Two-Carbon Ring Enlargement of Five-, Six-, and Seven-Membered 1-Aza-2-vinylcycloalk-2-enes with Dimethyl Acetylenedicarboxylate and Subsequent Thermal Isomerization Reactions*

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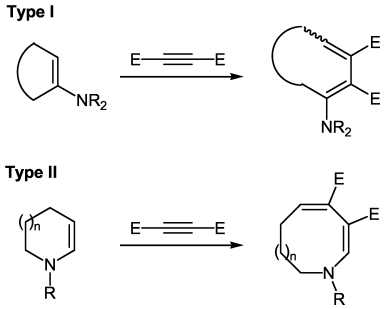
Z. Naturforsch. **61b,** 385 – 395 (2006); received October 6, 2005

2-Aminodienes, in which the enamine function is incorporated in a five-, six-, or seven-membered ring, react with dimethyl acetylenedicarboxylate in a sequence of [2+2] cycloaddition and electrocyclic ring-opening to form the two-carbon ring expanded unsaturated heterocycles, *i.e.*, 3,4-dicarboxylate substituted 6,7-dihydro-1*H*-azepines **3**, **8** and **21**, 1,6,7,8-tetrahydroazocines **22**, and 6,7,8,9-tetrahydro-1*H*-azonines **13**. Similarly, 2-[(2-thienyl)ethynyl]-4,5,6,7-tetrahydro-1*H*-azepine **9** is converted into 2-[(2-thienyl)ethynyl]-6,7,8,9-1*H*-azonine-3,4-dicarboxylate **10** which was characterized by X-ray structure determination. The eight- and nine-membered azaheterocycles **22** and **13**, which have not been isolated, undergo thermal isomerization at elevated temperatures. Thus, ring contraction by a 6π-electrocyclic reaction takes place for *N*-methyl substituted azonine **13**, while the *N*-allyl moiety of azocines **22** engages in an intramolecular Diels-Alder reaction or a 1,7-electrocyclization reaction.

Key words: Enamines, 2-Aminodienes, Medium-Sized Aza Heterocycles, Ring Enlargement, Ring Contraction

Introduction

The two-carbon ring expansion of enamines derived from cyclic ketones (*i. e.* 1-(dialkylamino)cycloalkenes) with electron-deficient alkynes, in particular acetylenic esters, has often been applied to the synthesis of medium-sized carbocyclic and heterocyclic compounds (Scheme 1, type I); see lit. [1] and cited references. Careful investigations have shown that in an unpolar solvent, [2+2] cycloaddition initially generates 3-amino-cyclobutenes which undergo conrotatory ring opening to form *cis,trans*-cycloalkadienes [1]. The condensed cyclobutenes derived from five- and six-membered enamines could be isolated under careful work-up conditions and were found to rearrange slowly into the *cis,cis*-cycloalkadienes, while the latter were obtained directly from larger-sized aminocycloalkenes. The *cis,trans*-dienes underwent thermal isomerization to form *cis,cis*-cycloalkadienes more or less readily, depending on the ring size.



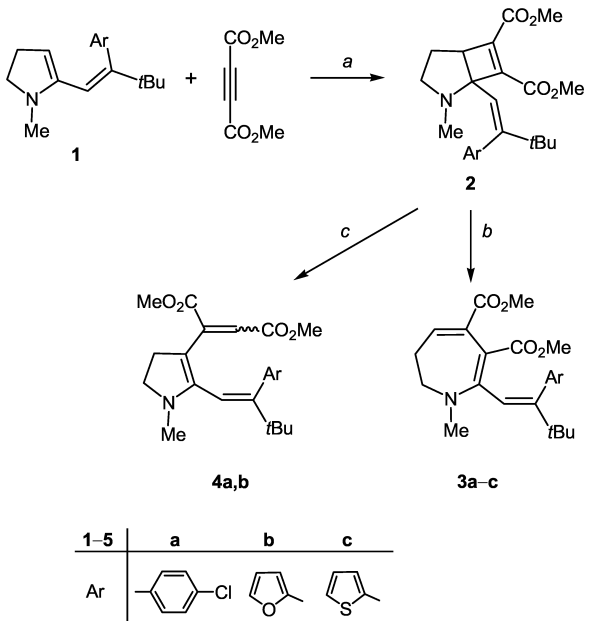
Scheme 1. Ring expansion of 1-amino-cycloalkenes (type 1) and 1-aza-2-cycloalkenes (type 2) with acetylenedicarboxylates (E = CO_2Me).

The two-carbon ring expansion strategy can also be used to convert endocyclic enamines into unsaturated seven-, eight-, and nine-membered azaheterocycles (Scheme 1, type II) [2 – 5]. Some years ago, we have worked out a method to prepare 1-aza-2-vinylcycloalk-2-enes, *i. e.*, semicyclic 2-amino-1,3-dienes, with the enamine functionality incorporated in five-, six-, and seven-membered rings [6]. We report now on the ring expansion of these cyclic enamines with dimethyl acetylenedicarboxylate and on subsequent thermally induced isomerization reactions [7].

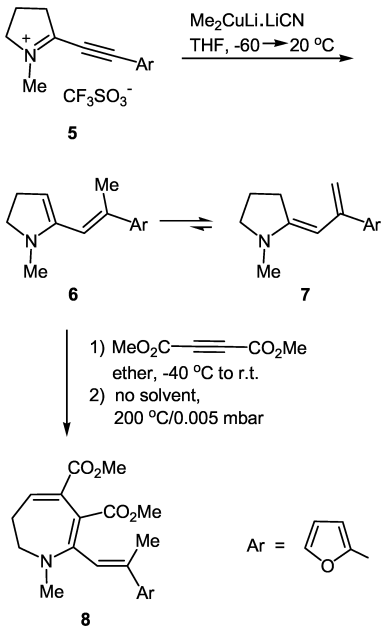
* Presented in part at the 7th Conference on Iminium Salts (ImSaT-7), Bartholomä/Ostalbkreis, September 6 – 8, 2005.

Results and Discussion

The 2-alkenyl-4,5-dihydropyrroles **1a – c** were prepared from the corresponding 1-((het)aryl)-2-(1-methylpyrrolidin-2-ylidene)ethan-1-one in three steps [6]. The reaction with dimethyl acetylenedicarboxylate (DMAD) was conducted in diethyl ether below room temperature to obtain the bicyclic [2+2] cycloaddition products **2** (Scheme 2). However, the latter could not be separated from the reaction mixture. When the work-up was done by Kugelrohr distillation, yellow oils distilled at $\geq$ 200 °C/0.005 mbar which yielded yellow crystals (45 – 65% yield) that were identified as 6,7-dihydro-1*H*-azepine-3,4-dicarboxylates **3a – c**. On the other hand, work-up of the reaction mixture obtained from **1a, b** by column chromatography over silica gel yielded the (dihydropyrrolyl)maleates or fumarates **4a, b**; since only one diastereomer was obtained, the available NMR data did not allow to assign the configuration at the ester-substituted olefinic bond (δ(=CH) = 4.92 ppm). Thus, the initially formed cycloaddition products **2** undergo the expected electrocyclic cyclobutene ring-opening/ring expansion reaction on thermal impact, while the formation of dihydropyrroles **4** can be interpreted as a proton-catalyzed ring-opening of the push-pull-substituted cyclobutene



Scheme 2. Reaction conditions: *a*) Et_2O, −40 °C → r. t.; *b*) no solvent, bulb-to-bulb distillation at 200 – 240 °C/ 0.005 mbar (45 – 62% yield from **1a – c**); *c*) chromatographic work-up (silica gel) (76 – 82% yield from **1a**, **b**).

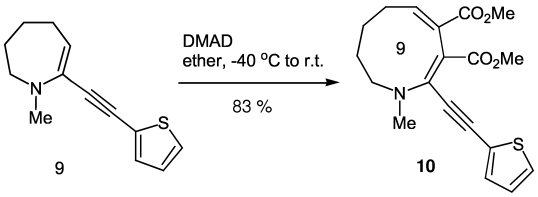


Scheme 3. Synthesis of aminodienes **6**/**7** and reaction with DMAD. Yield of **8**: 56% from **5**.

substructure. Analogous reactions take place when [2+2] cycloaddition products of 1-dialkylamino-cycloalkenes and acetylenic esters are dissolved in methanol or $CDCl_3$ [1a, 1b, 8, 9].

When the *tert*-butyl group in aminodienes **1** is replaced by a methyl group, a tautomeric equilibrium between the semicyclic 2-aminodiene form **6** and the exocyclic 1-aminodiene form **7** is possible (Scheme 3). In contrast to the *tert*-butyl analogues **1**, 1-aminodiene **7** (Ar = 4-chlorophenyl and 2-thienyl) has been observed exclusively by ^{1}H NMR spectroscopy [6]. The same is true for the 2-furyl substituted aminodiene (**7**, Ar = 2-furyl) which we have now prepared by dimethylcuprate addition to propyne iminium salt **5** (Scheme 3). Since **7** could not be isolated in pure form, the crude product was directly combined with DMAD and the mixture was subsequently heated at 200 °C. By analogy to the transformation **1** → **3**, dihydroazepine **8** was isolated in 58% yield. This result suggests indeed that DMAD does not react with the 1-aminodiene **7** but rather with the minute amount of the semicyclic aminodiene **6** which is in dynamic equilibrium with **7**.

