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New Tandem Reactions of Metal Carbenoids. Intermolecular Formation of Azomethine Ylide from Methyl 2-Diazo-2-phenylacetate and Schiff Base: Intramolecular 1,3-Dipolar Cycloaddition

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Abstract—Rhodium acetate-catalyzed decomposition of methyl 2-diazo-2-phenylacetate in the presence of substituted *N*-methylbenzylideneamines possessing an activated alkenyl fragment (dipolarophile) in the side chain gives products of intramolecular cycloaddition of intermediate *Z*,*E*- and *E*,*Z*-azomethine ylides. The cycloaddition is regioselective, and the products are hexahydrochromeno[4,3-*b*]pyrrole derivatives. The stereoselectivity of the process depends on the temperature. In the temperature range from 20 to 80°C, the major stereoisomer is that with *cis* junction of the tetrahydropyran and pyrrolidine rings. *N*-Phenylazomethine ylides generated from methyl 2-diazo-2-phenylacetate and alkyl 4-[2-(phenyliminomethyl)phenoxy]-2-butenoates at 40°C undergo cyclization to aziridines at a higher rate, as compared to the rate of cycloaddition to the internal dipolarophile. *N*-Phenylazomethine ylides generated by thermolysis of the corresponding aziridine or by the "deprotonation" method react with equal regio- and stereoselectivity to give intramolecular cycloaddition products, hexahydrochromeno[4,3-*b*]pyrrole derivatives with *trans*-fused tetrahydropyran and pyrrolidine rings. Analysis of the experimental and calculation data suggests preference of the *endo* transition state in the cycloaddition of the examined azomethine ylides.

Intramolecular 1,3-dipolar cycloadditions of azomethine ylides underlie effective procedures for the synthesis of various fused, bridged, and cage-like polycyclic nitrogen-containing compounds [1]. An important problem is the stereoselectivity of cycloaddition of ylide intermediates, for it determines the efficiency of this approach as applied to a particular synthetic task. Low stereoselectivity often results from configurational heterogeneity of ylide intermediate owing to fairly severe conditions of its generation [2–4]. The stereoselectivity problem may be solved by development of such methods for generation of azomethine ylides which would allow their geometry to be controlled. One of these methods is based on reactions of carbenes or carbenoids with compounds possessing a C=N bond and is referred to as "carbene" technique. These reactions occur as a rule under mild conditions, and they make it possible to generate ylides which cannot be obtained by other methods [5].

The synthetic sequence intermolecular carbene generation of azomethine ylide–intramolecular cycloaddition almost was not studied as a method of synthesis of nitrogen-containing polycyclic compounds. Only recently, we described examples of such syntheses with the use of difluorocarbene and dichlorocarbene [6–8].

The goal of the present study was to develop approaches to tandem synthesis of fused heterocycles via the above reaction sequence involving carbenoids generated from diazo compounds. As model system we used azomethine ylides generated by addition of carbene-like species derived from methyl 2-diazo-2-phenylacetate to *N*-methyl- and *N*-phenylbenzylideneamines **I**–**IV** possessing an activated alkenyl fragment (dipolarophile) in the *ortho* position of the aromatic ring. While analyzing factors determining the stereoselectivity of intramolecular cycloaddition of azomethine ylides we used for comparison so-called "deprotonation" technique which is based on thermal

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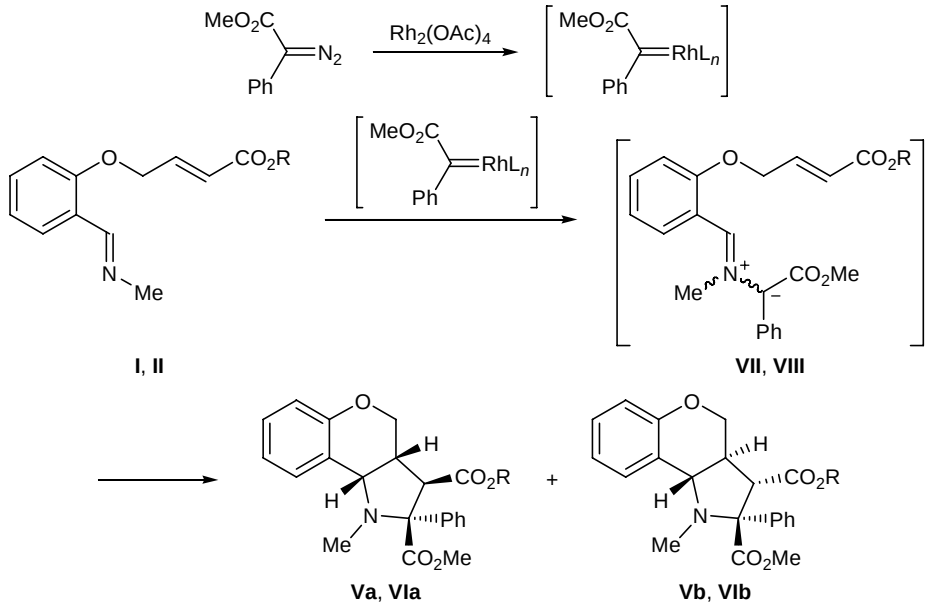
Scheme 1.



I, **Va**, **Vb**, **VII**, R = Et; **II**, **VIa**, **VIb**, **VIII**, R = Me.

condensation of the corresponding aldehyde with amine [9].

The reaction of Schiff base **I** with methyl 2-diazo-2-phenylacetate in boiling methylene chloride in the presence of a catalytic amount of $Rh_2(OAc)_4$ gave two stereoisomeric chromeno[4,3-*b*]pyrroles **Va** and **Vb** as a result of intramolecular 1,3-dipolar cycloaddition of the ylide moiety to the C=C bond in intermediate azomethine ylide **VII** (Scheme 1). The major isomer (compound **Va**) was obtained in 59% yield, whereas minor isomer **Vb** was not isolated in the pure state. The *cis*-junction of the pyran and pyrrolidine rings in **Va** follows from the spin–spin coupling constant between 3a-H and 9b-H, which is equal to 8.3 Hz, and from the presence of two coupling constants (J = 4.4, 5.5 Hz) between the 3a-H and 4-H protons. It is known that the *cis* coupling constant between 3a-H and 9b-H in analogous 5+6-fused systems ranges from 6 to 9 Hz, while the corresponding *trans* constant is equal to 11–12 Hz. Moreover, both coupling constants between 3a-H and 4-H in *cis*-fused systems are lesser than 10 Hz, while in *trans*-fused systems one of these exceeds 10 Hz [2–4, 10, 11].

The configuration of C^3 is determined by stereoselectivity of 1,3-dipolar cycloaddition and *trans*-configuration of the double C=C bond in the initial Schiff base. The configuration of C^2 in molecules **Va** and **Vb** cannot be established on the basis of the ^{1}H NMR spectra; therefore, further experiments were performed with Schiff bases **II** and **III** in which the activating group is CO_2Me rather than CO_2Et. The relative position of the phenyl group on C^2 and CO_2Me group on C^3 can readily be determined from the chemical shift of the methoxy protons in the ^{1}H NMR spectrum. The structure of compound **Va** was unambiguously proved by X-ray analysis (Fig. 1).

