Tri- and Tetracyclic Azepine Derivatives by Thermally Induced Cyclization of Aminoallenes and Semicyclic 2-Dienamines

Robert Reinhard,† Martina Glaser,‡ Ralf Neumann,‡ and Gerhard Maas*,‡

Abteilung Organische Chemie I, Universität Ulm, Albert-Einstein-Allee 11, D-89081 Ulm, Federal Republic of Germany, and Fachbereich Chemie, Universität Kaiserslautern, Erwin-Schrödinger-Strasse, D-67663 Kaiserslautern, Federal Republic of Germany

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The 3,3-dimethylindoline-derived allenes **5** are conveniently prepared by organocuprate addition to 2-(phenylethynyl)-3,3-dimethyl-1-methylindolium triflate **4**. Their thermal isomerization affords tetracyclic azepine derivatives **6**. The semicyclic 2-amino 1,3-dienes **11**, formed by spontaneous tautomerization of the corresponding aminoallenes, are transformed by thermal reaction into either tricyclic azepine derivatives **13** or benzothiophene-annelated azaheterocycles **14** and **15**, depending on the ring size of the enamine moiety and the (hetero)aryl group at C-4 of the 2-dienamine.

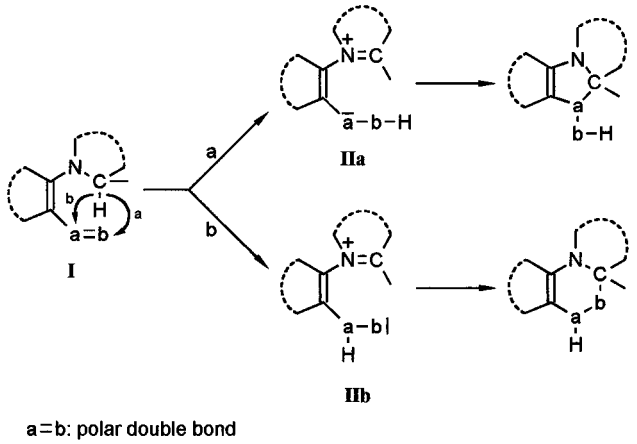
Introduction

The thermally induced cyclization of *N*,*N*-dialkyl-1,3-dien-1-amines **I** is a remarkably general strategy for the construction of five- and six-membered azaheterocycles. The chain → ring isomerization includes a 1,6- or a 1,5-H shift from the N−C−H unit to the polar double bond, followed by 1,5- or 1,6-cyclization of dipoles **IIa**,**b** (Scheme 1).

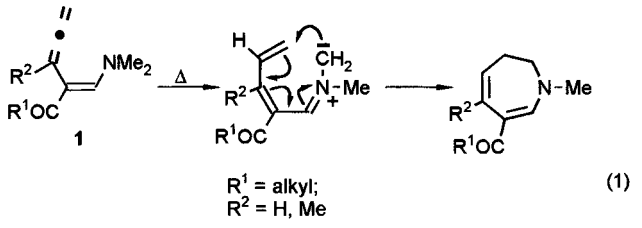
The term "*tert*-amino effect" was originally assigned to this category of reactions by Suschitzky and Meth-Cohn.[1] More recently, Viehe[2] introduced the more descriptive term "α-cyclization of tertiary amines." Reactions of this type were first observed for tertiary anilines bearing in *ortho* position a double-bond function with at least one heteroatom[1] (**I**, a=b: N=O, NO_2, N=NR, C=NR, $C=N^+R_2$,[3] C=O), but it was later realized that the *ortho* substituent could also be an acceptor-substituted vinyl group. Reinhoudt and co-workers exploited the possibilities of this structural variation extensively,[4] and they were also the first ones to recognize that the essential and sufficient structural moiety to undergo this type of isomerization is that of a *N*,*N*-dialkyl-1(*Z*),3-dien-1-amine.[5] In the last decade or so, work by Reinhoudt's[4] group and others[2,3,6,7] has amply demonstrated the broad applicability of the reaction principle outlined in Scheme 1.

Another manifestation of the α-cyclization of tertiary amines has not yet come to general attention. Examples

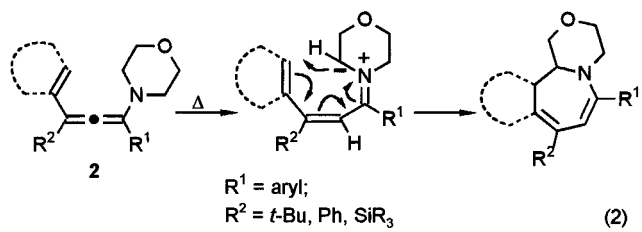
Scheme 1. Thermal Isomerization of *N*,*N*-Dialkyl-1,3-dien-1-amines



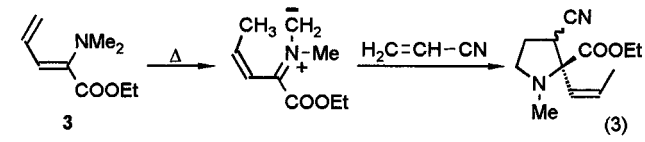
of this type include the thermal isomerization reactions of 1-(dimethylamino)-1,3,4-pentatrienes[8] and of 1-morpholino-3-vinylallenes (or 3-arylallenes) (eq 1 and 2),[9] leading to azepine derivatives in both cases.



(1)



(2)



(3)

Although the mechanistic details have not been established, it seems reasonable to assume the formation of

* To whom correspondence should be addressed.
† University of Kaiserslautern.
‡ University of Ulm.
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(1) (a) Suschitzky, H.; Meth-Cohn, O. *Adv. Heterocycl. Chem.* **1972**, *13*, 211−278. (b) Meth-Cohn, O. *Adv. Heterocycl. Chem.* **1996**, *65*, 1−37.
(2) (a) Jiang, S.; Janousek, Z.; Viehe, H. G. *Bull. Soc. Chim. Belg.* **1993**, *102*, 663−668. (b) Jiang, S.; Janousek, Z.; Viehe, H. G. *Tetrahedron Lett.* **1994**, *35*, 1185−1188. (c) De Boeck, B.; Jiang, S.; Janousek, Z.; Viehe, H. G. *Tetrahedron* **1994**, *50*, 7075−7092. (d) De Boeck, B.; Janousek, Z.; Viehe, H. G. *Tetrahedron* **1995**, *51*, 13239−13246.
(3) Meth-Cohn, O.; Taylor, D. L. *J. Chem. Soc., Chem. Commun.* **1995**, 1463−1464.
(4) Verboom, W.; Reinhoudt, D. N. *Recl. Trav. Chim. Pays-Bas* **1990**, *109*, 311−324.
(5) Reinhoudt, D. N.; Visser, G. W.; Verboom, W.; Benders, P. H.; Pennings, M. L. M. *J. Am. Chem. Soc.* **1983**, *105*, 4775−4781.
(6) (a) Kirschke, K.; Moller, A.; Schmitz, E.; Kuban, R. J.; Schulz, B. *Tetrahedron Lett.* **1986**, *27*, 4281−4284. (b) Ojea, V.; Muinelo, I.; Figueroa, M. C.; Ruiz, M.; Quintela, J. M. *Synlett* **1995**, 622−624. (c) Chantegrel, B.; Deshayes, C.; Faure, R. *Tetrahedron Lett.* **1995**, *36*, 7859−7862. (d) Noguchi, M.; Mizukoshi, T.; Kakehi, A. *Tetrahedron* **1996**, *52*, 13081−13096. (e) Noguchi, M.; Mizukoshi, T.; Uchida, T.; Kuroki, Y. *Tetrahedron* **1996**, *52*, 13097−13110.

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an α,β,γ,δ-unsaturated azomethine ylide by a 1,4- and 1,6-H shift, respectively, followed by 1,7-electrocyclization. Since the termini of the H shift, the δ-position of a dienamine in **1** and the β-position of an enamine in **2**, are electron-rich centers, a proton transfer is likely to occur in both cases, in contrast to the hydridic nature[10] of the H shift occurring in compounds **I**. Indirect evidence for the azomethine ylide came from the interception of such a 1,3-dipole by [3 + 2] cycloaddition, when 1-dienamine **3** was heated in the presence of acrylonitrile (eq 3).[11] In a reaction sequence comparable to that shown in eq 2, [(dialkylamino)methylene]ketenes, under the conditions of their generation from the corresponding dialkylaminomethylene Meldrum's acid by flash vacuum pyrolysis, yield pyrrolin-4-ones by 1,5-cyclization of intermediate azomethine ylides.[12]

