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The Preparation and the Cascade Reactions of *N*-Butadienyl-*N*-Alkylketene *N,O-tert*-Butyldimethylsilyl acetals

Andreas Franz, Pierre-Yves Eschler, Manuel Tharin and Reinhard Neier*

Institut de Chimie de l'Université de Neuchâtel, CH-2000 Neuchâtel

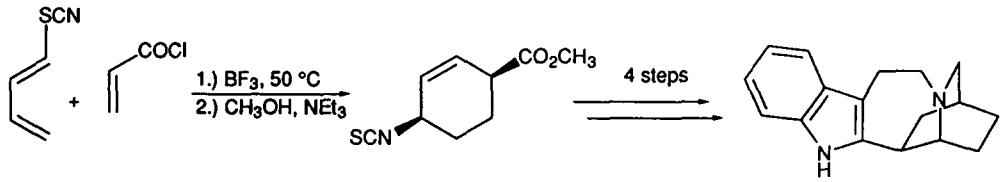
Abstract: The preparation of *N*-butadienyl-*N*-alkylketene *N,O-tert*-butyldimethylsilyl acetals **(11a - d)**from readily available starting materials is described. The cascade *Diels-Alder* reaction followed by acylation of these ketene acetals yields bicyclic and tricyclic products **7**, **13a,b** and **14c,d** with high diastereoselectivity. Copyright © 1996 Elsevier Science Ltd

INTRODUCTION

Some of the most attractive biosynthetic transformations are tandem or cascade reactions[1-3]. They have fascinated biochemists as well as well as synthetic organic chemists. The imitation of processes occurring in nature has been successfully used as guideline for the planning of organic synthesis[4-6]. The beauty and the efficiency of multistep reactions was a strong motivation for the synthetic organic chemists to imitate the biosynthetic pathways[7,8]. Tandem or cascade processes have been known for a long time. Many name reactions[9-12], belong to this category.

In recent years some spectacular applications of cascade reactions to the synthesis of complex natural products have been reported using either the biogenetic approach[13] or cascade reactions specifically designed for their synthetic utility[14]. Lately the interest in developing new tandem or cascade reactions has increased considerably. The systematic search has been motivated by the recognition of the higher efficiency which can be obtained [15,16]. Tandem or cascade reactions represent one of the best ways to decrease the number of synthetic steps to a specific target. Therefore developing and applying tandem or cascade reactions is an excellent method to approach the goal of an "ideal" synthesis [17]. The increasing interest in those processes has been documented by the publication of review articles on tandem or cascade reactions [15,16]. A systematic nomenclature for tandem or cascade reactions has been proposed as well, which allows a classification of tandem or cascade processes[15,18].

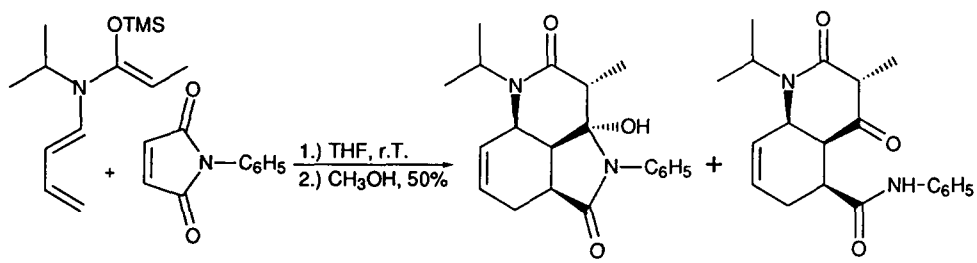
Our interest in cascade reactions composed of a *Diels-Alder* reaction and a [3,3]-sigmatropic shift is motivated by the obvious advantages of combing two synthetically important electrocyclic reactions[19-21]. The successful application of this cascade using (*E*)-buta-1,3-dienyl-thiocyanate (**1**) as suitably substituted diene in the synthesis of the *iboga* skeleton **3** in five steps and with remarkable "atom economy" is a proof for the synthetic utility of this approach (Scheme 1) [22].



1 **2** **3**

Scheme 1

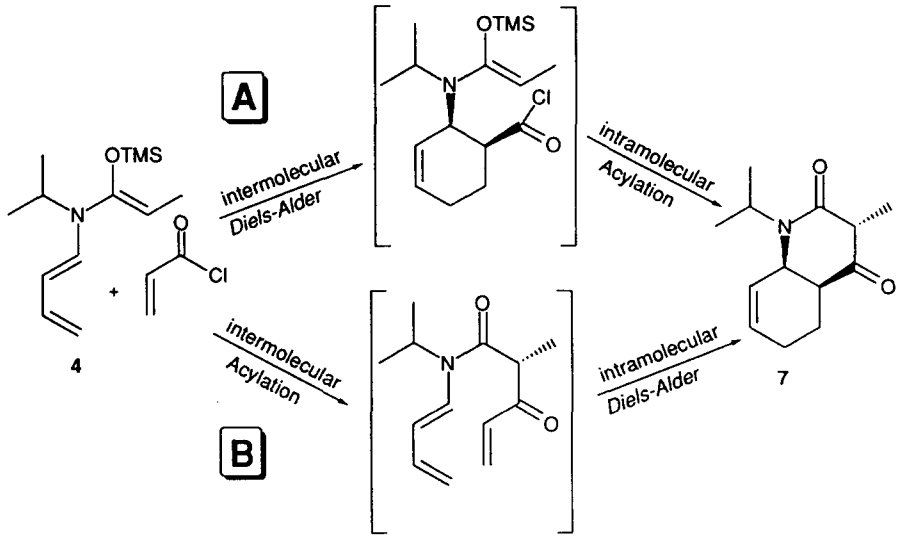
Incorporating into this novel cascade a [3,3]-sigmatropic shift producing a C-C bond would increase the synthetic utility. We therefore studied the synthesis of *N*-butadienyl-*N*-isopropylketene *N,O*-trimethylsilyl acetal of propionamide (**4**) and its reactivity against *N*-phenylmaleimide and acryloyl chloride [23-25] (Scheme 2). Instead of the planned cascade, an unexpected process combining a *Diels-Alder* reaction with an acylation step occured leading to interesting bicyclic and tricyclic products **5** and **6** in good yields.



