Modification of the Tiemann Rearrangement: One-Pot Synthesis of *N*,*N*-Disubstituted Cyanamides from Amidoximes

Stanislav A. Bakunov,[a#] Alexey V. Rukavishnikov,[b‡] Alexey V. Tkachev*[c]

[a] Novosibirsk State University, Novosibirsk 630090, Russia

[b] Novosibirsk Institute of Organic Chemistry, Novosibirsk 630090, Russia

[c] Novosibirsk State University, Novosibirsk Institute of Organic Chemistry, 9 Acad. Lavrentjev Ave., Novosibirsk, 630090, Russia

Fax +7(3832)344752; E-mail: atkachev@nioch.nsc.ru

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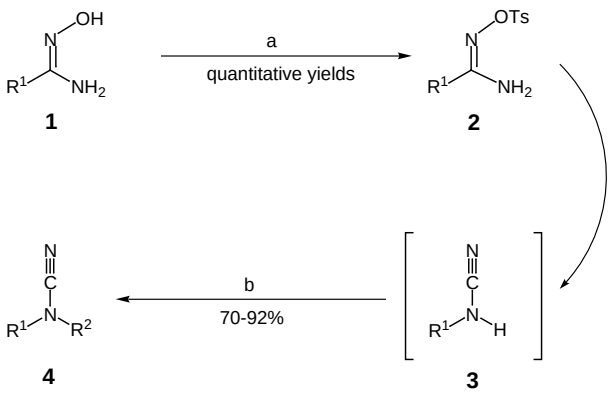
Abstract: A three-stage one-pot synthetic procedure for transformation of amidoximes to *N*,*N*-disubstituted cyanamides in 70−92% yield is described.

Key words: Tiemann rearrangement, phase-transfer catalysis, amidoximes, cyanamides, alkylations

Cyanamides (RR'N−C≡N) have been widely employed as intermediates in organic synthesis and as biomolecules precursors. The CN-group can be easily removed from a cyanamide, and hence it can be used as a protective group in the syntheses of secondary and tertiary amines.[1,2] On the other hand, transformation of the CN-group leads to different classes of organic compounds such as ureas, carbamates, heterocycles, etc.[3,4] Direct alkylation of cyanamide[1] or its salts,[5] including the alkylation under phase-transfer conditions,[6] as well as reaction of phosgene imminium salts with ammonia[7] are the simplest methods for the preparation of substituted cyanamides.

However, despite of conciseness and simplicity of the reactions cited, these methods are not suitable for preparation of the most attractive non-symmetrical cyanamides (RR'N−C≡N, R≠R'). The latter compounds can be obtained by treatment of tertiary or secondary amines with cyanohalides.[8] Among the other possible approaches to the non-symmetrical cyanamides, the following methods should be mentioned: cyanation of halogen amines,[9] treatment of secondary amines with 1-cyanobenzotriazole,[10] and dehydration of *N*,*N*-disubstituted ureas.[11]

In this paper we report a mild and convenient procedure for the conversion of amidoximes to *N*,*N*-disubstituted cyanamides with the loss of one carbon atom from the amidoxime molecule. We focused on the Tiemann rearrangement[12] to generate the crucial monosubstituted cyanamides that were alkylated afterwards. When heated with arylsulfonyl halides in a pyridine solution followed by acidic hydrolysis, amidoximes are known to form monosubstituted ureas as a result of the Tiemann rearrangement, cyanamides being the stable intermediates in this reaction. Despite their high lability in acidic media, cyanamides remain invariable under basic conditions at pH >10 due to deprotonation and formation of cyanamide anion.[13] We have found that formation of monosubstituted cyanamides was possible under the action of a base in the two-phase system in presence of a phase-transfer catalyst. This allowed us to develop the three-stage one-pot synthetic procedure from amidoximes to *N*,*N*-disubstituted cyanamides. A solution of an amidoxime and triethylamine in CH_2Cl_2 is treated with an equimolar amount of TsCl followed by addition of an alkyl halide, 30% aqueous solution of NaOH and phase-transfer catalyst followed by reflux. At the first stage of the reaction sequence, an amidoxime **1** is transformed to the corresponding *O*-tosylated derivative **2** which is then rearranged (Tiemann rearrangement) to give the monosubstituted cyanamide **3**. Alkylation of **3** under phase-transfer conditions affords the *N*,*N*-disubstituted non-symmetrical cyanamide **4** (Scheme 1).



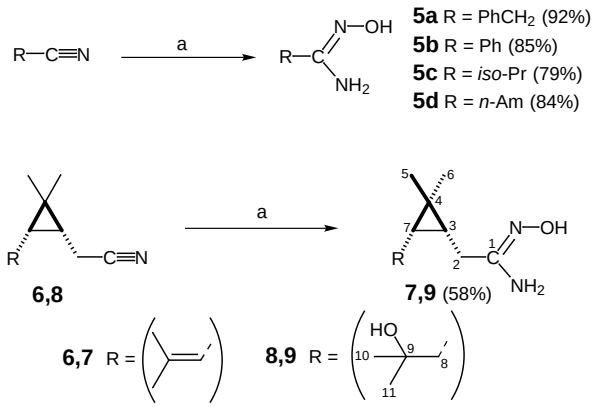
Reagents and conditions: a) $TsCl/Et_3N/CH_2Cl_2$, 0 °C; b) R^2-Hal/30% aq $NaOH/Et_3N^+CH_2PhCl^-$, reflux

Scheme 1

We found a number of aromatic, aliphatic and terpenic amidoximes can be easily converted in good yields (40−90%) to disubstituted cyanamides. The one-pot version of the synthetic pathway was found to be the most suitable one because many *O*-tosyl derivatives of amidoximes and some cyanamides **3** are too unstable for isolation.

To study the new reaction sequence we have synthesized a number of amidoximes of different structures: (a) the simplest aliphatic and aromatic amidoximes without additional functions, (b) amidoximes of *seco*-terpenic nature having additional functions or labile groups (cyclopropyl group, carbon-carbon double bond, hydroxy and keto groups). Two different methods were used to prepare

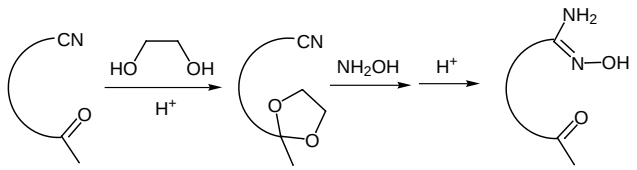
starting amidoximes. Scheme 2 shows the formation of the amidoximes by the addition of hydroxylamine to nitriles.



Reagents and conditions: a) NH_2OH•HCl/Na_2CO_3/95% aq EtOH, reflux, 21 h
The numbering of the C-atoms does not coincide with the numbering of the system according to IUPAC and is given for NMR interpretation only.

Scheme 2

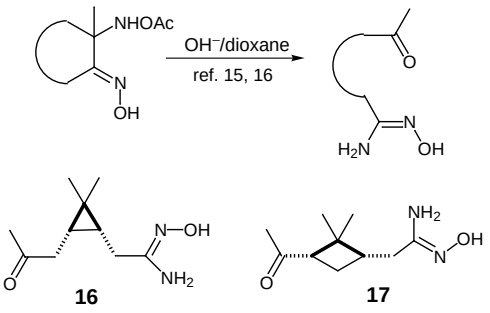
In the case of oxonitriles, protection of the carbonyl group is required prior to the addition of hydroxylamine (Scheme 3).