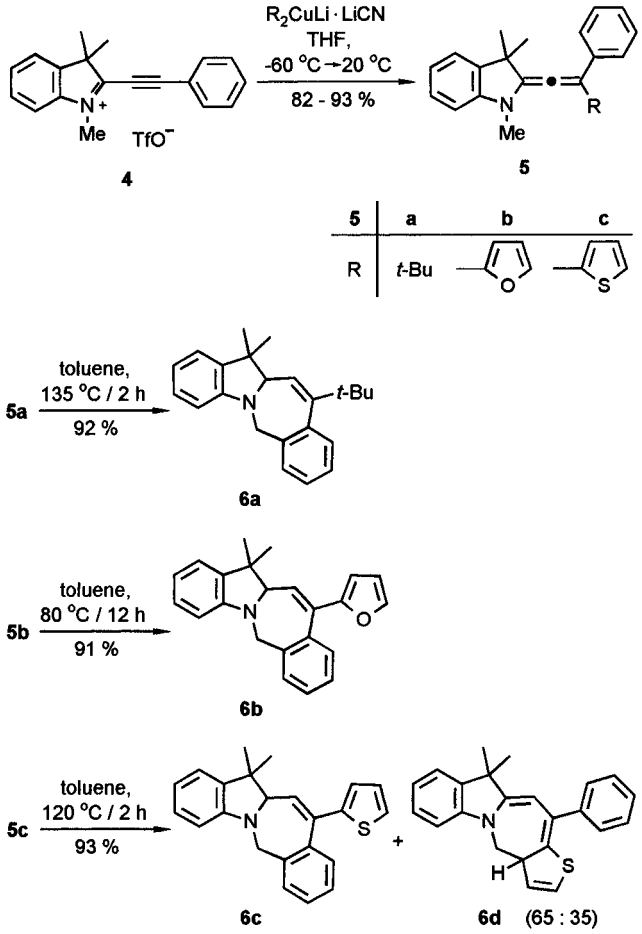
In this paper, we show that the 1-amino-3-vinyl (or -aryl)allene → dihydroazepine isomerization is not restricted to morpholinoallenes, but can be generalized to construct other fused azepine derivatives as well. Furthermore, for the first time we report that the azomethine ylide route to azepine derivatives is also viable for *N*-methyl-substituted 2-amino 1,3-dienes.

Results

Thermal Isomerization of Aminoallenes. The availability of aminoallenes is limited for two reasons: (a) (*N*,*N*-Dialkylamino)allenes bearing a CHR_2 substituent at either terminus of the allene unit usually tautomerize readily to form 1- or 2-amino 1,3-dienes.[13,14] (b) Aminoallenes with no or little substitution at the allene function tend to hydrolyze or oligomerize rather easily. Therefore, we envisaged aminoallenes **5** as suitable objects of study, where such complications cannot occur. We have recently introduced conjugate organocuprate addition to propyne iminium salts as a versatile route to aminoallenes and amino-1,3-dienes.[13] In the same manner, reaction of 2-(phenylethynyl)-3*H*-indolium triflate **4**[15] with so-called higher-order cyanocuprates provided the desired aminoallenes **5a**−**c** in good yield as crystalline compounds (Scheme 2). The constitution of these novel allenes[16] is indicated by the ν(C=C=C) stretching vibration in the IR spectrum (1910−1950 cm^{-1}) and by a ^{13}C NMR signal at 186.8 (**5a**) or 193.5 ppm (**5b**,**c**) for the central allenic carbon atom.

When concentrated solutions of allenes **5a**−**c** in toluene (ca. 0.5−1 M) were heated in Schlenk pressure tubes, clean isomerization/cyclization occurred, and the expected indolo[2]benzazepines **6a**−**c** were isolated. It is interesting to note that the furyl ring in **5b** does not compete with the phenyl group in the cyclization process, whereas

Scheme 2. Synthesis and Thermal Isomerization of Exocyclic Aminoallenes 5



the thienyl ring in **5c** does so.[17] In the latter case, a 65:35 mixture of the condensed systems **6c** and **6d** was isolated, and the same ratio of the two isomers was obtained when a solution of **5c** in toluene was kept at ambient temperature for 5 weeks. Remarkably, no rearomatization of the thiophene ring occurs in **6d**, although a thermally allowed 1,5-sigmatropic H shift should be feasible. It is assumed that extended π-conjugation including the two heteroatoms is possible in **6d**, which stabilizes the molecule enough to compensate for the loss of resonance energy of the thiophene ring.

We then tried to prepare the S,N-substituted allene **8** from 2-(4-chlorophenyl)-1-methyl-1,3-benzothiazolium triflate **7**[15] and the appropriate higher-order cyanocuprate. However, this particularly electron-rich allene could not be separated from byproducts since crystallization was not successful and liquid chromatography led to decomposition. Therefore, the crude product mixture was heated in toluene solution at 125 °C. Again, isomerization/cyclization occurred, and the 1,3-benzothiazolo[2]-benzazepine **9** was obtained in good overall yield (Scheme 3).

Thermal Reactions of Semicyclic 2-Amino 1,3-Dienes. The scope of the 1-amino-3-arylallene → dihydroazepine isomerization would be wider if aminoallenes with a CHR_2 substituent were stable compounds. As mentioned above, this subset of aminoallenes tends to

(7) The thermal isomerization of 1-[allyl(phenyl)amino]-1,3-dienenitriles yields dihydroazepines in a 1,7-cyclization reaction: Fang, J.-M.; Yang, C.-C.; Wang, Y.-W. *J. Org. Chem.* **1989**, *54*, 481−484.

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(11) Bourhis, M.; Vercauteren, J. *Tetrahedron Lett.* **1994**, *35*, 1981−1984.

(12) Hermecz, I.; Keresztúri, G.; Vasvári-Debreczy, L. *Adv. Heterocycl. Chem.* **1992**, *54*, 259−271.

(13) (a) Mayer, T.; Maas, G. *Synlett* **1990**, 399−400. (b) Maas, G.; Mayer, T. *Synthesis* **1991**, 1209−1215.

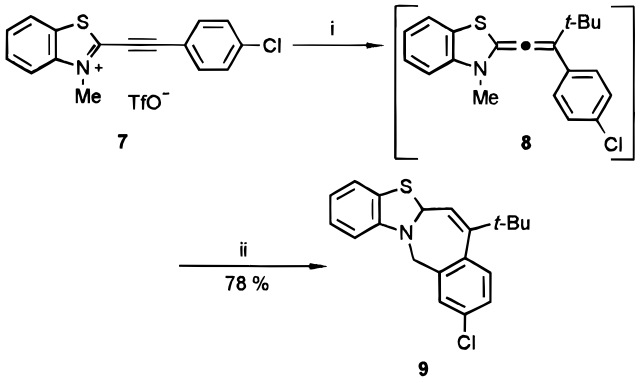
(14) Maas, G.; Reinhard, R.; Neumann, R.; Glaser, M. *J. Prakt. Chem.* **1996**, *338*, 441−450.

(15) Reinhard, R.; Maas, G.; Bohrisch, J.; Liebscher, J. *Liebigs Ann. Chem.* **1994**, 429−432.

(16) Allenes capped with two 1,3,3-trimethyl-3*H*-indoline units are known: Grahn, W. *Liebigs Ann. Chem.* **1981**, 107−121.

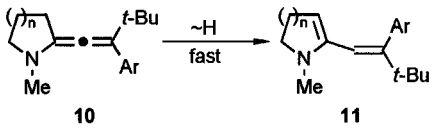
(17) In contrast to these results, the participation of a thienyl ring was found to be favored by a factor of >100 over that of a phenyl ring in 1,7-electrocyclization reactions of diene-conjugated nitrilium ylide dipoles: Cullen, K. E.; Sharp, J. T. *J. Chem. Soc., Perkin Trans. 1* **1995**, 2565−2579.

Scheme 3. One-Pot Synthesis of Azepine Derivative 9[a]

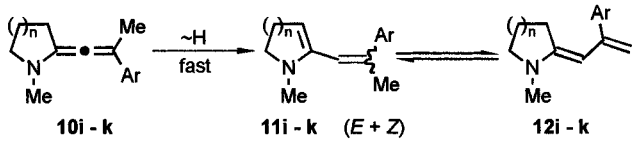


[a]Key: (i) $(t\text{-Bu})_2$CuLi·LiCN, THF, −60 → 20 °C; (ii) toluene, 125 °C, 25 h.