4 **5** **6**

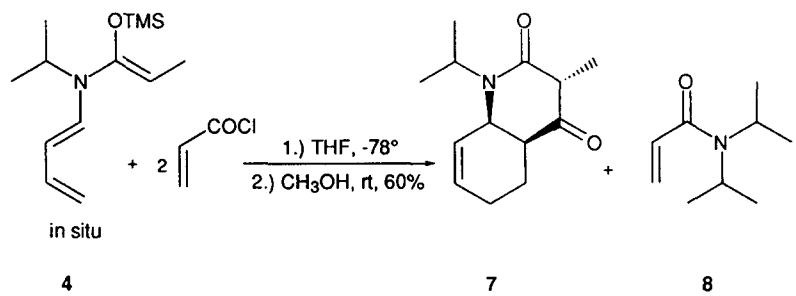
Scheme 2

The combination of a *Diels-Alder* reactions with an acylation step has not been reported very often[26-29]. In the reported cases the *N*-acylations of an adequate imine leads to an *N*-butadienyl amide, which undergoes the subsequent intramolecular *Diels-Alder* reaction. In contrast to the cases reported in the literature the novel cascade forms three C-C bonds: one during the acylation and two during the *Diels-Alder* reaction. The formation of the product **7** can be explained by either of the two following sequences: A) intermolecular *Diels-Alder* reaction first followed by intramolecular acylation second or B) intermolecular acylation between the ketene *N,O*-silyl acetal and an acid chloride forming a C-C bond first followed by an intramolecular *Diels-Alder* reaction (Scheme 3).



Scheme 3

We prefer the first sequence because of the high diastereoselectivity of our cascade: only one diastereoisomer was formed. In order to study the scope and limitations of this new cascade process it was important to synthesise a series of stable and isolable derivatives of *N*-butadienyl-*N*-isopropylketene *N,O*-silyl acetal of propionamide. The trimethylsilyl acetal **4** was created *in situ* and then directly applied in the cascade reaction without isolating the ketene trimethylsilyl acetal. Serious disadvantages of this procedure are the sensitivity of the ketene trimethylsilyl acetal **4** toward hydrolysis and the formation of the diisopropylamide **8** as side product (Scheme 4).

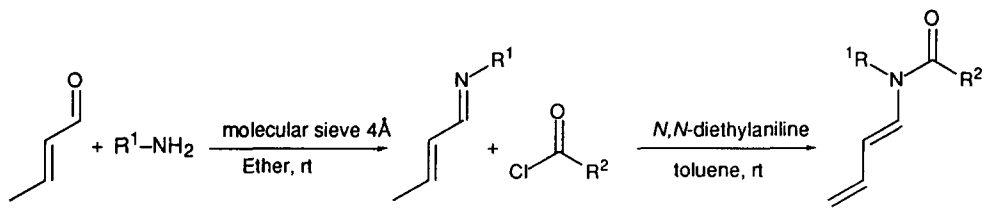


Scheme 4

RESULTS AND DISCUSSION

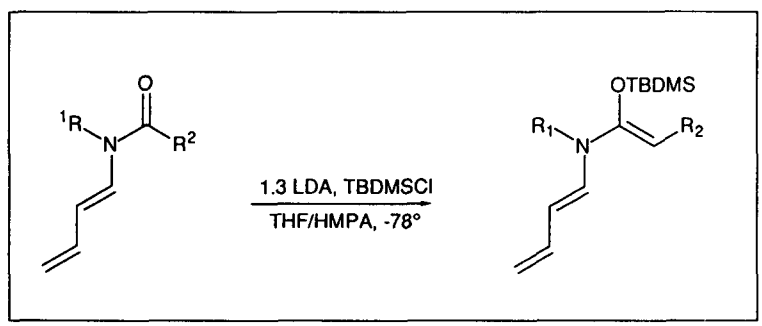
A series of *N*-alkyl-*N*-butadienyl amides were synthesised using the two step procedure: imine formation **9a,b** catalysed by molecular sieves[30] followed by base catalysed acylation with the corresponding acid chloride[31-34] (Scheme 5).

The *N*-alkyl-*N*-butadienyl amides **10a - d** were obtained in good to excellent yields starting from crotonaldehyde, the alkyl amine and the corresponding acid chloride. We decided to try to synthesise the *N*-butadienyl-*N*-isopropylketene *N,O-tert*-butyldimethylsilyl acetal of propionamide (**11a**) first, which should be considerably more stable than the trimethylsilyl derivatives.



9a R^1 = -$CH(CH_3)_2$
9b R^1 = -$CH_2C_6H_5$

10a R^1 = -iC_3H_7, R^2 = -C_2H_5
10b R^1 = -$CH_2C_6H_5$, R^2 = -C_2H_5
10c R^1 = -iC_3H_7, R^2 = -$CH_2C_6H_5$
10d R^1 = -iC_3H_7, R^2 = -$CH_2C_6H_4pOCH_3$



10a-d

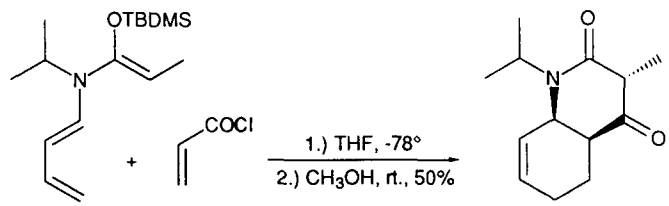
11a R^1 = -iC_3H_7, R^2 = -CH_3 (98 %)
11b R^1 = -$CH_2C_6H_5$, R^2 = -CH_3 (98 %)
11c R^1 = -iC_3H_7, R^2 = -C_6H_5 (97 %)
11d R^1 = -iC_3H_7, R^2 = -$C_6H_4pOCH_3$ (98 %)

Scheme 5

The *in situ* deprotonation/silylation which had been highly successful for the synthesis of the *N*-butadienyl-*N*-isopropylketene *N,O*-trimethylsilyl acetal of propionamide 4[23-25] could not be applied for the synthesis of the ketene *N,O-tert*-butyldimethylsilyl acetal **11a**. Only after considerable optimisation using the

procedure described by *Rathke*[35] could good and reproducible yields of the *N*-butadienyl-*N*-isopropylketene *N,O-tert*-butyldimethylsilyl acetals **11a - d** be obtained (Scheme 5). The amides **10a - d** were deprotonated in the solvent mixture THF/HMPA = 10 : 1 at - 78°C with LDA. After 10 minutes a solution of the *tert*-butyldimethylsilyl chloride in THF was added at the same temperature. The reaction mixture was allowed to warm to rt. and then diluted with pentane. Extraction against brine and evaporation of the solvent yielded the *N*-butadienyl-*N*-isopropylketene *N,O-tert*-butyldimethylsilyl acetals **11a - d** in almost quantitative yield as oils. The *tert*-butyldimethylsilyl acetals **11a - d** could be purified via extraction and could be stored over months in the refrigerator. However trials to purify the ketene *N,O*-acetals **11a - d** via chromatography lead to hydrolysis. Even the use of deactivated silica gel or aluminium oxide allowed only the isolation of the hydrolysed starting material.