A 7 → 9 ring expansion took place when the 2-[(2-thienyl)ethynyl]-4,5,6,7-tetrahydro-1*H*-azepine **9** [10] was exposed to DMAD at $\leq$ 20 °C (Scheme 4). Extraction of the reaction mixture with ether and crystallization yielded the tetrahydro-1*H*-azoninedicarboxylate **10** in 83% yield. Again, the initial [2+2] cycloaddition product was not observed because the electro-



Scheme 4. 7 → 9 Ring expansion of tetrahydroazepine **9**.

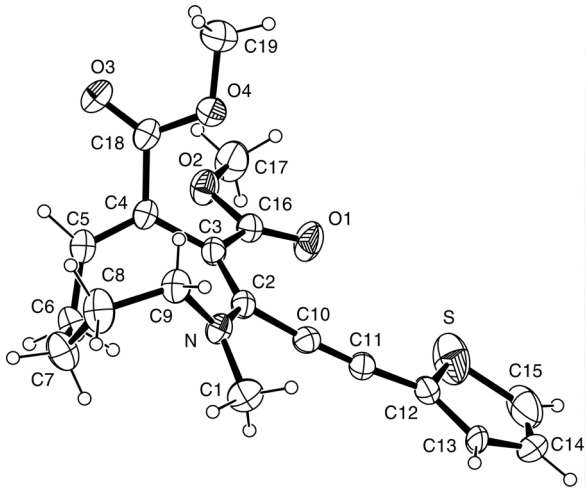
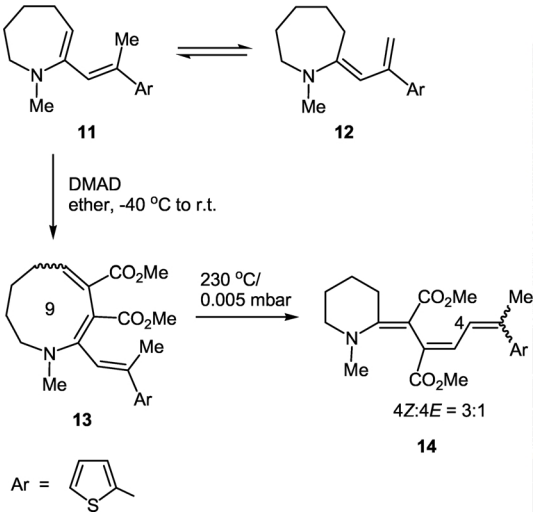


Fig. 1. Solid-state structure of **10**; ellipsoids of thermal vibration are shown at the 30% probability level. Selected bond lengths [Å] and torsion angles [°]: N–C2 1.367(6), C2–C3 1.375(7), C3–C16 1.470(7), C3–C4 1.486(6), C4–C18 1.504(7), C4–C5 1.334(7), C2–C10 1.441(7), C10–C11 1.195(7); C9–N–C2–C3 −25.4(7), N–C2–C3–C4 −5.6(8), C2–C3–C4–C5 −54.3(7). The thiophene ring is probably disordered over two position, with a minor component related to the major one by a 180° rotation around the C11–C12 bond. However, this disorder model was not included in the refinement.

cyclic ring-opening took place already at room temperature or below. The NMR data of **10** did not allow to firmly establish the configuration of the double bonds in the azonine ring. A crystal structure determination revealed the *cis,cis*-configuration of **10** (Fig. 1). It is interesting to note that the reaction of 1-dialkylaminocycloheptenes and -cyclooctenes with DMAD at room temperature generates the expected two-carbon ring-expanded cycloalka-1,3-dienes with *cis,trans* configuration [1] which have been isolated and were transformed into the *cis,cis*-isomer on heating. Thus, it is not clear whether *cis,cis*-**10** is formed *via* the *cis,trans*-isomer, the latter resulting from an orbital symmetry-allowed conrotatory ring-opening of the initial [2+2] cycloaddition product (see Introduction). The possibility has been discussed that push-pull substituted



Scheme 5. 7 → 9 Ring expansion of dihydroazepine **11** and subsequent thermal isomerization. Yield of **14**: 61% from **11**/**12**.

3-aminocyclobutene-1-carboxylates may undergo the ring opening by a disrotatory concerted electrocyclic process [11] or stepwise *via* a dipolar intermediate [12] (see also lit. [1]).

The crystal structure analysis of **10** shows that the tetrahydro-1*H*-azonine ring adopts a distorted boat conformation (Fig. 1). The dienamine moiety is not fully conjugated, because the torsion angle between the two double bonds (C2–C3–C4–C5) arises to −54.3°. On the other hand, the torsion angles of the enaminoester moiety N–C=C–COOMe allow extended π-conjugation with the expected bond length changes due to the push-pull character of this conjugated system.

In contrast to the five-membered enamine **6**, the seven-membered analogue **11** is the major component in the tautomeric equilibrium with the 1-aminodiene form **12** (**11**:**12** ≈ 2.7:1) [6] (Scheme 5). Trapping of the more reactive 2-aminodiene form **11** with DMAD was expected to furnish tetrahydroazonine **13** by analogy with the conversion **9** → **10**. As **13** could not be isolated in pure form from the reaction mixture by crystallization or chromatography, a bulb-to-bulb distillation was applied which unexpectedly gave the acyclic hexatriene **14** as a 3:1 mixture of diastereomers. The structure of **14** was elucidated by X-ray diffraction analysis of a crystal taken from the mixture of diastereoisomers (Fig. 2). The ^{1}H chemical shifts of the two diastereomers are quite similar except for the significantly different values of the olefinic proton at the thienyl-substituted double bond. The chemical shift

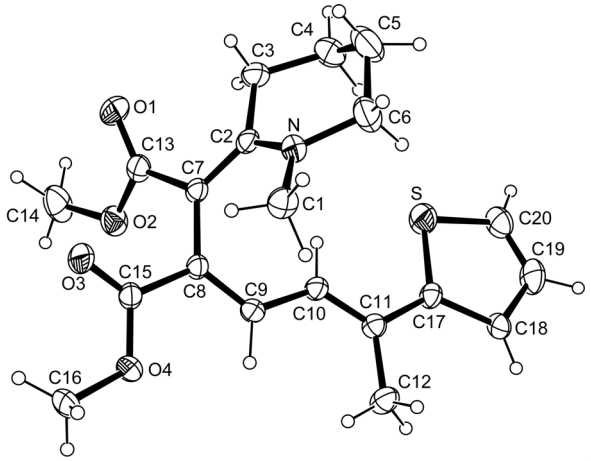
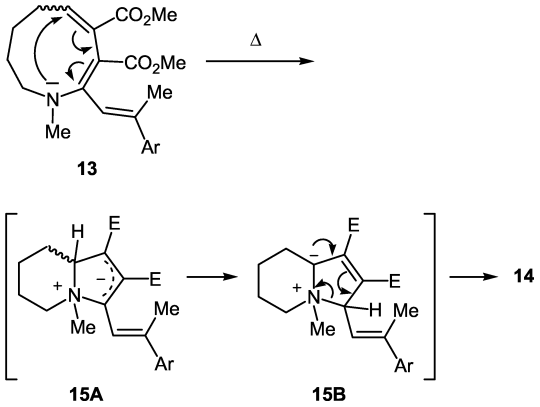


Fig. 2. Solid-state structure of $(1E,2E,4E)$-**14**; ellipsoids of thermal vibration are shown at the 30% probability level. Selected bond lengths [Å] and torsion angles [°]: N–C2 1.352(4), C2–C7 1.379(5), C7–C13 1.466(5), C7–C8 1.480(4), C8–C15 1.492(4), C8–C9 1.355(5), C9–C10 1.435(4), C10–C11 1.343(5); N–C2–C7–C8 −22.1(5), C2–C7–C8–C9 −52.2(5), C7–C8–C9–C10 −0.9(5), C8–C9–C10–C11 172.1(4), C9–C10–C11–C17 179.3(3), C10–C11–C17–C18 172.3(3). The thiophene ring is probably disordered over two position, with a minor component related to the major one by a 180° rotation around the exocyclic C–C bond. However, this disorder model was not included in the refinement.

of this proton is found at $\delta = 6.27$ ppm for the major diastereomer and at $\delta = 6.62$ ppm for the minor, corresponding to the *Z* and *E* configuration, respectively, in line with the assignment made for the starting material, aminodiene **11** [6]. Thus, a partial geometrical isomerization of the thienyl-substituted double bond has occurred, and the crystal structure has been determined for the minor diastereoisomer $1E,2E,4E$-**14**.

The formation of piperidinylidene-hexatriene **14** can be explained by a thermally induced isomerization of azonine **13** (Scheme 6). Ring contraction by transannular formation of an N–C bond yields betaine **15A** which rearranges to ylide **15B** by a hydrogen shift. Ring-opening of the cyclopentene ring finally generates **14**. It should be noted that this rearrangement can occur by a series of three concerted pericyclic processes with defined stereochemistry: disrotatory 6π electrocyclization of **13**, suprafacial [1,4-H] shift of **15a**, and disrotatory six-electron ring opening of **15B**. In order to arrive at the observed *E*(2,3)-configuration of triene **14**, this sequence must begin with the *cis,trans*-azonine **13** which undergoes electrocyclization to form trans-fused **15A**. However, we have no spectroscopic proof of the double bond con-

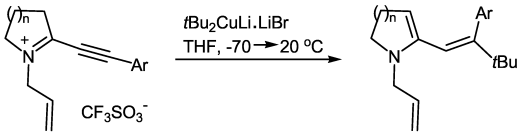


Scheme 6. Possible mechanism for the formation of triene **14**; Ar = 2-thienyl, E = CO_2Me.

figuration of **13**, and the case of azonine **10**, as described above, shows that the *cis,cis*-form is formed already at room temperature. The electrocyclic ring contraction of *cis,cis*-**13a** would generate *cis*-fused **15A**; a suprafacial H shift of the latter would lead to trans-disubstituted **15b** from which Z(3,4)-**14** would result after disrotatory opening of the N–C bond in the five-membered ring. Thus, if the thermal isomerization really starts with *cis,cis*-azonine **13**, at least one of the three steps cannot be under the predicted stereochemical control. For example, an isomerization of *cis*-fused **15a** to *trans*-disubstituted **15b** could be caused by (intermolecular) proton transfer, and the ring opening of **15b** could be a thermally induced homolytic process.