Scheme 4



10, 11	n	Ar
a	1	4-chlorophenyl
b	1	4-methoxyphenyl
c	1	2-thienyl
d	2	4-chlorophenyl
e	2	2-thienyl
f	2	3-thienyl
g	3	4-chlorophenyl
h	3	2-thienyl



10 - 12	n	Ar
i	2	4-chlorophenyl
j	2	2-thienyl
k	3	2-thienyl

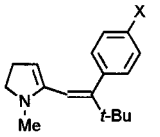
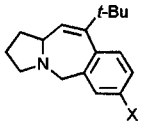
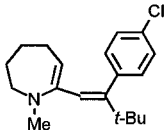
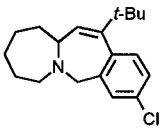
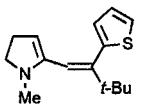
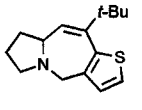
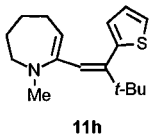
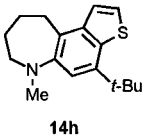
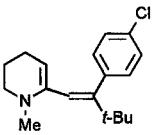
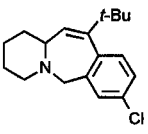
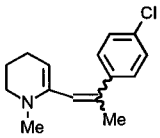
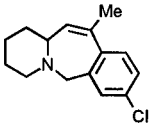
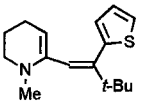
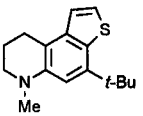
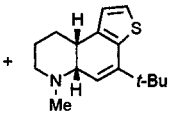
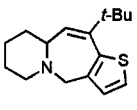
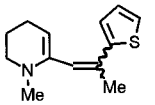
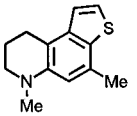
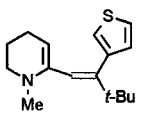
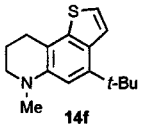
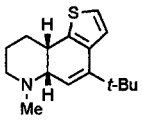
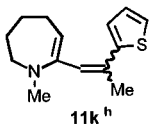
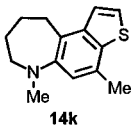
isomerize readily by a prototropic shift to form 1- or 2-amino 1,3-dienes. For example, when we tried to synthesize the allenes **10a**−**h** by analogy with the procedure described in Scheme 2, we isolated the semicyclic 2-amino 1,3-dienes **11a**−**h** (Scheme 4).[14] Similarly, the aminoallenes **10i**−**k**, bearing CHR_2 substitutents at the two ends of the cumulene system, rearranged under the conditions of their synthesis, and a mixture of 2- and 1-amino 1,3-dienes (**11** and **12**) was obtained. Equilibria exist between *Z*-**11**, *E*-**11**, and **12i**−**k**, and the ratio **11**:**12** depends on the size of the heterocycle.[14] Thus, the endocyclic form (**11i**,**j**) prevails for the six-membered rings, and a more balanced equilibrium is observed for the amino dienes **11k**/**12k**.

To our great satisfaction, some of these semicyclic dienamines underwent thermal isomerization to give the same azepine derivatives which would have been expected from their nonavailable tautomers, aminoallenes **10**. However, more energetic conditions than in the case of aminoallenes **5** and **7** were required. The results are collected in Table 1. It can be seen that thermal impact on dienamines **11** leads, in general, either to fused azepine derivatives **13** or to benzo-annelated azaheterocycles **14**. Azepines are formed in the case of the dihydropyrrole-derived semicyclic dienamines **11a**−**c**, no matter whether an aryl or a thienyl ring is present. In contrast, the six- and seven-membered semicyclic dienamines yield the fused azepine systems only for the dienamines with a 4-chlorophenyl substituent (**11d**,**g**,**i**). In the case of the thienyl-substituted systems, however, benzothiophene derivatives are formed (**14f**,**h**,**j**,**k**; **15e**,**f**). Dienamine **11e** turned out to be a special case since it was converted thermally to a mixture of azepine derivative **13e**, benzothiophene **14e**, and dihydrobenzothiophene **15e** under a variety of conditions (see below). The alkyl substituent (*tert*-butyl or methyl) at the exocyclic double bond of the dienamines does not influence the course of the thermal reaction, but a qualitative comparison of the reaction conditions for the pairs **11d**/**i**, **11e**/**j**, and **11g**/**11k** suggests that the *t*-Bu substituent facilitates both cyclization modes. These observations are summarized in Scheme 5 along with a mechanistic proposal (see Discussion section).

Several efforts were made to lower the activation energies for the isomerization **11** → **13**. Replacement of toluene by the more polar solvents DMF or DMSO resulted in a slower reaction rate for **11c**. For example, a reaction run in DMF gave, after 5 h at 120 °C, the starting material and product **13c** in yields of 13 and 79%, respectively, in contrast to complete conversion in toluene under identical conditions. We noticed, however, that isomerization in DMF gave less byproducts according to NMR than in toluene or in DMSO. Addition of an amine base led to contradictory results. In a kinetic run monitored by ^{1}H NMR, pyridine or ethyldiisopropylamine did not have a beneficial effect on the rate of the isomerization **11c** → **13c**. On the other hand, isomerization of the tetrahydropyridine system **11d** at 200 °C was significantly faster in the presence than in the absence of ethyldiisopropylamine (94% conversion in 29 h vs 75% conversion in 33 h). The same is true for the reaction **11i** → **13i**, but extensive decomposition occurred under the harsh reaction conditions, no matter whether the amine was present or absent. Finally, the presence of the same amine base in the thermal isomerization of **11g** resulted in extensive decomposition, and the product yield decreased from 81 to 29%.

As mentioned above, dienamine **11e** was converted to a mixture of **13e**, **14e**, and **15e** under a variety of conditions, and considerable effort was spent in order to selectively favor the pathway leading to dihydroazepine **13e** by checking the influence of solvent, concentration, and additives. These experiments were carried out on the NMR scale, and the relative composition of the product mixture was estimated from the integration of characteristic ^{1}H NMR signals of the different species; due to partial overlap of some signals, this method is of course only approximate. Although it turned out that the results so obtained were not always reproducible, mixtures were typically obtained in which **14e** + **15e**, taken together, dominated over **13e**, and the following trends were noticed: A polar solvent (DMF vs toluene) and a low concentration of the dienamine (0.1 M vs 1.06 M) both favor the formation of the benzothiophene derivatives. In contrast, a lower reaction temperature provides the azepine derivative as the major product; for example, complete consumption of **11e** was achieved after being heated in toluene at 110 °C for 45 days or at 200 °C for 12 h, leading to a **13e**/**14e**/**15e** ratio of 1.0/0.27/0.29 and 1.0/1.7/2.3, respectively. The addition of NEt(*i*-Pr)$_2$ (0.3 equiv) to a toluene solution of **11e** does not

Table 1. Thermally Induced Cyclization Reactions of Semicyclic Dienamines 11[a]

dienamine	conditions	product	yield (%)	dienamine	conditions	product	yield (%)
 X = Cl: **11a**; X = OMe: **11b**	145 °C, 9 h 145 °C, 9 h	 **13a** **13b**[b]	70 56	 **11g**[d]	155 °C, 36 h	 **13g**	81
 **11c**	120 °C, 4 h	 **13c**	88	 **11h**	135 °C, 2 h	 **14h**	70
 **11d**	200 °C, 29 h, NEt(*i*-Pr)$_2$	 **13d**	85	 **11i**[e]	200 °C, 70 h, NEt(*i*-Pr)$_2$	 **13i**	f
 **11e**	200 °C, 11-12 h (NEt(*i*-Pr)$_2$)	 **14e** +  **15e** +  **13e**	see text	 **11j**[g]	200 °C, 40 h, NEt(*i*-Pr)$_2$	 **14j**	62
 **11f**	190 °C, 1 h or 120 °C, 9 h	 **14f** +  **15f**	35 c	 **11k**[h]	180 °C, 2 h	 **14k**	54

[a] All reactions were carried out in toluene solution in thick-walled Schlenk tubes. [b] The product has a purity of only ca. 60%. [c] The ratio of **14f** and **15f** was 1:1 in the crude product mixture, but **15f** could not be isolated. [d] A mixture of ***Z*-11g** and ***E*-11g** (14:1) was used. [e] A mixture of **11i** ($Z + E$) and **12i** (94:6) was used. [f] The ^{1}H NMR spectrum indicated the absence of **11i**, the presence of **13i**, and also extensive decomposition; **13i** could not be isolated in pure form. [g] A mixture of ***Z*-11j**, ***E*-11j**, and **12j** (52:45:3) was used. [h] A mixture of ***E*-11k** and **12k** (73:27) was used.

shorten the reaction time appreciably nor does it alter dramatically the composition of the product mixture. On the other hand, thermal treatment of a sample of **11e** and NEt(*i*-Pr)$_2$ in toluene-d_8, which had been stored at −28 °C for 8 weeks, produced nearly exclusively azepine derivative **13e**. Unfortunately, this sample could not be purified further by bulb-to-bulb distillation (240 °C) nor could **13e** be recovered after column chromatography on basic alumina or silica gel, while florisil allowed partial purification but with significant loss of **13e**.

The unsatisfactory reproducibility of some of these results suggested that the "history" of the dienamine was also an important factor, i.e., whether a sample of **11e** was freshly prepared and distilled or whether it was taken at the workup stage before distillation (i.e., pentane extract of the preparation of **11e** by organocuprate addition to the corresponding propyniminium salt[14]) and perhaps contained traces of copper salts. Therefore, a sample of freshly distilled **13e** (which contained no copper salts according to atomic absorption spectroscopy), an undistilled sample (obtained from the pentane extract mentioned before and containing significant amounts of copper salts), and a distilled sample to which some CuCN (20% w/w) had been added were all heated in toluene solution at 185 °C. The results were not very conclusive since mixtures of **13e**, **14e**, and **15e** were obtained in all cases, but a reliable comparison by ^{1}H NMR integration was not possible due to the formation of large amounts of byproducts in the samples containing copper salts. As a net result of all these studies, it appears that the cyclization of dienamine **11e** to form azepine derivative **13e** selectively and reproducibly is not possible under thermal conditions. The opposite aspect, namely selective synthesis of **14e** at the complete expense of the azepine route (e.g., by established photocyclization procedures), was not a goal of our present study.

