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Microwave-assisted solvent-free intramolecular 1,3-dipolar cycloaddition reactions leading to hexahydrochromeno[4,3-*b*]-pyrroles: scope and limitations

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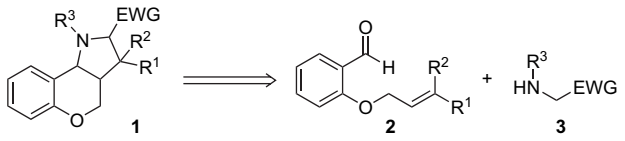
Abstract—We report the microwave-assisted solvent-free synthesis of hexahydrochromeno[4,3-*b*]pyrroles. Intramolecular 1,3-dipolar cycloadditions proceed under these conditions within 15–40 min in 16–84% yields. An influence of the microwave irradiation upon various [3+2] cycloaddition reaction intermediates was studied. Additionally, a scope and limitations of these reactions including an influence of the dipolarophile geometry upon the cycloaddition selectivity and steric demands of the dipole upon its reactivity were also disclosed. These observations led us to postulate a preferable transition state of the reaction. Finally, an influence of the microwave irradiation to the isomerization of activated olefins was also described.

1. Introduction

Short and efficient synthesis of complex organic structures is a dream of each chemist. Moreover nowadays, ecological aspects and atom efficiency processes enter into the consideration when a new compound synthesis is proposed. Aware of this situation, we have focused our attention on the synthesis of fused heterocycles by intramolecular 1,3-dipolar cycloaddition[1] under solvent-free conditions.[2] We anticipated that microwave initiation of the reaction is essential in our case to avoid the degradation of the newly formed heterocycles.[3]

To demonstrate our approach, a family of compounds containing hexahydrochromeno[4,3-*b*] pyrrolidine skeleton (**1**) was chosen (Scheme 1). Such compounds are known to be non-competitive antagonists of the muscular nicotin receptor.[4] Moreover, similar structure motive is contained in various natural compounds, such as martinelline[5] and sceletium alkaloid A-4.[6]



Scheme 1.

Keywords: Intramolecular cycloaddition; Azomethine ylides; Solvent-free synthesis; Microwave-assisted synthesis; 1,3-Dipolar cycloaddition.
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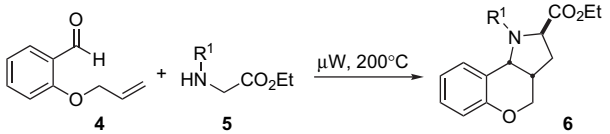
Such compounds can be accessible by the cycloaddition reaction between aldehyde **2** and amine **3**. These particular reagents were previously studied under the classical reaction conditions[6] (various solvents, classical heating, various catalysts) and microwave heating using toluene as a solvent,[7] but low reaction yields, selectivity and/or long reaction times dissuade from the more systematic study of the reaction. Therefore, understanding of the substitution influence on the reactivity and reaction selectivity has not been known. Recently, we have reported a development of a simple, rapid, one pot and solvent-free synthesis of compounds with general pattern **6** (Table 1).[8] In that paper, the steric properties of the nitrogen atom substitution upon the reaction yields were discussed. We have observed that increasing steric

Table 1. The influence of the nitrogen atom substitution on the reaction yields



Entry	Amine	R^1	Reaction time [min]	Product	Yield[a] [%]
1	**5a**	Benzyl	15	**6a**	83
2	**5b**	Ethyl	15	**6b**	81
3	**5c**	*n*-Butyl	15	**6c**	80
4	**5d**	Isopropyl	30	**6d**	79
5	**5e**	1-Adamantyl	60	—	—
6	**5f**	*tert*-Butyl	60	—	—

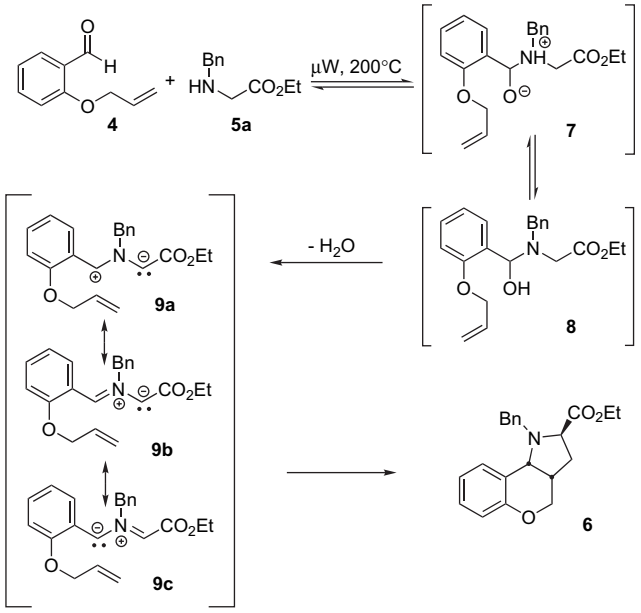
[a] All yields are for pure, fully characterized, products.

demands of the nitrogen atom substituent decreased the reaction yield. However, in none of the cases, any of the starting materials, neither aldehyde **4** nor amine **5**, were reisolated after the reaction. In all cases, only the products of degradation[9] were obtained along with desired cycloadducts **6**. Therefore, the evaluation of all possible reaction intermediates and their ability to degradation was investigated.

Herein, we would like to discuss our results obtained during our reaction intermediates stability testing. Additionally, the influence of other substituents placed on the amine **5** as well as on aldehyde **4** upon the reaction yield and selectivity will be discussed.

2. Results and discussion

The reaction mechanism of the 1,3-dipolar reactions between aldehyde **4** and amine **5a** has been postulated as shown in Scheme 2.[1e] As one can see, all three putative intermediates **7**, **8** and **9** are possible candidates to undergo decomposition under the microwave irradiation, because they possess a dipole in the molecule. It is known that microwaves interact only with molecules containing a dipole.[10]



Scheme 2.

First we focused our attention on the stability of intermediates **7** and **8**. To evaluate if these two intermediates undergo decomposition under the reaction conditions, amine **10** having another acidic hydrogen in the molecule was used in the reaction with aldehyde **4** and tested under microwave conditions (Scheme 3). We expected that amine **10** would bring additional acidic hydrogen into the reacting system, and therefore a competitive reaction to azomethine ylide **13** formation leading to intermediate **16** might be expected.

As one can see, the first two steps of the reaction (leading to intermediates **11** and **12**) are the same as in the case of Scheme 2. In the structures, the ester group has been substituted by a secondary amide group. Consequently, during the water elimination step, the hydrogen atom in intermediate **12** attached to the nitrogen atom might compete with the hydrogen atom attached to the α-carbon next to the carbonyl group. Hence, the reaction could proceed via two different intermediates, **13** and **16**, respectively, leading then to three possible products **14**, **15** and **17**.

Since an amide hydrogen atom is more acidic (pK_a~20 (DMSO))[11] than the hydrogen atom situated on an α-carbon next to the amide group (pK_a~26 (DMSO))[11] and because the water elimination step is irreversible under the reaction conditions,[12] only the intermediate **16** formation should be anticipated (pathway B).

According to our expectation, compound **17** was observed as the only product of the reaction and isolated in 85% yield (GC yield—92%).[13] In this stage, we have concluded that the degradation of dipole intermediate **13** is responsible for the degradation products observed in the reaction.[14]

To bring the evidence for our conclusions, we have decided to use other electron-withdrawing groups to stabilize the generated dipole intermediate **19** (Table 2). Different electron-withdrawing groups should have two main impacts on the dipole **19**, stability and reactivity.