Scheme 3

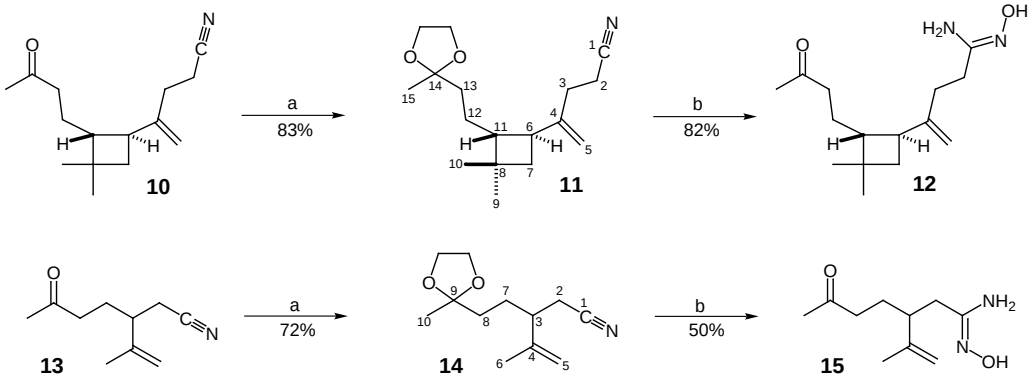
Due to the presence of carbon-carbon double bonds capable of migration in the molecules **10** and **13**, we used pyridinium chloride[14] instead of traditionally applied *p*-toluenesulfonic acid, to prepare 1,3-dioxalane derivatives **11** and **14** from the corresponding oxonitriles of *seco*-limonene and *seco*-caryophyllene types (Scheme 4).

The second method is the based-promoted cleavage of *O*-acylated α-hydroxylamino oximes (Scheme 5). Derivatives of seco-pinane type **17**[15] and seco-carane type **16**[16] were prepared by this method.



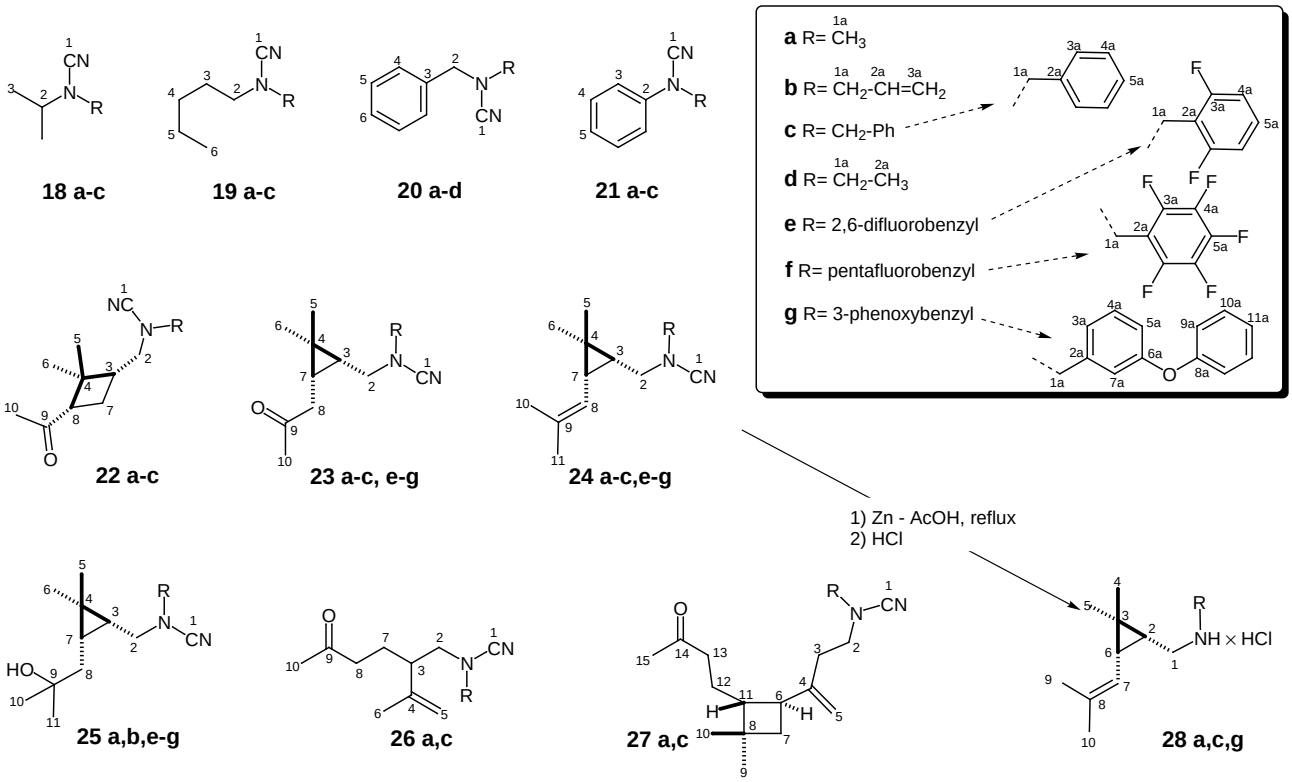
Scheme 5

A number of amidoximes listed above were used in the one-pot syntheses of *N*,*N*-disubstituted cyanamides. Testing of different alkyl halides as alkylating agents at the stage of transformation of unsubstituted cyanamides to the *N*,*N*-disubstituted ones shows that only the most active alkyl halides (methyl iodide and ethyl bromide, allyl and benzyl halides) are suitable for the reaction. Our attempts to use other alkyl halides (primary and secondary alkyl chlorides, bromides and iodides) resulted in poor yields of the corresponding disubstituted cyanamides, although alkylation of monosubstituted cyanamides with these halides under phase transfer conditions was reported.[6] The list of *N*-disubstituted cyanamides synthesized is shown in Scheme 6.



Reagents and conditions: a) $HOCH_2CH_2OH$/Py•HCl, reflux in benzene, 5−7 h; b) NH_2OH•HCl/Na_2CO_3/95% aq EtOH, reflux, 21 h
The numbering of the C-atoms does not coincide with the numbering of the systems according to IUPAC and are given for NMR interpretation only.

Scheme 4



The numbering of the C-atoms does not coincide with the numbering of the systems according to IUPAC and are given for NMR interpretation only.

Scheme 6

The method developed is useful for the preparation of different non-symmetric *N*,*N*-disubstituted cyanamides. For example, the method allowed us to prepare easily *N*,*N*-disubstituted (1*R*)-*cis*-chrysanthemyl amine derivatives **28a**, **28c** and **28g**, which are of interest because of their insecticidal properties.

Yields, melting points, optical rotations and analytical data (obtained both by HRMS and combustion analysis) for the new compounds are listed in Table 1. IR, MS and NMR spectral data for the compounds synthesized are listed in Table 2.