The constitution of the novel azepine derivatives **6**, **9**, and **13** is fully supported by the NMR spectra. Some characteristic chemical shifts of the azepine ring are given in Table 2. We have not established the stereo-

Scheme 5. Thermally Induced Isomerization Pathways of Dienamines 11

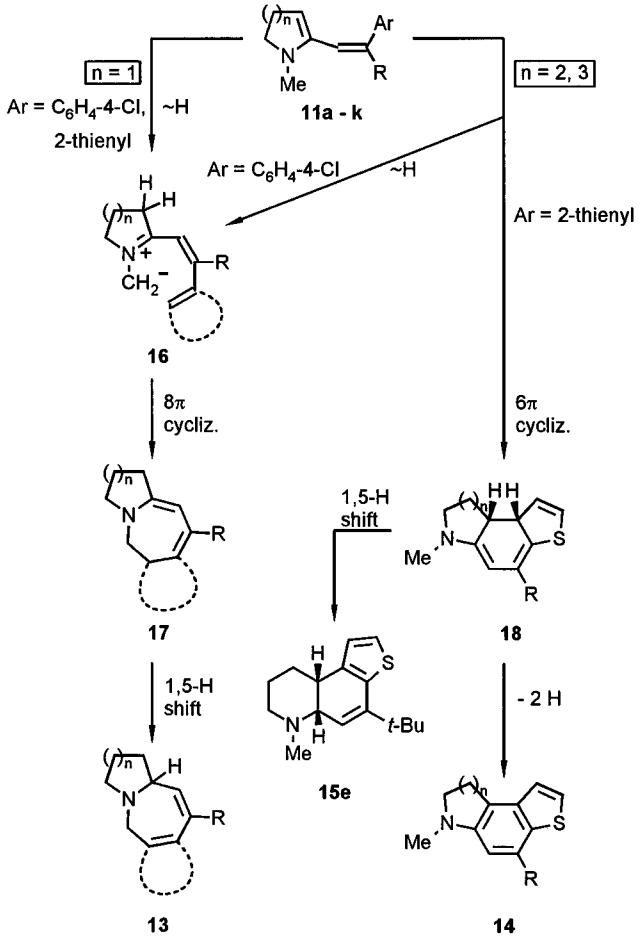


Table 2. NMR Chemical Shifts of the Azepine Ring in 6, 9, and 13 ($CDCl_3$, TMS, δ/ppm)

	$\delta(^1H)$			$\delta(^{13}C)$	
compd	NCH_2[a]	NCH[b]	N−C−CH=[c]	NCH_2	NCH
6a	3.60, 4.20	3.26	6.07	49.9	70.5
6b	3.78, 4.33	3.56	6.68	49.9	70.7
6c	3.80, 4.35	3.55	*d*	50.0	71.1
9	3.59, 4.14	4.90	6.10	50.2	66.4
13a	3.14, 3.63	3.06	5.73	54.7[e]	56.8
13b	3.17, 3.65	3.11	5.68	*f*	*f*
13c	3.00, 3.87	3.21	5.82	49.9[e]	58.3
13d	3.31, 3.83	2.73	5.78	58.8[e]	58.2
13g	3.36, 3.73	2.94	5.83	60.2[e]	60.2

[a] AB quartet, $|^2J| = 10.9-13.3$ Hz. [b] Multiplet. [c] Doublet, $^3J = 6.0-6.8$ Hz. [d] Signal overlap with **6d**. [e] Assignment by $^1H,^{13}C$ correlation. [f] Not assigned.

chemistry of the fused rings containing the bridgehead nitrogen atom. We notice, however, that for 5,6,8,13,14,14a-hexahydroisoquino[2,1-*b*][2]benzazepines ("C-homoberbines"), which are closely related structurally to **13d**,**i**, *cis*-fused rings with the angular hydrogen in equatorial positon at the six-membered ring have been found both in the solid state and in chloroform solution.[18] The 3,4,5,12b-tetrahydro-1*H*-[1,4]oxazino[4,3-*a*][2]benzazepines that result from thermal isomerization of 1-morpholino-3-phenylallenes (eq 2) have the same configuration.[9]

Discussion

The thermal isomerization of aminoallenes **5** and **8** to the tetracyclic azepine derivatives **6** and **9** follows the same pattern as that for 3-phenyl (or -vinyl)-1-morpholinoallenes **2**[9] (eq 2). This suggests that a broad range of condensed azepine derivatives can be synthesized from appropriate alkylamino-substituted allenes. As mentioned before, CH-substituted aminoallenes tautomerize easily to the corresponding conjugated amino dienes and are, therefore, not available for the azepine synthesis under discussion. However, we show in this paper that the semicyclic 2-amino 1,3-dienes **11** can be isomerized, in principle, to the same azepine derivatives (**13**) that would result from the tautomeric, but nonavailable, aminoallenes **10**. Depending on the ring size of the enamine moiety and the π-system at C-4 of the dienamine, another cyclization process leading to **14** can supersede the azepine route. A mechanistic scheme for the two competing pathways is shown in Scheme 5. We assume that the azepine route begins with a H shift leading to the $\alpha,\beta,\gamma,\delta$-unsaturated azomethine ylide **16**, which then undergoes a 1,7 ring closure by an 8π electrocyclic reaction.[19,20] The reaction sequence closes with a 1,5-sigmatropic H shift (**17** → **13**) that reestablishes the aromaticity of the newly fused (hetero)aromatic ring.

On the other hand, formation of the benzothiophene derivatives **14** and **15** is initiated by disrotatory 6π electrocyclic ring closure. Under the reaction conditions, the resulting 1,3-cyclohexadiene **18** is either dehydrogenated to form **14** or isomerized to dihydrobenzothiophene **15** by a suprafacial 1,5-H shift. Scheme 5 shows this for the 2-thienyl case, but the same scenario applies for the 3-thienyl-dienamine **11f**. Obviously, both reaction modes are accessible in the case of the six-membered azaheterocycles (formation of **14e**,**f** + **15e**,**f**), while in the seven-membered cases the 1,5-H shift cannot compete with the dehydrogenation of **18** (formation of **14h**,**k**).

It is evident that both cyclization modes shown in Scheme 5 require the *Z* configuration for the exocyclic double bond of dienamines **11**. Since the *tert*-butyl-substituted dienamines exist exclusively or nearly so in this configuration, whereas pronounced *Z*/*E* equilibria were observed for the methyl-substituted dienamines **11i**−**k**,[14] it is reasonable to assume that the more forcing reaction conditions in the latter cases (see above) are due to the additional energy required for the *E* → *Z* isomerization.

By analogy with the isomerization of (alkylamino)allenes **2**, we assume that dipoles **16** are generated from dienamines **11** by a 1,4 proton transfer from the *N*-methyl group to the β-carbon atom of the enamine function. It was expected that this step would be assisted by a base, and we have indeed observed qualitatively the rate-enhancing effect of ethyldiisopropylamine in some cases (see above). The cases of the thienyl-substituted dienamines **11f**,**j**,**k** show, however, that the presence of this base is not sufficient to render the azepine route competitive with the 6π electrocyclization leading ultimately to the benzothiophene derivatives **14** and **15**. Proton transfer as the rate-limiting step of the isomerization **11** → **17** would also explain why the five-membered dienamines all isomerize to the azepine derivatives, no matter whether the cyclization includes an aryl (**11a**,**b**) or a

(18) Meise, W.; Arth, C.; Zlotos, D.; Jansen, M.; Feldmann, C. *Liebigs Ann. Chem.* **1994**, 1135−1142.

(19) 1,7-Electrocyclization reactions of $\alpha,\beta,\gamma,\delta$-unsaturated 1,3-dipoles constitute an established route to seven-membered heterocycles: Zecchi, G. *Synthesis* **1991**, 181−188.

(20) For the formation of 4,5-dihydroazepines by an 8π electrocyclic ring closure of 4-azaheptatriene anions, see: Klötgen, S.; Würthwein, E.-U. *Tetrahedron Lett.* **1995**, *36*, 7065−7068.

thienyl ring (**11c**), whereas the six- and seven-membered dienamines bearing a thienyl ring behave differently. The β-carbon atom of the enamine function, which accepts the transferred proton, is more basic in the five-membered than in the two larger rings. Indications for this are given by the pK_a values of 2,3-dihydro-1,5-dimethylpyrrole (11.94) and 1,2,3,4-tetrahydro-1,6-dimethylpyridine (11.42),[21] the conjugate acids being the C-protonated forms. Furthermore, a comparison of the δ(N−C=*C*H) ^{13}C NMR values[14] of dienamines **11** with those of the corresponding carbocycles[22] shows that the largest upfield shift, suggesting the highest electron density, is observed for the five-membered cyclic enamines; $\Delta\delta$ values of −26.6 (**11a**), −22.6 (**11d**), and −17.8 ppm (**11g**) are found in the 4-chlorophenyl series, and $\Delta\delta$ values of −27.2 (**11c**), −23.8 (**11e**), and −17.8 (**11h**) are found in the 2-thienyl series. Obviously, the rather small basicity differences between the five- and six-membered enamine functions are sufficient to retard the proton transfer enough to let the electrocyclization of the hexatriene unit in the thienyl-substituted dienamines take over.[23] In this context, it is interesting to note that the photochemically induced 6π electrocyclization of 1-(2-pyridyl)-2-(2-thienyl)ethene to form thieno[3,2-*f*]quinoline, the fully unsaturated analogue of **14e**, could not be achieved.[24]

The results presented in this paper show that small changes in ring size and substituents of the starting dienamines can have a strong impact on the ease and outcome of their thermal isomerization reactions. A better understanding of the factors responsible for the two competing reaction pathways is clearly desirable. Along these lines, we are currently studying the effects of altering the substituent at nitrogen in dienamines **11**. As a first result, we have found that replacement of *N*-methyl by *N*-benzyl leads to a dramatic decrease of the activation energy for the isomerization **11** → **13**. This observation corroborates our proposal that 1,4-proton transfer is the rate-determining step in this transformation.