The ring contraction **13** → **15a** could also be considered as a transannular nucleophilic addition of the ring nitrogen atom to the electron-deficient 4,5-double bond. The nucleophilicity of the nitrogen atom may be considered too low because of the partial delocalization of its lone pair of electrons in the enaminoester moiety (see the structure of **10** discussed above), but conformational changes at elevated temperatures may change this situation. Transannular interactions of medium-sized azaheterocycles with carbonyl functions are known [13] and have been studied by molecular mechanics calculations [14]. Transannular cyclization reactions such as the electrophile-induced cyclization of unsaturated nine- and ten-membered *N*-benzyl lactams [15] and *N*-nucleophilic epoxide-ring opening reactions of nine-membered ring lactams [16] have recently been used for the synthesis of quinolizidine and indolizidine ring systems.

Next, we were interested to learn whether the presence of an allyl instead of a methyl substituent on the



16a: n = 1, Ar = C_6H_4-4-Cl
16b: n = 1, Ar = 2-thienyl
17a: n = 2, Ar = C_6H_4-4-Cl
17b: n = 2, Ar = 2-thienyl

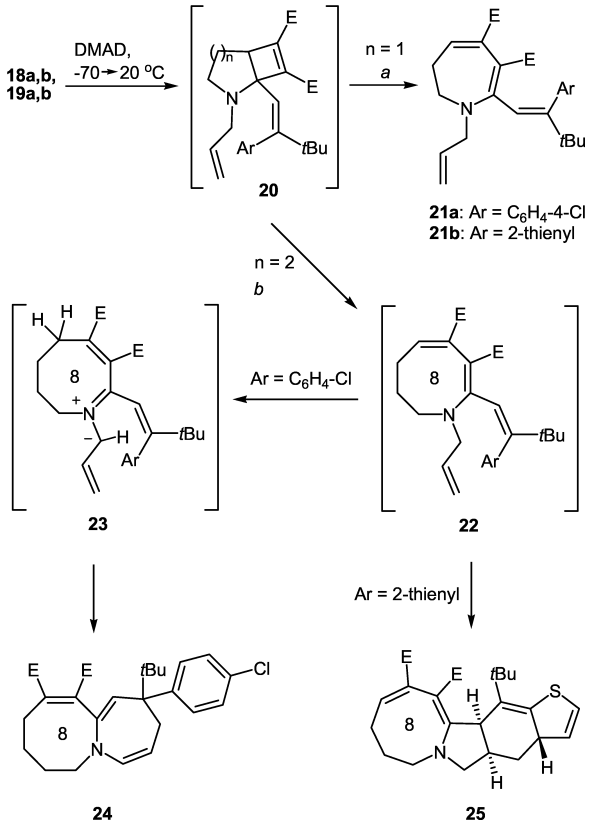
18a: n = 1, Ar = C_6H_4-4-Cl
18b: n = 1, Ar = 2-thienyl
19a: n = 2, Ar = C_6H_4-4-Cl
19b: n = 2, Ar = 2-thienyl

Scheme 7. Preparation of semicyclic N-allyl-aminodienes **18** and **19**.

nitrogen atom of compounds such as dihydroazepines **3** would open other pathways for thermal isomerization reactions. To this end, we prepared *N*-allyl-2,3-dihydropyrroles **18** and *N*-allyl-1,2,3,4-tetrahydropyridines **19** by organocuprate addition to the semicyclic propyniminium triflates **16** and **17** [17], respectively (Scheme 7). In all cases, only one diastereoisomer was found to which the *E* configuration of the *tert*-butyl-substituted C=C bond could be assigned by NOE NMR experiments.

As none of the 2-aminodienes **18** and **19** could be isolated in pure form, the crude products were treated directly with DMAD at ≤ 20 °C. Starting from **18a, b** and by full analogy with the behavior of the *N*-methyl analogues **1** (see Scheme 2), the expected initial cycloaddition products **20** (n = 1) were not isolated and the crude product mixture was heated in toluene at 120 °C (Scheme 8). This procedure yielded the 6,7-dihydro-1*H*-azepine-3,4-dicarboxylates **21a, b** in 47 and 52% yield. The characteristic NMR data match those of **3a**–**c**. In addition, the allyl NCH_2 protons were found to be diastereotopic which indicated the persistance of a chiral conformation. As the strongly broadened signals of both the o,o'- and m,m'-CH groups in **21a** indicated that these nuclei were on the way to chemical nonequivalence, it can be concluded that steric hindrance between the *N*-allyl substituent and the alkenyl group attached to C-2 restricts the free rotation around the ring/substituent bonds.

The reaction of aminodienes **19a, b** with DMAD and subsequent heating at 160 °C in toluene did not furnish the expected tetrahydroazocines **22** (Scheme 8). From 4-chlorophenyl-substituted **19a**, the azepino[1,2-*a*]azocine **24** was obtained in 68% yield (relative to the precursor of **19a**, iminium salt **17a**), while thienyl-substituted **19b** gave the tetracyclic azocino[2,1-*a*]thieno[3,2-*f*]isoindole **25** in 42% yield. The structure of **24** and **25** was established by X-ray crystal structure determination (Figs 3 and 4) and all ^1H and ^{13}C NMR chemical shifts were assigned from 1D and 2D spec-



20

21a: Ar = C_6H_4-4-Cl
21b: Ar = 2-thienyl

23 **22**

24 **25**

Scheme 8. 6 → 8 Ring expansion of aminodienes **18** and **19** and subsequent thermal isomerization reactions (E = CO_2Me); (*a*) toluene, 120 °C, 5 h; (*b*) toluene, 160 °C, 5 h.

tra (see Experimental Section). It is obvious that **24** and **25** are derived from *N*-allylazocines by subsequent thermally induced isomerization. Conversion of monocyclic **22** into tetracyclic **25** occurs by an intramolecular Diels-Alder reaction with the 2-vinylthiophene unit as the diene component. If no suitable diene unit is present (Ar = 4-chlorophenyl), a [1,6] shift of an allylic NCH hydrogen atom generates the conjugated azomethine ylide **23** which yields bicyclic **24** by an 8π 1,7-electrocyclic ring closure. 1,7-Electrocyclizations of conjugated 1,3-dipoles are an established route to seven-membered heterocycles [18].

In conclusion, semicyclic 2-amino-1,3-dienes in which the enamine function is incorporated in a five-, six-, or seven-membered ring were found to react with DMAD at the enamine C=C bond to give two-carbon ring-expanded products, while a [4+2] cycloaddition was not observed. 6,7-Dihydro-1*H*-azepines could be isolated in good yield and were thermally quite stable at high temperatures, surviving treatment at more

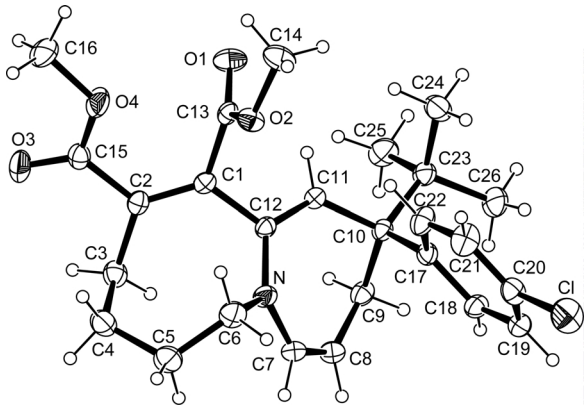


Fig. 3. Solid-state structure of **24**; ellipsoids of thermal vibration are shown at the 30% probability level. Selected bond lengths [Å], bond angles [°], and torsion angles [°]: C1–C2 1.342(2), C1–C13 1.504(3), C2–C15 1.494(3), C1–C12 1.500(3), C11–C12 1.340(2), C7–C8 1.328(3); C6–N–C12 120.73(16), C6–N–C7 115.90(17), C7–N–C12 123.37(16); C13–C1–C2–C15 1.9(3), C10–C11–C12–N −3.4(3), C6–N–C12–C1 −32.0(2).