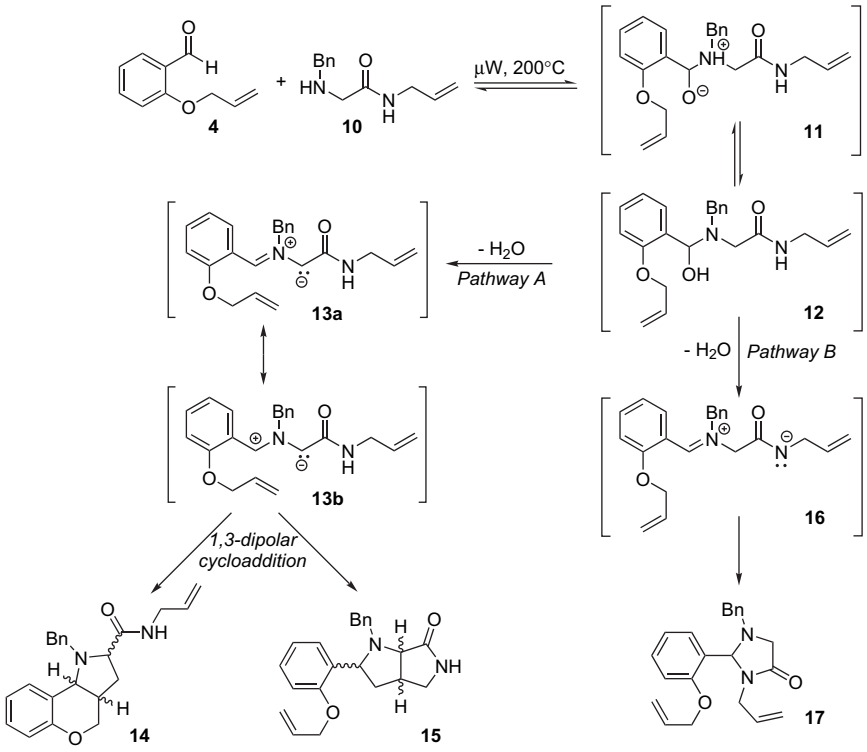
Stronger electron-withdrawing groups like cyano group should facilitate the H_2O molecule elimination during intermediate **19** generation due to higher acidity of the hydrogen atom attached to the carbon next to cyano group.[15] Thus, the generation of the 1,3-dipole should be faster.

On the contrary, the presence of the cyano group on the dipole **19** causes decreasing of the HOMO orbital energy of the 1,3-dipole.[1e,16] Since in all cases the dipoles react with the same dipolarophile, the reaction of the cyano derivative of **19** should require higher $\Delta G^{\neq}$ than similar ester or amide derivatives. Therefore, the generated 1,3-dipole should be present in the reaction mixture longer than its ester analogue and the prolonged interaction of microwaves with it could cause the 1,3-dipole degradation and would be reflected in the lower reaction yield.

Based on the same logic, the presence of less electron-withdrawing groups on the dipole **19** should lead to the higher reaction yields, even though the acidity of the hydrogen atom next to electron-withdrawing group is lower compared to ester stabilized 1,3-dipole. The gap between HOMO of the dipole and LUMO of the dipolarophile should be smaller. The results obtained in the reaction using various EWG groups on the dipole intermediate **19** are presented in Table 2.

The reaction of cyano-stabilized dipole **19** gave, as expected, desired cycloadduct even at prolonged time only in low yield (Table 2, entry 1).[14] On the other hand, the presence of ethyloxy carbonyl group on the dipole **19** furnished desired tricycle in 84% yield (Table 2, entry 2).[17] To our great surprise, when *iso*-propyloxy and *tert*-butyloxy carbonyl groups were used, the drop in the yield of corresponding cycloadducts was observed (Table 2, entries 3 and 4).

We expect that in these cases the reactivity of the dipole is the same as in the case of ethyloxy carbonyl stabilized



Scheme 3.

dipole, but that sterically bulkier groups presented on the dipole caused additional obstacle during the dipole–dipolarophile interaction. Thus, the dipoles interact with the dipolarophiles in the microwave field only when treated for a longer time. The longer time causes degradation of generated dipole.

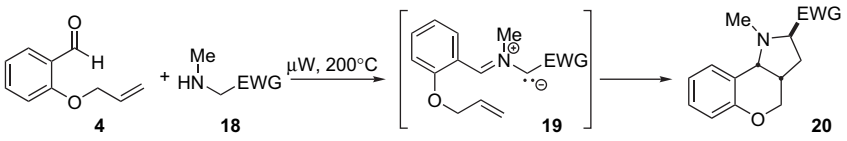
The same phenomena was observed also in the case of *N*,*N*-dialkylamino carbonyl groups, which were used to stabilize the generated dipole **19** (Table 2, entries 5–7).

Next, we have focused on trapping the generated azomethine ylide before its decomposition. Therefore, maleic anhydride and *N*-*tert*-butylmaleimide, respectively, as excellent dipolarophiles,[18] were added to the reaction mixture (Scheme 4).

Addition of maleic anhydride to the reaction mixture of aldehyde **4** and amine **5a** resulted in the formation of two products, **6a** and **21**, in 95% yield. Products of intramolecular cycloaddition **6a** and that of an intermolecular reaction **21** were formed in a 1:4 ratio. The addition of *N*-*tert*-butylmaleimide resulted in the formation of intra- (**6a**) and intermolecular products (*exo*-**22** and *endo*-**22**) in a 1:3.3 ratio and 85% yield. The products of intermolecular reaction, *endo*-**22** and *exo*-**22**, resulting from *exo* and *endo* approach of the dipolarophile to dipole (Fig. 1) are formed in a 1:1.3 ratio.

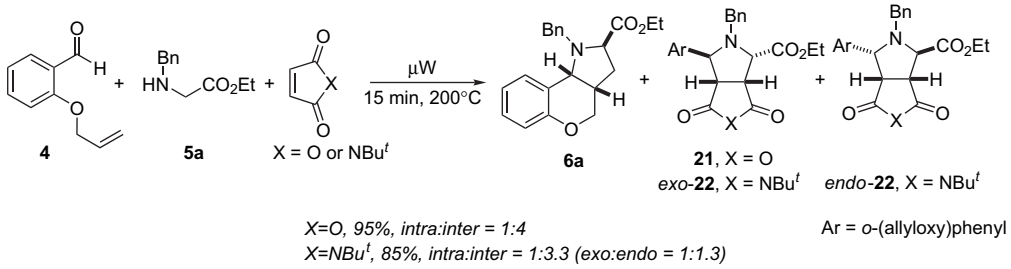
In both cases, intermolecular product(s) are preferred. This is probably due to the high concentration of components in the reaction mixture (no molecules of solvent, which can dilute it, are present). Thus, intermolecular reaction of the

Table 2. The reactivity of the dipole **19** substituted with different EWG groups



Entry	Amine	EWG	Time [min]	Product	Yield[a] [%]
1	**18a**	CN	30	**20a**	17
2	**18b**	CO_2Et	15	**20b**	84
3	**18c**	CO_2Pr^i	40	**20c**	38
4	**18d**	CO_2Bu^t	40	**20d**	17
5	**18e**	$CONMe_2$	40	**20e**	45
6	**18f**	$CONPr^i_2$	40	**20f**	16
7	**18g**	CON(Et)Ts	60	—	—

[a] All yields are for pure, fully characterized, products.



Scheme 4.

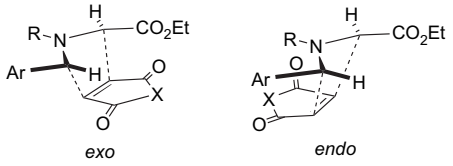


Figure 1.

dipole with the highly reactive dipolarophile (maleic anhydride) is preferred over the intramolecular one.

The overall yield in the case of reaction with maleic anhydride is 95%. Therefore, we can conclude that most of the generated azomethine ylide **9** reacts with the dipolarophile present and forms the products **6a** and **21**. Probably only a small quantity of generated azomethine ylide **9** under the reaction conditions decomposes. It implies that azomethine ylide is rather stable if there is a proper dipolarophile available for rapid transformation to the product.

In the case of *N*-*tert*-butylmaleimide, the overall yield of the reaction is only 85%. Thus, probably a little bit larger quantity of the generated azomethine ylide decomposes during the reaction. We suppose that in this case an approach of the dipole to the dipolarophile might be complicated by the presence of the bulky group (*tert*-butyl) on the dipolarophile.

2.1. *cis/trans* Disubstituted intramolecular dipolarophiles and their reaction selectivity

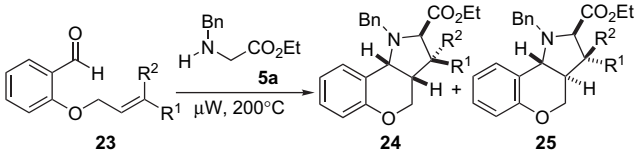
The question, whether the change of the substituent in ω-position of a dipolarophile or the change of dipolarophile configuration is reflected in the substrate reactivity and consequently in the reaction selectivity, became another field of our interest.

