 4.0 Hz, 1 H, 5a-H), 1.90–2.30 (m, 5 H), 3.50 (dt, J = 5.0 Hz, J = 4.0 Hz, 1 H, 9a-H), 5.18–5.28 (m, 1 H, 7-H), 7.18–7.30 (m, 1 H, p-3-Ph), 7.32–7.50 (m, 5 H, m-3-Ph, m-1-Ph, p-1-Ph), 7.60–7.70 (m, 2 H, o-3-Ph), 7.85–7.95 (m, 2 H, o-1-Ph); MS, m/z 370 (100, M^+), 355 (12, M – CH_3), 327 (81, M – C_3H_7), 315 (34, M – C_4H_7), 314 (14, M – C_4H_8), 302 (93, M – C_5H_8), 287 (76, M – C_6H_{11}). Anal. Calcd for $C_{25}H_{26}N_2O$: 370.2045. Found: 370.2045.

Fraction 2. (5a*RS*,9a*SR*)-5,5,8-Trimethyl-1,3-diphenyl-3,5,5a,6,7,9a-hexahydro[2]benzopyrano[3,4-*c*]pyrazole (29c): R_f 0.30 (ethyl acetate/petroleum ether, 1:10); mp 157–159 °C (ethyl acetate); UV 240 (4.15), 271 (4.35); IR 1600, 1575, 1515, 1490, 770, 705; ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.20–1.44 (m, 1 H), 1.49 (s, 6 H, 5-CH_3), 1.56 (s, 3 H, 8-CH_3), 1.69 (ddd, J = 12.0 Hz, J = 6.0 Hz, J = 2.5 Hz, 1 H, 5a-H), 1.80–2.04 (m, 3 H), 3.77 (t, br, J = 5–6 Hz, 1 H, 9a-H), 5.62 (d, br, J = 5 Hz, 1 H, 9-H), 7.18–7.30 (m, 1 H, p-3-Ph), 7.36–7.52 (m, 5 H, m-1-Ph, p-1-Ph, m-3-Ph), 7.72–7.82 (m, 2 H, o-3-Ph), 7.85–7.94 (, 2 H, o-1-Ph). Anal. Calcd for $C_{25}H_{26}N_2O$: C, 81.05; H, 7.07; N, 7.56. Found: C, 80.98; H, 7.17; N, 7.63.

Fraction 3. (5a*RS*,9a*RS*)-5,5,8-Trimethyl-1,3-diphenyl-3,5,5a,6,7,9a-hexahydro[2]benzopyrano[3,4-*c*]pyrazole (30c): UV 239 (4.14), 269 (4.36); IR 1600, 1575, 1510, 1125, 760, 705; ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.21–1.37 (m, 1 H, 6-H ax.*), 1.32 (s, 3 H, 5-CH_3 ax.), 1.46–1.66 (m, 1 H, 7-H ax.*), 1.51 (s, br, 3 H, 8-CH_3), 1.68–1.75 (m, 1 H, 5a-H), 1.55 (s, 3 H, 5-CH_3 eq), 1.85–1.99 (m, 1 H, 6-H eq), 2.10–2.22 (m, 1 H, 7-H eq), 3.47 (dsextet, J = 10.0 Hz, J = 2.5 Hz, 1 H, 9a-H), 5.57 (mc, 1 H, 9-H), 7.23 (mc, 1 H, p-3-Ph), 7.30–7.50 (m, 5 H, m-1-Ph, p-1-Ph, m-3-Ph), 7.71–7.80 (m, 2 H, o-1-Ph), 7.89–7.91 (o-3-Ph); MS, m/z 370 (100, M^+), 355 (47, M – CH_3), 327 (30, M – C_3H_7), 315 (7, M – C_4H_7), 314 (m, M – C_4H_8), 302 (41, M – C_5H_8), 287 (63, M – C_6H_{11}). Anal. Calcd for $C_{25}H_{26}N_2O$: 370.2045. Found: 370.2045.