The reaction of Schiff base **II** with methyl 2-diazo-2-phenylacetate in the presence of $Rh_2(OAc)_4$ led to formation of two stereoisomeric chromeno[4,3-*b*]pyrroles **VIa** and **VIb**. By column chromatography we isolated a mixture of compounds **VIa** and **VIb** (overall yield 59%) at a ratio of 7:1. The pure isomers were isolated by fractional crystallization from methanol–hexane. The NMR spectra of compound **VIa** were almost similar to those of **Va**, except for signals belonging to protons in the ester fragments. Therefore, isomer **VIa** was assigned the same structure as **Va**. It should be noted that the chemical shift of methyl protons in the CO_2Me group on C^3 is 3.7–3.9 ppm, i.e., it is typical of *trans* arrangement of the methoxycarbonyl group and phenyl group on C^2.

The structure of compound **VIb** was determined by analysis of the NMR spectra. The coupling constant between 3a-H and 9b-H in the ^{1}H NMR spectrum is equal to 11.7 Hz, and interaction between the 3a-H and 4-H protons is characterized by two constants, one of which is large (5.4 and 11.8 Hz). These data indicate *trans* junction of the pyran and pyrrolidine rings in

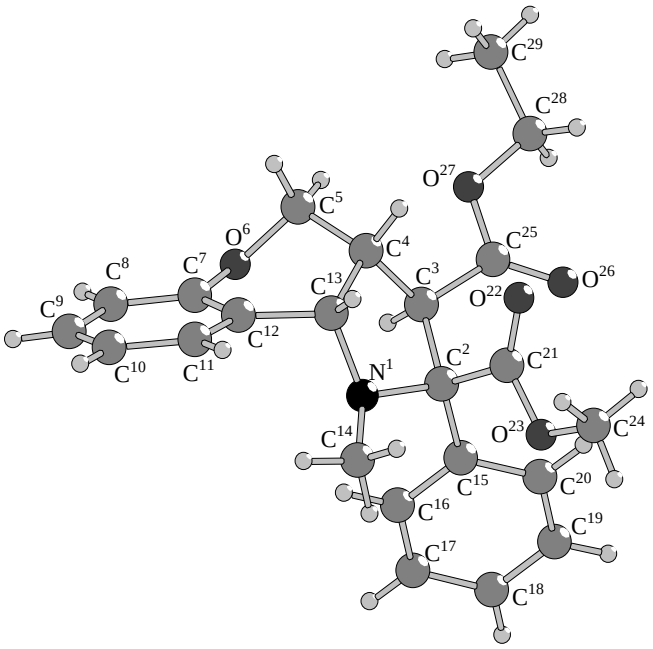
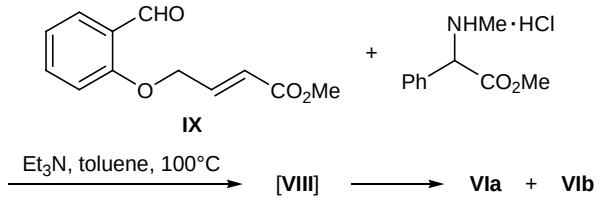


Fig. 1. Structure of the molecule of ethyl (2*RS*,3*RS*,3a*RS*,-9b*SR*)-1-methyl-2-methoxycarbonyl-2-phenyl-1,2,3,3a,4,9b-hexahydrochromeno[4,3-*b*]pyrrole-3-dicarboxylate (**Va**) according to the X-ray diffraction data.

isomer **VIb**. The configuration of C^3 is determined by stereoselectivity of 1,3-dipolar cycloaddition and *trans*-configuration of the double C=C bond in the initial Schiff base. In addition, the 3-H and 3a-H protons are coupled through a constant ($J_{3,3a}$) of 11.9 Hz, typical of their *trans* arrangement [23, 25, 26, 28, 30]. The configuration of C^2 in **VIb** follows from the chemical shift of methyl protons in the CO_2Me group on C^3 (δ 3.31 ppm). The upfield shift of the CO_2Me signal relative to its usual position (δ 3.7–3.9 ppm) is caused by the *cis* arrangement of the methoxycarbonyl group on C^3 and phenyl group on C^2 [12–15].

It is known that *N*-alkyl-substituted azomethine ylides can also be generated by condensation of the corresponding aldehyde and secondary amine ("deprotonation" technique) [9]. With a view to estimate the efficiency of the carbene procedure for generation of azomethine ylides and compare the selectivities in cycloaddition of ylides generated by different methods,

Scheme 2.



we examined intramolecular cycloaddition in azomethine ylide **VIII** generated by deprotonation [11, 16]. For this purpose, a mixture of aldehyde **IX** and methyl 2-methylamino-2-phenylacetate in toluene was heated at the boiling point with simultaneous removal of water as azeotrope. As a result, we obtained the same products (**VIa** and **VIb**, Scheme 2) as in the reaction with ylide **VIII** generated by the carbene method, but the isomer ratio was different (2:1).

The ratio of stereoisomers depends on a number of factors, one of which is the reaction temperature. We performed a series of experiments in which ylide **VIII** was generated using both carbene and deprotonation techniques at various temperatures. The results are collected in Table 1. It is seen that the selectivity decreases as the temperature rises. This may be due to leveling of the rates of reactions leading to isomers **VIa** and **VIb** and isomerization of **VIb** into **VIa**. By special experiments we found that isomers **VIa** and **VIb** are stable under the given conditions. According to the ^{1}H NMR data, heating of compound **VIa** or **VIb** for 4 h in benzene in the presence of 4 mol % of $Rh_2(OAc)_4$ or for 40 h in the presence of $Et_3N{\cdot}HCl$ gives no isomerization products.

The reactions of Schiff bases **III** and **IV** with methyl 2-diazo-2-phenylacetate in boiling methylene chloride afforded the corresponding 1,3-cyclization products **XII** and **XIII** (yield 40 and 60%, respectively) instead of 1,3-dipolar cycloaddition products of intermediate azomethine ylides **X** and **XI** (Scheme 3). According to Doyle *et al*. [17], *N*-benzylideneanilines under analogous conditions give rise to aziridines with *cis* orientation of the aryl groups in positions *2* and *3*. For comparison, we synthesized methyl *cis*-1,2,3-triphenylaziridine-2-carboxylate (**XIV**) whose steric structure was determined [17] by X-ray analysis; however, its ^{1}H NMR spectrum was not reported. On the basis of the spectral data, compounds **XII** and **XIII** were assigned the structure with *cis*-oriented aromatic substituents.

Aziridines having a strong π-acceptor group at a ring carbon atom are known to readily undergo ring opening at the C^2–C^3 bond at elevated temperature to give azomethine ylides [1]. Aziridine **XII** was subjected to thermolysis in order to estimate the stereoselectivity of intramolecular cycloaddition in *N*-aryl-substituted azomethine ylides generated by the "aziridine" technique. A solution of aziridine **XII** was heated in anhydrous xylene under reflux, and we thus obtained 87% of diastereoisomeric products **XVa** and **XVb** at

Table 1. Ratios of stereoisomeric cycloaddition products obtained from azomethine ylide **VIII** generated by the carbene and deprotonation methods