It is known that the properties of dipolarophile substituents[16] have a great influence upon dipolarophile reactivity in the course of 1,3-dipolar cycloaddition. For azomethine ylides, better reactivity was found in the presence of an EWG group on the dipolarophile than in the presence of an EDG.[19] The electronic influence of dipolarophile substituents could be divided into three basic groups: (1) alkyl substituents (increasing HOMO and decreasing LUMO energy of dipolarophile), (2) EWG substituents (decreasing HOMO and decreasing LUMO energy) and (3) EDG substituents (increasing HOMO and increasing LUMO energy).[1,18,19] Therefore, for our purposes three different dipolarophile substituents were chosen, the methyl group (aldehydes **23d**,**e**), the methoxycarbonyl group (aldehydes **23a**,**b**) and the phenyl group (aldehyde **23c**).

The reactions of aldehydes containing *trans* ω-substituted double bond in the *ortho* position to the formyl group were carried out at first (Table 3, entries 1,3 and 4). We have observed that aldehydes **23a**,**c** afforded two pairs of products (Table 3, entries 1 and 3). Products **24a** and **25a** (from aldehyde **23a**) were formed in a 3.8:1 ratio. In the case of products **24c** and **25c** formed from aldehyde **23c**, the product ratio decreased to 2.2:1. During the reaction of aldehyde **23d** with amine **5a** no traces of the desired product(s) were observed (Table 3, entry 4). The overall yields decreased from very good (79%—with methoxycarbonyl group as the dipolarophile substituent, Table 3, entry 1) through moderate (54%—phenyl group, entry 3) to none (methyl group, entry 4).

Then reactions of aldehydes containing dipolarophiles in *cis* configuration (**23b**,**e**) and amine **5a** were then examined. The reaction of aldehyde **23b** and amine **5a** proceeded to the formation of three products, **24a**, **24b** and **25a** (Table 3, entry 2). Compound **24b** was the main product of the reaction and was formed in 82% yield. The traces of compounds **24a** and **25a** were detected only (by GC and ^{1}H NMR) in the reaction mixture and were not isolated. However, these two products are formed also in the case of reaction of the aldehyde **23a**. The possible explanation for this finding will be discussed later. The reaction of aldehyde

Table 3. Cycloaddition reaction of *cis/trans* intramolecular dipolarophiles



Entry	Aldehyde	R^1	R^2	Time [min]	Product(s)	Yield[a] [%]	Ratio[b]
1	**23a**	CO_2Me	H	15	**24a+25a**	79	3.8:1
2	**23b**	H	CO_2Me	15	**24b**[c]	82	>99:1
3	**23c**	Phenyl	H	30	**24c+25c**	54	2.2:1
4	**23d**	Methyl	H	60	—	—	—
5	**23e**	H	Methyl	40	**24e**	62	>99:1

[a] All yields are for pure, fully characterized, products.
[b] Determined by GC–MS.
[c] Another 4% of **24a** and 1% of **25a** were detected in the reaction mixture, however, not isolated.

23e with amine **5a** proceeded to the formation of only one stereoisomer **24e** in 63% yield.

The reaction yields in the cases of *cis* disubstituted dipolarophiles were higher than those in the cases of *trans* configuration, particularly, when the methyl group was used as a substituent on the dipolarophile. Product **24e** was formed in 63% yield (Table 3, entry 5) comparatively with no product in the reaction of the aldehyde **23d** and amine **5a** (Table 3, entry 4).

As one can see, there is a large difference between the reactions of dipolarophiles with *cis* and *trans* configuration. The dipolarophiles having *trans* configuration react with worse selectivity and give two cycloadducts. Dipolarophiles with *cis* configuration afford one stereoisomer only. The second most remarkable difference was observed in the case of a methyl substituent on the dipolarophile (aldehydes **23d**,**e**).

We assume that steric requirements might play a role in the TS of the reaction. On the base of the knowledge of Houk et al.,[20] who showed by quantum calculation methods that the 1,3-DC proceeds via an early TS as well as on the Hammond postulate,[21] we suggest two TSs leading to the products **24** and **25**, respectively (Fig. 2). TSs exhibiting a *syn* conformation of the azomethine ylide are not considered because no product containing such a configuration on the pyrrolidine ring was identified.

TS A leading to product **24** is characterized by a steric repulsion between the substituent R^1 and the ester group on the dipole. Such repulsion does not exist for the substituent R^2 and therefore the reaction of the dipolarophile with *cis* configuration ($R^2 \neq H$) via this TS A is energetically preferred.

In the case of TS B leading to compound **25**, there is negligible steric repulsion for the substituent R^1 and the thermodynamically more stable pyrrolidine ring is formed. Thus, TS B should be preferred by the dipolarophiles having *trans* geometry (R^2=H). On the other hand, there is a strong entropy factor influence on TS B formation. One can see that the second formed ring (six-membered ring) has to adopt for entropy reasons an energetically more demanding conformation, in which TS B is formed. For this reason TS B is disfavoured over TS A.

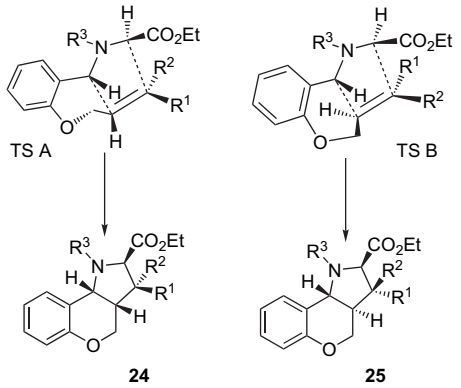
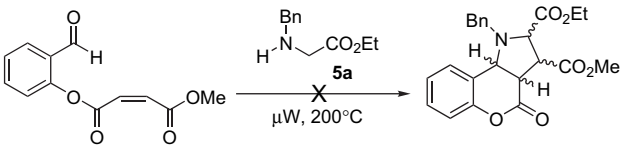


Figure 2.

Therefore, for *cis* dipolarophiles $\Delta G^{\neq}$ of TS A is smaller than $\Delta G^{\neq}$ of TS B and thus only one diastereomer **24** is formed under the reaction conditions.

For the formation of both TS, flexibility of the O–CH_2–CH═ group is important. Therefore to prove our assumption of TSs, aldehyde **26** was used as a dipolarophile. We suppose that exchange of the CH_2 group for CO diminishes the flexibility of the substrate and might prevent the TS A and TS B formation. From an electronic point of view, the additional EWG group on the dipolarophile should make the 1,3-dipolar cycloaddition more feasible.[16]

During the reaction of aldehyde **26** with amine **5a** no expected product **32** was observed in the reaction mixture (Scheme 5). Only isomerization of compound **26** to *trans* isomer **27** was detected as a newly formed product.



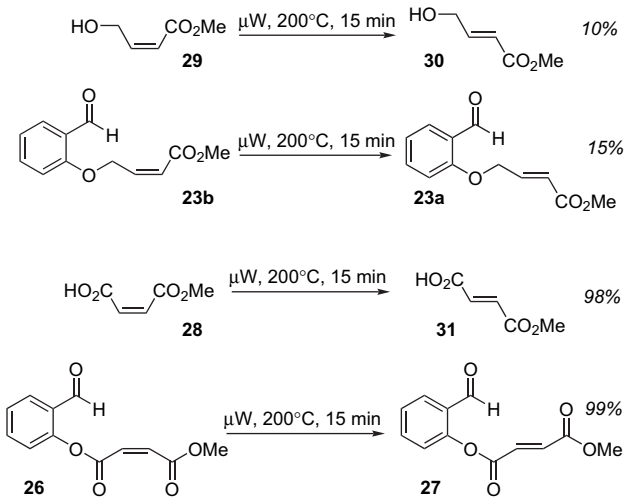
Scheme 5.