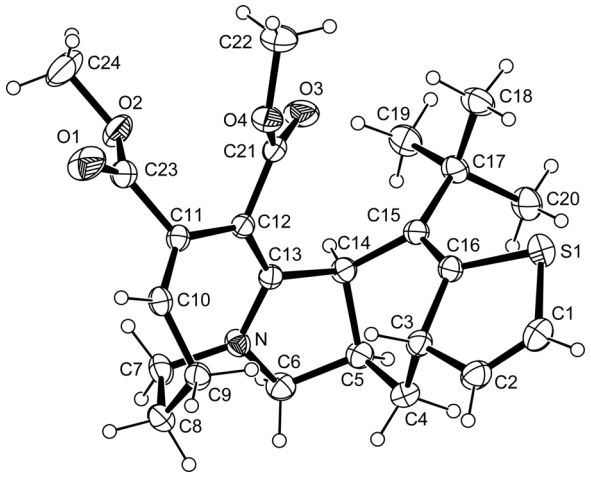


Fig. 4. Solid-state structure of **25**; ellipsoids of thermal vibration are shown at the 30% probability level. Selected bond lengths [Å], bond angles [°], and torsion angles [°]: C10–C11 1.338(2), C11–C12 1.488(2), C11–C23 1.500(2), C12–C21 1.462(2), C12–C13 1.380(2), C13–N 1.356(2), N–C6 1.458(2), C15–C16 1.337(3), C1–C2 1.315(3); C6–N–C7 117.46(15), C6–N–C13 114.21(14), C7–N–C13 127.75(15), C11–C12–C13–N 10.3(3), C10–C11–C12–C13 39.4(3).

than 200 °C (**3a – c**) or at 120 °C (**21a, b**). On the other hand, the homologous azocine and azonine derivatives were found to undergo a variety of thermally induced isomerization reactions, including transannular reaction as well as cyclization or cycloaddition reactions involving the exocyclic *N*-allyl and the adjacent alkenyl substituents. The greater conformational flexibility of the eight- and nine-membered ring systems is likely to favor these thermal isomerization reactions. The results reported here indicate once more that the two-carbon ring expansion of endocyclic enamines is a suitable method to prepare functionalized seven-, eight-, and nine-membered azaheterocycles. The latter two classes in particular, representing typical medium-sized ring systems, have been studied relatively little and are found only in a limited number of natural products [2, 19]. However, some azonine and azocine derivatives are known to have interesting pharmaceutical properties.

Experimental Section

General methods: Solvents were dried by standard methods and were stored under an argon atmosphere. The petroleum ether used had a boiling point range of 40 – 60 °C. Dimethyl acetylenedicarboxylate (DMAD) was distilled prior to use. All reactions involving aminodienes were carried out in rigorously dried glassware and under an argon atmosphere. Column chromatography was performed using hydrostatic pressure (silica gel 60, Macherey-Nagel, 0.063 – 0.2 mm) or under elevated pressure using Merck Lichroprep Si60 columns (particle size 40 – 63 μm, two columns of size A and B connected), a gradient pump (Merck-Hitachi L6200) and UV detection (Gilson Spectrochrom M, λ = 254 nm). For the bulb-to-bulb distillation experiments, the temperature of the heating mantle is given. The NMR spectra were recorded in $CDCl_3$ solution using as the internal standard tetramethylsilane for ^{1}H spectra ($\delta = 0$ ppm) and residual solvent signal ($\delta(CHCl_3) = 77.0$ ppm) for ^{13}C spectra; mc = centered multiplet. The signal assignment was based on proton-coupled ^{13}C spectra (^1J(C,H) multiplicities are given with the spectra), H,H COSY, and C,H (^{1}J) as well as C,H (^2J, ^3J) correlation spectra. IR spectra were recorded on Perkin Elmer IR 883 and IR 1310 spectrometers. Microanalyses were carried out in the Analytical Laboratories of the Universities of Ulm and Kaiserslautern.

*Dimethyl 2-[(Z)-2-(4-chlorophenyl)-3,3-dimethylbut-1-enyl]-6,7-dihydro-1-methyl-1H-azepine-3,4-dicarboxylate (**3a**):* A solution of aminodiene **1a** [6] (0.83 g, 3.0 mmol) in ether (10 ml) was cooled at −40 °C and DMAD (0.41 ml, 3.3 mol) was added. The cooling bath was removed and the mixture was stirred overnight. After removal of the solvent at 0.01 mbar, the residual oil was submitted to a Kugelrohr distillation. Excess DMAD was distilled off at 120 °C/0.005 mbar. The temperature was raised until a yellow oil distilled over at 220 °C/0.005 mbar. It was dissolved in ether, and pentane was added until the solution started to become turbid. Crystallization at −30 °C furnished yellow crystals (0.56 g, 45%), m. p. 93 °C. –

IR (KBr): ν = 2940 (m), 1730 – 1630 (s, broad) cm^{-1}. – ^1H NMR (400.13 MHz): δ = 1.16 (s, 9 H, *t*Bu), 1.80 – 2.15 (m, br, 2 H, 6-H_2), 2.67 (s, 3 H, NCH_3), 2.60 – 2.85 (m, 2 H, NCH_2), 3.65 (s, 3 H, OCH_3), 3.69 (s, 3 H, OCH_3), 6.52 (t, 1 H, J = 6.1 Hz, 5-H), 6.54 (s, 1 H, =$CH_{excycl.}$), 6.94/7.26 (AA'BB', 4 H_{aryl}). – ^{13}C NMR (100.61 MHz): δ = 27.7 (C-6), 29.2 (C*Me*$_3$), 36.3 (*C*Me$_3$), 41.1 (NCH_3), 50.9 (OCH_3), 51.9 (OCH_3), 57.7 (C-7), 99.7 (s, NC=*C*), 124.8 (d), 127.3 (d), 129.7 (d), 132.6 (s), 133.5 (s), 135.0 (d, C-5), 138.2 (s), 151.2 (s), 157.9 (s), 168.9 (C=O), 169.9 (C=O). – $C_{23}H_{28}ClNO_4$ (417.93): calcd. C 66.10, H 6.75, N 3.35; found C 66.1, H 6.8, N 3.3.

*Dimethyl 2-[(Z)-2-(furan-2-yl)-3,3-dimethylbut-1-enyl]-6,7-dihydro-1-methyl-1H-azepine-3,4-dicarboxylate (***3b***):* Prepared as described for **3a**, from aminodiene **1b** [6] (0.70 g, 3.0 mmol) and DMAD (0.41 ml, 3.3 mmol). Kugelrohr distillation at 200 °C/0.005 mbar. Yellow microcrystalline solid (0.59 g, 53%), m. p. 84 °C. – IR (KBr): ν = 3100 (w), 2940 (s), 1710 (s), 1685 (s) cm^{-1}. – ^1H NMR (200.1 MHz): δ = 1.22 (s, 9 H, *t*Bu), 2.36 (virtual q, 2 H, 6-H_2), 2.62 (s, 3 H, NCH_3), 2.99 (m, 2 H, NCH_2), 3.62 (s, 3 H, OCH_3), 3.71 (s, 3 H, OCH_3), 6.12 (dd, J = 3.2, 0.6 Hz, 1 H, 3-H_{furyl}), 6.32 (mc, 1 H, 4-H_{furyl}), 6.53 (t, J = 5.7 Hz, 1 H, 5-H), 6.58 (s, 1H, =$CH_{excycl.}$), 7.37 (dd, J = 1.7, 0.6 Hz, 1 H, 5-H_{furyl}). – ^{13}C NMR (100.61 MHz): δ = 28.5 (C-6), 29.1 (C*Me*$_3$), 36.4 (*C*Me$_3$), 41.0 (NCH_3), 50.5 (OCH_3), 51.6 (OCH_3), 57.7 (C-7), 98.9 (s, NC=*C*), 109.5 (d), 110.0 (d), 126.5 (d), 133.5 (d, J = 160.0 Hz, C-5), 141.3 (d, J = 211.3 Hz, 5-C_{furyl}), 143.6 (s), 152.3 (s), 158.5 (s), 168.7 (C=O), 170.2 (C=O). – $C_{21}H_{27}NO_5$ (373.45): calcd. C 67.54, H 7.29; N 3.75; found C 67.2, H 7.2, N 3.7.

*Dimethyl 6,7-dihydro-1-methyl-2-[(Z)-3,3-dimethyl-2-(thiophen-2-yl)but-1-enyl]-1H-azepine-3,4-dicarboxylate (***3c***):* Prepared as described for **3a**, from aminodiene **1c** [6] (0.74 g, 3.0 mmol) and DMAD (0.41 ml, 3.3 mmol); Kugelrohr distillation at 240 °C/0.005 mbar. Yellow crystals (0.76 g, 65%), m. p. 72 °C. – IR (KBr): ν = 3100 (w), 2940 (m), 1710 (s), 1680 (s), 1625 (m) cm^{-1}. – ^1H NMR (400.13 MHz): δ = 1.22 (s, 9 H, *t*Bu), 2.0 – 2.2 (m, 2 H, 6-H_2), 2.69 (s, 3 H, NCH_3), 2.7 – 3.1 (unresolved m, 2 H, NCH_2), 3.62 (s, 3 H, OCH_3), 3.68 (s, 3 H, OCH_3), 6.55 (t, J = 6.0 Hz, 1 H, 5-H), 6.62 (s, 1 H, =$CH_{exocycl.}$), 6.73 (dd, J = 3.4, 1.2 Hz, 1 H, 3-$H_{thienyl}$), 6.94 (mc, 1 H, 4-$H_{thienyl}$), 7.21 (dd, J = 5.1, 1.1 Hz, 5-$H_{thienyl}$). – ^{13}C NMR (100.61 MHz): δ = 27.6 (C-6), 28.8 (C*Me*$_3$), 36.0 (*C*Me$_3$), 40.7 (NCH_3), 50.3 (OCH_3), 51.3 (OCH_3), 57.8 (C-7), 99.4 (s, NC=*C*), 124.1 (d), 125.6 (d), 125.7 (d), 126.9 (d), 133.6 (s), 134.6 (d, J = 160.1 Hz, C-5), 138.9 (s), 154.3 (s), 157.4 (s), 168.4 (C=O), 169.4 (C=O). – $C_{21}H_{27}NO_4S$ (389.51): calcd. C 64.75, H 6.99, N 3.60; found C 64.5, H 7.0, N 3.5.