Reaction of 27d. (5a*RS*,9a*SR*)-1-*tert*-Butyl-5,5,8-trimethyl-3-phenyl-3,5,5a,6,7,9a-hexahydro[2]benzopyrano-[3,4-*c*]pyrazole (29d): R_f 0.31 (ether/petroleum ether, 1:20); reaction time, 90–150 min; yield, 61%; mp 81–83 °C (hexane); the compound was obtained crystalline only once in a small quantity; UV 254 (4.27); IR 1605, 1595, 1565, 1510, 760, 695; MS, m/z 350 (70, M^+), 335 (6, M – CH_3), 307 (12, M – C_3H_7), 295 (10, M – C_4H_7), 282 (54, M – C_5H_8), 267 (68, M – C_6H_{11}), 43 (100). Anal. Calcd for $C_{23}H_{30}N_2O$: C, 78.82; H, 8.63; N, 7.99. Found: C, 78.68; H, 8.50; N, 8.03.

Synthesis of [2-(2-Methyl-1-propenyl)phenoxy]acetaldehyde (31). [2-(2-Methyl-1-propenyl)phenoxy]acetic Acid Ethyl Ester. A mixture of 2-(2-methyl-1-propenyl)phenol (25.0 g, 169 mmol), bromoacetic acid ethyl ester (30.0 g, 180 mmol), and potassium carbonate (50.0 g, 360 mmol) in dry acetone (300 mL) was refluxed for 6 h. After filtration and washing with acetone, the solvent was removed under reduced pressure. The resulting oil was distilled (112–114 °C (0.01 Torr)) to yield 35.1 g (89%) of a colorless liquid: ^{1}H NMR (100 MHz, $CDCl_3$) δ 1.28 (t, J = 7 Hz, 3 H, CH_2CH_3), 1.82 (d, J = 1 Hz, 3 H, CH_3 cis), 1.93 (d, J = 1 Hz, 3 H, CH_3 trans), 4.22 (q, J = 7 Hz, 2 H, CH_2CH_3) 4.59 (s, 2 H, CH_2), 6.36 (s, br, 1 H, =CH), 6.64–7.26 (m, 4 H, Ar H). Anal. Calcd for $C_{14}H_{18}O_3$: 234.1256. Found: 234.1256.

2-[2-(2-Methyl-1-propenyl)phenoxy]ethanol. A solution of [2-(2-methyl-1-propenyl)phenoxy]acetic acid ethyl ester (15.9 g, 68 mmol) in *tert*-butyl methyl ether (20 mL) was added to a well-stirred suspension of lithium aluminum hydride (1.58 g, 42.0 mmol) in 100 mL of the same solvent. The rate of addition was controlled to achieve gentle reflux. After the addition of the ester, the mixture was refluxed for an additional 2 h. The hydrolysis of surplus hydride was carried out by cautious addition of water (5 mL), and then 10% KOH (30 mL) was added. The aqueous phase was removed and extracted twice with *tert*-butyl methyl ether. The combined organic phases were washed with brine and dried with sodium sulfate. Removal of the solvent under reduced pressure afforded an oil. Distillation (84 °C (0.06 Torr)) gave 11.5 g (88%) of a colorless liquid: IR (film) 3600–3100, 1250, 760; ^{1}H NMR (100 MHz, $CDCl_3$) δ 1.81 (d, J = 1.3 Hz, 3 H, CH_3 cis), 1.92 (d, J = 1.5 Hz, 3 H, CH_3 trans), 2.36 (s, br, 1 H, OH), 3.80–4.15 (m, 4 H, 1-H, 2-H), 6.29 (s, br, 1 H, =CH), 6.75–7.30 (m, 4 H, Ar H). Anal. Calcd for $C_{12}H_{16}O_2$: C, 74.97; H, 8.39. Found: C, 74.90; H, 8.28.