2.2. *cis/trans* Isomerization of activated double bonds under the microwave irradiation

Finally another important fact, which appeared during the experiments, has to be discussed. Traces of stereoisomers **24a** and **25a** were found in the reaction mixture when aldehyde **23b** reacted with amine **5a**. Because these two products are the main products of the reaction of aldehyde **23a** and amine **5a**, we propose that *cis/trans* isomerization occurred in the reaction mixture during the reaction.

To prove the assumption, a series of experiments were carried out during which the *cis/trans* isomerization of compounds **23a**,**b**,**d**,**e**, **26**, **27**, **28**, **29**, **30** and **31** was examined. Because the direct observation of *cis/trans* isomerization during the reaction is impossible, a different approach was used. The previously mentioned compounds were irradiated for 15 min and then they were rapidly cooled to 0 °C. The cooled reaction mixture was analyzed and the presence of *cis* and *trans* isomers was identified by GC and/or ^{1}H NMR.

During our experiments, an isomerization of olefins substituted by EDG as well as an isomerization of *trans* olefin to *cis* isomer was not observed. However, in the case of *cis* olefins substituted by EWG substituents, the situation was different. The isomerization of *cis* to *trans* isomers was observed if there was at least one carboxylic group on the irradiated olefin. In the case of compounds **23b** and **29**, 15% of *trans* isomer **23a** and 10% of *trans* isomer **30**, respectively, were identified after 15 min of irradiation (Scheme 6 and Graph S-2).[22] In the case of two carboxylic groups on the olefin (compounds **26** and **28**), the *trans* isomers **27** and **31**, respectively, were formed in the reaction mixture nearly quantitatively within 15 min (Graph S-3).



Scheme 6.

Therefore, we can assume that the small amount of products **24a** and **25b** in the reaction mixture of aldehyde **23b** and amine **5a** could be explained by the isomerization of a small amount of aldehyde **23b** to aldehyde **23a**. In situ formed aldehyde **23a** then reacts with amine **5a** and affords products **24a** and **25a**.

3. Conclusion

We have developed a simple protocol for intramolecular 1,3-dipolar cycloadditions of azomethine ylides leading to tricyclic hexahydrochromeno[4,3-*b*]pyrroles skeletons. The desired tricyclic molecules were prepared in moderate to very good yield and selectivity. Moreover, an influence of various electron-withdrawing groups upon the dipole stability and reactivity was established. Additionally, the influence of the dipolarophile double bond geometry on the reaction selectivity was observed and rationalized. These observations led us to propose preferred TSs of the cycloaddition.

Finally, an isomerization of activated double bond under the microwave irradiation was described.

4. Experimental section

4.1. General remarks

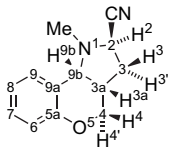
Melting points were measured on a Kofler hot stage VEB Wagetechnik Rapido 79/2106. IR spectra were recorded on a FTIR ATI MATTSON spectrophotometer in NaCl cell or KBr tablets (w—week, m—medium, s—strong signals). Microwave irradiation was carried out in PROLABO 402 Synthewave oven (power 300 W, frequency 2450 MHz). NMR spectra were recorded on Avance 300 Varian apparatus with working frequency of 300 MHz for ^{1}H and 75 MHz for ^{13}C in $CDCl_3$ with TMS as an internal standard. Chemical shifts are given in parts per million, coupling constants *J* in Hertz. Mass spectra were recorded on a FISONS INSTRUMENTS TRIO 1000 spectrometer in positive mode with EI. Gas chromatography was carried out on SPIRA KI 8 column (30 m, 5% diphenyldimethylsiloxane) with FISONS INSTRUMENTS TRIO 1000 spectrometer as a detector. HPLC chromatography was carried out on SHIMADZU LC-20AD with RP-HPLC glass column SGC C-18 (7 μm; 3×150 nm). SHIMADZU SPD-10 A was used as UV detector. Flash column chromatography was carried out on Merck silica 63–100 μm using petroleum ether/ethyl acetate as a mobile phase (for the precise ratio consult data below).

The structure determination was carried out with a help of 2D-COSY, HSQC, HMBS and 2D-NOESY NMR experiments.

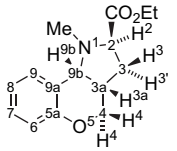
Experimental procedures and characterization of amines **5**, **10** and **18a–g**,[23] aldehydes **4** and **23a–e**[24] and olefins **28**[25] and **29**[26] can be found in Supplementary data.

4.2. General method for the preparation of hexahydrochromeno[4,3-*b*]pyrroles

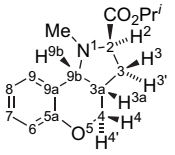
Mixture of aldehyde **4** or **23** (2.5 mmol) and amine **5**, **10** or **18a–f** (2.5 mmol) was irradiated under stirring from 15 to 60 min. Temperature of the reaction mixture was maintained at 200 °C. Reaction mixture was allowed to cool down to rt and separated by column chromatography (petroleum ether/ethyl acetate). The structure determination was made with help of 2D-COSY, HSQC, HMBS and 2D-NOESY experiments and by comparison with known compounds.[6b]



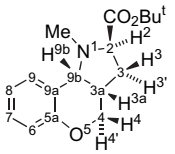
4.2.1. (2*R,3a*S**,9b*R**)-1-Methyl-1,2,3,3a,4,9b-hexahydrochromeno[4,3-*b*]pyrrole-2-carbonitrile (20a).** Compound **20a** was prepared by the reaction of aldehyde **4** (405 mg, 2.5 mmol) with amine **18a** (175 mg, 2.5 mmol), irradiated for 30 min. Flash chromatography (4:1) gave 91 mg (17%) of **20a** as a yellow oil. IR (NaCl) ν (cm^{-1}) 3061 (w), 2981 (m), 2935 (m), 2875 (w), 2265 (w, CN), 1607 (w), 1484 (w), 1456 (m), 1245 (m), 1184 (s), 1095 (s), 1008 (m), 751 (m). ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.84 (ddd, 1H, $^2J_{3,3'}$=13.5, $^3J_{3',2}$=8.9, $^3J_{3',3a}$=2.3 Hz, H-3′), 2.17 (ddd, 1H, $^2J_{3,3'}$=13.5, $^3J_{3,3a}$=8.3, $^3J_{3,2}$=4.3 Hz, H-3), 2.46–2.51 (m, 1H, H-3a), 2.60 (s, 3H, NCH_3), 3.92 (dd, 1H, $^2J_{4,4'}$=11.6, $^3J_{4,3a}$=2.7 Hz, H-4), 3.52 (d, 1H, $^3J_{9b,3a}$=6.3 Hz, H-9b), 4.17 (dd, 1H, $^2J_{4',4}$=11.6, $^3J_{4',3a}$=4.3 Hz, H-4′), 4.55 (dd, 1H, $^3J_{2,3'}$=8.9, $^3J_{2,3}$=4.3 Hz, H-2), 6.94–7.32 (m, 4H, arom. CH). ^{13}C NMR (75 MHz, $CDCl_3$) δ 31.1 (C-3), 34.4 (C-3a), 36.3 (N*C*H$_3$), 54.7 (C-2), 59.5 (C-9b), 67.8 (C-4), 117.8 (*C*N), 117.6, 120.3, 122.5, 129.0, 132.3, 155.8 (arom. CH and C$_q$). EI-MS *m*/*z* (%) 214.2 (M$^+$, 1), 198.2 (5), 186.8 (100), 130.9 (26), 115.0 (34), 62.9 (31), 50.9 (38). Calcd for $C_{13}H_{14}N_2O$ (214.26): C 72.87, H 6.59, N 13.07; found: C 72.89, H 6.61, N 13.03.