*Dimethyl 2-{2-[(Z)-2-(4-chlorophenyl)-3,3-dimethylbut-1-enyl]-4,5-dihydro-1-methyl-1H-pyrrol-3-yl}maleate (or fumarate) (***4a***):* The reaction of aminodiene **1a** (0.83 g, 3.0 mmol) and DMAD (0.41 ml, 3.3 mmol) was conducted as described above for **3a**. After stirring overnight, the solvent was evaporated at 25 °C/0.01 mbar, and the residue was worked up by column chromatography (silica gel, ether/CH_2Cl_2 (1:1)). Crystallization from ether yielded **4a** as a yellow powder (0.95 g, 76%), m. p. 103 °C. – IR (KBr): ν = 2970 (s), 2945 (s), 2920 (s), 2900 (s), 1725 (vs), 1685 (s) cm^{-1}. – ^1H NMR (200.1 MHz): δ = 1.15 (s, 9 H, *t*Bu), 2.25 – 2.50 (unresolved m, 2 H), 2.64 (s, 3 H, NCH_3), 3.10 (t, 2 H, NCH_2), 3.66 (s, 3 H, OCH_3), 3.95 (s, 3 H, OCH_3), 4.92 (s, 1 H, =C*H*–CO_2Me, 5.92 (s, 1 H, C*H*=C–Aryl), 7.11/7.21 (AA'BB', 4 H_{aryl}). – ^{13}C NMR (100.61 MHz): δ = 28.4 (NCH_2CH_2), 29.2 (C*Me*$_3$), 35.1 (NCH_3), 36.9 (*C*Me$_3$), 50.8 (OCH_3), 52.2 (NCH_2), 52.6 (OCH_3), 101.3 (*C*H–CO_2Me), 105.6 (s, NC=*C*), 113.7 (*C*H=C–Aryl), 127.3 (d), 130.0 (d), 132.9 (s), 136.9 (s), 146.0 s), 155.7 (s), 158.8 (s), 167.6 (C=O), 169.8 (C=O). – $C_{23}H_{28}ClNO_4$ (417.93): calcd. C 66.10, H 6.75, N 3.35; found C 65.9, H 6.8, N 3.3.

*Dimethyl 2-{2-[(Z)-2-(2-furanyl)-3,3-dimethylbut-1-enyl]-4,5-dihydro-1-methyl-1H-pyrrol-3-yl}maleate (or fumarate) (***4b***):* The reaction of aminodiene **1b** [6] (0.69 g, 3.0 mmol) and DMAD (0.41 ml, 3.3 mmol) was conducted as described above for **3a**. After stirring overnight, the solvent was evaporated at 25 °C/0.01 mbar, and the residue was worked up by column chromatography (silica gel, ether/CH_2Cl_2 (1:1)). Crystallization from ether yielded **4b** as light-red crystals (0.92 g, 82%), m. p. 164 °C. – IR (KBr): ν = 2960 (m), 2900 (m), 1715 (vs), 1670 (s) cm^{-1}. – ^1H NMR (400.13 MHz): δ = 1.26 (s, 9 H, *t*Bu), 2.42 (s, 3 H, NCH_3), 2.61 (mc, 2 H), 3.20 – 3.40 (unresolved m, 2 H), 3.65 (s, 3 H, OCH_3), 3.84 (s, 3 H, OCH_3), 4.99 (s, 1 H, =C*H*–CO_2Me), 5.92 (s, 1 H, C*H*=C–Aryl), 6.32 (dd, J = 3.3, 1.7 Hz, 1 H, 4-H_{furyl}), 6.42 (dd, J = 3.3, 0.7 Hz, 1 H, 3-H_{furyl}), 7.38 (dd, 1 H, J = 1.8, 0.8 Hz, 5-H_{furyl}). – ^{13}C NMR (100.61 MHz): δ = 28.2 (NCH_2CH_2), 29.4 (C*Me*$_3$), 33.9 (NCH_3), 36.9 (*C*Me$_3$), 50.6 (OCH_3), 52.1 (OCH_3), 52.7 (NCH_2), 100.4 (=*C*H–CO_2Me), 105.8 (s, NC=*C*), 110.6 (d), 111.4 (d), 115.1 (*C*H=C–Aryl), 141.6 (d, J = 201.8 Hz, C-5$_{furyl}$), 146.2 (s), 149.5 (s), 151.6 (s), 155.7 (s), 167.6 (C=O), 169.8 (C=O). – $C_{21}H_{27}NO_5$ (373.45): calcd. C 67.54, H 7.29, N 3.75; found C 67.0, H 7.4, N 3.6.

*Dimethyl 2-[(Z)-2-(furan-2-yl)-3,3-dimethylbut-1-enyl]-6,7-dihydro-1-methyl-1H-azepine-3,4-dicarboxylate (***8***):* (2*E*)-2-[2-(Furan-2-yl)prop-2-en-1-ylidene]-2,3,4,5-tetrahydro-1-methyl-1*H*-pyrrole (**7**) was prepared according to a procedure for similar aminodienes [6] and was used without purification. The reaction of crude aminodiene **7** (0.57 g, 3.0 mmol) and DMAD (0.41 ml, 3.3 mmol) was carried out as described above for **3a**. Bulb-to-bulb distillation at 200 °C/0.005 mbar followed by crystallization from ether/pentane furnished a yellow, microcrystalline solid (0.58 g, 58%), m. p. 93 °C. – IR (KBr): ν = 2950 (s), 1710

(sh), 1695 (s) cm^{-1}. – ^1H NMR (200.1 MHz): $\delta = 2.20$ (d, $^4J = 1.1$ Hz, 3 H, =C-CH_3), 2.61 (mc, 2 H, 6-H), 2.88 (s, 3 H, NCH_3), 3.40 (t, 2 H, NCH_2), 3.54 (s, 3 H, OCH_3), 3.72 (s, 3 H, OCH_3), 6.41 (mc, 1 H), 6.42 ("s", ^4J coupling not resolved, 1 H, $=CH_{exocycl.}$), 6.50 (t, 1 H, $J = 5.4$ Hz, 5-H), 6.84 (mc, 1 H), 7.41 (mc, 1 H). – ^{13}C NMR (100.61 MHz): $\delta =$ 14.3 (=C–*C*H_3), 29.2 (C-6), 40.7 (NCH_3), 50.7 (OCH_3), 51.8 (OCH_3), 55.6 (C-7), 98.5 (s, NC=*C*), 107.6 (d), 111.2 (d), 121.5 (d), 131.0 (s), 131.9 (d, $J = 156.4$ Hz, C-5), 133.4 (s), 142.4 (d, $J = 202.4$ Hz, C-5_{furyl}) 154.7 (s), 157.5 (s), 168.9 (C=O), 170.8 (C=O). – $C_{18}H_{21}NO_5$ (331.37): calcd. C 65.24, H 6.39, N 4.23; found C 64.0, H 6.7, N 3.8.

*Dimethyl 6,7,8,9-tetrahydro-1-methyl-2-[(thiophen-2-yl) ethynyl]-1H-azonine-3,4-dicarboxylate (***10***):* A solution of alkynyl-enamine **9** [10] (0.65 g, 3.0 mmol) in ether (10 ml) was cooled at −40 °C and DMAD (0.41 ml, 3.3 mmol) was added dropwise. The cooling bath was removed and the solution was stirred overnight. After evaporation of the solvent at 25 °C/0.01 mbar, the residue was extracted with ether (4 × 50 ml). The extracts were combined, the solvent was removed, and the residue was crystallized by addition of CH_2Cl_2/ether and cooling at −30 °C. Yellow crystals (0.89 g, 83%), m. p. 114 °C. – IR (KBr): $\nu = 3060$ (w), 2920 (s), 2180 (s, C ≡ C), 1700 (vs), 1670 (vs) cm^{-1}. – ^1H NMR (400.13 MHz): $\delta = 1.60-1.88$ (m, 4 H), 2.26 (mc, 2 H), 3.03 (s, 3 H, NCH_3), 3.34 (mc, 2 H, NCH_2), 3.68 (s, 3 H, OCH_3), 3.73 (s, 3 H, OCH_3), 6.98 (t, $J = 9.2$ Hz, 1 H, 5-H), 7.02 (dd, $J = 5.2$, 3.8 Hz, 1 H, 4-$H_{thienyl}$), 7.33 (dd, $J = 3.5$, 1.1 Hz, 1 H, 3-$H_{thienyl}$), 7.37 (dd, $J = 5.2$, 1.1 Hz, 1 H, 5-$H_{thienyl}$). – ^{13}C NMR (100.61 MHz): $\delta = 22.7$ (CH_2), 24.9 (CH_2), 27.5 (CH_2), 41.1 (NCH_3), 49.8 (CH_2), 51.1 (OCH_3), 51.8 (OCH_3), 88.4 and 91.7 (*C*≡*C*), 104.4 (s, C-3), 122.0 (s), 127.1 (d), 128.7 (d), 132.4 (s), 132.9 (d), 142.0 (d, $J = 156.8$ Hz, C-5), 142.2 (s), 168.0 (C=O), 168.2 (C=O). – $C_{19}H_{21}NO_4S$: calcd. C 63.49, H 5.89, N 3.90; found C 63.5, H 5.8, N 3.9.