[2-(2-Methyl-1-propenyl)phenoxy]acetaldehyde (31). To a solution of oxalyl chloride (1.92 mL, 22 mmol) in dry toluene (80 mL) at –60 °C was slowly added a mixture of dimethyl sulfoxide (3.55 mL, 44 mmol) in toluene (11 mL). After the mixture was stirred at this temperature for 5 min, a solution of [2-(2-methyl-1-propenyl)phenoxy]acetic acid ethyl ester (3.88 g, 20.2 mmol) in toluene (20 mL) was added over 10 min. Stirring at –60 °C was continued for 30 min, then triethylamine (14 mL) was added and the mixture was allowed to warm to room temperature after 5 min. After addition of water (50 mL), the phases were separated and the aqueous phase was extracted twice with methylene chloride. The combined organic phases were washed with brine and dried with Na_2SO_4. After removal of the solvent in vacuo, a yellow oil was obtained. Kugelrohr distillation (150

°C (0.02 Torr)) afforded 2.28 g (60%) of the aldehyde. The compound proved to be not very stable. Part of the material was directly used for the tandem-Knoevenagel-Diels-Alder reaction; a 2,4-dinitrophenylhydrazone was prepared for characterization: mp 141-143.5 °C (ethyl acetate); ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.83 (d, J = 1.3 Hz, 3 H, CH_3 cis), 1.95 (d, J = 1.4 Hz, 3 H, CH_3 trans), 4.86 (d, J = 4.9 Hz, 2 H, CH_2), 6.36 (s, br, 1 H, =CH), 6.92-7.12 (m, 2 H, 4'-H, 6'-H), 7.20-7.28 (m, 2 H, 3'-H, 5'-H), 7.69 (td, J = 4.9 Hz, J = 0.8 Hz, 1 H, N=CH), 7.96 (d, J = 9.5 Hz, 1 H, 6'-H), 8.38 (ddd, J = 9.5 Hz, J = 2.5 Hz, J = 0.8 Hz, 1 H, 5''-H), 9.17(d, J = 2.5 Hz, 1 H, 3''-H), 11.16 (s, br, 1 H, NH). Anal. Calcd for $C_{18}H_{18}N_4O_4$: C, 58.37; H, 4.90; N, 15.13. Found: C, 58.49; H, 4.91; N, 15.27.

Reaction of 31 with *N*,*N*-Dimethylbarbituric Acid (32). To a stirred suspension of **32** (302 mg, 1.94 mmol) and EDDA (14 mg, 0.07 mmol) in dry acetonitrile (20 mL) was added a solution of aldehyde **31** (5.14 mg, 2.70 mmol) in acetonitrile (10 mL). The mixture was stirred for 22 h at room temperature, the solvent was then removed in vacuo, and the residue was flash chromatographed on silica gel (*tert*-butyl methyl ether/petroleum ether, 1:1).

Fraction 1. (3'*RS*,4'*RS*)-5-(4-Isopropenyl-3,4-dihydro-1*H*-[1]benzopyran-3-yl)-1,3-dimethyl-2,4,6(1*H*,3*H*,5*H*)-pyrimidinetrione (34): R_f 0.34; yield, 28%; UV 218 (4.09), 266 (3.86), 282 (sh); IR 1750, 1700-1670, 755; ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.47 (d, J = 0.5 Hz, 3 H, =CCH_3), 3.10-3.24 (m, 1 H, 3'-H), 3.26 (s, 3 H, NCH_3), 3.35 (s, 3 H, NCH_3), 3.55 (d, J = 2.0 Hz, 1 H, 5-H), 3.83 (d, br, J = 11.0 Hz, 1 H, 4'-H), 4.20-4.30 (m, 2 H, 2'-H ax. and eq), 4.88-4.94 (m, 1 H, =CH), 4.98-5.06 (m, 1 H, =CH), 6.80-7.20 (m, 4 H, 5'-H to 8'-H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 17.33 (CH_3C=), 28.46 (NCH_3), 38.67 (C-3'), 47.24 (C-4'*), 49.29 (C-5*), 67.70 (C-2), 116.75 (C-8'), 116.99 (=CH_2), 120.93 (C-6'), 122.07 (C-4'a), 127.79, 128.69 (C-5', C-7') 144.93 (C=C_2), 151.19 (C-2), 154.44 (C-8'a), 166.69, 167.14 (C-4, C-6); some signals of the minor cis isomer **35** are seen, δ 21.27 (CH_3C=), 40.20 (C-3'), 44.67 (C-4'*), 48.95 (C-5*), 66.44 (C-2); ratio **34**:**35** = 5.2:1; MS, m/z 328 (6, M^+), 313 (0.2, M - CH_3), 285 (0.8, M - C_3H_7), 172 (100, $C_{12}H_{12}O$), 157 (69, $C_6H_9N_2O_3^+$). Anal. Calcd for $C_{18}H_{20}N_2O_4$: C, 65.84; H, 6.14; N, 8.53. Found: C, 65.78; H, 6.22; N, 8.55.