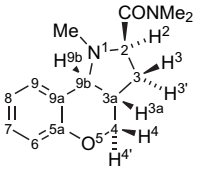
4.2.2. Ethyl-(2*R,3a*S**,9b*R**)-1-methyl-1,2,3,3a,4,9b-hexahydrochromeno[4,3-*b*]pyrrole-2-carboxylate (20b).** Compound **20b** was prepared by the reaction of aldehyde **4** (405 mg, 2.5 mmol) with amine **18b** (293 mg, 2.5 mmol), irradiated for 15 min. Flash chromatography (7:1) gave 549 mg (84%) of **20b** as a yellowish oil. IR (NaCl) ν (cm^{-1}) 3022 (m), 2944 (s), 2882 (s), 1722 (s, C=O), 1609 (m), 1580 (m), 1490 (m), 1451 (m), 1230 (w), 1195 (m), 1048 (w), 761 (w). ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.32 (t, 3H, ^3J=7.3 Hz, OCH_2CH_3), 1.99 (ddd, 1H, $^2J_{3',3}$=13.5, $^3J_{3',2}$=8.6, $^3J_{3',3a}$=4.0 Hz, H-3′), 2.19 (ddd, 1H, $^2J_{3,3'}$=13.5, $^3J_{3,3a}$=8.5, $^3J_{3,2}$=3.0 Hz, H-3), 2.52–2.63 (m, 1H, H-3a), 2.63 (s, 3H, NCH_3), 3.87 (dd, 1H, $^3J_{2,3'}$=8.6, $^3J_{2,3}$=3.0 Hz, H-2), 3.96 (dd, 1H, $^2J_{4,4}$=11.7, $^3J_{4,3a}$=4.6 Hz, one of H-4), 4.00 (dd, 1H, $^2J_{4,4}$=11.7, $^3J_{4,3a}$=2.0 Hz, the other of H-4), 4.11 (d, 1H, $^3J_{9b,3a}$=6.3 Hz, H-9b), 4.18 (dq, 2H, ^3J=7.3, ^2J=2.3 Hz, OCH_2CH_3), 6.81–7.23 (m, 4H, arom. CH). ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.6 (OCH_2CH_3), 30.4 (C-3), 35.2 (C-3a), 38.7 (NCH_3), 58.3 (C-2), 60.0 (C-9b), 60.3 (OCH_2CH_3), 68.3 (C-4), 117.3, 120.3, 122.5, 128.9, 132.4, 156.0 (arom. CH and C_q), 174.5 (C=O). EI-MS *m*/*z* (%) 262.3 (M^++H, 39), 203.7 (7), 202.3 (100), 173.2 (15), 159.0 (21), 144.7 (22), 131.0 (58), 115.0 (12), 107.1 (13), 55.9 (13). Calcd for $C_{15}H_{19}NO_3$ (261.32): C 68.94, H 7.33, N 5.36; found: C 68.92, H 7.34, N 5.32.



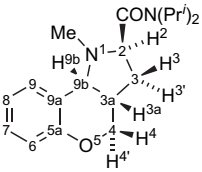
4.2.3. 2-Propyl-(2*R,3a*S**,9b*R**)-1-methyl-1,2,3,3a,4,9b-hexahydrochromeno[4,3-*b*]pyrrole-2-carboxylate (20c).** Compound **20c** was prepared by the reaction of aldehyde **4** (405 mg, 2.5 mmol) with amine **18c** (328 mg, 2.5 mmol), irradiated for 40 min. Flash chromatography (5:1) gave 261 mg (38%) of **20c** as a yellow oil. IR (NaCl) ν (cm^{-1}) 3064 (w), 2980 (m), 2935 (m), 2879 (w), 2802 (w), 1732 (s, C=O), 1608 (w), 1484 (w), 1456 (m), 757 (m), 1198 (s), 1106 (s), 1018 (m), 756 (m). ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.30 (dt, 6H, ^3J=6.6, 4.5 Hz, $CH(CH_3)_2$), 1.84 (ddd, 1H, $^2J_{3,3'}$=13.1, $^3J_{3',2}$=9.9, $^3J_{3',3a}$=2.3 Hz, H-3′), 2.17 (ddd, 1H, $^2J_{3,3'}$=13.1, $^3J_{3,3a}$=7.3, $^3J_{3,2}$=4.3 Hz, H-3), 2.40–2.46 (m, 1H, H-3a), 2.65 (s, 3H, CH_3), 3.92 (dd, 1H, $^2J_{4,4'}$=10.6, $^3J_{4,3a}$=3.3 Hz, H-4), 3.96 (d, 1H, $^3J_{9b,3a}$=6.6 Hz, H-9b), 4.17 (dd, 1H, $^2J_{4',4}$=10.6, $^3J_{4',3a}$=4.6 Hz, H-4′), 4.55 (dd, 1H, $^3J_{2,3'}$=9.9, $^3J_{2,3}$=4.3 Hz, H-2), 5.07–5.12 (m, 1H, $CH(CH_3)_3$), 6.86–7.41 (m, 4H, arom. CH). ^{13}C NMR (75 MHz, $CDCl_3$) δ 22.1 ($CH(CH_3)_2$), 30.8 (C-3), 38.7 (NCH_3), 42.3 (C-3a), 64.6 (C-9b), 68.2 (C-2), 68.2 ($CH(CH_3)_2$), 71.0 (C-4), 116.6, 120.2, 122.6, 128.9, 132.6, 154.2 (arom. CH and C_q), 173.6 (C=O). EI-MS *m*/*z* (%) 275.5 (M^+, 7), 274.3 (7), 261.6 (5), 260.2 (35), 233.4 (11), 232.2 (100), 218.1 (11). Calcd for $C_{16}H_{21}NO_3$ (275.34): C 69.79, H 7.69, N 5.09; found: C 69.82, H 7.72, N 5.09.



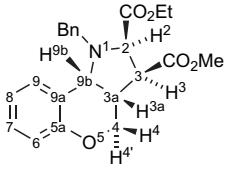
4.2.4. *tert*-Butyl-(2*R,3a*S**,9b*R**)-1-methyl-1,2,3,3a,4,9b-hexahydrochromeno[4,3-*b*]pyrrole-2-carboxylate (20d).** Compound **20d** was prepared by the reaction of aldehyde **4** (405 mg, 2.5 mmol) with amine **18d** (363 mg, 2.5 mmol), irradiated for 40 min. Flash chromatography (19:1) gave 123 mg (17%) of **20d** as a slightly yellow oil. IR (NaCl) ν (cm^{-1}) 3071 (w), 2967 (m), 2936 (m), 2871 (m), 2791 (w), 1723 (s, C=O), 1609 (w), 1488 (m), 1452 (w), 1260 (m), 1150 (s), 1052 (m), 755 (m). ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.52 (s, 9H, $C(CH_3)_3$), 1.96 (ddd, 1H, $^2J_{3,3'}$=13.2, $^3J_{3',2}$=8.6, $^3J_{3',3a}$=4.5 Hz, H-3′), 2.17 (ddd, 1H, $^2J_{3,3'}$=13.2, $^3J_{3,3a}$=8.8, $^3J_{3,2}$=3.3 Hz, H-3), 2.52 (s, 3H, NCH_3), 2.64–2.69 (m, 1H, H-3a), 3.64 (dd, 1H, $^3J_{2,3'}$=8.6, $^3J_{2,3}$=3.3 Hz, H-2), 3.89 (dd, 1H, $^2J_{4,4'}$=10.6, $^3J_{4,3a}$=8.3 Hz, H-4), 3.96 (dd, 1H, $^2J_{4',4}$=10.6, $^3J_{4',3a}$=4.6 Hz, H-4′), 4.04 (d, 1H, $^3J_{9b,3a}$=6.3 Hz, H-9b), 6.90–7.22 (m, 4H, arom. CH). ^{13}C NMR (75 MHz, $CDCl_3$) δ 28.5 ($C(CH_3)_3$), 30.8 (C-3), 35.2 (C-3a), 35.9 (NCH_3), 59.0 (C-9b), 65.2 (C-2), 68.5 (C-4), 80.3 ($C(CH_3)_3$), 117.5, 120.4, 122.7, 128.7, 133.1, 156.0 (arom. CH and C_q), 173.8 (C=O). EI-MS *m*/*z* (%) 289.9 (M^+, 2), 168.3 (4), 167.0 (34), 150.2 (7), 149.0 (100), 113.3 (8), 83.0 (8), 71.0 (13), 70.0 (11), 57.0 (43), 42.9 (28), 40.9 (33). Calcd for $C_{17}H_{23}NO_3$ (289.37): C 70.56, H 8.01, N 4.84; found: C 70.58, H 7.99, N 4.86.