Melting points were determined using a Kofler hot-stage. IR spectra were recorded on a Specord M-80 spectrophotometer. ^{1}H and ^{13}C NMR spectra were recorded for 5-10% solutions on a Bruker AC 200 spectrometer (200.13 MHz for ^{1}H, 50.32 MHz for ^{13}C and 188.28 MHz for ^{19}F). Proton and carbon chemical shifts were calculated relative to the solvent signals used as the internal standards: δ_H = 7.24 ($CDCl_3$) and 3.31 (CD_3OD); δ_C = 76.90 ($CDCl_3$) and 49.00 (CD_3OD), whereas ^{19}F chemical shifts are based relative to the internal standard (C_6F_6, δ_F = 0.00). Optical rotations were measured on a Polamat A polarimeter at 20−23 °C for solutions in $CHCl_3$. MS spectra were recorded on a Finnigan MAT 8200 mass spectrometer using electron impact ionization technique (70 eV). Elemental analyses were performed using a Hewlett Packard 185 and Carlo Erba 1106 analyzers. All reagents and solvents were of commercial quality. Petroleum ether refers to the fraction that boiled in the range 40−70 °C. Preparative chromatography was performed on a silica gel column (100−200 mesh) and the solvents used as eluents were distilled prior to use.

Preparation of Amidoximes from Nitriles; General Procedure

Method A, Addition of Hydroxylamine to Nitriles: Powdered Na_2CO_3 (1.0 g, 9.4 mmol) and NH_2OH•HCl (0.65 g, 9.4 mmol) were added to a solution of a nitrile (7.2 mmol) in 95% aq EtOH (40 mL) and the reaction mixture was stirred under reflux for 7 h. An additional amount of Na_2CO_3 (0.5 g) and NH_2OH•HCl (0.33 g) were added and the mixture was stirred under reflux for 7 h. Additional portions of Na_2CO_3 and NH_2OH•HCl (as indicated above) were added and the mixture was stirred under reflux for 7 h more. The mixture was cooled to r.t., filtered, and concentrated in vacuum. The residue was treated with Et_2O (30 mL) and 1 M aq HCl (3 × 15 mL), the aqueous phase was separated, neutralized with ammonia, saturated with NaCl and extracted with Et_2O (2 × 15 mL). The combined extracts were dried ($MgSO_4$) and concentrated at reduced pressure to give the crude product, which was then purified by column chromatography (silica gel, Et_2O/light petroleum).

The treatment of the simplest nitriles, phenylacetonitrile, benzonitrile, 3-methylbutyronitrile and hexanenitrile, afforded corresponding amidoximes as yellowish viscous oils: *N*-hydroxy-2-phenylacetamidine (**5a**, yield 92%), *N*-hydroxybenzamidine (**5b**, 85%), *N*-hydroxyisobutyramidine (**5c**, 79%), *N*-hydroxyhexanamidine (**5d**, 84%). All the above amidoximes gave satisfactory microanalyses: C±0.35%, H±0.39%, N±0.38%.

Homochrysanthemyl amidoxime **7** was synthesized from the corresponding nitrile **6** as reported earlier.[17] *N*-Hydroxy-2-[3-(2-hydroxy-2-methylpropyl)-2,2-dimethylcyclopropyl]acetamidine (**9**) was prepared by the above method from the corresponding hydroxy

Table 1 Yields, Melting Points, Optical Rotation, HRMS and Analytical Data for the New Compounds.

Product[a]	Yield (%)	mp (solvent)	$[\alpha]_{578}$ ($CHCl_3$)	Molcular Formula	HRMS (M^+)	
					Found	Calcd
9	58	80–82 °C (95% aq EtOH)	–24.0 (*c* = 3.33)	$C_{11}H_{22}N_2O_2$	197.1637[b]	197.1654[b]
11	83	oil	+74.0 (*c* = 5.43)	$C_{17}H_{27}NO_2$	277.2044	277.2042
12	82	oil	+71.3 (*c* = 8.27)	$C_{15}H_{26}N_2O_2$	249.1975[b]	249.1967[b]
14	72	oil	–	$C_{12}H_{19}NO_2$	209.1417	209.1416
15	50	oil	–	$C_{10}H_{18}N_2O_2$	181.1352[b]	181.1341[b]
18a	85	oil	–	$C_5H_{10}N_2$	98.0848	98.0844
18b	89	oil	–	$C_7H_{12}N_2$	124.1002	124.1000
18c	70	oil	–	$C_{11}H_{14}N_2$	174.1156	174.1157
19a	85	oil	–	$C_7H_{14}N_2$	126.1158	126.1157
19b	80	oil	–	$C_9H_{16}N_2$	152.1301	152.1313
19c	81	oil	–	$C_{13}H_{18}N_2$	202.1466	202.1470
20a	90	oil	–	$C_9H_{10}N_2$	146.0848	146.0844
20b	90	oil	–	$C_{11}H_{12}N_2$	172.1003	172.1001
20c	92	38–41 °C (hexane/EtOAc)	–	$C_{15}H_{14}N_2$	222.1163	222.1157
20d	85	oil	–	$C_{10}H_{12}N_2$	160.0988	160.1001
21a	88	oil	–	$C_8H_8N_2$	132.0688	132.0687
21b	91	oil	–	$C_{10}H_{10}N_2$	158.0836	158.0844
21c	92	oil	–	$C_{14}H_{12}N_2$	208.1010	208.1000
22a	75	oil	+10.8 (*c* = 3.33)	$C_{11}H_{18}N_2O$	194.1417	194.1419
22b	79	oil	+9.0 (*c* = 2.90)	$C_{13}H_{20}N_2O$	220.1570	220.1576
22c	70	oil	+7.1 (*c* = 3.95)	$C_{17}H_{22}N_2O$	270.1734	270.1732
23a	87	oil	–5.0 (*c* = 10.4)	$C_{11}H_{18}N_2O$	194.1421	194.1419
23b	82	oil	–8.7 (*c* = 8.26)	$C_{13}H_{20}N_2O$	220.1576	220.1576
23c	83	oil	–8.9 (*c* = 6.27)	$C_{17}H_{22}N_2O$	270.1743	270.1732
23e	82	oil	–6.6 (*c* = 3.35)	$C_{17}H_{20}N_2OF_2$	306.1484	306.1544
23f	84	oil	–9.1 (*c* = 5.15)	$C_{17}H_{17}N_2OF_5$	360.1264	360.1261
24a	81	oil	+71.5 (*c* = 4.00)	$C_{12}H_{20}N_2$	192.1629	192.1626
24b	84	oil	+56.7 (*c* = 5.64)	$C_{14}H_{22}N_2$	218.1783	218.1783
24c	75	oil	+49.3 (*c* = 5.12)	$C_{18}H_{24}N_2$	268.1942	268.1939
24e	79	oil	+43.1 (*c* = 4.50)	$C_{18}H_{22}N_2F_2$	304.1750	304.1751
24f	82	oil	+40.8 (*c* = 4.44	$C_{18}H_{19}N_2F_5$	358.1467	358.1468
25a	78	oil	+16.1 (*c* = 2.12	$C_{12}H_{22}N_2O$	210.1733	210.1732
25b	73	oil	+14.7 (*c* = 1.90)	$C_{14}H_{24}N_2O$	236.1887	236.1889

Table 1 (continued)