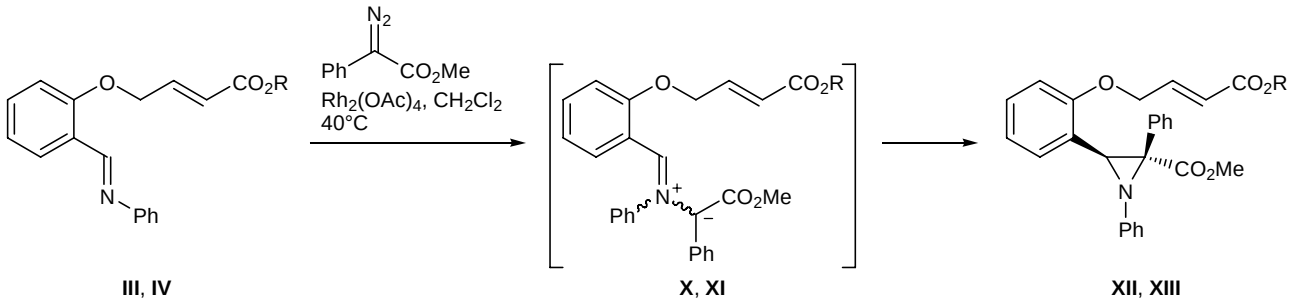
Carbene method					
Schiff base **II**, mmol	$PhC(N_2)CO_2Me$, mmol	Temperature, °C	Solvent	Reaction time, h	Ratio **VIa**:**VIb**
0.1	0.25	20	CH_2Cl_2	8	8:1
1.0	1.9	40	CH_2Cl_2	8	7:1
0.125	0.25	80	Benzene	4	4:1
Deprotonation method					
Aldehyde **IX**, mmol	$PhCH(NHMe)CO_2Me$, mmol				
0.25	0.50	80	Benzene	58	3:1
1.00	2.00	110	Toluene	4	2:1

a ratio of 3:1 (Scheme 4). The isomers were separated by fractional crystallization from methanol–heptane. Their structure was determined on the basis of their NMR spectra. The *trans* junction of the pyran and pyrrolidine rings in molecules **XVa** and **XVb** follows from the coupling constant between the 3a-H and 9b-H protons, which is equal to 11.6 Hz, and from the presence of one large coupling constant between 3a-H and 4-H (J 5.4 and 11.7 Hz) [2–4, 10, 11]. The configuration at C^3 is determined by stereoselectivity of 1,3-dipolar cycloaddition and *trans*-configuration of the double C=C bond in the initial Schiff base; also, a large coupling constant between 3-H and 3a-H ($J_{3,3a}$ = 12.5 Hz) is typical of *trans* arrangement of the 3-H and 3a-H protons [2–4, 10, 11]. The configuration at the C^2 atom in isomer **XVa** follows from the chemical shift of methyl protons in the CO_2Me group on C^3 (δ 3.38 ppm). The signal from these protons appears in a stronger field (as compared to its usual position) due to *cis* orientation of the methoxycarbonyl group on C^3 with respect to the phenyl group on C^2. By contrast, the chemical shift of the CO_2Me protons in isomer **XVb** has its usual value (δ 3.87 ppm), indicating *trans* arrangement of the methoxycarbonyl group on C^3 and phenyl group on C^2 [12–15]. The structure of isomer **XVa** was finally proved by X-ray analysis (Fig. 2).

It should be noted that thermolysis of aziridine **XIII** in the presence of a small amount of water gives the corresponding cycloadducts as minor products (overall yield less than 15%), while the major products are aldehyde **XVI** and ethyl 2-phenyl-2-phenylaminoacetate. The latter are formed by hydrolysis of ylide **XI** (Scheme 5). These data suggest that the hydrolysis of ylide intermediate occurs at a much higher rate than does the intramolecular cycloaddition at the activated C=C bond.

In order to compare the selectivities in the reactions of ylide **X** generated by different methods (thermolysis of aziridine **XII** and deprotonation) we performed condensation of aldehyde **IX** with methyl 2-phenyl-2-phenylaminoacetate (Scheme 6). This reaction also afforded compounds **XVa** and **XVb**. However, to ensure an acceptable rate, the reaction was carried out in boiling xylene, which should affect the diastereo-

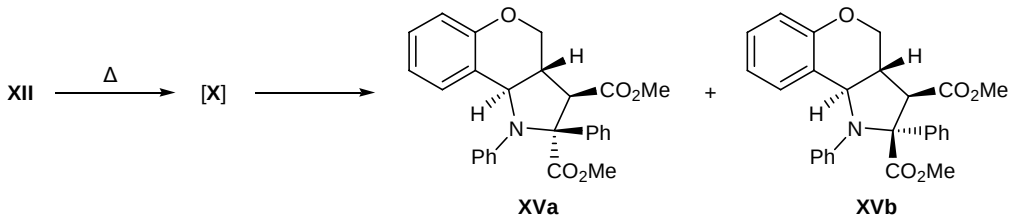
Scheme 3.



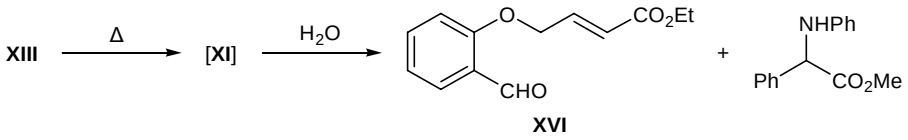
III, **IV** **X**, **XI** **XII**, **XIII**

III, **X**, **XII**, R = Me; **IV**, **XI**, **XIII**, R = Et.

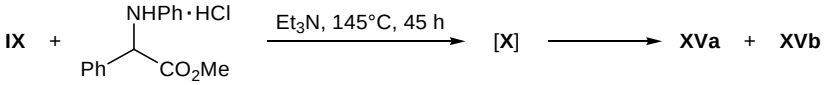
Scheme 4.



Scheme 5.



Scheme 6.

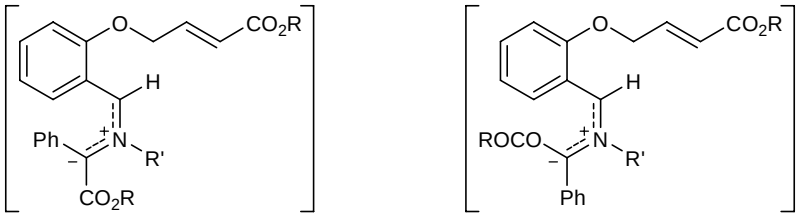


isomer ratio. Therefore, we performed a similar reaction in toluene with incomplete conversion of the initial compounds. In this case, the cycloaddition stereoselectivity was almost the same as in the transformation of azomethine ylide **X** generated by the aziridine technique (Table 2). By special experiments we found that isomers **XVa** and **XVb** are stable under the given conditions: according to the ^{1}H NMR data, no isomerization of **XVa** and **XVb** occurred on heating for 40 h in toluene in the presence of an equimolar amount of $Et_3N \cdot HCl$.

Thus, all the examined azomethine ylides capable of undergoing intramolecular 1,3-dipolar cycloaddition at activated double C=C bond react in a regioselective fashion, yielding only fused polycyclic compounds (no regioisomeric bridged structures were detected; cf.

Scheme 7.

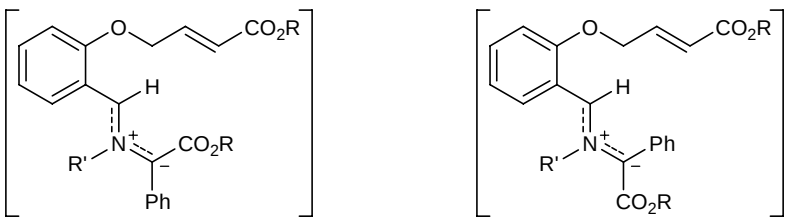
Carbene ylides



(*E*,*Z*)-Ylide (*Z*,*Z*)-Ylide

Δ*H*°, kcal/mol:	R' = Me	–90.7	–90.8
	R' = Ph	–57.1	–57.6

Noncarbene ylides



(*Z*,*E*)-Ylide (*E*,*E*)-Ylide

Δ*H*°, kcal/mol:	R' = Me	–98.8	–98.5
	R' = Ph	–62.5	–61.9

Table 2. Ratios of stereoisomeric cycloaddition products obtained from azomethine ylide **X** generated by the aziridine and deprotonation methods

Deprotonation method					
Aldehyde **IX**, mmol	PhCHN(Ph)CO_2Me, mmol	Temperature, °C	Solvent	Reaction time, h	Ratio **XVa**:**XVb**
1.50	3.00	110	Toluene	50[a]	1:3
1.50	3.00	145	Xylene	35	1:3
Aziridine method					
Aziridine **XII**		110	Toluene	4	1:3

[a] Conversion ≈ 40%.