Acylation reactions of ketene *N,O*-acetals are usually catalysed by Lewis acids. In the cascade process no Lewis acid had been added. The LiCl present in the reaction mixture, using the ketene *N,O*-trimethylsilyl acetal **4** synthesised *in situ*, could possibly act as a weak Lewis acid. Using the pure ketene *N,O-tert*-butyldimethylsilyl acetal **11a** free of LiCl and diisopropylamine and submitting it to the reaction conditions optimised for the ketene *N,O*-trimethylsilyl acetal, the bicyclic product **7** could be obtained in 50 % yield (Scheme 6). This result clearly indicates that the presence of LiCl is not necessary for the success of the tandem reaction. Work-up and crystallisation of the products were considerably facilitated by the fact that no diisopropylacryloyl amide **8** had been formed as side product.



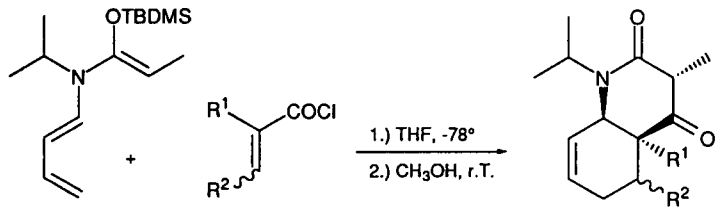
11a **7**

Scheme 6

The cascade product **7** could also be obtained in 34 % yield using CH_2Cl_2 as solvent. Trials to improve the yield by adding a series of Lewis acids in catalytic amounts ($AlCl_3$, $ZnCl_2$, $TiCl_4$, $BF_3{\cdot}OEt_2$, $(nBu)_4NF$ 10 mol % of each of these Lewis acids was added) were unsuccessful. The addition of up to 50 mol % of $ZnCl_2$ did not improve the yield of the tandem reaction either. In all cases the yields were considerably lower (yields between 10 and 22 %) than for the uncatalysed reaction. TLC analysis clearly indicated the formation of large amounts of side products.

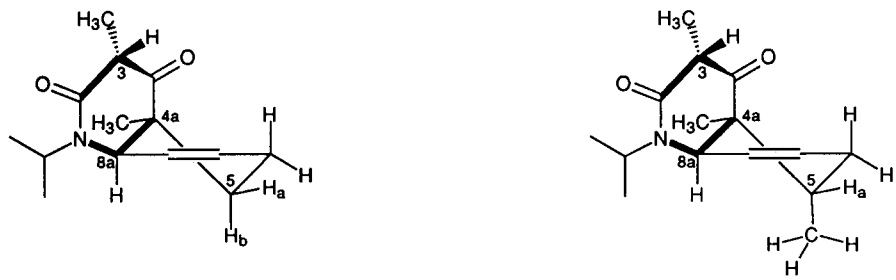
Crotonyl chloride (**12b**) or methacryl chloride (**12a**) could also be used as dienophiles for the cascade reaction (Scheme 7). The yields (19 % of **13a** and 12 % of **13b**) were unfortunately only moderate. The TLC-analysis of the reaction mixture indicated that during the reaction several side products were formed. The chromatographic isolation of the bicyclic products **13a,b** proved to be tedious and time consuming. Using methacryl chloride (**12a**) as dienophile one single diastereoisomer **13a** was obtained. In the case of the crotonyl chloride (**12b**), this starting material was a 4 : 1 mixture of isomers and thus yielded adduct **13b** as a

mixture of diastereoisomers at the position C(5). One of the two diastereoisomers of **13b** could be crystallised directly from the mixture. The relative configuration of the cascade products was determined with the help of NOESY-spectra. The *cis*-junction of the two rings was evident from the cross-peaks between the protons at the bridgehead positions. The bicycles are in a half-chair/boat conformation locked by the isopropyl group of the lactam nitrogen (Scheme 8).



11a **12a** $R^1 = CH_3$, $R^2 = H$; **12b** $R^1 = H$, $R^2 = CH_3$ **13a** $R^1 = CH_3$, $R^2 = H$ (19 %); **13b** $R^1 = H$, $R^2 = CH_3$ (12 %)

Scheme 7



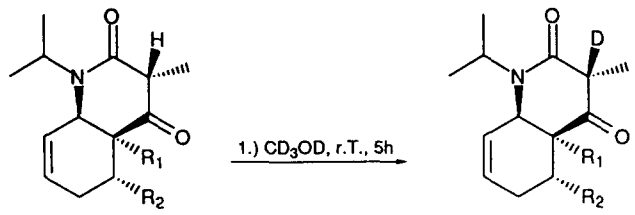
7 **13b**

Scheme 8

The cross-peaks between the methine H at C(3) and the olefinic H at C(8) as well as the cross-peaks between the H at C(8a) and the pseudo-axial H of the methylene group at C(5) are only compatible with such a locked conformation. A further indication for this strong conformational preference came from the deuterium exchange experiment (Scheme 9).

Dissolving the bicyclic products **7**, **13a** and **13b** in deuteromethanol and observing the ^{1}H-NMR spectrum during 5 h at room temperature showed complete exchange of the H at C(3), keeping the configuration at C(3) intact. The isolated product must be the thermodynamically preferred diastereoisomer because the deuteration occurs without any epimerisation at C(3). This observation can be explained assuming a stereoelectronic control of the deprotonation deuteration process starting from the locked conformations shown in Scheme 8.