Product[a]	Yield (%)	mp (solvent)	$[\alpha]_{578}$ ($CHCl_3$)	Molcular Formula	HRMS (M^+) Found	HRMS (M^+) Calcd
25e	77	63–65 °C (EtOAc/hexane)	+15.2 (*c* = 2.24)	$C_{18}H_{24}N_2OF_2$	322.1856	322.1856
25f	80	oil	+14.7 (*c* = 1.88)	$C_{18}H_{21}N_2OF_5$	376.1575	376.1574
26a	72	oil	–	$C_{11}H_{18}N_2O$	194.1420	194.1419
26c	70	oil	–	$C_{17}H_{22}N_2O$	270.1743	270.1732
27a	78	oil	–	$C_{16}H_{26}N_2O$	262.2049	262.2045
27c	70	oil	+60.1 (*c* = 9.76)	$C_{22}H_{30}N_2O$	338.2365	338.2358
28a	81	218–220 °C (EtOAc/MeCN)	+74.1 (*c* = 0.43)	$C_{11}H_{22}NCl$	–	–
28c	83	204–206 °C (EtOAc/MeCN)	+60.2 (*c* = 1.29)	$C_{17}H_{26}NCl$	–	–
28g	68	143–145 °C (EtOAc/MeCN)	+42.8 (*c* = 2.15)	$C_{23}H_{30}NOCl$	–	–

[a] Satisfactory microanalyses obtained: C±0.5, H±0.4, ±0.5.
[b] The molecular ion has insufficient intensity, so the analysis was carried out for the ion $M^+ - OH$.

nitrile **8**.[18] 4-[(1*S*,2*R*)-3,3-Dimethyl-2-(3-oxobutyl)cyclobutyl]-*N*-hydroxypent-4-enamidine (**12**) and (±)-*N*-Hydroxy-4-methyl-3-(3-oxobutyl)pent-4-enamidine (**15**) were prepared from the protected compounds **11** and **14**, correspondingly.

4-{(1*S*,2*R*)-3,3-Dimethyl-2-[2-(2-methyl-1,3-dioxolan-2-yl)ethyl]cyclobutyl}-pent-4-enenitrile (11)

Method A, Using Py•HCl: A solution of **10**[19] (9.33 g, 40 mmol), ethylene glycol (4.5 mL, 80 mmol) and Py•HCl (0.5 g, 4.8 mmol) in benzene (120 mL) was allowed to reflux with a Dean−Stark water separator until the starting ketone had disappeared (5−7 h). The solvent was removed under reduced pressure and the residue was taken up into Et_2O (50 mL). The ethereal extract was then washed with 1 M HCl (10 mL), 0.5 M aq Na_2CO_3 solution (10 mL), brine (10 mL), and dried ($MgSO_4$). The solvent was removed in vacuum and the crude product was then purified by column chromatography to give **11** (9.20 g, 83%) as a viscous colorless oil.

(±)-4-Methyl-3-[2-(2-methyl-1,3-dioxolan-2-yl)-ethyl]-pent-4-enenitrile **(14)** was prepared by the same method from the corresponding keto nitrile **13** whose synthesis was described in Ref.[19]

Method B, Base-Promoted Cleavage of O-Acylated α-Hydroxyamino Oximes: Keto amidoximes **17** and **16** were prepared from α-pinene ($[\alpha]_D$ +20.0) and 3-carene ($[\alpha]_D$ +16.0) via the corresponding monoacylated derivatives according to Ref.[15,16]

Preparation of Cyanamides from Amidoximes; General Procedure

A solution of TsCl (0.92 g, 4.8 mmol) in CH_2Cl_2 (15 mL) was added dropwise during 1 h to a cooled (0 °C) stirred solution of an amidoxime (4.8 mmol) and Et_3N (0.7 mL, 4.8 mmol) in CH_2Cl_2 (15 mL). The reaction mixture was allowed to warm to r.t. and stirred for 1 h more. An alkyl halogenide (9.6 mmol, 2 equiv), 30% aq solution of NaOH (20 mL) and $BzEt_3NCl$ (0.05 g) were added and the mixture was stirred under reflux for 1 h, then cooled to r.t., poured into H_2O (50 mL), and extracted with CH_2Cl_2 (2 × 15 mL). The combined organic extracts were washed with H_2O (15 mL), 1 M aq HCl (15 mL), 0.5 M aq Na_2CO_3 solution (15 mL), brine (15 mL) and dried (Na_2SO_4). The solvent was removed under reduced pressure to give the crude product which was then chromatographed (silica gel, 5→20% Et_2O in light petroleum) to give an analytical sample of the corresponding *N*-substituted *N*-cyanamide.

The following *N*,*N*-disubstituted *N*-cyanamides were prepared according to this procedure:

Isopropylmethylcyanamide (**18a**), allylisopropylcyanamide (**18b**), benzylisopropylcyanamide (**18c**), methylpentylcyanamide (**19a**), allylpentylcyanamide (**19b**), benzylpentylcyanamide (**19c**), benzylmethylcyanamide (**20a**), allylbenzylcyanamide (**20b**), dibenzylcyanamide (**20c**), benzylethylcyanamide (**20d**), methylphenylcyanamide (**21a**), allylphenylcyanamide (**21b**), benzylphenylcyanamide (**21c**), [(1*R*,3*S*)-3-acetyl-2,2-dimethylcyclobutylmethyl]methylcyanamide (**22a**), [(1*R*,3*S*)-3-acetyl-2,2-dimethylcyclobutylmethyl]allylcyanamide (**22b**), [(1*R*,3*S*)-3-acetyl-2,2-dimethylcyclobutylmethyl]benzylcyanamide (**22c**), [(1*R*,3*S*)-2,2-dimethyl-3-(2-oxopropyl)cyclopropylmethyl]methylcyanamide (**23a**), allyl[(1*R*,3*S*)-2,2-dimethyl-3-(2-oxopropyl)cyclopropylmethyl]-cyanamide (**23b**), benzyl[(1*R*,3*S*)-2,2-dimethyl-3-(2-oxopropyl) [(1*R*,3*S*)-2,2-dimethyl-3-(2-oxopropyl)cyclopropylmethyl]cyanamide (**23e**), [(1*R*,3*S*)-2,2-dimethyl-3-(2-oxopropylcyclopropylmethyl]pentafluorophenylmethylcyanamide (**23f**), [(1*R*,3*S*)-2,2-dimethyl-3-(2-oxopropyl)cyclopropylmethyl]-(3-phenoxybenzyl)-cyanamide (**23g**, yield 80%, described earlier[17]), [(1*R*,3*S*)-2,2-dimethyl-3-(2-methylpropenyl)cyclopropylmethyl]methylcyanamide (**24a**), allyl[(1*R*,3*S*)-2,2-dimethyl-3-(2-methylpropenyl)cyclopropylmethyl]cyanamide (**24b**), benzyl[(1*R*,3*S*)-2,2-dimethyl-3-(2-methylpropenyl)cyclopropylmethyl]cyanamide (**24c**), (2,6-difluorobenzyl)-[(1*R*,3*S*)-2,2-dimethyl-3-(2-methylpropenyl)cyclopropylmethyl]cyanamide (**24e**), [(1*R*,3*S*)-2,2-dimethyl-3-(2-methylpropenyl)cyclopropylmethyl]pentafluorophenylmethylcyanamide (**24f**), [(1*R*,3*S*)-2,2-dimethyl-3-(2-methylpropenyl)cyclopropylmethyl]-(3-phenoxy-benzyl)cyanamide (**24g**, yield 82%, described earlier[17]), [(1*R*,3*S*)-3-(2-hydroxy-2-methylpropyl)-2,2-dimethylcyclopropylmethyl]methylcyanamide (**25a**), allyl[(1*R*,3*S*)-3-(2-hydroxy-2-methylpropyl)-2,2-dimethylcyclopropylmethyl]cyan-