[7]). The stereoselectivity of this process depends on the substituent at the nitrogen atom, ylide generation method, and temperature.

Each ylide **VII**, **VIII**, **X**, and **XI** can exist as four stereoisomeric structures which, in keeping with the generally accepted denotations [9], may be referred to as (*E*,*Z*), (*Z*,*Z*), (*Z*,*E*), and (*E*,*E*) isomers (Scheme 7). In addition, the first two isomers may be regarded as carbene-like, for just these isomers should be formed by addition of electrophilic carbene (carbenoid) at the lone electron pair on the nitrogen atom of Schiff base having *E* configuration. Scheme 7 also shows enthalpies of formation of the above ylides, calculated by the PM3 semiempirical method with full geometry optimization.

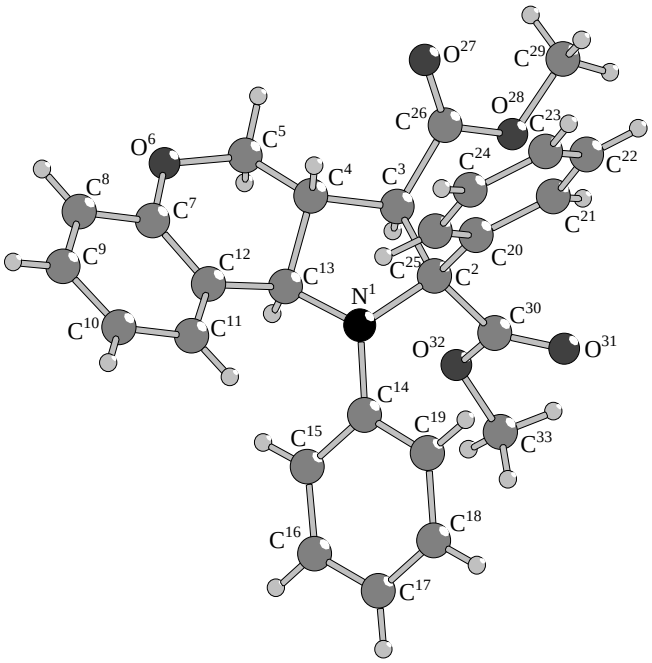


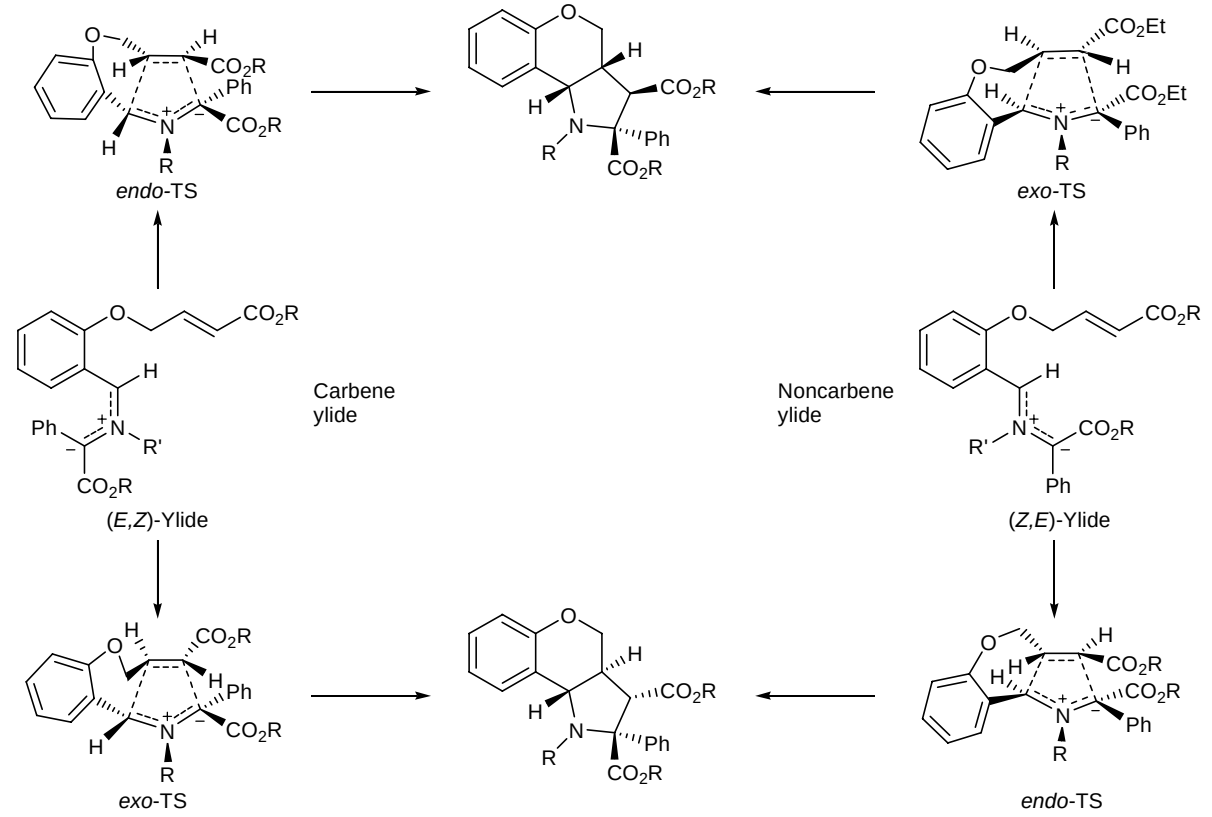
Fig. 2. Structure of the molecule of dimethyl (2*RS*,3*RS*,-3a*RS*,9b*SR*)-1,2-diphenyl-1,2,3,3a,4,9b-hexahydrochromeno-[4,3-*b*]pyrrole-2,3-dicarboxylate (**XVa**) according to the X-ray diffraction data.

1,3-Dipolar cycloaddition can involve transition states (TS) of two types, *endo* and *exo*; in *endo*-TS the activating group and ylide nitrogen atom are oriented at one side, and in *exo*-TS these fragments are oriented at opposite sides. As shown in Schemes 8 and 9, the four isomeric ylide could give rise to four stereoisomeric intramolecular cycloaddition products. It is seen that stereoisomers **Va**/**Vb** and **VIa**/**VIb** obtained in the reactions with *N*-methyl-substituted Schiff bases could be formed only from (*E*,*Z*)- or (*Z*,*E*)-ylide and that the major isomer could be formed from carbene (*E*,*Z*)-ylide through *endo*-TS and from noncarbene (*Z*,*E*)-ylide through *exo*-TS. On the other hand, the minor isomer could be formed from carbene (*E*,*Z*)-ylide through *exo*-TS and from noncarbene (*Z*,*E*)-ylide through *endo*-TS (Scheme 10).