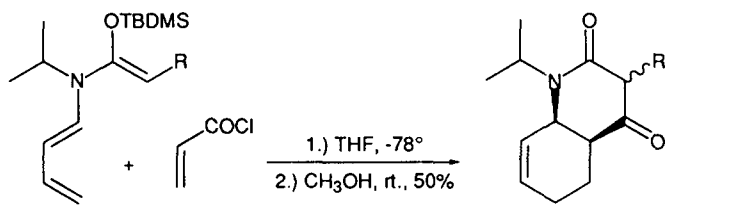
The ketene *N,O-tert*-butyldimethylsilyl acetals **11c,d** also underwent the cascade reaction with acryloyl chloride. The yields of the bicyclic products **14c,d** were considerably lower than in the case of the ketene *N,O-tert*-butyldimethylsilyl acetals **11a** (Scheme 10).



7 $R^1=R^2=H$
13a $R^1=CH_3$, $R^2=H$
13b $R^1=H$, $R^2=CH_3$

Scheme 9

The bicyclic products **14c,d** were obtained as a 2 : 1 mixture of the two diastereoisomers at C(3). The configuration at the ring junction was *cis* as would be expected for the cascade process. The relative configuration of the major diastereoisomer corresponds to the relative configuration observed for **7**. The presence of an aromatic substituent at C(3) certainly increases the acidity of the proton at C(3) which should facilitate the epimerisation at this position. In the deprotonated form the two carbonyl groups and the aromatic ring have to be arranged in one plane in order to allow an optimal overlap with the carbanionic centre at C(3). This creates a strong steric interaction. Therefore either the aromatic ring or the two carbonyl groups have to be twisted out of the plane. This twisted conformation of the deprotonated form is probably responsible for the occurrence of both diastereoisomers at C(3).



11c $R=C_6H_5$
11d $R=C_6H_5pOCH_3$

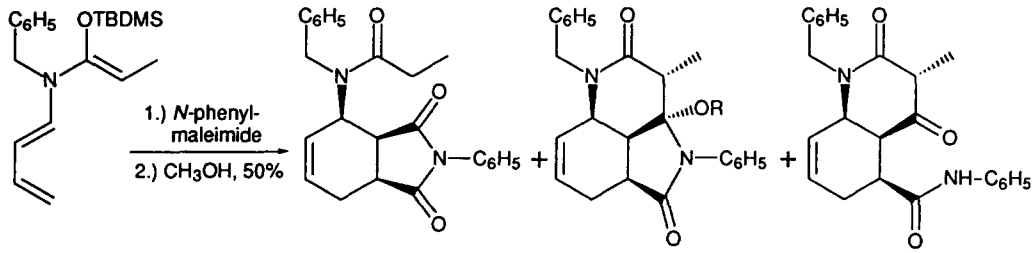
14c $R=C_6H_5$ (19 %)
14d $R=C_6H_5pOCH_3$ (12 %)

Scheme 10

Reaction of the ketene *N,O-tert*-butyldimethylsilyl acetal **11b** with N-phenylmaleimide in THF at rt. yielded, after hydrolysis with methanol, mainly the *Diels-Alder* product **15** obtained from an *endo* selective cycloaddition (38 %). Only small amounts of the bicyclic **17** (10 % yield) and tricyclic **16a** (3 % yield) tandem products could be isolated (Scheme 11). The reaction mixture ketene *N,O-tert*-butyldimethylsilyl acetals **11b** and N-phenylmaleimide had to be heated to reflux in toluene to obtain larger quantities (19 % yield) of the tricyclic cascade product in its silylated form **16b** (Scheme 11).

The following experiments were carried out to obtain information on the reaction sequence. Reacting the ketene *N,O-tert*-butyldimethylsilyl acetals **11a** with benzoyl chloride in THF varying the temperature from -78 °C to reflux, no acylation product could be isolated. However using fumaronitrile as dienophile, the

cycloadduct **18** could be obtained in 62 % yield (Scheme 12). These experiments clearly indicate that the *Diels-Alder* reaction smoothly occurs under the reaction conditions whereas the acylation step needs special conditions (intramolecularisation?).

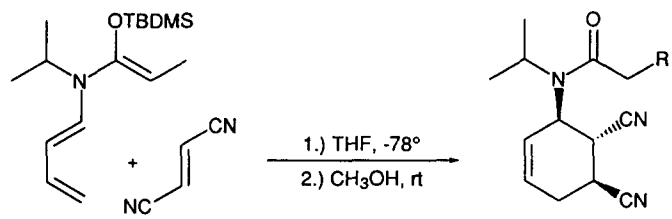


11b **15** **16a** R=H **16b** R=TBDMS **17**

a) rt in THF: **15 : 16a : 17** = 38% : 3% : 10%

a) toluene 110°C: **15 : 16b** = 6% : 19%

Scheme 11



11a **18** (62 %)

Scheme 12

The *trans-trans*-diastereoisomer **18** was the only product isolated. The relative configuration at the three chiral centres was determined with the help of a NOESY-spectrum. The cross peak observed between the protons at C(1) and C(3) can be best explained if the substituents at C(1) and C(3) are in a *cis* position and the six membered ring is in a half chair conformation. Other cross peaks especially between the protons at C(2) and C(3) can be rationalised only if we assume that the six membered ring posses two conformations: a half chair and a boat conformation

In conclusion, a series of *N*-butadienyl-*N*-alkyl amides **10a - d** have been synthesised and a method has been developed to obtain the stable, storable ketene *N,O-tert*-butyldimethylsilyl acetals **11a - d** in excellent yields. These ketene *N,O*-acetals **11a - d** undergo cascade *Diels-Alder* reaction/acylation in good to moderate yields using acryloyl, crotonyl or methacryl chloride. The bicyclic products **7**, **13a,b** and **14c,d** are formed in high chemo- and diastereoselectivity by this cascade process. Model studies indicate that the acylation reaction is probably the rate limiting step of the cascade sequence.