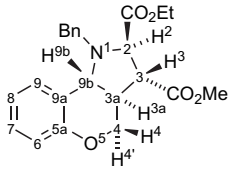
4.2.5. *N*,*N*-Dimethyl-(2*R,3a*S**,9b*R**)-1-methyl-1,2,3,3a,4,9b-hexahydrochromeno[4,3-*b*]pyrrole-2-carboxamide (20e).** Compound **20e** was prepared by the reaction of aldehyde **4** (405 mg, 2.5 mmol) with amine **18e** (190 mg, 2.5 mmol), irradiated for 40 min. Flash chromatography (10:1) gave 293 mg (45%) of **20e** as white crystals. Mp (58–59 °C). IR (KBr) ν (cm^{-1}) 3007 (w), 2968 (m), 2930 (m), 2871 (w), 2833 (w), 1737 (s, C=O), 1582 (w), 1480 (w), 1441 (m), 1257 (m), 1044 (m), 758 (m). ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.99 (ddd, 1H, $^2J_{3,3'}$=13.1, $^3J_{3',2}$=8.1, $^3J_{3',3a}$=4.5 Hz, H-3′), 2.19 (ddd, 1H, $^2J_{3,3'}$=13.1, $^3J_{3,3a}$=8.7, $^3J_{3,2}$=3.9 Hz, H-3), 2.49 (s, 3H, NCH_3), 2.85 (m, 1H, H-3a), 2.95 and 2.99 (two s, 3H+3H, $N(CH_3)_2$), 3.92 (dd, 1H, $^2J_{4,4'}$=10.6, $^3J_{4,3a}$=3.2 Hz, H-4), 3.96 (dd, 1H, $^3J_{2,3'}$=8.1, $^3J_{2,3}$=3.9 Hz, H-2), 4.25 (dd, 1H, $^2J_{4',4}$=10.6, $^3J_{4',3a}$=4.6 Hz, H-4′), 4.32 (d, 1H, $^3J_{9b,3a}$=6.8 Hz, H-9b), 6.90–7.27 (m, 4H, arom. CH). ^{13}C NMR (75 MHz, $CDCl_3$) δ 34.2 (C-3), 36.8 (NCH_3), 37.5 (C-3a), 38.6 ($N(CH_3)_2$), 60.0 (C-9b), 63.2 (C-2), 66.7 (C-4), 115.1, 120.1, 122.2, 129.4, 132.6, 156.8 (arom. CH and C_q), 165.5 (C=O). Calcd for $C_{15}H_{20}N_2O_2$ (260.33): C 69.20, H 7.74, N 10.76; found: C 69.19, H 7.73, N 10.76.



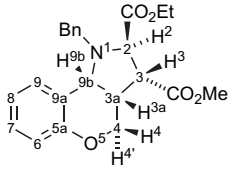
4.2.6. *N*,*N*-Di-(2-propyl)-(2*R,3a*S**,9b*R**)-1-methyl-1,2,3,3a,4,9b-hexahydrochromeno[4,3-*b*]pyrrole-2-carboxamide (20f).** Compound **20f** was prepared by the reaction of aldehyde **4** (405 mg, 2.5 mmol) with amine **18f** (431 mg, 2.5 mmol), irradiated for 40 min. Flash chromatography (9:1) gave 127 mg (16%) of **20f** as white crystals. Mp (91–92 °C). IR (KBr) ν (cm^{-1}) 3004 (w), 2967 (m), 2931 (m), 2869 (w), 2834 (w), 1735 (s, C=O), 1583 (w), 1486 (w), 1444 (m), 1256 (m), 1045 (m), 760 (m). ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.26 (d, 6H, ^3J=6.6 Hz, one of $CH(CH_3)_2$), 1.41 (d, 6H, ^3J=6.6 Hz, the other of $CH(CH_3)_2$), 2.02 (ddd, 1H, $^2J_{3,3'}$=12.9, $^3J_{3',2}$=8.3, $^3J_{3',3a}$=4.6 Hz, H-3′), 2.22 (ddd, 1H, $^2J_{3,3'}$=12.9, $^3J_{3,3a}$=8.6, $^3J_{3,2}$=4.0 Hz, H-3), 2.52 (s, 3H, CH_3), 2.78–2.83 (m, 1H, H-3a), 3.76–3.81 (m, 2H, $N(CH(CH_3)_2)_2$) 3.92 (dd, 1H, $^2J_{4,4'}$=10.7, $^3J_{4,3a}$=3.2 Hz, H-4), 3.96 (dd, 1H, $^3J_{2,3'}$=8.3, $^3J_{2,3}$=4.6 Hz, H-2), 4.17 (dd, 1H, $^2J_{4',4}$=10.7, $^3J_{4',3a}$=4.5 Hz, H-4′), 4.34 (d, 1H, $^3J_{9b,3a}$=6.9 Hz, H-9b), 6.91–7.20 (m, 4H, arom. CH). ^{13}C NMR (75 MHz, $CDCl_3$) δ 22.0 ($CH(CH_3)_2$), 31.4 (C-3), 35.4 (NCH_3), 36.2 (C-3a), 46.1 ($CH(CH_3)_2$), 60.0 (C-9b), 61.9 (C-2), 68.6 (C-4), 117.3, 119.9, 122.4, 128.8, 132.9, 156.0 (arom. CH and C_q), 165.1 (C=O). EI-MS *m*/*z* (%) 317.4 (M^++1, 6), 315.5 (4), 314.4 (3), 189.5 (15), 188.2 (100), 130.9 (14), 81.8 (8), 42.8 (13). Calcd for $C_{19}H_{28}N_2O_2$ (316.44): C 72.12, H 8.92, N 8.85; found: C 72.15, H 8.90, N 8.84.



4.2.7. 2-Ethyl-3-methyl-(2*R,3*S**,3a*S**,9b*R**)-1-benzyl-1,2,3,3a,4,9b-hexahydrochromeno[4,3-*b*]pyrrole-2,3-dicarboxylate (24a).** Compound **24a** was prepared by the reaction of aldehyde **23a** (586 mg, 2.5 mmol) with amine **5a** (483 mg, 2.5 mmol), irradiated for 15 min. Flash chromatography (7:1) gave 620 mg (62%) of **24a** as a yellowish oil. IR (NaCl) ν (cm^{-1}) 3067 (m), 3020 (m), 2945 (s), 2876 (s), 1725 (s, C=O), 1608 (m), 1580 (m), 1490 (m), 1445 (m), 1230 (w), 1189 (w), 1049 (w), 762 (w). ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.31 (t, 3H, ^3J=7.3 Hz, OCH_2CH_3), 3.39 (dddd, 1H, $^3J_{3a,3}$=9.3, $^3J_{3a,9b}$=8.3, $^3J_{3a,4'}$=3.6, $^3J_{3a,4}$=1.7 Hz, H-3a), 3.43 (dd, 1H, $^3J_{3,3a}$=9.3, $^3J_{3,2}$=6.6 Hz, H-3), 3.58 (d, 1H, ^2J=13.2 Hz, one of NCH_2Ph), 3.72 (s, 3H, OCH_3), 3.93 (d, 1H, $^3J_{2,3}$=6.6 Hz, H-2), 3.97 (dd, 1H, $^3J_{4',4}$=11.6, $^3J_{4',3a}$=3.6 Hz, H-4′), 4.11 (d, 1H, $^3J_{9b,3a}$=8.3 Hz, H-9b), 4.22 (d, 2H, ^2J=13.2 Hz, NCH_2Ph), 4.27 (q, 2H, ^3J=7.3 Hz, OCH_2CH_3), 4.31 (dd, 1H, $^3J_{4,4'}$=11.6, $^3J_{4,3a}$=1.7 Hz, H-4), 6.90–7.41 (m, 9H, arom. CH). ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.6 (OCH_2CH_3), 41.4 (C-3a), 47.7 (C-3), 52.1 (NCH_2Ph), 52.1 (OCH_3), 58.8 (C-9b), 60.6 (OCH_2CH_3), 63.6 (C-2), 69.8 (C-4), 118.0, 121.5, 127.3, 128.3, 128.7, 130.5, 138.7, 157.7 (m, 9H, arom. CH and C_q), 171.5 and 172.1 (C=O). EI-MS *m*/*z* (%) 396.8 (M^++H ,1), 395.1 (M^+, 1), 324.2 (15), 222.3 (95), 320.5 (15), 260.5 (5), 174.2 (2), 173.1 (14), 172.1 (15), 131.0 (13), 92.1 (8), 90.9 (100), 64.8 (18). Calcd for $C_{23}H_{25}NO_5$ (395.45): C 69.86, H 6.37, N 3.54; found: C 69.81, H 6.32, N 3.49.