Fraction 2. (4b*RS*,10b*SR*)-1,2,3,4,4b,5,10b,11-Octahydro-1,3,11,11-tetramethyl[1]benzopyrano[3',4':4,5]pyrano[2,3-*d*]pyrimidine-2,4-dione (36): R_f 0.17-0.30; yield, 42%; mp 215-217 °C (methanol/water); UV 219 (4.16), 262 (3.99), 283 (3.36); IR 1705, 1640, 1230, 750; ^{1}H NMR (200 MHz, 50 °C, DMSO-d_6) δ 1.36 (s, 3 H, 11-CH_3 ax.), 1.95 (s, 3 H, 11-CH_3 eq), 2.78 (td, J = 11.0 Hz, J = 4.5 Hz, 1 H, 4b-H), 3.12 (d, br, J = 11.0 Hz, 1 H, 10b-H), 3.16 (s, 3 H, NCH_3), 3.21 (s, 3 H, NCH_3), 3.84 (dd, J = 11.0 Hz, J = 10.0 Hz, 1 H, 5-H ax.), 5.35 (dd, J = 10.0 Hz, J = 4.5 Hz, 1 H, 5-H eq), 6.84 (dd, J = 8.0 Hz, J = 1.5 Hz, 1 H, 7-H), 6.89 (td, J = 8.0 Hz, J = 1.5 Hz, 1 H, 9-H), 7.19 (tdd, J = 8.0 Hz, J = 1.8 Hz, J = 1.0 Hz, 1 H, 8-H), 7.37 (dt, J = 8.0 Hz, J = 1.0 Hz, 1 H, 10-H); ^{13}C NMR (20 MHz, $CDCl_3$) δ 20.26 (11-CH_3 ax.), 27.84, 28.68 (NCH_3), 29.96 (11-CH_3 eq), 31.18 (C-4b*), 45.71 (C-10b*), 70.02 (C-5), 84.22, 85.59 (C-4a, C-11), 117.51 (C-7), 119.89 (C-9), 122.36 (C-10a), 125.01, 128.38 (C-8, C-10), 151.07 (C-2), 155.26, 155.43 (C-6a, C-12a), 162.18 (C-4); MS, m/z 328 (30, M^+), 313 (6, M - CH_3), 285 (24, M - C_3H_7), 181 (100, $C_8H_9N_2O_3^+$), 147 (8, $C_{10}H_{11}O^+$). Anal. Calcd for $C_{18}H_{20}N_2O_4$: C, 65.84; H, 6.14; N, 8.53. Found: C, 65.97; H, 6.22; N, 8.52.