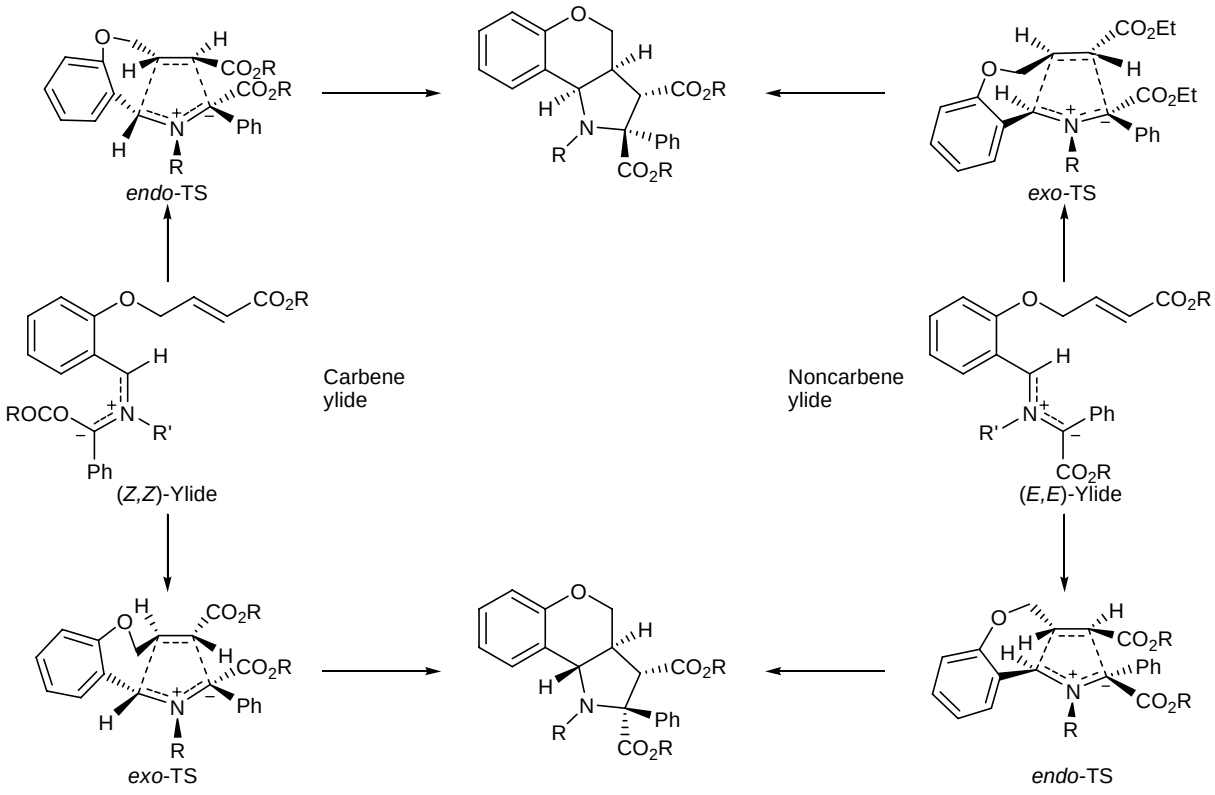
Taking into account that noncarbene ylides are more stable than carbene ylides (according to the calculations) and that the reaction stereoselectivity decreases as the temperature rises, we believe that ylide generation by the carbene method at low temperature gives rise mainly to the reaction channel involving *endo*-TS, which leads to formation of major products **Va** and **VIa** with *cis*-fused pyran and pyrrolidine rings. Elevated temperature favors isomerization of the carbene ylide into noncarbene, and the fraction of minor isomers **Vb** and **VIb** (which are also formed through the corresponding *endo*-TS) with s *trans*-fused rings increases. The *endo*-TS was also preferred over *exo*-TS in many other 1,3-dipolar cycloaddition reactions of azomethine ylides [9]. Unfortunately, it is difficult to estimate the relative rates of formation of carbene and noncarbene ylides generated by the deprotonation method.

Increase in steric hindrances to cycloaddition in *N*-phenyl-substituted ylides **X** and **XI** generated by the carbene procedure at 40°C is responsible for formation of only 1,3-cyclization products, aziridines **XII** and **XIII**. These compounds could be formed via thermally

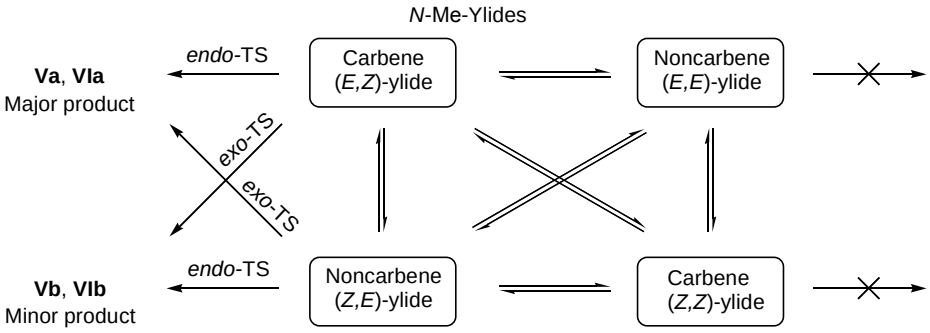
Scheme 8.



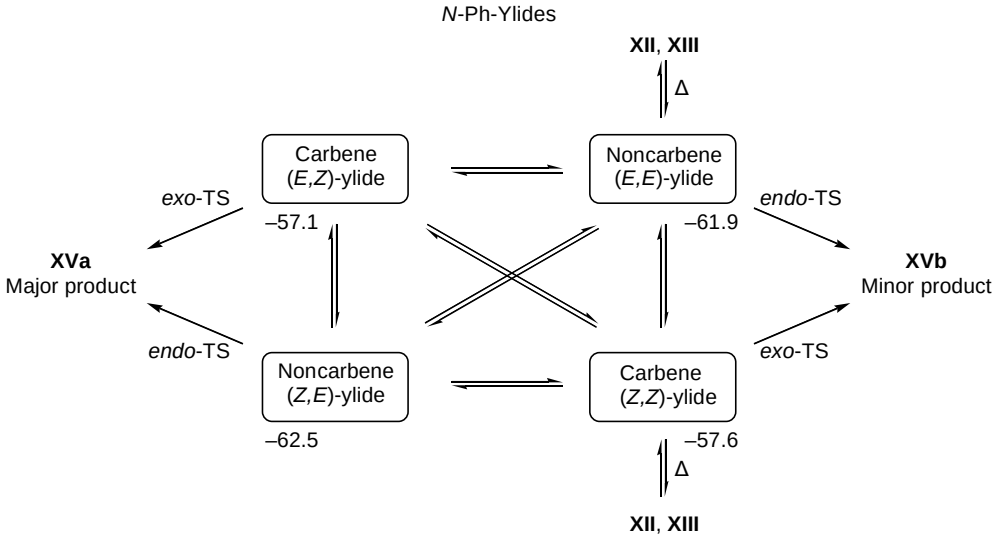
Scheme 9.



Scheme 10.



Scheme 11.



allowed conrotatory closure of carbene (*Z*,*Z*)-ylide or noncarbene (*E*,*E*)-ylide. Presumably, the first channel involving kinetically preferred carbene (*Z*,*Z*)-ylide is operative at low temperature.

The rate of intramolecular cycloaddition in *N*-phenyl-substituted ylides **X** and **XI** generated by thermolysis (145°C) and deprotonation is lower; therefore, these ylides are likely to exist in equilibrium. In this case, the observed stereoselectivity is readily rationalized in terms of the above assumed preference of *endo*-TS in the cycloaddition process: both products are formed from the two most stable isomers of the azomethine ylide through *endo*-TS: more stable (*Z*,*E*)-ylide gives rise to major isomer **XVa**, and less stable (*E*,*E*)-ylide, to minor isomer **XVb** (Scheme 11).