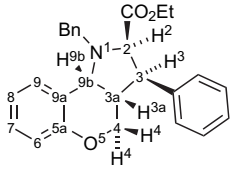


4.2.8. 2-Ethyl-3-methyl-(2*R,3*R**,3a*R**,9b*R**)-1-benzyl-1,2,3,3a,4,9b-hexahydrochromeno[4,3-*b*]pyrrole-2,3-dicarboxylate (25a).** Compound **25a** was prepared by the reaction of aldehyde **23a** (586 mg, 2.5 mmol) with amine **5a** (483 mg, 2.5 mmol), irradiated for 15 min. Flash chromatography (7:1) gave 170 mg (17%) of **25a** as a yellowish oil. IR (NaCl) ν (cm^{-1}) 3067 (m), 3020 (m), 2945 (s), 2876 (s), 1727 (s, C=O), 1608 (m), 1578 (m), 1467 (m), 1445 (m), 1230 (w), 1189 (w), 1049 (w), 762 (w). ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.19 (t, 3H, ^3J=7.3 Hz, OCH_2CH_3), 2.80 (dddd, 1H, $^3J_{3a,3}$=11.0, $^3J_{3a,9b}$=11.0, $^3J_{3a,4}$=10.5, $^3J_{3a,4'}$=2.0 Hz, H-3a), 3.22 (dd, 1H, $^3J_{3a,3}$=10.9, $^3J_{3,2}$=5.4 Hz, H-3), 3.59 (d, 1H, ^2J=13.2 Hz, one of NCH_2Ph), 3.79 (s, 3H, OCH_3), 4.10 (dd, 1H, $^3J_{4',4}$=9.9, $^3J_{4',3a}$=2.0 Hz, H-4′), 4.18 (d, 1H, $^3J_{2,3}$=5.4 Hz, H-2), 4.21 (d, 1H, $^3J_{9b,3a}$=11.0 Hz, H-9b), 4.25 (q, 2H, ^3J=7.3 Hz, OCH_2CH_3), 4.34 (d, 1H, ^2J=13.2 Hz, the other of NCH_2Ph), 4.52 (dd, 1H, $^3J_{4,3a}$=10.9, $^3J_{4,4'}$=9.9 Hz, H-4), 6.90–7.49 (m, 9H, arom. CH). ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.2 (OCH_2CH_3), 42.5 (C-3), 49.4 (C-3a), 52.7 (OCH_3), 53.4 (NCH_2Ph), 58.8 (C-9b), 61.1 (OCH_2CH_3), 64.8 (C-2), 69.8 (C-4), 116.9, 125.9, 126.3, 128.4, 128.6, 128.9, 130.5, 138.7, 157.7 (arom. CH and C_q), 172.3 and 173.4 (C=O). EI-MS *m*/*z* (%) 396.8 (M^++1, 1), 395.1 (M^+, 1), 324.2 (12), 323.2 (25), 222.3 (80), 320.5 (16), 260.5 (7), 174.2 (5), 173.1 (20), 172.1 (10), 131.0 (15), 92.1 (5), 90.9 (100), 64.8 (18). Calcd for $C_{23}H_{25}NO_5$ (395.45): C 69.86, H 6.37, N 3.54; found: C 69.84, H 6.35, N 3.52.

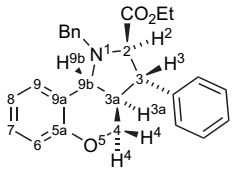


4.2.9. 2-Ethyl-3-methyl-(2*R,3*R**,3a*S**,9b*R**)-1-benzyl-1,2,3,3a,4,9b-hexahydrochromeno[4,3-*b*]pyrrole-2,3-dicarboxylate (24b).** Compound **24b** was prepared by the reaction of aldehyde **23b** (586 mg, 2.5 mmol) with amine **5a** (483 mg, 2.5 mmol), irradiated for 15 min. Flash chromatography (8:1) gave 811 mg (82%) of **24b** as a yellowish oil. IR (NaCl) ν (cm^{-1}) 3064 (m), 3019 (m), 2940 (s), 2876 (s), 1725 (s, C=O), 1723 (s, C=O), 1605 (m), 1581 (m), 1486 (m), 1447 (m), 1235 (w), 1189 (w), 1049 (w), 754 (w). ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.32 (t, 3H, ^3J=7.3 Hz, OCH_2CH_3), 3.40 (m, 1H, H-3a), 3.51 (dd, 1H, $^3J_{3,3a}$=7.2, $^3J_{3,2}$=6.9 Hz, H-3), 3.62 (d, 1H, ^2J=13.2 Hz, one of NCH_2Ph), 3.75 (s, 3H, OCH_3), 3.99 (d, 1H, $^3J_{2,3}$=6.9,

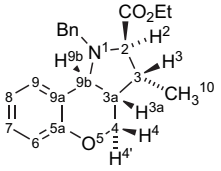
H-2), 4.05 (dd, 1H, $^3J_{4',4}$=11.3, $^3J_{4',3a}$=3.4 Hz, H-4′), 4.15 (d, 1H, $^3J_{9b,3a}$=8.3 Hz, H-9b), 4.23 (d, 2H, ^2J=13.2 Hz, NCH_2Ph), 4.27 (q, 2H, ^3J=7.3 Hz, OCH_2CH$_3$), 4.31 (dd, 1H, $^3J_{4,4'}$=11.3, $^3J_{4,3a}$=1.8 Hz, H-4), 6.91–7.42 (m, 9H, arom. CH). ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.5 (OCH$_2$CH$_3$), 41.6 (C-3), 47.6 (C-3a), 51.8 (NCH$_2$Ph), 53.4 (OCH$_3$), 59.5 (C-2), 61.2 (OCH$_2$CH$_3$), 63.8 (C-9b), 70.2 (C-4), 117.3, 126.2, 126.7, 128.5, 128.7, 129.1, 130.7, 138.5, 158.1 (arom. CH and C$_q$), 171.6 and 172.2 (C=O). EI-MS *m/z* (%) 396.8 (M$^+$+H, 1), 395.1 (M$^+$, 1), 324.2 (12), 222.3 (95), 320.5 (15), 260.5 (5), 174.2 (6), 173.1 (19), 172.1 (18), 131.0 (13), 92.1 (8), 91.0 (100), 64.8 (18). Calcd for $C_{23}H_{25}NO_5$ (395.45): C 69.86, H 6.37, N 3.54; found: C 69.84, H 6.39, N 3.51.