EXPERIMENTAL SECTION

All reagents were of commercial quality if not specially mentioned. The reactions were carried out under argon. Solvents were dried by distillation using the following drying agents: THF (Na), Et_2O (CaH_2), CH_2Cl_2 (CaH_2), MeOH (Mg), EtOH (Mg). Silica Gel 60 (*Merck*) was used for flash-chromatography (FC). Melting points (mp) were determined in open capillary tubes on a *Kofler* melting point apparatus (Thermovar, C. *Reichert* AG, Vienna) and are uncorrected. IR spectra: *Perkin Elmer* 1720 X FT IR spectrophotometer (liquid films between potassium chloride discs or in $CHCl_3$- or CCl_4-solution). NMR spectra: ^1H- and ^{13}C-NMR spectra were measured on a *Bruker* AMX 400 (400 and 100 MHz) or on a *VARIAN* Gemini 200 (200 and 50 MHz). If not otherwise mentioned spectra were measured in $CDCl_3$ with $CHCl_3$ as internal standard. Coupling constants (*J*) are given in Hz. Mass spectra: The HRMS (high resolution mass spectra) were measured on a *Vacuum Generator Micromass 7070E* and on a *NERMAG R30-10* (70 eV) for the rest of the mass spectra; relative peak intensities are given as a percentage of the base peak. Microanalyses were performed in the micro analytical laboratories of *CIBA-GEIGY Ltd.*, Marly/Fribourg.

Starting materials available by literature methods: N-*Isopropyl*-(E)-*2-butene-1-imine* (9a)[30]; N-*Benzyl*-(E)-*2-butene-1-imine* (9b)[30]; (E)-N-*Isopropyl*-N-*propionyl-1-amino-1,3-butadiene* (10a)[31]; (E)-N-*Benzyl*-N-*propionyl-1-amino-1,3-butadiene* (10b)[31].

Typical procedure for the synthesis of *N*-butadienyl-*N*-alkyl amides (10c,d):
A solution of phenylacetyl chloride (12.53 g, 80 mmol) and *N,N*-diethyl aniline (14.9 g, 80 mmol) in toluene (40 ml) was treated dropwise with the imine **9a** (9.0 g, 0.1 mol). After the addition was complete the mixture was stirred over night at rt.. The mixture was filtered over Celite and the residue was washed with toluene (2 × 50 ml). The combined organic layers were combined and washed with 1M aq. HCl solution (2 × 100 ml), sat. aq. $NaHCO_3$ solution (2 × 100 ml) and H_2O (2 × 100 ml). The organic phase was dried ($MgSO_4$) and evaporated under reduced pressure. Distillation (107 °C/ 0.02 Torr) of the residue furnished the dienamide **10c** (9.43 g, 52 %) as a light yellow oil.
(E)-N-*Isopropyl*-N-*phenylacetyl-1-amino-1,3-butadiene* (10c): IR (KBr): ν = 3085, 3065, 3030, 2975, 2935, 1745, 1665, 1635, 1600, 1495, 1455, 1425, 1400, 1345, 1220, 1170, 1000 cm^{-1}. **^1H NMR** (200 MHz, $CDCl_3$): δ = 7.36-7.21 (m, 5H), 6.41-6.22 (br m, 2H), 6.04-5.92 (br t, 1H), 5.19 (d, 1H, *J* = 16.9 Hz), 5.12 (d, 1H, *J* = 11.1 Hz), 4.68 (br sept., 1H, *J* = 6.6 Hz), 3.75 (br s, 2H), 1.19 (d, 6H, *J* = 6.9 Hz). **^{13}C NMR** (50 MHz, $CDCl_3$):δ = 170.6, 135.2, 134.0, 129.4, 129.1, 129.0, 127.2, 117.8, 47.4, 42.7, 20.5. **MS** (EI): *m/z* = 229 (42, M^+), 111 (44), 96 (71), 91 (100), 65 (18), 41 (14). **HRMS** for $C_{15}H_{19}NO$ (M^+) found 229.1467.
(E)-N-*Isopropyl*-N-*(4-methoxy-phenyl)-acetyl-1-amino-1,3-butadiene* (10d): 62 % yield of **10d** purified by filtration over silica gel (EtOAc). **IR** (film): ν = 3065, 2965, 2935, 2835, 1740, 1640, 1625, 1585, 1555, 1515, 1465, 1425, 1340, 1300, 1250, 1180, 1035, 1000, 810 cm^{-1}. **^1H NMR** (400 MHz, DMSO, 373 K): δ = 7.30 and 7.24 (m, 2H), 6.97 (m, 2H), 6.73 (d, 1H, *J* = 14.0 Hz), 6.50 (dxt, 1H, *J* = 17.0, 10.5, 10.3 Hz), 6.17 (dd, 1H, *J* = 14.0, 10.5 Hz), 5.30 (dd, 1H, *J* = 17.0, 1.8 Hz), 5.15 (dd, 1H, *J* = 10.2, 1.8 Hz), 4.64 and 3.98 (sept, 1H, *J* = 6.9), 3.87 and 3.86 (s, 3H), 3.82 and 3.45 (s, 2H), 1.32 and 1.20 (d, 6H, *J* = 6.8 Hz). **^{13}C NMR** (100 MHz, DMSO, 373 K): δ = 169.4, 168.9, 157.8, 157.7, 134.5, 129.4, 129.3, 129.3, 127.1, 121.8, 114.9, 113.6, 113.4, 54.7, 46.4, 41.3, 40.0, 21.8, 19.3. **MS** (EI): *m/z* = 260 (72, M^+ + 1), 259 (73, M^+), 122 (56), 121 (84), 112 (36), 111 (89), 97 (20), 96 (100), 91 (32), 89 (11), 78 (32), 77 (34), 68 (12), 43 (35). **HRMS** for $C_{16}H_{21}NO_2$ (M^+) found 259.1566.

Typical procedure for the synthesis of the ketene-*N,O-tert*-butyldimethylsilyl acetals (11a - d):

In a flamedried three-necked flask fitted with magnetic stirrer, septum, argon bubbler and thermometer, a 1.6M solution of *n*-BuLi (hexane, 3.0 ml, 4.2 mmol) was added dropwise to a solution of anh. $(i\text{-}Pr)_2NH$ (0.6 ml, 4.3 mmol) in dry THF (10 ml) at –78 °C. After addition was complete the mixture was allowed to reach 0 °C and stirred 30 min at this temperature. The mixture was cooled to –78 °C and freshly distilled HMPA (1.0

ml) was added in one stream to the solution. Afterwards a solution the dienamide **10a** (0.47 g, 3.0 mmol) in dry THF (2 ml) was added slowly at the same temperature and stirring was continued for 10 min at –78 °C. To this solution was added dropwise a solution of TBDMSCl (0.51 g, 3.4 mmol) in dry THF (2 ml) at -78 °C. After addition was complete, the mixture was warmed up to rt.. and stirred for 2h . After stirring pentane was added (30 ml) and the resulting solution was washed with water (2 × 10 ml) and with saturated. aq. NaCl solution. (2 × 10 ml). The organic. phase was dried (Na_2SO_4) and the solvent was removed to give pure silyl enol ether **11a** (0.86 g, quant.) as a yellow oil.