Table 2 IR, MS and NMR Spectral Data for the Compounds Synthesized

Product	IR ($CHCl_3$) ν (cm^{-1})	MS *m/z* (%)	^1H NMR[a,b] δ, *J*, $W_{1/2}$ (Hz)	^{13}C NMR[a,c] δ, *J* (Hz)
9	3505 (OH), 3478, 3400 (NH_2), 1658 (C=N), 1605, 1365, 1147	197 (2, M^+ – OH), 155 (100), 81 (48), 69 (35), 43 (86)	0.68–0.85 (m, 2 H, 3-H and 7-H), 0.87 (s, 6-H_3), 1.03 (s, 5-H_3), 1.20 (s, 10-H_3), 1.21 (s, 11-H_3), 1.35–1.50 (m, 2 H, 8-H_2), 1.90–2.20 (m, 2 H, 2-H_2), 4.72 (br, NH_2, OH)	15.22 (q, C-6), 16.50 (s, C-4), 21.82 (d, C-7 or C-3), 23.12 (d, C-3 or C-7), 26.26 (t, C-2), 28.21 (q, C-11), 28.61 (q, C-5), 30.66 (q, C-10), 37.38 (t, C-8), 70.64 (s, C-9), 153.99 (s, C-1)
11	2260 (C=N), 1640, 1470, 1390	277 (4, M^+), 262 (40), 234 (4), 170 (85), 155 (45), 115 (40), 108 (66), 93 (46), 91 (330, 87 (100)	0.95 (s, 6 H, 9-H_3 and 10-H_3), 1.18 (s, 3 H, 15-H_3), 1.3–1.6 (m, 5 H), 1.65–1.80 (m, 2 H), 2.15-2.50 (m, 5 H), 3.81 (s, 4 H, OCH_2CH_2O), 4.68 (br s $W_{1/2}$ = 4, 1 H, 5-H^a), 4.80 (br s $W_{1/2}$ = 4, 1 H, 5-H^b)	15.59 (t, C-2), 21.82 (q, C-9), 23.28 (q, C-15), 24.77 (t, C-12), 29.72 (t, C-3), 30.81 (q, C-10), 33.42 (s, C-8), 37.00 (t, C-13), 39.18 (t, C-7), 40.86 (d, C-6), 48.43 (d, C-11), 64.21 (t, 2 C, $OCHCH_2O$), 108.56 (t, C-5), 109.44 (s, C-14), 119.07 (s, C-1), 148.41 (s, C-4)
12	3605 (OH), 3520, 3415 (NH), 1710 (C=O), 1640 (C=N), 1620, 1585 (C=C), 910	249 (14, M^+ – OH), 209 (18), 193 (49), 167 (60), 136 (62), 124 (87), 110 (100), 95 (54), 83 (78)	0.97 (s, 6 H, 9-H_3 and 10-H_3), 1.36 (t, *J* = 10.5, 1 H, 7-H^a), 1.50–1.80 (m, 4 H, 7-H^b, 12-H_2, 11-H), 2.04 (s, 3 H, 15-H_3), 2.18–2.40 (m, 7 H, 2-H_2, 3-H_2, 6-H, 13-H_2), 4.63 (br s, $W_{1/2}$ = 12, NH_2), 4.68 (br s $W_{1/2}$ = 4, 1 H, 5-H^a), 4.70 (br s, $W_{1/2}$ = 4, 1 H, 5-H^b), 8.51 (br, $W_{1/2}$ = 20, NOH)	22.13 (q, C-9), 24.38 (t, C-12), 29.47 (t, C-3), 29.61 (q, C-15), 30.81 (q, C-10), 31.06 (t, C-2), 33.34 (s, C-8), 39.47 (t, C-7), 41.16 (d, C-6), 41.72 (t, C-13), 47.60 (d, C-11), 107.37 (t, C-5), 151.12 (s, C-4), 153.58 (s, C-1), 208.89 (s, C-14)
14	2260 (C≡N), 1645 (C=C), 890	209 (33, M), 194 (31), 181 (100), 121 (18), 108 (19), 95 (28), 81 (27), 55 (13)	1.27 (s, 3 H, 10-H_3), 1.57 (m, 4 H, 7-H_2, 8-H_2), 1.69 (br s, 3 H, 6-H_3), 2.36–2.61 (m, 3 H, 2-H_2, 3-H), 3.91 (m, 4 H, OCH_2CH_2O), 4.86 (br s, $W_{1/2}$ = 3.5, 1 H, 5-H^a), 4.90 (dq, *J* = 1.5, 1.5, 1 H, 5-H^b)	18.81 (q, C-6), 22.43 (t, C-2), 24.11 (q, C-10), 27.52 (t, C-7), 37.29 (t, C-8), 44.70 (d, C-3), 65.56 (t, 2 C, OCH_2CH_2O), 110.71 (s, C-9), 114.04 (t, C-5), 120.02 (s, C-1), 145.87 (s, C-4)
15	3605 (OH), 3520, 3420, 1710 1665, 1585, 1380, 900	181 (100, M^+ – OH), 122 (19), 108 (14), 95 (26), 81 (25), 55 (11), 42(18), 41(13)	1.30–1.70 (m, 2 H), 1.58 (s, 3 H, 6-H_3), 2.04 (s, 3 H, 10-H_3), 2.10–2.30 (m, 2 H), 2.50 (m, 3 H), 4.60 (br s, $W_{1/2}$ = 10, 2 H, NH_2), 4.69 (s, 1 H, 5-H^a), 4.73 (s, 1 H, 5-H^b), 8.0 (br, $W_{1/2}$ = 25, 1 H, OH)	18.16 (q, C-6), 25.92 (t, C-7), 29.75 (q C-10), 35.15 (t, C-2), 40.72 (t, C-8), 43.80 (d, C-3), 112.77 (t, C-5), 145.84 (s, C-4), 152.68 (s, C-1), 208.71 (s, C-9)
18a	2210 (C≡N), 1465, 1455, 1392, 1367, 1090	98.08480 (59, M^+), 83 (83), 57 (38), 56 (41), 43 (100), 41 (45)	1.24 (d, *J* = 6.5, 6 H, 3-H_6), 2.86 (s, 3 H, 1a-H_3), 3.19 (sept, *J* = 6.5, 1 H, 2-H)	20.20 (q, 2 C, C-3), 37.26 (q, C-1a), 54.26 (d, C-2), 118.42 (s, C-1)
18b	2220 (C≡N), 1455, 1412, 1393, 1360, 1180, 1090, 990, 935	124 (24, M^+), 109 (45), 81 (5), 69 (6), 55 (33), 43 (28), 41 (100)	1.24 (d, *J* = 6.5, 6 H, 3-H_6), 3.24 (sept, *J* = 6.5, 1 H, 2-H), 3.68 (ddd, *J* = 6.5, 1.5, 1.5, 2 H, 1a-H_2), 5.30 (ddt, *J* = 10.5, 1.5, 1.5, 1 H, 3a-H^a), 5.33 (ddt, *J* = 17.0, 1.5, 1.5, 1 H, 3a-H^b), 5.90 (ddt, *J* = 17.0, 10.5, 6.5, 1 H, 2a-H)	20.84 (q, 2 C, C-3), 53.02 (d, C-2), 53.86 (t, C-1a), 117.39 (s, C-1), 119.96 (t, C-3a), 133.37 (d, C-2a)
18c	2220 (C≡N), 1495, 1450, 1362, 1165, 703	174 (16, M^+), 159 (4), 131 (2), 91 (100), 77 (3), 65 (11), 41 (5)	1.19 (d, *J* = 6.5, 6 H, 3-H_6), 3.27 (sept, *J* = 6.5 Hz, 1 H, 2-H), 4.18 (s, 2 H, 1a-H_2), 7.33 (m, 5 H, Ar-H)	20.77 (q, 2C, C-3), 52.93 (d, C-2), 55.18 (t, C-1a), 117.69 (s, C-1), 129.39 (d, C-5a), 129.60 (d, 2 C, C-3a), 129.91 (d, 2 C, C-4a), 137.00 (s, C-2a)
19a	2220 (C≡N), 1370, 1180	126 (13, M^+), 111 (12), 97 (16), 83 (9), 69 (100), 57 (15), 44 (35)	0.95 (t, *J* = 6.5, 3 H, 6-H_3), 1.25-1.41 (m, 4 H, 5-H_2 and 4-H_2), 1.65 (m, 2 H, 3-H_2), 2.87 (s, 3 H, 1a-H_3), 3.05 (t, *J* = 6.5, 2 H, 2-H_2)	14.33 (q, C-6), 23.28 (t, C-5), 27.98 (t, C-3), 29.63 (t, C-4), 39.07 (q, C-1a), 53.73 (t, C-2), 119.79 (s, C-1)