Thus we have studied intramolecular 1,3-dipolar cycloaddition in azomethine ylides generated by the carbene method, i.e., by rhodium acetate-catalyzed reaction of methyl 2-diazo-2-phenylacetate with *ortho*-substituted *N*-methylbenzylideneamines containing an activated C=C dipolarophilic fragment in the side chain. The product structure indicates that the process occurs as regioselective intramolecular cycloaddition of only (*Z*,*E*)-/(*E*,*Z*)-ylides with formation of fused polycyclic compounds, hexahydrochromeno[4,3-*b*]pyrrole derivatives. The reaction stereoselectivity depends on the temperature. In the temperature range from 20 to 80°C, isomers with *cis*-fused tetrahydropyran and pyrrolidine rings are mainly formed. Replacement of the methyl group on the nitrogen atom by bulky phenyl substituent changes the reaction direction. *N*-Phenyl-substituted azomethine ylides generated from methyl 2-diazo-2-phenylacetate and (2-phenyliminomethylphenoxy)-2-butenoic acid esters at 40°C undergo cyclization to the corresponding aziridine at a higher rate, as compared to the cycloaddition at the internal dipolarophile moiety. *N*-Phenyl azomethine ylides generated by thermolysis (110–145°C) of the corresponding aziridine or by the deprotonation method react with similar regio- and stereoselectivity to give intramolecular cycloaddition products, hexahydrochromeno[4,3-*b*]pyrrole derivatives with *trans*-fused tetrahydro-

pyran and pyrrolidine rings. Analysis of the experimental and calculation data showed that the *endo*-transition state is preferred in the cycloaddition of the examined azomethine ylides. Tandem process at about 40°C, which includes carbene generation of azomethine ylides by reaction of methyl 2-diazo-2-phenylacetate in the presence of rhodium acetate with *N*-alkylbenzylideneamines containing an activated C=C dipolarophilic fragment in the side chain, is preferred from the viewpoint of selective synthesis of hexahydrochromeno[4,3-*b*]pyrrole derivatives with *cis*-fused tetrahydropyran and pyrrolidine rings.

EXPERIMENTAL

The melting points were determined on a Boetius melting point apparatus; uncorrected values are given. The IR spectra were recorded on a Carl Zeiss UR-20 instrument using 400-μm cells. The NMR spectra were obtained on a Bruker DPX 300 spectrometer at 300 and 75 MHz for ^{1}H and ^{13}C, respectively. The elemental compositions were determined on an HP-185B CHN analyzer. The progress of reactions was monitored by thin-layer chromatography using Silufol UV-254 plates. Silica gel Merck 60 was used for column chromatography. Methylene chloride was dried by distillation over P_2O_5.

Reactions of Schiff bases I–IV and *N*-benzylideneaniline with methyl 2-diazo-2-phenylacetate. Schiff base **I**, 0.248 g (1 mmol), was mixed under argon with 4.4 mg (1.1 mol %) of $Rh_2(OAc)_4$ and 3.5 ml of methylene chloride. The mixture was heated to the boiling point, and a solution of 0.342 g (1.95 mmol) of methyl 2-diazo-2-phenylacetate in 6.5 ml of methylene chloride was added dropwise under stirring over a period of 6 h using a syringe. The progress of the reaction was monitored by TLC using hexane–ethyl acetate (10:1) as eluent. The isomer ratio of the products was determined as follows. A sample of the reaction mixture (2–3 ml) was filtered through a thin layer of silica gel, and the solvent was washed with 50 ml of methylene chloride. The filtrate was combined with the washings and evaporated, and ^{1}H NMR spectrum of the residue was recorded. The products were isolated by column chromatography (gradient elution with hexane–ethyl acetate, 15:1, to ethyl acetate). The major isomer (**Va**, 0.260 g) was recrystallized from hexane–diethyl ether.

Ethyl (2*RS*,3*RS*,3a*RS*,9b*SR*)-1-methyl-2-methoxycarbonyl-2-phenyl-1,2,3,3a,4,9b-hexahydrochromeno[4,3-*b*]pyrrole-3-carboxylate (Va). Yield 0.240 g (59%). mp 115–118°C (from hexane–diethyl ether). IR spectrum ($CHCl_3$), ν, cm^{-1}: 940, 1180, 1220, 1260, 1460, 1490, 1580, 1610, 1730, 2950, 3020, 3060. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.27 t (3H, SCH_3, J = 7.2 Hz), 2.21 s (3H, NCH_3), 3.00 d (1H, 3-H, J = 6.9 Hz), 3.31 d.d.d.d (1H, 3a-H, $J_{3a,3}$ = 6.9, $J_{3a,9b}$ = 8.3, $J_{3a,4}$ = 4.4, 5.5 Hz), 3.85 s (3H, OCH_3), 3.93 d (1H, 9b-H, $J_{9b,3a}$ = 8.3 Hz), 3.95 d.d (1H, 4-H, $J_{3a,4}$ = 4.5, $J_{4,4}$ = 11.0 Hz), 4.14 d.d (1H, 4-H, $J_{3a,4}$ = 5.5, ^2J = 11.0 Hz), 6.98–7.03 m (2H, H_{arom}), 7.20–7.32 m (5H, H_{arom}), 7.59–7.61 m (2H, H_{arom}). ^{13}C NMR spectrum (DEPT, $CDCl_3$), δ_C, ppm: 13.7 (CH_3); 33.6 (NCH_3); 39.5 (C^{3a}); 50.9 (OCH_3); 57.7 (C^3); 59.2 (C^{9b}); 60.5 ($CO_2\mathbf{C}H_2$); 69.2 (Ar$\mathbf{O}$CH_2); 76.9 (C^2); 117.3, 120.5, 123.48, 127.2, 127.4, 127.7, 128.4, 130.5, 139.8, 156.7 (C_{arom}); 169.8 (C=O); 170.9 (C=O). Found, %: C 69.81; H 6.58; N 3.20. $C_{23}H_{25}NO_5$. Calculated, %: C 69.86; H 6.37; N 3.54. The structure of **Va** was proved by the X-ray diffraction data (Fig. 1). $C_{23}H_{25}NO_5$, M 395.44. Unit cell parameters: a = 24.449(5), b = 24.449(5), c = 7.0278(18) Å; α = β = γ = 90°; V = 4201.0(17) Å^3; d_{calc} = 1.250 g/cm^3; tetragonal crystal system; space group I-4 (no. 82); Z = 8; λ = 0.71073 Å, temperature 293 K, crystal habit 0.5×0.4×0.2 mm, R_{All} = 0.063, wR_2 = 0.1151; 6703 reflections, 3126 independent reflections (R_{int} = 0.0285).