(Z)*-N-*[(E)*-*Buta-1,3-dienyl]*-N-*isopropyl-1-[(tert-butyl-dimethylsilyl)-oxy]prop-1-enamine **(11a): IR** (CCl_4): 3085, 3045, 2960, 2930, 2860, 1670, 1630, 1470, 1460, 1320, 1255, 1050, 995 cm^{-1}. **^{1}H NMR** (200 MHz, $CDCl_3$): δ = 6.23 (dxt, 1H, *J* =16.5, 10.6, 10.5), 6.18 (d, 1H, *J* = 14.1), 5.32 (dd, 1H, *J* = 13.7, 10.6 Hz), 4.75 (dd, 1H, *J* = 16.8, 2.2 Hz), 4.53 (dd, 1H, J = 10.3, 2.1 Hz), 4.33 (q, 1H, *J* = 6.7 Hz), 3.59 (sept, 1H, *J* = 6.7 Hz), 1.56 (d, 3H, *J* = 6.7 Hz), 1.22 (d, 6H, *J* = 6.7 Hz), 0.93 (s, 9H), 0.1 (s, 6H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 147.9, 138.1, 138.0, 106.6, 104.1, 99.6, 50.5, 26.4, 20.9, 18.8, 11.7, -3.5. **MS** (EI): *m/z* = 282 (13, M^+ + 1), 281 (19, M^+), 267 (16), 266 (22), 115 (8)), 75 (13), 74 (17), 73 (100).

(Z)*-N-*[(E)*-*Buta-1,3-dienyl]*-N-*benzyl-1-[(tert-butyl-dimethylsilyl)oxy]prop-1-enamine **(11b)** (yellowish oil): **IR** (CCl_4): ν = 3080-3010, 2960, 2950, 2885, 2860, 1670, 1635, 1460, 1425, 1385, 1360, 1330, 1255, 1200, 1060, 995, 885, 840 cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.35-7.19 (m, 5H), 6.66 (d, 1H, *J* =13.7 Hz), 6.26 (dxt, 1H, *J* = 16.7, 10.6 10.2 Hz), 5.19 (dd, 1H, *J* = 13.7, 10.6, Hz), 4.75 (dd, 1H, *J* =16.7, 1.8 Hz), 4.60 (dd, 1H, *J* = 10.2, 1.8 Hz), 4.49 (s, 2H), 4.23 (q, 1H, *J* = 6.7 Hz), 1.58 (d, 3H, *J* = 6.7 Hz), 1.02 (s, 9H), 0.17 (s, 6H).**^{13}C-NMR** (100 MHz, $CDCl_3$): δ = 149.6, 138.4, 137.6,137.4, 129.1, 127.5, 127.3, 108.1, 104.0, 91.0, 50.5, 26.4, 18.9, 11.7, -3.8. **MS** (EI): *m/z* = 329 (17, M^+), 314 (23), 288 (9), 238 (9), 159 (11), 91 (100), 75 (23), 73 (78), 65 (18).

***(Z)*-N-*[(E)*-*Buta-1,3-dienyl]*-N-*isopropyl-1-[(tert-butyl-dimethylsilyl)oxy]-phenyl-ethenamine* (11c)** (yellow oil): The dienamide **10c** (0.69 g, 3.0 mmol) was reacted as described for **10a.** The NMR analysis showed, that only 63 % of the starting material was converted into the silyl enol ether **11c**. Supplementary addition of *n*-BuLi (1.6 M, 3.0 ml, 4.2 mmol) followed by a solution of TBDMSCl (0.51 g, 3.4 mmol) in THF (2 ml) to the reaction mixture at -78 °C with normal workup and extraction as described for **11a** furnished the silyl enol ether **11c** (1.28 g, quantitative) as a yellow oil. **IR** (CCl_4): ν = 3025, 2960, 2930, 2885, 2860, 1630, 1470, 1465, 1390, 1255, 1165, 1115, 840 cm^{-1}. **^{1}H NMR** (200 MHz, $CDCl_3$): δ = 7.53-7.48 (m, 2H), 7.30-7.22 (m, 2H), 7.16-7.08 (m, 1H), 6.31 (dxt, 1H, *J* = 16.9, 10.7, 10.2 Hz), 6.28 (d, 1H, *J* = 13.6 Hz), 5.46 (dd, 1H, *J* = 13.7, 10.6 Hz), 5.33 (s, 1H), 4.81 (dd, 1H, *J* = 16.9, 2.0 Hz), 4.63 (dd, 1H, *J* = 10.2, 1.9 Hz), 3.75 (sept, 1H, *J* = 6.7 Hz), 1.29 (d, 6H, *J* = 6.7 Hz), 0.92 (s, 9H), 0.1 (s, 6H). **^{13}C NMR** (50 MHz, $CDCl_3$): δ = 147.6, 137.1, 136.2, 136.1, 128.3, 127.9, 125.6, 107.3, 105.6, 104.3, 50.5, 25.9, 20.4, 18.2, -3.8. **MS** (EI): *m/z* = 344 (1, M^+ + 1), 266 (1), 118 (3), 115 (23), 114 (12), 96 (13), 91 (33), 90 (13), 75 (23), 74 (11), 73 (100).