In conclusion, we have presented a versatile route to tri- and tetracyclic azepine derivatives which is based on the 1,7-cyclization of an $\alpha,\beta,\gamma,\delta$-unsaturated azomethine ylide intermediate. Although a number of ways exist to construct the azepine skeleton, most of them remain specific and inefficient.[25] With respect to the biological activities of various azepine derivatives, it should be emphasized that the method presented here is open to further variations of the ring systems (including their substituents) which are fused with the dihydroazepine substructure.[26]

Experimental Section

General Methods. For instrumentation used in this work, see refs 14 and 15. For the ^{1}H NMR spectra, tetramethylsilane was used as the internal standard whereas the solvent signal was used as standard in the ^{13}C NMR spectra [$\delta(CDCl_3) = 77.0$, $\delta(CD_3CN) = 118.2$ ppm]. The multiplicities given for the ^{13}C NMR spectra refer to ^1J(C−H) coupling. All reactions were carried out in rigorously dried glassware. Solvents were dried according to standard methods and stored under an argon atmosphere.

2,3-Dihydro-2-(3,3-dimethyl-2-phenyl-1-butenylidene)-1,3,3-trimethyl-1*H*-indole (5a). A solution of the cuprate (*t*-Bu)$_2$CuLi·LiCN was prepared as follows:[13b] To a magnetically stirred suspension of copper(I) cyanide (0.269 g, 3.0 mmol) in THF (20 mL), cooled at −60 °C, was slowly added a 1.7 M solution of *tert*-butyllithium in ether (3.53 mL, 6.0 mmol). The yellow suspension was brought to 0 °C within 5 min, and after 15 min the temperature was lowered again to −60 °C. To the cuprate solution so obtained was gradually added a suspension of iminium triflate **4**[15] (1.23 g, 3.0 mmol) in THF (15 mL). The temperature was raised to −35 °C, and after being stirred for 1 h the mixture was allowed to rise to room temperature. The solvent was evaporated at 0.01 mbar, and the residue was extracted with pentane (3 × 70 mL). From the pentane extracts, a yellow oil was isolated, which was already sufficiently pure for subsequent reactions. Analytically pure **5a** was obtained by crystallization from pentane at −30 °C, yielding 0.80 g (84%) of light yellow crystals: mp 79 °C; IR (film) ν 1945 (s, C=C=C), 1600 (vs), 1590 (sh) cm^{-1}; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.18 (s, 9 H), 1.26 (s, 3 H), 1.43 (s, 3 H), 2.90 (s, 3 H), 6.42 (d, J = 7.8 Hz, 1 H), 6.64 (dt, J = 7.8, 1.0 Hz, 1 H), 7.00−7.26 (m, 7 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 29.1 (q), 29.5 (q), 30.0 (q), 30.3 (q), 36.0 (s), 43.7 (s), 104.9 (d), 117.4 (d), 121.7 (d), 126.1 (d), 127.4 (d, 3 C), 128.9 (d, 2 C), 131.4 (s), 131.9 (s), 137.5 (s), 140.4 (s), 146.8 (s), 186.8 (s). Anal. Calcd for $C_{23}H_{27}N$ (317.5): C, 87.02; H, 8.57; N, 4.41. Found: C, 86.8; H, 8.6; N, 4.4.

2-[(2-Furyl)phenylvinylidene]-2,3-dihydro-1,3,3-trimethyl-1*H*-indole (5b). The synthesis was carried out in the same manner as described for **5a** from **4**[15] and (2-furyl)$_2$CuLi·LiCN,[14] yielding 0.81 g (82%) of an orange-colored solid: mp 85 °C (pentane); IR (KBr) ν 1940−1920 (w, br, C=C=C), 1590 (vs), 1475 (vs) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.40 (s, 3 H), 1.46 (s, 3 H), 2.97 (s, 3 H), 6.33 (dd, ^3J = 3.3 Hz, $|^4J|$ = 0.8 Hz, 1 H), 6.38 (dd, ^3J = 3.3 Hz, $|^4J|$ = 1.8 Hz, 1 H), 6.51 (d, ^3J = 7.8 Hz, 1 H), 6.72 (dt, J = 7.8, 0.7 Hz, 1 H), 7.07−7.13 (m, 2 H), 7.24−7.38 (m, 4 H), 7.55−7.57 (m, 2 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 29.1 (q), 29.2 (q), 30.5 (q), 45.2 (s), 105.2 (d), 108.7 (d), 111.2 (d), 114.9 (s), 117.9 (d), 121.7 (d), 127.6 (d), 127.7 (d), 128.1 (d), 128.2 (d), 136.0 (s), 137.4 (s), 137.6 (s), 142.1 (d), 146.6 (s), 151.4 (s), 193.5 (s). Anal. Calcd for $C_{23}H_{21}NO$ (327.4): C, 84.37; H, 6.46; N, 4.28. Found: C, 84.1; H, 6.6; N, 4.2.

2,3-Dihydro-1,3,3-trimethyl-2-[phenyl(2-thienyl)-vinylidene]-1*H*-indole (5c). The synthesis was carried out in the same manner as described for **5a** from **4**[15] and (2-thienyl)$_2$CuLi·LiCN,[14] yielding 0.96 g (93%) of yellow crystals: mp 112 °C (pentane); IR (film) ν 1910 (s, C=C=C), 1630 (w), 1595 (vs) cm^{-1}; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.40 (s, 3 H), 1.48 (s, 3 H), 2.96 (s, 3 H), 6.50 (d, J = 7.8 Hz, 1 H), 6.71 (dt, J = 7.8, 1.0 Hz, 1 H), 6.90−6.97 (m, 2 H), 7.05−7.14 (m, 2 H), 7.24−7.36 (m, 3 H), 7.53−7.58 (m, 2 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 29.3 (q), 29.6 (q), 30.1 (q), 45.8 (s), 105.8 (d), 118.6 (d), 118.9 (d), 122.1 (d), 125.4 (d), 126.1 (d), 127.6 (d), 127.9 (d), 128.1 (d), 128.6 (d, 2 C), 128.7 (2 C), 135.3 (s), 137.7 (s), 139.1 (s), 144.5 (s), 146.8 (s), 193.5 (s). Anal. Calcd for $C_{23}H_{21}NS$ (343.5): C, 80.42; H, 6.16; N, 4.08. Found: C, 80.4; H, 6.3; N, 4.1.

11-(1,1-Dimethylethyl)-12a,13-dihydro-6a*H*-13,13-dimethylindolo[1,2-*b*][2]benzazepine (6a). Aminoallene **5a** (0.64 g, 2 mmol) was placed in a thick-walled Schlenk tube fitted with a screw cap and was dissolved in a minimal volume of toluene (1−2 mL). The solution was heated in an oil bath

(21) Adams, R.; Mahan, J. E. *J. Am. Chem. Soc.* **1942**, *64*, 2588−2593.

(22) ^{13}C NMR δ(=CH) values: 130.8 (cyclopentene), 127.4 (cyclohexene), 130.4 ppm (cycloheptene); see: Kalinowski, H.-O.; Berger, S.; Braun, S. *^{13}C-NMR-Spektroskopie*; Thieme: Stuttgart, 1984.

(23) The observation that the course of the thermal isomerization reaction (i.e., azomethine ylide formation/cyclization vs 6π electrocyclization) depends on the ring size is likely to be associated only in part with the ease of proton transfer (initial step of the first-mentioned route) in the five-, six-, and seven-membered cyclic enamines. Several factors can make the electrocyclic reaction more or less competitive; specifically, factors associated with the ring size, such as the conformation of the azaheterocycle and the exocyclic bond angle at the enamine α-carbon, are likely to influence the energy of the pericyclic transition state. The importance of these factors would be worth studying by theoretical calculations.

(24) Marzinzik, A. L.; Rademacher, P. *Synthesis* **1995**, 1131−1134.

(25) Evans, P. A.; Holmes, A. B. *Tetrahedron* **1991**, *47*, 9131−9166.