4.2.10. Ethyl-(2*R,3*R**,3a*S**,9b*R**)-1-benzyl-3-phenyl-1,2,3,3a,4,9b-hexahydrochromeno[4,3-*b*]pyrrole-2-carboxylate (24c).** Compound **24c** was prepared by the reaction of aldehyde **23c** (596 mg, 2.5 mmol) with amine **5a** (483 mg, 2.5 mmol), irradiated for 30 min. Flash chromatography (19:1) gave 383 mg (37%) of **24c** as an orange oil. IR (NaCl) ν (cm^{-1}) 3062 (w), 3028 (w), 2959 (m), 2924 (m), 2853 (m), 1727 (s, C=O), 1605 (m), 1490 (m), 1452 (m), 1261 (m), 1183 (s), 1029 (m), 748 (m), 699 (m). ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.83 (t, 3H, ^3J=7.4 Hz, OCH$_2$CH_3), 3.35–3.39 (m, 1H, H-3a), 3.71 (dd, 1H, $^3J_{3,2}$=6.3, $^3J_{3,3a}$=7.3 Hz, H-3), 3.79 (d, 1H, ^2J=13.5 Hz, one of CH_2Ph), 3.84 (d, 1H, $^3J_{2,3}$=6.3 Hz, H-2), 3.98 (dd, 1H, $^2J_{4,4}$=11.2, $^3J_{4,3a}$= 3.6 Hz, one of the H-4), 4.06 (dd, 1H, $^2J_{4,4}$=11.2, $^3J_{4,3a}$=3.0 Hz, the other of H-4), 4.20 (q, 2H, ^3J=7.3 Hz, OCH_2CH$_3$), 4.34 (d, 1H, ^2J=13.5 Hz, the other of CH_2Ph), 4.38 (d, 1H, $^3J_{9b,3a}$=8.9 Hz, H-9b), 6.98–7.43 (m, 14H, arom. CH). ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.0 (OCH$_2$CH_3), 42.7 (C-3a), 48.4 (C-3), 58.0 (CH_2Ph), 59.4 (C-9b), 60.4 (OCH_2CH$_3$), 68.3 (C-2), 68.5 (C-4), 117.9, 120.1, 122.3, 125.1, 126.2, 127.6, 128.3, 128.6, 129.1, 130.3, 132.9, 134.8, 139.8, 157.0 (arom. CH and C$_q$), 172.3 (C=O). EI-MS *m/z* (%) 413.7 (M$^+$, 1), 374.4 (2), 300.2 (2), 283.4 (4), 211.5 (19), 210.2 (98), 192.2 (17), 181.1 (12), 92.1 (17), 90.9 (100), 64.9 (30). Calcd for $C_{27}H_{27}NO_3$ (413.51): C 78.42, H 6.58, N 3.39; found: C 78.45, H 6.57, N 3.41.



4.2.11. Ethyl-(2*R,3*S**,3a*R**,9b*R**)-1-benzyl-3-phenyl-1,2,3,3a,4,9b-hexahydrochromeno[4,3-*b*]pyrrole-2-carboxylate (25c).** Compound **25c** was prepared by the reaction of aldehyde **23c** (596 mg, 2.5 mmol) with amine **5a** (483 mg, 2.5 mmol), irradiated for 30 min. Flash chromatography (19:1) gave 176 mg (17%) of **25c** as an orange oil. IR (NaCl) ν (cm^{-1}) 3061 (w), 3028 (w), 2961 (m), 2928 (m), 2855 (m), 1728 (s, C=O), 1606 (m), 1491 (m), 1453 (m), 1261 (m), 1187 (s), 1029 (m), 753 (m), 699 (m). ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.98 (t, 3H, ^3J=7.1 Hz, OCH$_2$CH_3), 2.59–2.63 (m, 1H, H-3a), 3.35 (dd, 1H, $^3J_{3,2}$=7.6, $^3J_{3,3a}$=6.6 Hz, H-3), 3.56 (d, 1H, $^3J_{2,3}$=7.6 Hz, H-2), 3.70 (dq, 2H, ^3J=7.0, ^2J=5.9 Hz, OCH_2CH$_3$), 3.91 (d, 1H, ^2J=13.5 Hz, one of CH_2Ph), 4.10 (dd, 1H, $^2J_{4,4}$=11.2, $^3J_{4,3a}$=4.0 Hz, one of the H-4), 4.15 (d, 1H, $^3J_{9b,3a}$=7.3 Hz, H-9b), 4.28 (dd, 1H, $^2J_{4,4}$=11.1, $^3J_{4,3a}$=7.0 Hz, the other of H-4), 4.38 (d, 1H, ^2J=13.5 Hz, the other of CH_2Ph), 6.84–7.37 (m, 14H, arom. CH). ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.1 (OCH$_2$CH_3), 43.6 (C-3a), 50.2 (C-3), 58.4 (CH_2Ph), 60.8 (OCH_2CH$_3$), 61.4 (C-9b), 65.7 (C-4), 74.1 (C-2), 117.2, 119.4, 121.6, 125.4, 125.9, 127.4, 127.5, 128.1, 128.9, 130.2, 132.6, 135.2, 138.1, 148.5 (arom. CH and C$_q$), 172.9 (C=O). EI-MS *m/z* (%) 413.5 (M$^+$, 1), 374.1 (3), 300.6 (1), 283.1 (5), 211.7 (20), 210.1 (97), 192.1 (17), 181.5 (13), 92.0 (18), 90.9 (100), 64.8 (31). Calcd for $C_{27}H_{27}NO_3$ (413.51): C 78.42, H 6.58, N 3.39; found: C 78.44, H 6.56, N 3.38.



4.2.12. Ethyl-(2*R,3*R**,3a*S**,9b*R**)-1-benzyl-3-methyl-1,2,3,3a,4,9b-hexahydrochromeno[4,3-*b*]pyrrole-2-carboxylate (24e).** Compound **24e** was prepared by the reaction of aldehyde **23e** (441 mg, 2.5 mmol) with amine **5a** (483 mg, 2.5 mmol), irradiated for 40 min. Flash chromatography (9:1) gave 544 mg (62%) of **24e** as slightly brown crystals. Mp (70–72 °C). IR (KBr) ν (cm^{-1}) 3062 (m), 3029 (m), 2962 (m), 2929 (m), 2856 (m), 1726 (s, C=O), 1602 (w), 1489 (w), 1454 (w), 1218 (m), 1184 (s), 1139 (m), 1027 (m), 756 (m), 700 (m). ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.04 (d, 3H, $^3J_{10,3}$=6.9 Hz, H-10), 1.25 (t, 3H, ^3J=7.3 Hz, CO$_2$CH$_2$CH_3), 2.45–2.51 (m, 1H, H-3a), 2.51–2.64 (m, 1H, H-3), 3.55 (d, 1H, $^3J_{2,3}$=7.3 Hz, H-2), 3.73 (d, 1H, ^2J=13.2 Hz, one of NCH_2Ph), 3.91 (dd, 1H, $^2J_{4',4}$= 11.2, $^3J_{4',3a}$=3.6 Hz, H-4′), 4.09 (dd, 1H, $^2J_{4,4'}$=11.1, $^3J_{4,3a}$=3.0 Hz, H-4), 4.18 (q, 2H, ^3J=7.3 Hz, CO$_2$CH_2CH$_3$), 4.24 (d, 1H, ^3J=13.2 Hz, the other of NCH_2Ph), 4.47 (d, 1H, $^3J_{9b,3a}$=8.3 Hz, H-9b), 6.90–7.37 (m, 9H, arom. CH). ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.3 (C-10), 14.7 (CH$_2$CH_3), 36.7 (C-3), 45.6 (C-3a), 53.0 (CH$_2$Ph), 59.1 (C-9b), 60.0 (CH_2CH$_3$), 66.9 (C-2), 68.4 (C-4), 117.8, 121.3, 126.4, 127.1, 128.3, 128.4, 128.9, 130.5, 139.2, 157.0 (arom. CH and C$_q$), 178.3 (C=O). EI-MS *m/z* (%) 353.1 (M$^+$+2, 9), 352.0 (M$^+$+1, 17), 351.4 (M$^+$, 4), 279.5 (14), 278.2 (100), 260.1 (5), 187.3 (4), 186.3 (8), 148.9 (13), 130.7 (10), 90.8 (48). Calcd for $C_{22}H_{25}NO_3$ (351.44): C 75.19, H 7.17, N 3.99; found: C 75.20, H 7.19, N 3.98.

Acknowledgements

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Supplementary data

Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet.2006.10.074.

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9. This very polar fraction, which sticks on the silica gel, presented a very complicated mixture of probably decomposed reaction intermediates, which was not possible to analyze. At first, we have expected the formation of product of the Claisen rearrangement, however, this product was not observed in the reaction mixture.
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12. The condensation of the water was observed above the open reaction vessel in the course of the reaction.
13. This reaction is possible to extend to other aldehydes as well as *N*-alkyl 2-alkylaminoacetamides and represents an elegant way for the preparation of 1,2,3-trialkyl substituted imidazolin-4-ones. Desired compounds are formed generally in 5 min (200 °C, μW) in 90–96% yields. Interestingly, the reaction is possible to carry out under the classical heating with comparable yields, however, the reaction times are longer (30 min). See: Pospíšil, J.; Potáček, M. *Heterocycles* **2004**, *63*, 1165–1173.
14. Interestingly, no products of the intermolecular reaction (dimers, trimers,…) were observed in the reaction mixture (GC–MS).
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