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Registry No. 1, 56074-73-8; **8a**, 876-92-6; **8b**, 89-25-8; **8c**, 4845-49-2; **8d**, 6631-89-6; **8e**, 10234-66-9; **8f**, 2749-59-9; **8g**, 41927-50-8; **8h**, 87031-30-9; (*E*)-**9a**, 112296-87-4; (*Z*)-**9a**, 112296-88-5; (*E*)-**9b**, 112296-89-6; (*Z*)-**9b**, 112296-90-9; (*Z*)-**9f**, 112296-91-0; (*Z*)-**9h**, 112296-79-4; **10a**, 112296-60-3; **10b**, 112296-62-5; **10c**, 112296-64-7; **10d**, 112296-66-9; **10e**, 112296-68-1; **10f**, 112296-70-5; **10g**, 112296-72-7; **10h**, 112296-74-9; **11a**, 112296-61-4; **11b**, 112296-63-6; **11c**, 112296-65-8; **11d**, 112296-67-0; **11e**, 112296-69-2; **11f**, 112296-71-6; **11g**, 112296-73-8; **11h**, 112296-75-0; **12**, 112296-59-0; **13**, 112296-76-1; **14**, 112296-77-2; **15**, 58758-47-7; **16**, 112296-78-3; **17**, 1076-59-1; **18**, 112296-80-7; **19**, 112296-81-8; **20**, 112296-82-9; **21**, 28752-82-1; (*E*)-**22a**, 112296-83-0; (*Z*)-**22a**, 112297-19-5; (*E*)-**22b**, 112297-20-8; (*Z*)-**22b**, 112296-84-1; **22c**, 112296-85-2; **22d**, 112296-86-3; **23a**, 112296-92-1; **23b**, 112296-94-3; **23c**, 112296-96-5; **23d**, 112296-98-7; **24a**, 112296-93-2; **24b**, 112296-95-4; **24c**, 112296-97-6; **24d**, 112296-99-8; **25**, 5392-40-5; **27a**, 112297-00-4; **27b**, 112319-73-0; **27c**, 112297-01-5; **27d**, 112297-02-6; **28a**, 112297-03-7; **28b**, 112297-06-0; **28c**, 112297-08-2; **29a**, 112297-04-8; **29b**, 112421-49-5; **29c**, 112421-50-8; **29d**, 112297-10-6; **30a**, 112297-05-9; **30b**, 112297-07-1; **30c**, 112297-09-3; **30d**, 112297-11-7; **31**, 112297-14-0; **31** (2,4-dinitrophenylhydrazone deriv), 112297-15-1; **32**, 769-42-6; **34**, 112297-16-2; **35**, 112297-17-3; **36**, 112297-18-4; 4,5-dihydro-1-methyl-5-oxo-1*H*-pyrazole-4-carboxylic acid methyl ester, 112296-58-9; dimethyl (methoxymethylene)malonate, 22398-14-7; methylhydrazine, 60-34-4; ethyl 4,4-dimethyl-3-oxopentanoate, 17094-34-7; 2-(2-methyl-1-propenyl)phenol, 6395-29-5; bromoacetic acid ethyl ester, 105-36-2; [2-(2-methyl-1-propenyl)phenoxy]acetic acid ethyl ester, 112297-12-8; 2-[2-(2-methyl-1-propenyl)phenoxy]ethanol, 112297-13-9.

Some Observations on the Stereochemical and Regiochemical Outcome of Hydrostannylation of Substituted Propargyl Alcohols

Cristina Nativi and Maurizio Taddei*

Dipartimento di Chimica Organica "U. Schiff", Università, Via G. Capponi 9, I50121 Firenze, Italy

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A regio- and stereocontrolled hydrostannylation of substituted propargyl alcohols and derivatives has been performed. Tri-*n*-butylstannyl hydride reacts with different substituted propargyl alcohols to give a mixture of *Z*/*E* isomers of vinylstannane with the stannyl moiety bonded to the carbon closest to the OH or OR group. A careful study of the reaction conditions allowed the preparation and isolation of pure *Z* isomer for a wide set of compounds. The reaction products are unstable under the conditions of preparation. An outline of the possible mechanism of the reaction is described.

Hydrostannylation is a useful reaction for the preparation of carbon-functional organostannanes[1] and is the simplest and most direct route to transform alkynes into vinylstannanes.[1,2] This reaction, however, is not highly regio- and stereoselective, and analogously the mechanism does not appear to have been well established. The predominance of a free-radical mechanism or of a stepwise

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