(26) For recent syntheses of the fused ring structure contained in **13a**,**b** and **13e**, respectively, see: (a) Ikeda, M.; Akamatsu, S.; Kugo, Y.; Sato, T. *Heterocycles* **1996**, *42*, 155−158. (b) Berkes, D.; Decroix, B. *Bull. Soc. Chim. Fr.* **1994**, *131*, 986−991.

at 135 °C for 2 h. The residue obtained after evaporation of the solvent was dissolved in ether, and pentane was gradually added until the solution started to become turbid. After several hours at −30 °C, 0.58 g (92%) of **6a** was obtained as colorless crystals that turned reddish on prolonged storing: mp 111 °C; IR (KBr) ν 1600 (s), 1570 (m), 1472 (vs), 1447 (vs) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.13 (s, 3 H), 1.17 (s, 9 H), 1.35 (s, 3 H), 3.26 (d, ^3J = 6.8 Hz, 1 H), 3.60/4.20 (AB q, $|^2J|$ = 10.8 Hz), 6.07 (d, ^3J = 6.8 Hz), 6.49 (d, 1 H), 6.68 (t, 1 H), 6.96 (m_c, 1 H), 7.07 (t, 1 H), 7.20−7.29 (m, 2 H), 7.35 (d, 1 H), 7.45 (d, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 22.0 (q), 29.5 (q), 31.2 (q), 36.6 (s), 41.2 (s), 49.9 (t), 70.5, 107.1, 117.9, 120.3, 121.3, 126.7, 127.2, 127.4, 127.5, 129.4 (all d), 136.6, 139.2, 140.9, 149.2, 151.7 (all s). Anal. Calcd for $C_{23}H_{23}N$ (317.5): C, 87.02; H, 8.57; N, 4.41. Found: C, 86.8; H, 8.5; N, 4.4.

11-(2-Furyl)-12a,13-dihydro-13,13-dimethyl-6*H*-indolo[1,2-*b*][2]benzazepine (6b). Thermal treatment of **5b** (0.66 g, 2 mmol) at 80 °C for 12 h and workup were done as described above for **5a**. A beige solid **6b** (0.60 g, 91%) was obtained: mp 149 °C; IR (KBr) ν 1590 (s), 1472 (vs), 1445 (vs) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.22 (s, 3 H), 1.44 (s, 3 H), 3.56 (d, ^3J = 6.7 Hz), 3.78/4.33 (AB q, $|^2J|$ = 11.3 Hz, 2 H), 6.18 (d, ^3J = 3.4 Hz), 6.33 (dd, J = 3.4, 1.9 Hz), 6.51 (d, J = 7.8 Hz, 1 H), 6.68 (d, ^3J = 6.7 Hz), 6.71 (t), 7.00 (d, J = 6.9 Hz, 1 H), 7.09 (dt, J = 7.6, 1.0 Hz, 1 H), 7.32−7.37 (m, 3 H), 7.44 (m_c, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 22.3 (q), 29.2 (q), 41.8 (s), 49.9 (t), 70.7 (d), 107.1 (d), 108.8 (d), 111.2 (d), 118.2, 121.5, 122.2, 127.4, 127.6, 128.3, 128.6, 129.7 (all d), 133.4, 137.1, 138.0, 139.0 (all s), 142.1 (d), 149.2 (s), 153.4 (s). Anal. Calcd for $C_{23}H_{21}NO$ (327.4): C, 84.37; H, 6.46; N, 4.28. Found: C, 83.8; H, 6.6; N, 4.2.

12a,13-Dihydro-13,13-dimethyl-11-(2-thienyl)-6a*H*-indolo[1,2-*b*][2]benzazepine (6c) and 6,6a-Dihydro-12,12-dimethyl-10-phenyl-12*H*-indolo[1,2-*a*]thieno[2,3-*e*]-azepine (6d). A solution of **5c** (0.69 g, 2 mmol) in toluene (1−2 mL) was heated in a thick-walled Schlenk tube at 120 °C for 2 h. Workup as described above for **6a** furnished 0.64 g (93%) of a solid that was a 65:35 mixture of **6c** and **6d**. The following NMR data was obtained for this mixture (assignments to either **6c** or **6d** based on signal integration): ^1H NMR of **6c** ($CDCl_3$, 400 MHz) δ 1.24 (s, 3 H), 1.42 (s, 3 H), 3.53−3.58 (m, NCH, 1 H, partly overlapping with one NCH_2 signal of **6d**), 3.80/4.35 (AB q, $|^2J|$ = 11.4 Hz, 2 H, NCH_2), 6.49−7.54 (m, 12 H); ^1H NMR of **6d** δ 1.39 (s, 3 H), 1.41 (s, 3 H), 3.02 (X part of ABX), ca. 3.53−3.58 (m, NCH multiplet of **6c** and A part of ABX), 4.29 (*B* part of ABX, $|^2J|$ = 12.1 Hz, NCH_2), 5.07 (d, J = 2.0 Hz, NC=CH), 5.79 (dd, ^3J = 6.1 Hz, J = 2.7 Hz, 1 H, SC=CH), 6.35 (m_c, ^3J = 6.1 Hz, 1 H, SCH), 6.49−7.54 (m, 9 H); ^{13}C NMR ($CDCl_3$, 100 MHz) of **6c** δ 22.9 (q), 29.2 (q), 41.9 (s), 50.0 (t), 71.1 (d), 107.2 (d), 118.2 (d), 120.5−130.2 (10 CH), 137.2 (s, 2 C), 137.6 (s), 139.7 (s), 143.9 (s), 149.2 (s); ^{13}C NMR of **6d** δ 29.7 (q), 30.8 (q), 45.8 (s), 51.0 (t), 54.5 (d), 95.0 (d), 105.9 (d), 119.7 (d), 120.5−130.2 (9 CH), 132.0 (s), 137.6 (s), 138.9 (s), 144.8 (s), 145.5 (s), 154.7 (s). Anal. Calcd for $C_{23}H_{21}NS$ (343.5): C, 80.42; H, 6.16; N, 4.08. Found: C, 79.8; H, 6.3; N, 4.0.

7-*tert*-Butyl-10-chloro-5a,12-dihydro-1,3-benzothiazolo[3,2-*b*][2]benzazepine (9). A solution of $(t\text{-Bu})_2CuLi{\cdot}LiCN$ (3 mmol) in THF/ether was prepared as described above for **5a** and cooled at −60 °C. A suspension of 2-(4-chlorophenyl)-1,3-benzothiazolium triflate[15] (**7**, 1.30 g, 3.0 mmol) in THF (15 mL) was gradually added. The temperature was raised to −35 °C, and after being stirred for 1 h, the mixture was allowed to reach room temperature. After evaporation of the solvent, the residue was extracted with pentane (3 × 70 mL). The extracts were combined, and pentane was replaced by toluene (3 mL). This solution was placed in a thick-walled Schlenk tube fitted with a screw cap and heated at 125 °C for 2.5 h. After cooling, the solvent was removed, and the residue was subjected to flash chromatography (silica gel, ether). Crystallization from ether/pentane furnished **9** as an orange-colored solid (0.80 g, 78%): mp 114 °C; IR (KBr) ν 1610 (m), 1498 (s) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.16 (s, 9 H), 3.59/4.14 (AB q, $|^2J|$ = 10.6 Hz, 2 H), 4.90 (d, J = 6.3 Hz), 6.10 (d, J = 6.3 Hz, 1 H), 6.43 (d), 6.67 (t), 6.95−7.02 (m, 2 H), 7.30 (m_c, 1 H), 7.38 (m_c, 2 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 30.9 (q), 36.2 (s), 50.2 (t), 66.4, 108.2, 119.5, 121.5, 125.4, 126.2 (all d), 126.8 (s), 127.5 (d), 128.8 (d), 129.8 (d), 133.0 (s), 137.4 (s), 138.6 (s), 146.0 (s), 150.0 (s). Anal. Calcd for $C_{20}H_{20}ClNS$ (341.9): C, 70.26; H, 5.90; N, 4.10. Found: C, 70.0; H, 6.1; N, 4.0.

Thermally Induced Cyclization Reactions of Dienamines 11a−k, General Procedure. A solution of the respective dienamine (ca. 0.4−2.0 mmol; **11a−e**,**g−k**;[14] **11f**: see Supporting Information) in dry toluene (1−1.5 mL) was placed in a thick-walled Schlenk tube fitted with a screw cap. In some cases, 30 mol % of ethyldiisopropylamine was added. The solution was heated in an oil bath at the conditions summarized in Table 1. After cooling, the solvent was removed under reduced pressure, and the residual oil was processed as described for the individual compounds.

7-Chloro-10-(1,1-dimethylethyl)-2,3,5,11a-tetrahydro-1*H*-pyrrolo[1,2-*b*][2]benzazepine (13a). Thermal treatment of **11a** (0.55 g, 2.0 mmol) gave an oil which was subjected to bulb-to-bulb distillation at 150 °C/0.005 mbar. Crystallization from ether/pentane furnished **13a** (0.39 g, 70%) as yellow crystals: mp 38 °C; IR (KBr) ν 1465, 1445, 1090, 870, 835 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.22 (s, 9 H), 1.64−1.71 (m, 1 H), 1.85−2.06 (m, 3 H), 2.55 (q, 1 H), 2.92 (dt, 1 H), 3.06 (m_c, 1 H), 3.14/3.63 (AB q, $|^2J|$ = 10.5 Hz, 2 H), 5.73 (d, J = 6.6 Hz, 1 H), 7.23 (dd, J = 8.4, 2.3 Hz, 1 H), 7.32−7.36 (m, 2 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 24.4 (t), 29.8 (t), 31.2 (q), 36.0 (s), 52.1 (t), 54.7 (t), 56.8 (d), 126.2 (d), 126.4 (d), 128.2 (d), 128.8 (d), 132.0 (s), 139.2 (s), 139.9 (s), 150.1 (s). Anal. Calcd for $C_{17}H_{22}ClN$ (275.8): C, 74.03; H, 8.04; N, 5.08. Found: C, 74.2; H, 8.1; N, 5.0.