Table 2 (continued)

Product	IR ($CHCl_3$)[a] ν (cm^{-1})	MS *m/z* (%)	^{1}H NMR[b] δ, *J*, $W_{1/2}$ (Hz)	^{13}C NMR[b,c] δ, *J* (Hz)
19b	2205 (C≡N), 1460, 1380, 930	152 (6, M^+), 137 (14), 123 (7), 95 (31), 70 (22), 55 (19), 41 (100)	0.75 (t, *J* = 6.5, 3 H, 6-H_3), 1.05−1.20 (m, 4 H, 4-H_2 and 5-H_2), 1.40 (m, 2 h, 3-H_2), 2.74 (t, *J* = 6.5, 2 H, 2-H_2), 3.39 (ddt, *J* = 6.5, 1.0, 1.0, 2 H, 1a-H), 5.07 (ddt, *J* = 10.5, 1.0, 1.0, 1 H, 3a-H[a]), 5.10 (ddt, *J* = 17.0, 1.0, 1.0, 1 H, 3a-H[b]), 5.62 (ddt, *J* = 17.0, 10.5, 6.5, 1 H, 2a-H)	13.28 (q, C-6), 21.59 (t, C-5), 26.61 (t, C-3), 27.95 (t, C-4), 50.02 (t, C-2), 53.71 (t, C-1a), 115.94 (s, C-1), 119.00 (t, C-3a), 130.98 (d, C-2a)
19c	2205 (C≡N), 1450, 1165, 1090	202 (7, M^+), 201 (12), 111 (10), 91 (100), 83 (5), 69 (35), 65 (9), 44 (13)	0.79 (t, *J* = 6.5, 3 H, 6-H_3), 1.10−1.30 (m, 4 H, 5-H_2 and 4-H_2), 1.49 (m, 2 H, 3-H_2), 2.74 (t, *J* = 6.5, 2 H, 2-H_2), 4.00 (s, 2 H, 1a-H_2), ≈7.2 (m, 5 H, Ar-H)	13.43 (q, C-6), 21.70 (t, C-5), 26.61 (t, C-3), 28.09 (t, C-4), 49.72 (t, C-2), 55.34 (t, C-1a), 116.49 (s, C-1), 127.82 (d, C-5a), 127.87 (d, C-4a), 128.24 (d, 2 C, C-3a), 134.67 (s, C-2a)
20a	2220 (C≡N), 1460, 1380, 1038	146 (22, M^+), 104 (3), 91 (100), 65 (13), 39 (6)	2.74 (s, 3 H, 1a-H_3), 4.12 (s, 2 H, 2-H_2), ≈7.34 (m, 5 H, Ar-H)	37.63 (q, C-1a), 56.98 (t, C-2), 118.63 (s, C-1), 128.20 (d, C-6), 128.41 (d, C-4), 128.71 (d, C-5), 134.19 (s, C-3)
20b	2220 (C≡N), 1500, 1460, 1385, 1000, 942	172 (6, M^+), 160 (2), 130 (2), 117 (2), 92 (14), 91 (100), 77 (2), 65 (10), 51 (3)	3.53 (ddd, *J* = 7, 1.5, 1.5, 2 H, 1a-H_2), 4.15 (s, 2 H, 2-H_2), 5.27 (ddt, *J* = 17.0, 1.5, 1.5, 1 H, 3a-H[a]), 5.31 (ddt, *J* = 11.0, 1.5, 1.5, 1 H, 3a-H[b]), 5.82 (ddt, *J* = 17.0, 11.0, 7, 1 H, 2a-H), ≈7.34 (m, 5 H, Ar-H)	52.88 (t, C-1a), 54.58 (t, C-2), 117.70 (s, C-1), 120.54 (t, C-3a), 128.37 (d, C-6), 128.38 (d, 2 C, C-5), 128.74 (d, 2 C, C-4), 130.66 (d, C-2a), 134.39 (s, C-3)
20c	2200 (C≡N), 1465, 1250, 1000, 725	222.11625 (7, M^+), 131 (19), 92 (10), 91 (100), 65 (15), 28 (20)	4.07 (s, 4 H, 2-H_2 and 1a-H_2), ≈7.30 (m, 10 H, Ar-H)	54.16 (t, 2 C, C-2 and C-1a), 117.64 (s, C-1), 128.52 (d, 2 C, C-6 and C-5a), 128.53 (d, 4C, C-4 and C-3a), 128.79 (d, 4C, C-5 and C-4a), 134.33 (s, 2 C, C-3 and C-2a)
20d	2200 (C≡N), 1495, 1460, 1385, 1155, 1080	160 (16, M^+), 146 (4), 117 (2), 104 (2), 91 (100), 77 (3), 65 (10), 51 (3)	1.23 (t, *J* = 7, 3 H, 2a-H_3), 2.96 (q, *J* = 7, 2 H, 1a-H_2), 4.16 (s, 2 H, 2-H_2), ≈7.32 (m, 5 H, Ar-H)	12.49 (q, C-2a), 44.95 (t, C-1a), 55.44 (t, C-2), 117.52 (s, C-1), 128.18 (d, C-6), 128.71 (d, 2 C, C-5), 128.32 (d, 2 C, C-4), 134.74 (s, C-3)
21a	2216 (C≡N), 1595, 1495, 1385, 1105	132 (100, M^+), 117 (14), 91 (43), 77 (33), 65 (26), 51 (21), 42 (36)	3.22 (s, 3 H, 1a-H_3), ≈7.04 (m, 3 H, 3-H_2 and 5-H), ≈7.32 (m, 2 H, 4-H_2)	37.18 (q, C-1a), 115.17 (s, C-1), 115.86 (d, 2 C, C-3), 124.28 (d, C-5), 130.57 (d, 2 C, C-4), 141.68 (s, C-2)
21b	2220 (C≡N), 1598, 1497, 1360, 1190	158 (76, M^+), 131 (59), 130 (51), 118 (19), 91 (15), 77 (38), 65 (18), 51 (26), 41 (100)	4.26 (ddd, *J* = 6.0, 1.5, 1.5, 2 H, 1a-H_2), 5.33 (ddt, *J* = 10.5, 1.5, 1.5, 1 H, 3a-H[b]), 5.36 (ddt, *J* = 17.0, 1.5, 1.5, 1 H, 3a-H[a]), 5.96 (ddt, *J* = 17.0, 10.5, 6.0, 1 H, 2a-H), ≈7.08 (m, 3 H, 3-H_2 and 5-H), ≈7.29 (m, 2 H, 4-H_2)	52.99 (t, C-1a), 114.70 (s, C-1), 117.08 (d, 2 C, C-3), 119.98 (t, C-3a), 124.79 (d, C-5), 130.72 (d, 2 C, C-4), 131.91 (d, C-2a), 141.15 (s, C-2)
21c	2222 (C≡N), 1595, 1492, 1360, 740	208 (17, M^+), 91 (100), 77 (5), 65 (17), 28 (64)	4.83 (s, 2 H, 1a-H_2), 7.05−7.25 (m, 3 H, Ar-H), 7.30−7.45 (m, 7 H, Ar-H)	54.43 (t, C-1a), 115.03 (s, C-1), 117.43 (d, 2 C), 124.94 (d), 128.88 (d, 2 C), 129.48 (d), 129.95 (d, 2 C), 130.75 (d, 2 C), 136.09 (s), 141.22 (s)
22a	2220 (C≡N), 1700 (C=O), 1475, 1460, 1385, 1370, 910	194 (1, M^+), 179 (4), 151 (13), 123 (13), 109 (25), 99 (19), 83 (460), 69 (100), 43 (80)	0.84 (s, 3 H, 6-H_3), 1.32 (s, 3 H, 5-H_3), 1.80−2.05 (m, 2 H), 1.99 (s, 3 H, 10-H_3), 2.30 (m, 1 H), 2.70−3.15 (m, 3 H), 2.77 (s, 3 H, 1a-H_3)	16.94 (q, C-6), 20.94 (t, C-7), 30.05 (q, C-10), 30.32 (q, C-5), 38.81 (d, C-3), 39.09 (q, C-1a), 42.39 (s, C-4), 53.22 (d, C-8), 53.16 (t, C-2), 118.09 (s, C-1),206.92 (s, C-9)