***(Z)*-N-*[(E)*-*Buta-1,3-dienyl]*-N-*isopropyl-1-[(tert-butyl-dimethylsilyl)oxy]-p-methoxy-phenylethenamine* (11d)** (yellow oil): **IR** (CCl_4): ν = 3045, 2960, 2930, 2900, 2860, 1740, 1630, 1610, 1585, 1575, 1560, 1510, 1465, 1420, 1390, 1365, 1295, 1250, 1175, 1115, 1025, 1005, 840 cm^{-1}. **^{1}H NMR** (200 MHz, $CDCl_3$): δ = 7.46 (m, 2H), 6.81 (m, 2H), 6.32 (dxt, 1H, *J* = 16.9, 10.7, 10.5 Hz), 6.31 (d, 1H, *J* = 13.7 Hz), 5.43 (dd, 1H, *J* = 13.8, 10.5 Hz), 5.29 (s, 1H), 4.80 (dd, 1H, *J* = 16.8, 1.9 Hz), 4.60 (dd, 1H, *J* = 10.4, 1.8 Hz), 3.80 (s, 3H), 3.73 (sept, 1H, *J* = 6.7 Hz), 1.27 (d, 6H, *J* = 6.7 Hz), 0.97 (s, 9H), 0.06 (s, 6H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 158.3, 147.1, 137.7, 137.2, 130.1, 129.4, 114.1, 107.6, 105.8, 105.1, 51.1, 26.6, 20.9, 18.8, -3.2. **MS** (EI): *m/z* = 374 (16, M + 1^+), 261 (38), 260 (100), 259 (67), 121 (32), 111 (61), 97 (12), 96 (80), 91 (32), 78 (24), 77 (28), 75 (12), 73 (31).

Tandem reactions:

(3*RS,*4a*SR,*8a*RS)-*1,2,3,4,4a,5,6,8a-Octahydro-1-isopropyl-3-methyl-chinoline-2,4-dione **(7)**[2,3]: In a flamedried three-necked flask fitted with magnetic stirrer, septum, argon bubbler and thermometer a solution of silyl enol ether **11a** (0.8 g, 2.9 mmol) in dry THF (15 ml) was treated dropwise with acryloyl chloride (0.3 ml, 3.5 mmol) at –78 °C. After addition was complete the mixture was stirred for 2h at this temperature and allowed over night to reach rt.. The mixture was hydrolysed with MeOH (5 ml) and the solvent was removed by evaporation under reduced pressure. The residue was dissolved in $CHCl_3$ (40 ml) and washed with 1M aq. HCl solution. (2 × 20 ml) and with saturated aq. NaCl solution (2 × 20 ml). The organic layer was dried

(Na_2SO_4) and the solvent was removed to liberate the crude material, which was purified by flash column chromatography on silica gel (EtOAC/hexane, 1:1) to furnish the product **7** (0.32 g, 50 %) as a yellow oil which could be crystallised. (m p 79 °C; Lit. 80 °C[23]).

(3RS,4aSR,8aRS)-1,2,3,4,4a,5,6,8a-Octahydro-1-isopropyl-3-methyl-4a-methyl-chinoline-2,4-dione **(13a):** A solution of silyl enol ether **11a** (0.81 g, 2.9 mmol) and methacryloyl chloride (0.6 ml, 6.3 mmol) in THF (15 ml) was reacted and worked up as described for **7** to give **13a** (130 mg, 19 %) after flash chromatography on silica gel (EtOAc/hexane, 1:1). R_f: 0.39 (EtOAc/hexane = 1:1); **IR** (KBr): ν = 2975, 2940, 2875, 1720, 1640, 1450, 1375, 1320, 1260, 1210, 1180, 1130, 1070, 1030 cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 5.84 (m, 1H), 5.54 (m, 1H), 4.94 (sept, 1H, *J* = 6.9 Hz), 3.89 (m, 1H), 3.42 (q, 1H, *J* = 6.9 Hz), 2.31-2.26 (m, 1H), 2.01-1.94 (m, 2H), 1.63-1.56 (m, 1H), 1.26 (d, 3H, *J* = 6.9 Hz), 1.22 and 1.14 (d, 6H, *J* = 6.9 Hz), 1.06 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 211.2, 168.0, 131.8, 128.7, 55.2, 51.4, 46.5, 45.4, 33.2, 25.3, 23.1, 21.2, 20.8, 9.3. **MS** (EI): *m/z* = 236 (30, M^+ + 1), 235 (93, M^+), 220 (54), 207 (16), 192 (26), 151 (23), 150 (15), 136 (17), 126 (31), 121 (46), 113 (21), 98 (49), 95 (16), 94 (100), 93 (50), 91 (55), 85 (12), 83 (19), 79 (100), 70 (49), 69 (19), 58 (83). **HRMS** for $C_{14}H_{21}NO_2$ (M^+) found 235.1673.

(3RS,4aSR,5RS,8aRS)-1,2,3,4,4a,5,6,8a-Octahydro-1-isopropyl-3-methyl-5-methyl-chinoline-2,4-dione **(13b):** A solution of silyl enol ether **11a** (0.81 g, 2.9 mmol) and crotonyl chloride (0.6 ml, 6.3 mmol) in THF (15 ml) was reacted and worked up as described for **7** to give a diastereoisomeric mixture **13b** (81 mg, 12 %) after flash chromatography on silica gel (EtOAc/hexane, 1:1). From this mixture one diastereoisomer **13b** was purified by recrystallisation. Spectroscopic data of the pure diastereoisomer **13b** (deliquescent crystals): R_f: 0.50 (EtOAc/hexane = 1:1). **IR** (CCl_4): ν = 2975, 2875, 1725, 1665, 1550, 1435, 1255, 1210, 1065, 1005, 980 cm^{-1}. **^{1}H NMR** (200 MHz, $CDCl_3$): δ = 5.80 (*m*, 1H), 5.60 (m, 1H), 4.99 (sept. 1H, *J* = 6.9 Hz), 4.23 (m, 1H), 3.51 (m, 1H), 2.73 (m, 1H), 2.26 (m, 1H), 2.17-2.04 (m, 1H), 1.78-1.64 (m, 1H), 1.27 (d, 3H, *J* = 6.7 Hz), 1.25 (d, 3H, *J* = 6.9 Hz), 1.16 (d, 3H, *J* = 7.3 Hz), 1.13 (d, 3H, *J* = 6.7 Hz). **^{13}C-NMR** (50 MHz, $CDCl_3$): δ = 208.3, 167.6, 129.6, 126.3, 51.7, 51.4, 44.9, 44.6, 29.5, 27.7, 20.4, 19.9, 19.1, 8.0. **MS** (EI): *m/z* = 236 (31, M^+ + 1), 235 (52, M^+), 220 (20), 192 (29), 172 (62), 167 (20), 150(11), 130 (32), 121 (17), 98 (34), 96 (13), 94 (91), 93 (45), 91(47), 79 (93), 77 (65), 73 (20), 70 (57), 69 (53), 58 (100). **HRMS** for $C_{14}H_{21}NO_2$ (M^+) found 235.1572.