10-(1,1-Dimethylethyl)-7-methoxy-2,3,5,11a-tetrahydro-1*H*-pyrrolo[1,2-*b*][2]benzazepine (13b). The reaction was carried out starting from **11b** (0.54 g, 2.0 mmol) as described above. Bulb-to-bulb distillation at 180 °C/0.02 mbar afforded **13b** (0.30 g, 56%) as a colorless oil: IR (film) ν 1590 (vs), 1560 (w), 1485 (s), 1460 (s) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.22 (s, 9 H), 1.60−1.70 (m, 1 H), 1.85−2.05 (m, 3 H), 2.51−2.56 (m, 1 H), 2.88−2.91 (m, 1 H), 3.11 (dt, 1 H), 3.17/3.65 (AB q, $|^2J|$ = 10.3 Hz, 2 H), 3.79 (s, 3 H), 5.68 (d, J = 6.6 Hz, 1 H), 6.70 (m_c, 1 H), 6.91 (d, J = 2.7 Hz, 1H), 7.32 (d, J = 8.6 Hz, 1H); according to ^1H NMR, the product has a purity of only ca. 60%. Anal. Calcd for $C_{18}H_{25}NO$ (271.4): C, 79.66; H, 9.29; N, 5.16. Found: C, 79.8; H, 9.3; N, 5.0.

10-(1,1-Dimethylethyl)-6,7,8,8a-tetrahydro-4*H*-pyrrolo[1,2-*a*]thieno[2,3-*e*]azepine (13c). Amino diene **11c** (0.26 g, 1.0 mmol) was submitted to the procedure described above. Bulb-to-bulb distillation at 160 °C/0.009 mbar yielded a yellow oil which was crystallized from ether/pentane to give **13c** (0.23 g, 88%) as yellow crystals: mp 43 °C; IR (KBr) ν 1640−1590 (w, br), 1460 (s), 1440 (s) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.23 (s, 9 H), 1.64−1.71 (m, 1 H), 1.86−2.09 (m, 3 H), 2.62 (q, 1 H), 2.91 (dt, 1 H), 3.00/3.87 (AB q, $|^2J|$ = 10.9 Hz, 2 H), 3.21 (m_c, 1 H), 5.82 (d, J = 6.0 Hz, 1 H), 7.04 (d, J = 5.1 Hz, 1 H), 7.20 (d, J = 5.1 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 24.6 (t), 29.8 (q), 30.2 (t), 36.0 (s), 49.9 (t), 52.2 (t), 58.3 (d), 123.7 (d), 127.4 (d), 127.7 (d), 138.8 (s), 140.8 (s), 148.4 (s). Anal. Calcd for $C_{15}H_{21}NS$ (247.4): C, 72.82; H, 8.56; N, 5.66. Found: C, 73.1; H, 8.8; N, 5.5.

8-Chloro-11-(1,1-dimethylethyl)-1,2,3,4,6,12a-hexahydropyrido[1,2-*b*][2]benzazepine (13d). A solution of **11d** (0.17 g, 0.6 mmol) and ethyldiisopropylamine (0.03 mL, 0.18 mmol) in toluene (1 mL) was heated at 200 °C for 29 h. Bulb-to-bulb distillation at 245 °C/0.02 mbar afforded **13d** (0.15 g, 85%) as an orange-colored oil which solidified on standing: mp 53−55 °C; IR (film) ν 1580 (w), 1460 (s), 1440 (s) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 0.95−1.05 (m, 2 H), 1.12 (s, 9 H), 1.41−1.64 (m, 4 H), 1.79 (m_c, 1 H), 2.31−2.37 (m, 1 H), 2.71−2.76 (m, 1 H), 3.31/3.83 (AB q, $|^2J|$ = 13.3 Hz, 2 H), 5.78 (d, J = 6.8 Hz, 1 H), 7.11 (d, $|^4J|$ = 2.3 Hz, 1 H), 7.20 (dd, J = 8.4 Hz, $|^4J|$ = 2.3 Hz, 1H), 7.34 (d, J = 8.4 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 23.8 (t), 26.1 (t), 30.8 (q), 30.8 (t), 36.0 (s), 53.3 (t), 58.2 (d), 58.8 (t), 126.4 (d), 127.2 (d), 128.2 (d), 129.0 (d), 131.9 (s), 137.4 (s), 139.3 (s), 150.4 (s). Anal. Calcd for $C_{18}H_{23}ClN$ (288.8): C, 74.85; H, 8.03; N, 4.85. Found: C, 74.46; H, 8.09; N, 4.85.

8,9-Dihydro-4-(1,1-dimethylethyl)-6(7*H*)-methylthieno[3,2-*f*]quinoline (14e), 4-(1,1-Dimethylethyl)-6-methyl-5a,6,7,8,9,9a-hexahydrothieno[3,2-*f*]quinoline (15e), and 11-(1,1-Dimethylethyl)-4,6,7,8,9,9a-hexahydro-

pyrido[1,2-*a*]thieno[2,3-*e*]azepine 13e. (a) The reaction was performed according to the general procedure starting from **11e** (0.26 g, 1.0 mmol), ethyldiisopropylamine (0.05 mL, 0.3 mmol), and toluene (1.0 mL). The ^{1}H NMR spectrum of the crude product mixture showed the presence of **13e**, **14e**, and **15e** in the ratio 1.0:1.7:1.8. Separation by flash chromatography over Florisil (100−200 mesh, 15 g) followed by preparative column chromatography on Florisil (50 g) with ether as eluant furnished **14e** (0.09 g, 35%). Further eluation with ether−MeOH (2:1 v/v) gave a fraction containing **13e**, **15e**, and some impurities. This mixture was chromatographed again (Florisil, 30 g; eluant ether−MeOH, 4:1 v/v), providing first **13e** (0.01 g, 3.8%) and then **15e** (0.04 g, 15.4%). Compound **14e** was obtained as an oil which solidified on standing. Recrystallization from ether/pentane gave light brown crystals: mp 82−83 °C; IR (KBr) ν 1654 (w), 1586 (s), 1558 (w), 1476 (m), 1456 (m) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.54 (d, ^5J = 0.9 Hz, 9 H), 2.06 (m_c, 2 H), 2.95 (s, 3 H), 2.96 (t, J = 6.6 Hz, 2 H), 3.16 (t, J = 5.5 Hz, 2 H), 6.86 (d, ^5J = 0.9 Hz, 1 H), 7.22 (d, J = 5.6 Hz, 1 H), 7.34 (d, J = 5.6 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 22.2 (t), 24.8 (t), 29.7 (q), 35.8 (s), 40.6 (q), 51.7 (t), 109.4 (d), 114.2 (s), 120.9 (d), 125.8 (d), 126.1 (s), 140.4 (s), 142.7 (s), 144.0 (s). Anal. Calcd for $C_{16}H_{21}NS$ (259.4): C, 74.08; H, 8.16; N, 5.39. Found: C, 73.6; H, 8.6; N, 5.6.

Compound **15e** was obtained as a yellow oil after bulb-to-bulb distillation at 130 °C/5 × 10^{-5} mbar. IR (film) ν 1695 (w), 1460 (m), 1364 (m), 1269 (m), 1207 (m), 1117 (m), 1063 (m) cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.30 (s, 9 H), 1.44−1.47 (m, 1 H), 1.75−1.79 (m, 2 H), 2.09−2.14 (m, 1 H), 2.26−2.29 (m, 1 H), 2.40 (s, 3 H), 2.48 (dd, J = 14.8, 1.6 Hz, 1 H), 2.58 (ddd, J = 15.0, 11.8, 4 Hz, 1 H), 2.97−3.00 (m, 1 H), 5.91 (d, J = 1 Hz, 1 H), 6.95 (dd, J = 5.1, 0.4 Hz, 1 H), 7.16 (d, J = 5.1 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 125.8 MHz) δ 24.8 (t), 27.9 (t), 29.7 (q), 35.1 (s), 39.2 (d), 42.7 (q), 57.2 (t), 67.0 (d), 121.1 (d), 122.7 (d), 123.8 (d), 133.6 (s), 141.8 (s), 142.3 (s). A peak assignment of ^{1}H and ^{13}C signals based on H,H and C,H correlation experiments is given in the Supporting Information. Anal. Calcd for $C_{16}H_{23}NS$ (261.4): C, 73.51; H, 8.87; N, 5.36. Found: C, 73.6; H, 8.87; N, 5.31.