*Dimethyl (1(2')E,2E,4Z)- and (1(2')E,2E,4E)-1-(1-methylpiperidin-2-ylidene)-5-(thiophen-2-yl)hexa-2,4-diene-1,2-dicarboxylate (***14***):* A solution of aminodiene **11**/**12** [6] (0.70 g, 3.0 mmol) in ether (10 ml) was cooled at −40 °C and DMAD (0.41 ml, 3.3 mmol) was added dropwise. The solution was brought to r. t. and submitted to a Kugelrohr distillation. Excess DMAD was distilled off at 100–120 °C/0.005 mbar. At 230 °C/0.005 mbar, a red oil distilled over from which orange crystals were obtained after crystallization from ether/pentane. Yield: 0.69 g (61%); mixture of diastereomers, (1*(2')E*,2*E*,4*Z*):(1*(2')E*,2*E*,4*E*) = 3:1. M. p. 119 °C. – IR (KBr): $\nu = 2930$ (m), 1670 (s, br) cm^{-1}. – ^1H NMR (400.13 MHz) of (1*(2')E*,2*E*,4*Z*)-**14**: $\delta = 1.72-1.84$ (m, 4 H, $NCH_2CH_2CH_2$), 2.30 (s, 3 H, =C-CH_3), 2.56 (s, 3 H, NCH_3), 3.06–3.19 (m, 4 H), 3.59 (s, 3 H, OCH_3), 3.75 (s, 3 H, OCH_3), 6.27 (broadened d, $^3J = 11.6$ Hz, C*H*=C–Thienyl), 6.99 (dd, $J = 5.1$, 3.7 Hz, 1 H, 4-$H_{thienyl}$), 7.11 (d, $J = 3.6$ Hz, 1 H, 3-$H_{thienyl}$), 7.21 (d, $J = 5.1$ Hz, 1 H, 5-$H_{thienyl}$), 7.51 (d, $J = 11.6$ Hz, 1 H, ester–C=C*H*); (1*(2')E*,2*E*,4*E*)-**14**: $\delta = 6.62$ (d, $J = 11.6$ Hz, C*H*=C-Thienyl). – ^{13}C (100.61 MHz): $\delta = 16.1$ (=C–*C*H_3), 20.5 (CH_2), 22.8 (CH_2), 29.8 (CH_2), 44.4 (NCH_3), 50.5 (OCH_3), 51.4 (CH_2), 51.7 (OCH_3), 93.0 (s, NC=*C*), 121.3 (d, *C*H=C-Thienyl), 124.4 (d), 125.0 (d), 127.5 (d), 130.2 (d, ester–C=*C*H), 131.3 (s), 135.7 (s), 146.5 (s), 164.1 (s, NC=), 169.36 (C=O), 169.40 (C=O). – $C_{20}H_{25}NO_4S$ (375.49): calcd. C 63.98, H 6.71, N 3.73; found C 64.0, H 6.8, N 3.9.

*1-Allyl-5-[(Z)-2-(4-chlorophenyl)-3,3-dimethylbut-1-enyl]-2,3-dihydro-1H-pyrrole (***18a***):* To a stirred suspension of copper(I) bromide dimethylsulfide (0.432 g, 2.1 mmol) in THF (10 ml), cooled at −70 °C, was slowly added a 1.7 M solution of *tert*-butyl lithium in hexane (2.37 ml, 4.2 mmol). The yellow suspension was then brought at −40 °C within 10 min and kept at this temperature until a homogeneous pale-yellow solution had formed which was cooled again at −70 °C. A solution of iminium salt **16a** [17] (0.788 g, 2.0 mmol) in THF (10 ml) was added dropwise. The mixture was warmed at −40 °C within 15 min and kept at this temperature for 1 h, then brought to r. t. within 2 h, whereupon a black color appeared. The solvent was evaporated at 0.01 mbar and the residue was extracted with pentane (3 × 50 ml). The extracts were combined and the solvent was completely evaporated at 0.01 mbar to leave a yellow oil which could not be purified further and was used directly (*vide infra*). Yield of crude **18a**: 0.520 g (1.72 mmol, 86%). – IR (film): $\nu = 2960$ (m), 2867 (m), 1643 (m), 1487 (m), 1171 (m), 1091 (m) cm^{-1}. – ^1H NMR (500.14 MHz): $\delta = 1.09$ (s, 9 H, *t*Bu), 2.19 (mc, 2 H, 3-H_2), 2.87 (t, 2 H, 2-H_2), 3.40 (d, 2 H, NC*H*$_2$CH=), 3.91 (mc, 1 H, 4-H), 5.12 (dd, $^3J = 10.2$, $^2J = 1.6$ Hz, 1 H, CH_2CH=C*H*$_2$), 5.19 (dd, $^3J = 17.2$, $^2J = 1.6$ Hz, 1 H, CH_2CH=C*H*$_2$), 5.83 (mc, 1 H, CH_2CH=CH_2), 5.95 (s, 1 H, 5-CH=), 6.95/7.26 (AA'BB', 4 H_{aryl}). – ^{13}C NMR (125.77 MHz): $\delta = 29.0$ (C-3), 29.6 (C*Me*$_3$), 36.7 (*C*Me$_3$), 52.4 (C-2), 55.3 (NCH$_2$CH=), 104.9 (C-4), 115.4 (*C*H=C–Aryl), 116.8 (CH_2CH=*C*H$_2$), 127.7 (d), 130.9 (d), 132.2 (s, C-Cl), 135.8 (CH_2CH=CH_2), 139.0 (s), 147.6 (CH=*C*–Aryl), 153.0 (s, C-5). – $C_{19}H_{24}ClN$ (301.86).

*1-Allyl-5-[(Z)-3,3-dimethyl-2-(thiophen-2-yl)but-1-enyl]-2,3-dihydro-1H-pyrrole (***18b***):* The synthesis was achieved as described for **18a**, from a solution of (*t*-Bu)$_2$CuLi·LiBr (4.2 mmol) in THF (10 ml) and a solution of iminium salt **16b** [17] (0.731 g, 2.0 mmol) in THF (10 ml). An orange oil was obtained which could not be purified further and was used directly (*vide infra*). Yield of crude **18b**: 0.494 g (90%). – IR (film): $\nu = 3070$ (w), 2962 (m), 2865 (m), 1613 (m), 1462 (m), 1224 (m) cm^{-1}. – ^1H NMR (500.14 MHz): $\delta = 1.14$ (s, 9 H, *t*Bu), 2.20 (t, 2 H, 3-H_2), 2.90 (t, 2 H, 2-H_2), 3.39 (d, 2 H, NC*H*$_2$CH=), 4.20 (t, 1 H, 4-H), 5.11 (dd, $^3J = 10.3$, $^2J = 1.6$ Hz, 1 H, CH_2CH=C*H*$_2$),

5.18 (dd, ^3J = 17.1, ^2J = 1.8 Hz, 1 H, $CH_2CH{=}CH_2$), 5.83 (mc, 1 H, $NCH_2CH{=}$), 6.06 (s, 1 H, C*H*=C–Thienyl), 6.69 (dd, ^3J = 3.4, ^4J = 1.2 Hz, 1 H, 3-$H_{thienyl}$), 6.94 (dd, ^3J = 5.0, ^3J = 3.4 Hz, 1 H, 4-$H_{thienyl}$), 7.21 (dd, ^3J = 5.0, ^4J = 1.0 Hz, 1 H, 5-$H_{thienyl}$). – ^{13}C NMR (125.77 MHz): δ = 29.0 (C-3), 29.5 (C*Me*$_3$), 36.8 (*C*Me$_3$), 52.3 (C-2), 55.4 ($NCH_2CH{=}$), 104.2 (C-4), 116.6 ($CH_2CH{=}CH_2$), 119.9 (*C*H=C–Thienyl), 124.4 (C-5$_{thienyl}$), 126.0 (C-4$_{thienyl}$), 126.5 (C-3$_{thienyl}$), 135.8 ($NCH_2CH{=}$), 140.3 (C-2$_{thienyl}$), 146.6 (CH=*C*–Thienyl), 147.7 (s, C-5). – $C_{17}H_{23}NS$ (273.44).

*1-Allyl-6-[(Z)-2-(4-chlorophenyl)-3,3-dimethylbut-1-enyl]-1,2,3,4-tetrahydropyridine (***19a***):* The synthesis was performed as described for **18a**, from a solution of (*t*-Bu)$_2$CuLi·LiBr (4.2 mmol) in THF (10 ml) and a solution of iminium salt **17a** [17] (0.759 g, 2.0 mmol) in THF (10 ml). A yellow oil was obtained which could not be purified further and was used directly (see below). Yield of crude **19a**: 0.555 g (88%). – IR (film): ν = 3074 (w), 2960, 1686, 1591, 1487, 1392, 1245 (all m) cm^{-1}. – ^{1}H NMR (500.14 MHz): δ = 1.08 (s, 9 H, *t*Bu), 1.48 (quin, 2 H, 3-H_2), 1.73 (mc, 2 H, 4-H_2), 2.79 (t, 2 H, 2-H_2), 3.48 (d, 2 H, $NCH_2CH{=}$), 4.08 (s, 1 H, 5-H), 5.09 (d, ^3J = 10.3 Hz, 1 H, $CH_2CH{=}CH_2$), 5.14 (d, ^3J = 17.4 Hz, 1 H, $CH_2CH{=}CH_2$), 5.76 (mc, 1 H, $CH_2CH{=}CH_2$), 6.00 (s, 1 H, C*H*=C–Aryl), 6.94/7.21 (AA'BB', 4 H, H_{aryl}). – ^{13}C NMR (125.77 MHz): δ = 21.1 (C-3), 22.7 (C-4), 29.7 (C*Me*$_3$), 36.3 (*C*Me$_3$), (C-2), 54.8 ($NCH_2CH{=}$), 104.0 (C-5), 116.1 ($CH_2CH{=}CH_2$), 123.3 (*C*H=C–Aryl), 127.0 (d), 131.1 (d), 131.6 (C-Cl), 136.4 ($CH_2CH{=}CH_2$), 138.6 (s), 141.6 (C-6), 151.2 (CH=*C*–Aryl). – $C_{20}H_{26}ClN$ (315.88).