Following the general procedure, from 0.233 g (1 mmol) of Schiff base **II** in 3.5 ml of methylene chloride, 20 mg (4.5 mol %) of $Rh_2(OAc)_4$, and 0.336 g (1.9 mmol) of methyl 2-diazo-2-phenylacetate in 8 ml of methylene chloride we obtained 0.225 g (59%) of a mixture of dimethyl (2*RS*,3*RS*,3a*RS*,9b*SR*)-1-methyl-2-phenyl-1,2,3,3a,4,9b-hexahydrochromeno-[4,3-*b*]pyrrole-2,3-dicarboxylate (**VIa**) and dimethyl (2*RS*,3*SR*,3a*SR*,9b*SR*)-1-methyl-2-phenyl-1,2,3,3a,-4,9b-hexahydrochromeno[4,3-*b*]pyrrole-2,3-dicarboxylate (**VIb**) at a ratio of 7:1. Isomer **VIa** was isolated by repeated crystallization from hexane–methanol. mp 122–123°C. IR spectrum ($CHCl_3$), ν, cm^{-1}: 990, 1010, 1130, 1250, 1450, 1490, 1585, 1605, 1740, 2850, 3040. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 2.22 s (3H, NCH_3), 3.04 d (1H, 3-H, $J_{3,3a}$ = 6.9 Hz), 3.32 d.d.d.d (1H, 3a-H, J = 4.5, 5.4, 6.9, 8.3 Hz), 3.72 s (3H, OCH_3), 3.85 s (3H, OCH_3), 3.94 d (1H, 9b-H, $J_{9b,3a}$ = 8.3 Hz), 3.95 d.d (1H, 4-H, $J_{4,3a}$ = 4.5, ^2J = 11.1 Hz), 4.15 d.d (1H, 4-H, $J_{4,3a}$ = 5.4, ^2J = 11.1 Hz), 6.98–7.03 m (2H, H_{arom}), 7.21–7.36 m (5H, H_{arom}), 7.58–7.61 m (2H, H_{arom}). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 34.5 (NCH_3); 40.4 (C^{3a}); 51.9 (OCH_3); 52.5 (OCH_3); 58.6 (C^3); 60.1 (C^{9b}); 70.1 (CH_2); 74.6 (C^2); 121.4, 124.4, 128.1, 128.4, 128.5, 129.3, 131.4, 140.6, 157.7 (C_{arom}); 170.8 (C=O); 172.3 (C=O). $C_{22}H_{23}NO_5$. Found, %: C 69.29; H 5.98; N 3.92. Calculated, %: C 69.28; H 6.08; N 3.67.

Following the general procedure, from 0.590 g (2.0 mmol) of Schiff base **III** in 4 ml of methylene chloride, 4.4 mg (3.75 mol %) of $Rh_2(OAc)_4$, and 0.220 g (1.25 mmol) of methyl 2-diazo-2-phenylacetate in 6 ml of methylene chloride we isolated by column chromatography (gradient elution with hexane–ethyl acetate, 10:1, to ethyl acetate) 0.248 g (40%) of methyl (2*RS*,3*RS*)-3-{2-[(*E*)-3-(methoxycarbonyl)-2-propenyloxy]phenyl}-1,2-diphenylaziridine-2-carboxylate (**XII**). mp 104–105°C (from CH_2Cl_2–hexane). IR spectrum ($CHCl_3$), ν, cm^{-1}: 965, 1030, 1120, 1255, 1280, 1305, 1445, 1495, 1595, 1660, 1715, 2850, 3050. ^1H NMR spectrum ($CDCl_3$), δ, ppm: 3.59 s (3H, OCH_3), 3.78 s (3H, OCH_3), 4.73 s (1H, 3-H), 4.68–4.84 m (2H, CH_2), 6.39 d.t (1H, =CH, J = 2.2, 15.7 Hz), 6.69–6.77 m (2H, H_{arom}), 7.05–7.40 m (13H, H_{arom}, =CH). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 48.6 (C^3); 51.3 (CH_3O); 52.2 (CH_3O); 55.7 (C^2); 65.7 (CH_2O); 109.9, 118.8, 120.3, 120.6, 122.5, 123.4, 127.1, 127.2, 128.2, 128.3, 128.4, 128.7, 134.0, 142.2, 149.5, 155.8 (C_{arom}); 166.3 (C=O); 168.2 (C=O). Found, %: C 73.24; H 5.58; N 3.04. $C_{27}H_{25}NO_5$. Calculated, %: C 73.12; H 5.68; N 3.16.

Following the general procedure, from 0.154 g (0.5 mmol) of Schiff base **IV** in 4 ml of methylene chloride, 4.4 mg (2.21 mol %) of $Rh_2(OAc)_4$, and 0.220 g (1.25 mmol) of methyl 2-diazo-2-phenylacetate in 6 ml of methylene chloride we isolated by column chromatography (gradient elution with hexane–ethyl acetate, 15:1, to ethyl acetate) 0.140 g (60%) of methyl (2*RS*,3*RS*)-1,2-diphenyl-*t*-3-{2-[(*E*)-3-(ethoxycarbonyl)-2-propenyloxy]phenyl}aziridine-*r*-2-carboxylate (**XIII**). mp 85–87°C (from diethyl ether). IR spectrum ($CHCl_3$), ν, cm^{-1}: 940, 1110, 1250, 1310, 1460, 1490, 1595, 1660, 1720, 2980, 3040. ^1H NMR spectrum ($CDCl_3$), δ, ppm: 1.31 t (3H, CCH_3, J = 7.1 Hz), 3.59 s (3H, OCH_3), 4.24 q (2H, $OC\mathbf{H}_2CH_3$, J = 7.1 Hz), 4.73 s (1H, 3-H), 4.68–4.84 m (2H, CH_2), 6.36 d.d.d (1H, =CH, J = 1, 2.3, 15.7 Hz), 6.69–6.77 m (2H, H_{arom}), 7.04–7.35 m (13H, H_{arom}, =CH). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 13.9 (CH_3); 48.6 (C^2 or C^3); 52.1 (OCH_3); 55.6 (C^2 or C^3); 60.2 (CH_2O); 65.8 (CH_2O); 109.9, 118.8, 120.3, 121.0, 122.5, 123.4, 127.1, 127.2, 128.1, 128.2, 128.4, 128.7, 134.0, 141.9, 149.4, 155.8 (C_{arom}, CH=); 165.9 (C=O); 168.2 (C=O). Found, %: C 73.49; H 6.09; N 2.97. $C_{28}H_{27}NO_5$. Calculated, %: C 73.51; H 5.95; N 3.06.

Methyl *cis*-1,2,3-triphenylaziridine-2-carboxylate (XIV). A solution of 47 mg (0.27 mmol) of methyl 2-diazo-2-phenylacetate in 1 ml of methylene chloride was added dropwise under stirring at 40°C to a solution of 48 mg (0.27 mmol) of *N*-benzylideneaniline and 5 mg (4.5 mol %) of $Rh_2(OAc)_4$ in 1 ml of methylene chloride. The product was isolated by column chromatography (eluent hexane–ethyl acetate, 20:1), followed by recrystallization from hexane–diethyl ether. Yield 35 mg (56%). ^1H NMR spectrum ($CDCl_3$), δ, ppm: 3.56 s (3H, OCH_3), 4.50 s (1H, 3-H), 7.05–7.75 m (18H, H_{arom}).

Reactions of aldehyde IX with methyl 2-methylamino-2-phenylacetate and methyl 2-phenyl-2-phenylaminoacetate. A 25-ml flask equipped with a reflux condenser and a Dean–Stark trap was charged with 0.234 g (1 mmol) of aldehyde **IX**, 0.431 g (2 mmol) of methyl 2-methylamino-2-phenylacetate hydrochloride, 15 ml of toluene, and 0.202 g (2 mmol) of triethylamine. The mixture was heated for 4 h under reflux, the progress of the reaction being monitored by TLC (hexane–ethyl acetate, 7:1). When the reaction was complete, the solvent was removed, the residue was extracted with diethyl ether, and the extract was concentrated and subjected to column chromatography using hexane–ethyl acetate (10:1) as eluent to isolate 0.342 g (90%) of a mixture of diastereoisomers **VIa** and **VIb**. Analytically pure samples of **VIa** and **VIb** were obtained by fractional recrystallization from methanol–hexane. The data for **VIa** are given above.