(3RS,3SR,4aSR,8aRS)-1,2,3,4,4a,5,6,8a-Octahydro-1-isopropyl-3-phenyl-chinoline-2,4-dione **(14c)**[23]: A solution of silyl enol ether **11c** (0.53 g, 1.53 mmol) and acryloyl chloride (0.22 ml, 2.5 mmol) in THF (15 ml) was reacted and worked up as described for **7** to give **14c** (130 mg, 30 %) after flash chromatography on silica gel (EtOAc/hexane, 1:1). R_f: 0.41 (EtOAc/hexane = 1:1). **^{1}H NMR** (200 MHz, $CDCl_3$): δ = 7.41-7.11 (*m*, 5H), 6.01-5.92, 5.79-5.69 and 5.61-5.42, (*m*, 2H), 4.99 (*sept.*, 1H, J = 6.8 Hz), 4.72 and 4.38 (*s*, 1H), 4.42-4.25 (*m*, 1H), 2.81-2.71 (*m*, 1H), 2.53-2.41 (*m*, 1H), 2.09-1.72 (*m*, 3H), 1.27 and 1.23 (*d*, 6H, J = 6.9 Hz). The ratio of the diastereoisomers is 70:30. **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 206.5, 206.1, 168.7, 166.8, 135.0, 133.9, 132.3, 131.2, 130.9, 128.9, 128.8, 128.8, 128.7, 128.3, 128.0, 64.5, 61.9, 49.9, 48.7, 47.3, 47.0, 46.5, 46.1, 24.3, 22.3, 21.5, 21.0, 20.8, 20.7, 20.6. **MS** (EI): *m/z* = 283 (6, M^+), 198 (16), 119 (9)), 118 (100), 91 (15), 90 (53), 89 (23), 80 (23), 79 (34), 77 (24).

(3RS,3SR,4aSR,8aRS)-1,2,3,4,4a,5,6,8a-Octahydro-1-isopropyl-3-p-methoxy-phenyl-chinoline-2,4-dione **(14d):** A solution of silyl enol ether **11d** (0.68 g, 1.82 mmol) and acryloyl chloride (0.41 ml, 4.6 mmol) in THF (15 ml) was reacted and worked up as described for **7** to give **14d** (124 mg of a yellowish oil as a 2 : 1 mixture of the 2 diastereoisomers, 22 %) after flash chromatography on silica gel (EtOAc/hexane, 1:1). R_f: 0.29 (EtOAc/hexane = 1:1). **IR** (CCl_4): ν = 3035, 2975, 2960, 2935, 1730, 1665, 1620, 1550, 1515 1430, 1300, 1250, 1210, 1180, 1040, 1005, 980 cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.12 and 6.91 (d, 2H), 6.87 and 6.72 (d, 2H), 5.95-5.92 and 5.50-5.41 (*m*, 1H), 5.72-5.68 and 5.54-5.50 (*m*, 1H), 4.95 (sept, J = 6.8 Hz), 4.62 and 4.27 (*s*, 1H), 4.36-4.33 and 4.28-4.25 (*m*, 1H), 3.78 and 3.74 (*s*, 3H), 2.75-2.69 (*m*, 1H), 2.49-2.41 (*m*, 1H), 2.12-1.71 (*m*, 3H), 1.30, 1.27, 1.25 and 1.21 (*d*, 6H, J = 6.9 Hz). **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 206.8, 206.4, 168.9, 167.1, 159.5, 159.4, 132.3, 132.2, 130.9, 130.1, 129.9, 128.4, 127.2, 125.9, 114.5, 114.4, 63.9, 61.2, 55.8, 50.0, 48.8, 47.3, 47.2, 46.5, 46.1, 24.5, 22.4, 21.5, 21.1, 20.9, 20.7, 20.6. **MS** (EI): *m/z* =314 (5, M^+), 148 (100), 121 (7), 120 (23), 91 (21), 77 (9).

(1SR, 2RS, 3RS)-1,2-Dinitril-3-(N-propionyl-N-isopropyl-amino)cyclohex-4-en **(18):** To a solution of the silyl enol ether **11a** (0.41 g, 1.46 mmol) in THF (15 ml) fumaronitrile (0.18 g, 2.3 mmol) in 2 ml THF was added at -78°C. After the addition the solution was slowly warmed to rt. and stirred for 36 h. Hydrolysis with MeOH (10 ml), removal of the solvent in the rotavap and chromatography over a silica gel column

(EtOAc/hexane = 1:1) yielded 0.22 g (62 %) of the crystalline product **18**. **mp**: 101-102 °C. R_f: 0.25 (EtOAC/hexane = 1:1) **IR**(KBr): 2970*m*, 2940*m*, 2900*m*, 2245*m*(CN); 1635*s*(C=O); 1475*m*, 1435*m*, 1375*m*, 1350*m*, 1330*m*, 1310*m*, 1300*m*, 1290*m*, 1195*m*, 1165*m*, 1075*m*.. **^{1}H-NMR** (200 MHz, $CDCl_3$): δ = 5.74 (*dxm*, 1H), 5.44 (*dxq*, 1H); 4.47 (br.*t*, J = 10.8 Hz, 1H); 4.17 (*sept.* 1H, J(=6.6 Hz); 3.89 (br.*m*, 1H); 3.09 (*dxt*, 1H, J = 12.2, 8.4 Hz); 2.57 (*m*, 2H); 2.49 (*dxq*, 1H, J = 16.7, 7.8 Hz,) 2.36 (*dxq*, 1H, J = 16.4, 7.4 Hz); 1.39 and 1.22 (2x*d*, 2x3H, J = 6.8 Hz); 1.14 (*t*, 3H, J = 7.3 Hz). **^{13}C-NMR**(100MHz, $CDCl_3$): δ = 175.0; 129.4; 125.1; 119.3; 118.9; 52.0; 49.4; 31.9; 30.5; 28.5; 22.3; 22.2; 9.7. **MS**(EI): 246 (6, $[M + 1]^+$), 245 (16, $[M]^+$), 202 (14), 174 (24), 140 (16), 111 (43), 104 (16), 96 (29), 77 (13), 58 (14), 57 (100). Anal. calc. for $C_{14}H_{19}N_3O$: C 68.53, H 7.82, N 17.12; found C 67.81, H 7.81, N 16.91.

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