*1-Allyl-6-[(Z)-3,3-dimethyl-2-(thiophen-2-yl)but-1-enyl]-1,2,3,4-tetrahydropyridine (***19b***):* As described above for **18a**, the compound was prepared from a solution of (*t*-Bu)$_2$CuLi·LiBr (4.2 mmol) in THF (10 ml) and a solution of iminium salt **17b** [17] (0.759 g, 2.0 mmol) in THF (10 ml). A yellow oil was obtained which could not be purified further and was used directly (*vide infra*). Yield of **19b**: 0.523 g (91%). – IR (film): ν = 3070 (w), 2954, 2833, 1632, 1462, 1434, 1360, 1225, 1171, 1129 (all m) cm^{-1}. – ^{1}H NMR (500.14 MHz): δ = 1.14 (s, 9 H, *t*Bu), 1.55 (quin, 2 H, 3-H_2), 1.79 (mc, 2 H, 4-H_2), 2.84 (t, 2 H, 2-H_2), 3.48 (d, 2 H, $NCH_2CH{=}$), 4.29 (s, br, 1 H, 5-H), 5.10 (dd, ^3J = 10.2, ^2J = 1.8 Hz, 1 H, $CH_2CH{=}CH_2$), 5.16 (dd, ^3J = 17.1, ^2J = 1.7 Hz, 1 H, $CH_2CH{=}CH_2$), 5.80 (mc, 1 H, $NCH_2CH{=}$), 6.09 (s, 1 H, C*H*=C–Thienyl), 6.71 (dd, ^3J = 3.5, ^4J = 1.1 Hz, 1 H, 3-$H_{thienyl}$), 6.92 (dd, ^3J = 5.1, ^3J = 3.5 Hz, 1 H, 4-$H_{thienyl}$), 7.18 (dd, ^3J = 5.1, ^4J = 1.2 Hz, 1 H, 5-$H_{thienyl}$). – ^{13}C NMR (125.77 MHz): δ = 21.1 (C-3), 22.9 (C-4), 29.7 (C*Me*$_3$), 36.6 (*C*Me$_3$), 47.5 (C-2), 55.3 ($NCH_2CH{=}$), 103.4 (C-6), 116.2 ($CH_2CH{=}CH_2$), 123.8 (C-5$_{thienyl}$), 125.8 (C-4$_{thienyl}$), 126.5 (*C*H=C–Thienyl), 126.7 (C-3$_{thienyl}$), 136.6 ($NCH_2CH{=}$), 140.8 (s, C-2$_{thienyl}$), 142.1 (s, C-6), 145.0 (CH=*C*–Thienyl). – $C_{18}H_{25}NS$ (287.46).

*Dimethyl 1-allyl-2-[(Z)-2-(4-chlorophenyl)-3,3-dimethylbut-1-enyl]-6,7-dihydro-1H-azepine-3,4-dicarboxylate (***21a***):* Freshly prepared crude aminodiene **18a** (0.520 g, 1.7 mmol) was dissolved in ether (15 ml) and cooled at −70 °C. DMAD (0.233 ml, 1.9 mmol) was added dropwise and the mixture was allowed to come to r.t. over 12 h. The solvent was replaced by toluene (5 ml) and the solution was heated at 120 °C during 5 h in a thick-walled Schlenk tube. Evaporation of the solvent left an oil which was first submitted to flash chromatography (10 g of silica gel, CH_2Cl_2), then to column chromatography (Merck Lobar columns, ether/petroleum ether 1:4→1:1). Yield of **21a**: 0.412 g (47% rel. to iminium salt **16a**); dark-yellow oil. – ^{1}H NMR (500.14 MHz, 253 K): δ = 1.16 (s, 9 H, *t*Bu), 1.83 – 1.92 (m, 1 H, 6-H), 2.23 – 2.41 (m, 2 H, 6-H, 7-H), 2.85 – 2.93 (m, 1 H, 7-H), 3.06 (dd, ^2J = 15.1, ^3J = 8.1 Hz, 1 H, $NCH_2CH{=}$), 3.68 (s, 3 H, OCH_3), 3.72 (s, 3 H, OCH_3), 4.34 (d, ^2J = 14.8 Hz, 1 H, $NCH_2CH{=}$), 5.10 – 5.19 (m, 2 H, $CH_2CH{=}CH_2$), 5.61 (mc, 1 H, $CH_2CH{=}CH_2$), 6.52 (t, 1 H, 5-H), 6.56 (s, 1 H, C*H*=C-Aryl), 6.80 – 7.00 (broad coalescing signal, 2 H_{aryl}), 7.24 – 7.35 (m, 2 H, H_{aryl}). – ^{13}C NMR (125.77 MHz, 253 K): δ = 28.9 (C*Me*$_3$), 29.5 (C-6), 36.2 (*C*Me$_3$), 51.1 (OCH_3), 52.1 (OCH_3), 54.8 (C-7), 56.9 ($NCH_2CH{=}$), 99.9 (C-3), 117.8 ($CH_2CH{=}CH_2$), 123.9 (*C*H=C-Aryl), 127.2 (broadened d, o/m-C_{aryl}), 132.2 (s, 2 C, $C1_{aryl}$, C-4), 134.0 ($CH_2CH{=}CH_2$), 135.1 (d, C-5), 137.7 (s, C-Cl), 151.6 (s, C-2), 158.0 (s, =*C*–Aryl), 169.1 (C=O), 170.4 (C=O). – $C_{25}H_{30}ClNO_4$ (443.97): calcd. C 67.63, 6.81, N 3.15; found C 68.19, H 6.69, N 3.17.

*Dimethyl 1-allyl-2-[(Z)-3,3-dimethyl-2-(thiophen-2-yl)-but-1-enyl]-6,7-dihydro-1H-azepine-3,4-dicarboxylate (***21b***):* The preparation was carried out as described for **21a**, from crude aminodiene **18b** (0.494 g, 1.8 mmol) and DMAD (0.246 ml, 2.0 mmol) in ether (15 ml). Yield of **21b**: 0.434 g (52% rel. to iminium salt **16b**); yellow oil. – IR (film): ν = 2950 (m), 1720 (s), 1536 (m), 1434 (m), 1252 (s), 1123 (m) cm^{-1}. – ^{1}H NMR (500.14 MHz, 253 K): δ = 1.21 (s, 9 H, *t*Bu), 2.02 – 2.12 (m, 1 H, 6-H), 2.24 – 2.35 (m, 1 H, 6-H), 2.53 (pseudo-t, 1 H, 7-H), 2.88 – 2.97 (m, 1 H, 7-H), 3.18 (dd, ^2J = 15.0 Hz, ^3J = 8.1 Hz, 1 H, $NCH_2CH{=}$), 3.68 (s, 3 H, OCH_3), 3.73 (s, 3 H, OCH_3), 4.23 (broadened, $^2J \approx$ 15 Hz, 1 H, $NCH_2CH{=}$), 5.09 – 5.18 (m, 2 H, $CH_2CH{=}CH_2$), 5.63 (mc, 1 H, $CH_2CH{=}CH_2$), 6.54 (t, 1 H, J = 5.4 Hz, 5-H), 6.63 (s, 1 H, C*H*=C–Thienyl), 6.70 (dd, ^3J = 3.5, ^4J = 1.2 Hz, 1 H, 3-$H_{thienyl}$), 6.96 (dd, ^3J = 5.1, ^3J = 3.5 Hz, 1 H, 4-$H_{thienyl}$), 7.22 (dd, ^3J = 5.1, ^4J = 1.2 Hz, 1 H, 5-$H_{thienyl}$). – ^{13}C NMR (125.77 MHz, 253 K): δ = 28.9 (C*Me*$_3$), 30.1 (C-6), 36.4 (*C*Me$_3$), 51.1 (OCH_3), 52.1 (OCH_3), 54.6 (C-7), 56.7 ($NCH_2CH{=}$), 100.0 (s, C-3), 118.1 ($CH_2CH{=}CH_2$), 124.5 (C-5$_{thienyl}$), 126.0 (d, 2 C, C-3$_{thienyl}$, C-4$_{thienyl}$), 126.4 (*C*H=C–thienyl), 132.1 (s, C-4), 134.1 ($CH_2CH{=}CH_2$), 134.9 (d, C-5),

Table 1. Summary of crystallographic data and structure refinement for compounds **10**, (1*E*,2*E*,4*E*)-**14**, **24**, and **25**.