Compound **13e** was subjected to bulb-to-bulb distillation at 240 °C/7 × 10^{-5} mbar, but could not be obtained in pure form. It was identified by the following NMR signals: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.22 (s, 9 H), 1.58−1.73 (m, 6 H), 2.00−2.04 (m, 1 H), 2.46−2.51/2.81−2.86 (2 m, 2 H), 3.42/3.63 (AB system, ^2J = 13.3 Hz, 2 H), 5.88 (d, J = 6.5 Hz, 1 H), 6.96 (d, J = 5.1 Hz,1 H), 7.26 (d, 1 H); ^{13}C NMR ($CDCl_3$, 50.3 MHz) δ 23.8 (t), 26.1 (t), 29.6 (q), 31.0 (t), 35.8 (s), 53.8 (t), 54.1 (t), 59.6 (d), 123.7 (d), 127.6 (2 d), 132.4 (s), 139.0 (s), 148.6 (s).

(b) Dienamine **11e** (0.27 g, 1.04 mmol) was heated in toluene (1 mL) at 200 °C for 12 h. The crude reaction mixture contained **13e**, **14e**, and **15e** in the ratio 1.0:1.7:2.3 according to ^{1}H NMR. Flash chromatography on Florisil (15 g, eluant ether−MeOH, 1:1 v/v) followed by medium-pressure column chromatography on Florisil (50 g, eluant ether−MeOH, 95:5 v/v) provided successively **14e** (0.06 g, 22%), **15e** (0.08 g, 30%), and still impure azepine derivative **13e**. Another chromatographic step (same conditions as before) furnished 10 mg (3.7 %) of **13e**.

8,9-Dihydro-4-(1,1-dimethylethyl)-6(7*H*)-methylthieno[2,3-*f*]quinoline (14f) and 4-(1,1-Dimethylethyl)-6-methyl-5a,6,7,8,9,9a-hexahydrothieno[2,3-*f*]quinoline (15f). Thermal treatment of **11f** (0.52 g, 2.0 mmol) furnished an oil which after flash chromatography over Florisil (100−200 mesh, 15 g) gave an oily mixture of **14f** and **15f** in a 1:1 ratio (^{1}H NMR). Preparative medium-pressure column chromatography on Florisil (80 g, ether as eluant) provided **14f**, which was further purified by bulb-to-bulb distillation at 172 °C/7 × 10^{-5} mbar to give a yellow oil which turned into a red-brown solid on standing, mp 86−87 °C (yield: 0.18 g, 35%). Compound **15f**, which was identified in the crude product mixture by δ(^{1}H) values very similar to those of **15e**, was lost completely during chromatography. Spectral data of **14f**: IR (KBr) ν 1660 (w), 1589 (s), 1479 (m), 1453 (m) cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.50 (s, 9 H), 2.07−2.12 (m, 2 H), 2.83 (t, 2 H), 2.97 (s, 3 H), 3.01 (m_c, 2 H), 6.81 (s, 1 H), 7.11 (d, J = 5.6 Hz, 1 H), 7.59 (d, J = 5.6 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 125.8 MHz) δ 22.2 (t), 25.9 (t), 31.1 (q), 36.0 (s), 40.2 (q), 51.8 (t), 108.7 (d), 112.9 (s), 119.9 (d), 125.0 (d), 127.9 (s), 142.7 (s), 143.4 (s), 144.0 (s). Anal. Calcd for $C_{16}H_{21}NS$ (259.4): C, 74.08; H, 8.16; N, 5.40. Found: C, 74.16; H, 8.21, N, 4.59.

9-Chloro-12-(1,1-dimethylethyl)-2,3,4,5,7,13a-hexahydro-1*H*-azepino[1,2-*b*][2]benzazepine (13g). The synthesis was carried out in the same manner as described for **13a** starting from **11g** (0.13 g, 0.4 mmol). After purification by bulb-to-bulb distillation at 225 °C/0.009 mbar, **13g** (0.10 g, 81%) was obtained as a pale yellow oil: IR (film) ν 1575 (m), 1540 (w), 1440 (s) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.82−0.89 (m, 1 H), 1.19 (s, 9 H), 1.41−1.66 (m, 5 H), 1.74 (m_c, 1 H), 1.89−1.96 (m, 1 H), 2.29 (ddd, 1H), 2.38 (ddd, 1 H), 2.94 (m_c, 1 H), 3.36/3.73 (AB q, $|^2J|$ = 12.4 Hz, 2 H), 5.83 (d, ^3J = 6.8 Hz, 1 H), 7.24−7.27 (m, 2 H), 7.39 (d, ^3J = 9.0 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 24.5 (t), 26.7 (t), 28.8 (t), 30.9 (q), 35.7 (t), 36.1 (s), 54.4 (t), 60.2 (d), 60.2 (t), 125.4 (d), 126.5 (d), 129.0 (d), 129.3 (d), 131.9 (s), 138.4 (s), 139.2 (s), 149.5 (s). Anal. Calcd for $C_{19}H_{26}ClN$ (303.9): C, 75.10; H, 8.62; N, 4.61. Found: C, 75.24; H, 8.60; N, 4.64.

4-(1,1-Dimethylethyl)-6-methyl-7,8,9,10-tetrahydrothieno[3,2-*g*][1]benzazepine (14h). Amino diene **11h** (0.55 g, 2.0 mmol) was heated according to the general procedure. The solvent was removed in vacuo and the residue submitted twice to flash chromatography, eluating with ether. Crystallization from ether/pentane gave **14h** (0.38 g, 70%) as a colorless solid: mp 87 °C; IR (KBr) ν 1570 (s), 1470 (w), 1430 (s), 1420 (m) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.55 (s, 9 H), 1.68 (m_c, 2 H), 1.78 (m_c, 2 H), 2.95 (m_c, 2 H), 2.97 (s, 3 H), 3.10 (m_c, 2 H), 7.07 (s, 1 H), 7.37 (d, J = 5.7 Hz, 1 H), 7.43 (d, J = 5.7 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 24.6 (t), 29.6 (t), 29.7 (q), 29.7 (t), 36.0 (s), 43.0 (q), 56.5 (t), 112.8 (d), 122.2 (d), 125.2 (d), 126.9 (s), 129.9 (s), 140.6 (s), 142.2 (s), 148.9 (s). Anal. Calcd for $C_{17}H_{23}NS$ (273.4): C, 74.67; H, 8.48; N, 5.12. Found: C, 74.4; H, 8.7; N, 4.8.

8,9-Dihydro-4,6(7*H*)-dimethylthieno[3,2-*f*]quinoline (14j). Thermal treatment of **11j** (0.22 g, 0.9 mmol) and ethyldiisopropylamine (0.03 mL, 0.2 mmol) and workup were done as described above for **14e**. Light brown crystals of **14j** (0.12 g, 62%) were obtained: mp 74 °C; IR (KBr) ν 1655 (w), 1590 (s), 1520 (m), 1480 (m), 1445 (m) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.07 (m_c, 2 H), 2.49 (d, ^5J = 1.7 Hz, 3 H), 2.90 (s, 3 H), 2.97 (t, J = 6.6 Hz, 2 H), 3.18 (m_c, 2 H), 6.66 (s, 1 H), 7.22 (d, J = 5.5 Hz, 1 H), 7.36 (d, J = 5.6 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 20.5 (q), 22.3 (t), 24.8 (t), 40.5 (q), 51.6 (t), 112.2 (d), 113.8 (s), 121.7 (d), 125.9 (d), 129.3 (s), 129.5 (s), 139.1 (s), 144.6 (s). Anal. Calcd for $C_{13}H_{15}NS$ (217.3): C, 71.85; H, 6.96; N, 6.40. Found: C, 71.5; H, 7.1; N, 6.3.

4,6-Dimethyl-7,8,9,10-tetrahydrothieno[3,2-*g*][1]benzazepine (14k). The crude product obtained from heating of **11k** (0.55 g, 2.0 mmol) was purified by 2-fold flash chromatography (silica gel, ether), affording **14k** as a colorless solid (0.29 g, 54%): mp 50 °C; IR (KBr) ν 1570 (s), 1430 (vs) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.61 (m_c, 2 H), 1.73 (m_c, 2 H), 2.50 (s, 3 H), 2.87 (m_c, 2 H), 2.89 (s, 3 H), 3.07 (m_c, 2 H), 6.87 (s, 1 H), 7.29 (d, J = 5.5 Hz, 1 H), 7.35 (d, J = 5.5 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 20.5 (q), 24.7 (t), 29.7 (t), 29.8 (t), 43.2 (q), 56.7 (t), 115.5 (d), 122.8 (d), 125.2 (d), 126.8 (s), 128.9 (s), 133.0 (s), 139.2 (s), 149.5 (s). Anal. Calcd for $C_{14}H_{17}NS$ (231.4): C, 72.68; H, 7.41; N, 6.05. Found: C, 72.6; H, 7.4; N, 6.2.

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Supporting Information Available: Experimental procedures for the synthesis of **11f** and ^{1}H and ^{13}C NMR spectra of **6b**, mixture of **6c**/**6d**, **13e**, **14e**, **15e**, and **14f** (18 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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