Table 2 (continued)

Product	IR ($CHCl_3$)[a] ν (cm^{-1})	MS *m/z* (%)	^{1}H NMR[b] δ, *J*, $W_{1/2}$ (Hz)	^{13}C NMR[b,c] δ, *J* (Hz)
22b	2205 (C≡N), 1700 (C=O), 1365, 1354, 938	220 (1, M^+), 205 (5), 177 (15), 149 (15), 135 (16), 123 (16), 99 (17), 95 (27), 83 (40), 81 (25), 43 (78), 41 (100)	0.91 (s, 3 H, 6-H_3), 1.39 (s, 3 H, 5-H_3), 1.76−2.01 (m, 2 H), 2.05 (s, 3 H, 10-H_3), 2.34 (m, 1 H), 2.96 (dd, *J* = 13.0, 7.0, 1 H, 2-H[a]), 3.01 (dd, *J* = 13.0, 8.0, 1 H, 2-H[b]), 3.11 (m, 1 H), 3.66 (ddt, *J* = 6.5, 1.5, 1.5, 2 H, 1a-H_2), 5.27 (ddt, *J* = 11, 1.5, 1.5, 1 H, 3a-H[b]), 5.33 (ddt, *J* = 17.0, 1.5, 1.5, 1 H, 3a-H[a]), 5.86 (ddt, *J* = 17.0, 11.0, 7.0, 1 H, 2a-H)	17.49 (q, C-6), 22.29 (t, C-7), 30.36 (q, C-10), 30.77 (q, C-5), 40.51 (d, C-3), 43.69 (s, C-4), 54.31 (d, C-8), 52.43 (t, C-2), 55.38 (t, C-1a), 118.74 (s, C-1), 120.49 (t, C-3a), 132.69 (d, C-2a), 209.71 (s, C-9)
22c	2210 (C≡N), 1700 (C=O), 1460, 1360	270 (6, M^+), 269 (12), 255 (2), 199 (6), 132 (5), 91 (100), 83 (11), 81 (9), 69 (24), 43 (26), 41 (15)	0.77 (s, 3 H, 6-H_3), 1.32 (s, 3 H, 5-H_3), 1.80−2.05 (m, 2 H), 1.98 (s, 3 H, 10-H_3), 2.30 (m, 1 H), 2.70−3.15 (m, 3 H), 4.10 (s, 2 H, 1a-H_2), ≈7.30 (m, 5 H, Ar-H)	16.84 (q, C-6), 20.59 (t, C-7), 30.00 (q, C-10), 30.24 (q, C-5), 38.80 (d, C-3), 42.34 (s, C-4), 50.55 (t, C-2), 53.16 (d, C-8), 56.04 (t, C-1a), 117.46 (s, C-1), 128.17 (d, 2C), 128.35 (d, C-5a), 128.65 (d, 2 C), 134.35 (s, C-2a), 206.87 (s, C-9)
23a	2220 (C≡N), 1720 (C=O), 1370, 1180	194 (2, M^+), 179 (2), 139 (100), 81 (48), 69 (35), 43 (86)	0.75−0.95 (m, 2 H, 3-H and 7-H), 0.82 (s, 3 H, 6-H_3), 0.98 (s, 3 H, 5-H_3), 2.00 (s, 3 H, 10-H_3), 2.27 (d, *J* = 7.0, 2 H, 8-H_2), 2.68 (s, 3 H, 1a-H_3), 2.73 (dd, *J* = 14.0, 8.0, 1 H, 2-H[a]), 2.82 (dd, *J* = 14.0, 7.0, 1 H, 2-H[b])	14.49 (q, C-6), 17.88 (s, C-4), 21.48 (d, C-7 or C-3), 22.82 (d, C-3 or C-7), 27.87 (q, C-5), 29.18 (q, C-10), 38.12 (q, C-1a), 38.66 (t, C-8), 49.36 (t, C-2), 118.04 (s, C-1), 207.27 (s, C-9)
23b	2220 (C≡N), 1715 (C=O), 1375	220 (1, M^+), 205 (3), 139 (42), 81 (24), 43 (100), 41 (37)	0.75−1.00 (m, 2 H, 3-H and 7-H), 0.83 (s, 3 H, 6-H_3), 1.00 (s, 3 H, 5-H_3), 2.01 (s, 3 H, 10-H_3), 2.27 (dd, *J* = 17.0, 8.0, 1 H, 8-H[a]), 2.29 (dd, *J* = 17.0, 7.0, 1 H, 8-H[b]), 2.76 (dd, *J* = 13.5, 8.0, 1 H, 2-H[a]), 2.84 (dd, *J* = 13.5, 7.0, 1 H, 2-H[b]), 3.48 (d, *J* = 7.0, 2 H, 1a-H_2), 5.15 (dd, *J* = 11.0, 1.5, 1 H, 3a-H[a]), 5.16 (dd, *J* = 17.0, 1.5, 1H), 5.70 (ddt, *J* = 17.0, 11.0, 7.0, 1 H, 2a-H)	14.53 (q, C-6), 17.96 (s, C-4), 21.57 (d, C-7 or C-3), 23.03 (d, C-3 or C-7), 27.91 (q, C-5), 29.20 (q, C-10), 38.72 (t, C-8), 47.32 (t, C-2), 53.64 (t, C-1a), 117.13 (s, C-1), 119.59 (t, C-3a), 130.70 (d, C-2a), 207.25 (s, C-9)