	10	(1*(2')E*,2*E*,4*E*)-**14**	**24**	**25**
Empirical formula	$C_{19}H_{21}NO_4S$	$C_{20}H_{25}NO_4S$	$C_{26}H_{32}ClNO_4$	$C_{24}H_{31}NO_4S \times 0.5C_3H_6O$ [a]
Formula weight	359.43	375.47	457.98	458.60
Temperature (K)	293(2)	293(2)	293(2)	293(2)
Crystal size [mm]	$0.75 \times 0.50 \times 0.35$	$0.60 \times 0.35 \times 0.25$	$0.38 \times 0.19 \times 0.12$	$0.54 \times 0.27 \times 0.11$
Crystal system	orthorhombic	triclinic	monoclinic	monoclinic
Space group	*P bca*	*P* -1	*P* $2_1/n$	*P* $2_1/n$
a [Å]	14.536(3)	8.807(2)	12.637(2)	6.3962(4)
b [Å]	11.447(2)	10.463(2)	13.786(1)	22.652(1)
c [Å]	22.273(4)	10.776(2)	14.149(2)	17.276(1)
α [°]	90	97.20(3)	90	90
β [°]	90	93.77(3)	100.41(2)	99.93(9)
γ [°]	90	96.40(3)	90	90
Volume [Å^3]	3706.1(12)	975.8(3)	2424.4(5)	2465.3(3)
Z	8	2	4	4
ρ_{ber} [g·cm^{-3}]	1.288	1.278	1.255	1.235
μ(Mo-K$_\alpha$) [cm^{-1}]	0.20	0.19	0.19	0.16
θ Range [°]	2.20 – 23.50	1.91 – 24.00	1.99 – 25.96	2.16 – 25.92
Index ranges	$-1 \le h \le 16$	$-1 \le h \le 10$	$-14 \le h \le 15$	$-7 \le h \le 7$
	$-1 \le k \le 12$	$-11 \le k \le 11$	$-16 \le k \le 16$	$-27 \le k \le 27$
	$-24 \le l \le 1$	$-12 \le l \le 12$	$-17 \le l \le 17$	$-21 \le l \le 21$
Reflections collected	3496	3730	18673	21317
Independent reflections (R_{int})	27408 (0.0302)	3054 (0.0345)	4691 (0.0707)	4582 (0.0277)
Completeness to θ_{max} [%]	99.9	99.8	98.8	95.6
Data / restraints / parameters	2740/ 0 / 265 [b]	3054 / 0 / 332 [c]	4691 / 0 / 294 [d]	4582 / 3 / 303 [d]
Goodness-of-fit on F^2	1.057	1.050	0.764	0.913
Final *R* indices [$I > 2\sigma(I)$]: R_1, wR_2 [e]	0.0757, 0.1869	0.0615, 0.1671	0.0376, 0.0714	0.0395, 0.1121
R Indices (all data): R_1, wR_2 [f]	0.1278, 0.2224	0.0842, 0.1856	0.0977, 0.0816	0.0568, 0.1226
Largest diff. peak and hole [e·Å^{-3}]	0.49, −0.70	0.48, −0.43	0.14, −0.17	0.33, −0.20

[a] Acetone hemisolvate; the acetone molecule is disordered around an inversion centre; [b] hydrogen atom positions at the azonine ring were taken from a ΔF map and refined freely; all other hydrogen positions were calculated and treated as riding on their bond neighbors; [c] all hydrogen atom positions were taken from a ΔF map and refined with isotropic temperature factors, except for H(18) (calculated position, riding model); [d] hydrogen atoms were calculated geometrically and treated as riding on their bond neighbors; the H atoms of the disordered acetone molecule in **26** were not located; [e] refinement based on F^2 values; [f] $R_1 = \Sigma||F_o| - |F_c||/\Sigma|F_o|$; $wR_2 = [\Sigma(w(F_o{}^2 - F_c{}^2)^2)/\Sigma w(F_o{}^2)^2]^{1/2}$.

139.0 (s, C-2$_{thienyl}$), 146.5 (s, =*C*–thienyl), 158.3 (s, C-2), 169.1 (C=O), 170.6 (C=O). – $C_{23}H_{29}NO_4S$ (415.55): calcd. C 66.48, H 7.03, N 3.37; found C 66.68, H 6.95, N 3.58.

*Dimethyl 2-(tert-butyl)-2-(4-chlorophenyl)-2,3,7,8,9,10-hexahydroazepino[1,2-a]azocine-11,12-dicarboxylate (***24***):* The preparation was carried out as described for **21a**, from crude aminodiene **19a** (0.555 g, 1.76 mmol) and DMAD (0.233 ml, 1.90 mmol) in ether (15 ml). Conditions for thermolysis: toluene, 160 °C, 5 h. The product was purified by flash chromatography (10 g of silica gel, CH_2Cl_2) and recrystallized from ethanol. Yield of **24**: 0.626 g (68% rel. to iminium salt **17a**); light-yellow crystals, m. p. 124 °C. – IR (KBr): ν = 3045 (w), 2952 (m), 1731 (s), 1713 (s), 1432 (m), 1263 (s) cm^{-1}. – ^{1}H NMR (500.14 MHz, 250 K): δ = 0.85 (broadened s, 9 H, *t*Bu), 1.26 – 1.37 (m, 2 H, 8-H, 9-H), 1.63 – 1.76 (m, 1 H, 8-H), 1.86 (quin, 1 H, 9-H), 2.40 – 2.51 (m, 2 H, 3-H, 10-H), 2.58 – 2.70 (m, 2 H, 7-H, 10-H), 2.92 (d, J = 15.2, 8.4 Hz, 1 H, 3-H), 3.27 (virtual t, 1 H, 7-H), 3.82 (s, 3 H, OCH$_3$), 3.94 (s, 3 H, OCH$_3$), 4.53 (virtual t, 1 H, 4-H), 5.50 (d, ^3J = 9.8 Hz, 1 H, 5-H), 5.54 (s, 1 H, 1-H), 7.12 – 7.24 (m, 4 H, H$_{aryl}$). – ^{13}C NMR (125.77 MHz, 250 K): δ = 23.2 (t, C-8), 24.9 (t, C-9), 25.8 (broadened q, C*Me*$_3$) 25.8 (t, C-10), 31.7 (t, C-3), 36.7 (*C*Me$_3$), 50.0 (t, C-7), 52.6 (OCH$_3$), 52.7 (OCH$_3$), 54.7 (s, C-2), 102.3 (d, C-4), 119.3 (d, C-1), 126.1/126.5 (both d, o-C$_{aryl}$), 129.7 (d, C-5), 130.4 (s, C-Cl), 130.8/132.8 (both d, m-C$_{aryl}$), 134.9 (s, C-11), 137.0 (s, C-12a), 140.3 (s, C-12), 142.7 (s, C-1$_{aryl}$), 167.7 (C=O), 170.0 (C=O). – $C_{26}H_{32}ClNO_4$ (458.00): calcd. C 68.19, H 7.04, N 3.06; found C 68.00, H 7.17, N 2.97.

*13-(tert-Butyl)-3a,4,4a,5,7,8,9,12b-octahydroazocino-[2,1-a]thieno[3,2-f]isoindole-11,12-dicarboxylate (***25***):* The preparation was carried out as described for **21a**, from crude aminodiene **19b** (0.523 g, 1.8 mmol) and DMAD (0.246 ml, 2.0 mmol) in ether (15 ml). Conditions for thermolysis: toluene, 160 °C, 5 h. The product was purified by flash chromatography (10 g of silica gel, CH_2Cl_2) followed by column chromatography (silica gel, ethyl acetate/petroleum ether 1:3) and was recrystallized from acetone/petroleum

ether. Yield of **25**: 0.364 g (42% rel. to iminium salt **17b**); light-yellow crystals, m. p. 124 °C. – IR (KBr): ν = 2940 (m), 1713 (s), 1550 (s), 1241 (vs) cm^{-1}. – ^{1}H NMR (500.14 MHz): δ = 1.08 – 1.19 (m, 1 H, 8-H), 1.33 (s, 9 H, *t*Bu), 1.35 – 1.45 (m, 1 H, 4-H), 1.67 – 1.83 (m, 2 H, 8-H, 4-H), 1.92 – 2.01 (m, 1 H, 4a-H), 2.29 – 2.47 (m, 2 H, 9-H), 2.87 (dd, J = 14.1, 3.6 Hz, 1 H, 7-H), 3.04 (d, J = 9.8 Hz, 1 H, 5-H), 3.57 (dd, J = 9.8, 4.9 Hz, 1 H, 5-H), 3.52 (s, 3 H, OCH_3), 3.69 (s, 3 H, OCH_3), 3.98 (t, 1 H, 7-H), 4.17 – 4.24 (m, 1 H, 3a-H), 4.30 (d, J = 6.0 Hz, 1 H, 12b-H), 5.63 (dd, J = 6.2, 2.8 Hz, 1 H, 3-H), 6.14 – 6.20 (m, 2 H, 2-H, 10-H). – ^{13}C NMR (125.77 MHz): δ = 13.5 (t, C-8), 24.9 (t, C-9), 28.7 (C*Me*$_3$), 31.3 (d, C-4a), 36.0 (*C*Me$_3$), 37.6 (t, C-4), 44.5 (t, C-7), 50.9 (d, C-3a), 51.1 (OCH_3), 51.5 (d, C-12b), 51.9 (OCH_3), 59.6 (t, C-5), 89.4 (s, C-12), 124.0 (d, C-2), 125.6 (d, C-3), 131.3 (d, C-10), 135.2 (s, 2 C, C-11, C-13a), 135.4 (s, C-13), 159.9 (s, C-12a), 169.6 (C=O), 169.9 (C=O). – $C_{24}H_{31}NO_4S$ (429.57): calcd. C 67.10, H 7.27, N 3.26; found C 66.03, H 7.29, N 3.02.

X-ray crystal structure determinations

Data collection was performed on a four-circle diffractometer (Siemens P4) for **10** and (1*(2')E*,2*E*,4*E*)-**14** and on an imaging-plate diffractometer (STOE IPDS) for **24** and **25**, using monochromatized Mo-K_α radiation. No absorption correction was applied. The structures were solved by direct methods and refined by a full-matrix least-squares procedure based on F^2 values using the program package SHELX-97 [20]. Crystallographic data and refinement details are given in Table 1.

CCDC-281834 (**10**), -281835 (1*(2')E*,2*E*,4*E*-**14**), -281836 (**24)** and -281837 (**25**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge at www.ccdc.cam.ac.uk/conts/retrieving.html [or from the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB2 1EZ, UK; fax: (internat.) +44-1223/336-033; E-mail: deposit@ccdc.cam.ac.uk].

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