Compound **VIb**. mp 172–174°C (from methanol–hexane). IR spectrum ($CHCl_3$), ν, cm^{-1}: 990, 1020, 1260, 1470, 1505, 1595, 1620, 1760, 2820, 3020. ^1H NMR spectrum ($CDCl_3$), δ, ppm: 2.70 m (1H, 3a-H, $J_{4,3a}$ = 5.4, $J_{9b,3a}$ = 11.7, $J_{4,3a}$ = 11.8, $J_{3,3a}$ = 11.9 Hz), 2.72 s (3H, NCH_3), 3.31 s (3H, OCH_3), 3.87 d (1H, 9b-H, $J_{9b,3a}$ = 11.7 Hz), 3.90 s (3H, OCH_3), 4.06 d (1H, 3-H, $J_{3,3a}$ = 11.9 Hz), 4.22 d.d (1H, 4-H, $J_{4,4}$ = 9.6, $J_{4,3a}$ = 11.8 Hz), 4.40 d.d (1H, 4-H, $J_{4,3a}$ = 5.4, $J_{4,4}$ = 9.6 Hz), 6.90–7.02 m (2H, H_{arom}), 7.19–7.30 m (4H, H_{arom}), 7.50–7.54 m (3H, H_{arom}). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 37.1 (NCH_3); 41.3 (C^{3a}); 51.3 (OCH_3); 52.0 (OCH_3); 54.3 (C^3); 63.0 (C^{9b}); 69.6 (CH_2); 80.4 (C^2); 116.4, 120.0, 122.7, 127.1, 127.6, 127.7, 128.1, 137.6, 154.9 (C_{arom}); 169.7 (C=O); 172.0 (C=O). Found, %: C 69.71; H 5.98; N 3.96. $C_{22}H_{23}NO_5$. Calculated, %: C 69.28; H 6.08; N 3.67.

Following an analogous procedure, from 0.351 g (1.5 mmol) of aldehyde **IX**, 0.431 g (3 mmol) of methyl 2-phenyl-2-phenylaminoacetate hydrochloride, and 0.303 g (3 mmol) of triethylamine in 15 ml of xylene (35 h under reflux) by column chromatography (hexane–ethyl acetate, 10:1) we isolated 0.382 g (86%) of a mixture of dimethyl (2*RS*,3*RS*,3a*RS*,9b*SR*)-1,2-diphenyl-1,2,3,3a,4,9b-hexahydrochromeno-[4,3-*b*]pyrrole-2,3-dicarboxylate (**XVa**) and dimethyl

(2*RS*,3*SR*,3a*SR*,9b*SR*)-1,2-diphenyl-1,2,3,3a,4,9b-hexahydrochromeno[4,3-*b*]pyrrole-2,3-dicarboxylate (**XVb**). Analytically pure samples of **XVa** and **XVb** were obtained by fractional crystallization from methanol–hexane.

Major isomer **XVa**. mp 203–234°C (decomp., from methanol–hexane). IR spectrum, ν, cm^{-1}: 990, 1050, 1260, 1325, 1460, 1490, 1500, 1605, 1703, 2890, 2850, 3045. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 2.82 m (1H, 3a-H, $J_{4,3a}$ = 5.4, $J_{9b,3a}$ = 10.6, $J_{4,3a}$ = 11.7, $J_{3,3a}$ = 12.5 Hz), 3.38 s (3H, OCH_3), 3.52 s (3H, OCH_3), 4.00 d (1H, 3-H, $J_{3,3a}$ = 12.5 Hz), 4.34 d.d (1H, 4-H, $J_{4,4}$ = 9.7, $J_{4,3a}$ = 11.7 Hz), 4.53 d.d (1H, 4-H, $J_{4,3a}$ = 5.4, $J_{4,4}$ = 9.7 Hz), 4.85 d (1H, 9b-H, $J_{9b,3a}$ = 10.6 Hz), 6.55–6.57 m (1H, H_{arom}), 6.79–7.37 m (11H, H_{arom}), 7.65–7.68 m (2H, H_{arom}). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 39.9 (C^{3a}); 51.6 (OCH_3); 52.1 (OCH_3); 56.7 (C^3); 58.9 (C^{9b}); 69.5 (CH_2); 80.9 (C^2); 116.1, 117.4, 119.0, 119.8, 121.0, 124.7, 126.1, 127.4, 127.8, 127.9, 128.0, 128.3, 128.6, 136.9, 146.9, 153.3 (C_{arom}); 168.3 (C=O); 170.8 (C=O). Found, %: C 73.04; H 5.74; N 2.96. $C_{27}H_{25}NO_5$. Calculated, %: C 73.12; H 5.68; N 3.16. The structure of **XVa** was proved by the X-ray diffraction data (Fig. 2). $C_{27}H_{25}NO_5$, *M* 443.50. Unit cell parameters: *a* = 8.5648(8), *b* = 13.2531(13), *c* = 20.023(2) Å; α = β = γ = 90°; *V* = 2272.81(40) $Å^3$; d_{calc} = 1.296 g/cm^3. Orthorhombic crystals, space group $P2_12_12_1$ (no. 19), *Z* = 4; λ = 0.71073 Å, temperature 293 K, crystal habit 0.45×0.4×0.35 mm; R_{All} = 0.046, wR_2 = 0.0827; 27626 reflections; 5355 independent reflections (R_{int} = 0.0285).

Minor isomer **XVb**. mp 184–185°C (from methanol–hexane). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 3.09 d.d.d.d (1H, 3a-H, $J_{4,3a}$ = 5.5, $J_{9b,3a}$ = 10.6, $J_{4,3a}$ = 11.5, $J_{3,3a}$ = 12.4 Hz), 3.23 (1H, 3-H, *J* = 12.4 Hz), 3.64 s (3H, OCH_3), 3.87 s (3H, OCH_3), 4.39 d.d (1H, 4-H, $J_{4,4}$ = 9.6, $J_{4,3a}$ = 11.5 Hz), 4.95 d.d (1H, 4-H, $J_{4,3a}$ = 5.5, $J_{4,4}$ = 9.6 Hz), 4.95 d (1H, 9b-H, $J_{9b,3a}$ = 10.6 Hz), 6.70–7.25 m (14H, H_{arom}). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 41.9 (C^{3a}); 51.6 (OCH_3); 52.5 (OCH_3); 60.4, 61.1 (C^3, C^{9b}); 70.7 (CH_2); 80.0 (C^2); 116.0, 119.2, 119.7, 124.7, 127.0, 127.3, 127.4, 127.5, 127.6, 128.8, 137.9, 144.7, 153.2 (C_{arom}); 169.4 (C=O); 171.6 (C=O). Found, %: C 73.14; H 5.98; N 3.14. $C_{27}N_{25}HO_5$. Calculated, %: C 73.12; H 5.68; N 3.16.

Thermolysis of methyl *t*-3-{2-[(*E*)-3-(methoxycarbonyl)-2-propenyloxy]phenyl}-1,2-diphenylaziridine-*r*-2-carboxylate (XII). A 25-ml flask equipped with a refluxed condenser capped with a drying tube was charged under argon with 77 mg (0.17 mmol) of aziridine **XII** in 10 ml of anhydrous toluene, and the resulting solution was heated for 4 h under reflux. According to the NMR data, the major products were cycloadducts **XVa** and **XVb**. An analytically pure sample of **XVa** was isolated by fractional crystallization from methanol–hexane.

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