23c	2220 (C≡N), 1715 (C=O), 1380, 920	270 (5, M^+), 139 (77), 121 (14), 91 (100), 81 (16), 43 (66)	0.80−1.00 (m, 2 H, 3-H and 7-H), 0.87 (s, 3 H, 6-H_3), 1.08 (s, 3 H, 5-H_3), 2.08 (s, 3 H, 10-H_3), 2.26 (dd, *J* = 17.5, 8.0, 1 H, 8-H[a]), 2.32 (dd, *J* = 17.5, 7.0, 1 H, 8-H[b]), 2.82 (dd, *J* = 13.0, 8.0, 1 H, 2-H[a]), 2.88 (dd, *J* = 13.0, 7.0, 1 H, 2-H[b]), 4.13 (s, 2 H, 1a-H_2), ≈7.30 (s, 5 H, Ar-H)	14.72 (q, C-6), 18.26 (s, C-4), 21.79 (d, C-7 or C-3), 23.13 (d, C-3 or C-7), 28.12 (q, C-5), 29.42 (q, C-10), 38.92 (t, C-8), 47.22 (t, C-2), 55.39 (t, C-1a), 117.78 (s, C-1), 128.02 (d, 2 C, C-3a or C-4a), 128.27 (d, C-5a), 128.65 (d, 2 C, C-4a or C-3a), 134.61 (s, C-2a), 207.53 (s, C-9)
23e	2225 (C≡N), 1715 (C=O), 1630, 1595 (C=C), 1485, 1360, 1040 (C-F)	306 (4, M^+), 287 (3), 263 (4), 139 (68), 127 (100), 95 (15), 81 (21), 43 (93)	0.65−0.90 (m, 2 H, 3-H and 7-H), 0.75 (s, 3 H, 6-H_3), 0.93 (s, 3 H, 5-H_3), 1.94 (s, 3 H, 10-H_3), 2.18 (dd, *J* = 17.5, 8.0, 1 H, 8-H[a]), 2.26 (dd, *J* = 17.5, 7.0, 1 H, 8-H_b), 2.78 (dd, *J* = 13.5, 8.0, 1 H, 2-H[a]), 2.88 (dd, *J* = 13.5, 7.0, 1 H, 2-H[b]), 4.08 (s, 2 H, 1a-H_2), 6.76 (dd, J_{HH} = 8.0, J_{HF} = 8.0, 2 H, 4a-H_2), 7.18 (tt, J_{HH} = 8.0, J_{HF} = 1.5, 1 H, 5a-H)	14.17 (q, C-6), 17.90 (s, C-4), 21.54 (d, C-7 or C-3), 22.70 (d, C-3 or C-7), 27.68 (q, C-5), 28.96 (q, C-10), 38.38 (t, C-8), 42.07 (t, C-1a), 47.53 (t, C-2), 110.26 (s, $^2J_{CF}$ = 19.5, C-2a), 110.96 (d, $^2J_{CF}$ = 25.2, C-4a), 116.18 (s, C-1), 130.49 (d, $^3J_{CF}$ = 10.4, C-5a), 161.07 (d, $^1J_{CF}$ = 250.4, $^3J_{CF}$ = 7.3, C-3a), 207.04 (s, C-9)
23f	2220 (C≡N), 1715 (C=O), 1660, 1530 (C=C), 1365, 1130, 1025 (C−F)	360 (1, M^+), 342 (1), 317 (1), 303 (1), 181 (40), 139 (42), 123 (29), 95 (25), 81 (45), 43 (100)	0.80−1.10 (m, 2 H, 3-H and 7-H), 0.94 (s, 3 H, 6-H_3), 1.12 (s, 3 H, 5-H_3), 2.13 (s, 3 H, 10-H_3), 2.40 (d, *J* = 7.5, 2 H, 8-H_2), 2.94 (dd, *J* = 13.0, 8.0, 1 H, 2-H[a]), 3.02 (dd, *J* = 13.0, 7.0, 1 H, 2-H[b]), 4.25 (t, J_{HF} = 1.5, 2 H, 1a-H_2)	14.73 (q, C-6), 18.56 (s, C-4), 22.10 (d, C-7 or C-3), 23.13 (d, C-3 or C-7), 28.13 (q, C-5), 29.50 (q, C-10), 38.99 (t, C-8), 42.32 (t, C-1a), 48.74 (t, C-2), 115.82 (s, C-1), 207.45 (s, C-9)

Table 2 (continued)

Product	IR ($CHCl_3$)[a] ν (cm^{-1})	MS *m/z* (%)	^1H NMR[b] δ, *J*, $W_{1/2}$ (Hz)	^{13}C NMR[b,c] δ, *J* (Hz)
24a	2205 (C≡N)	192 (33, M^+), 177 (7), 136 (11), 123 (100), 121 (13), 95 (22), 93 (15), 81 (65), 69 (23), 43 (25)	≈0.86 (m, 1 H, 3-H), 0.87 (s, 3 H, 6-H_3), 1.01 (s, 3 H, 5-H_3), 1.28 (dd, *J* = 8.0, 8.0, 1 H, 7-H), 1.53 (d, *J* = 1.5, 3 H, 10-H_3 or 11-H_3), 1.57 (d, *J* = 1.5, 3 H, 11-H_3 or 10-H_3), 2.69 (s, 3 H, 1a-H_3), 2.72 (dd, *J* = 13.0, 9.0, 1 H, 2-H^a), 2.78 (dd, *J* = 13.0, 7.0, 1 H, 2-H^b), 4.68 (dqq, *J* = 8.0, 1.5, 1.5, 1 H, 8-H)	15.01 (q, C-6), 18.05 (q, C-10), 19.92 (s, C-4), 25.21 (q, C-10), 25.53 (d, C-7 or C-3), 25.70 (d, C-3 or C-7), 27.97 (q, C-5), 38.12 (q, C-1a), 49.76 (t, C-2), 117.56 (s, C-1), 117.91 (d, C-8), 135.23 (s, C-9)
24b	2205 (C≡N)	218 (9, M^+), 203 (5), 136 (9), 123 (100), 121 (14), 105 (12), 95 (21), 91 (22), 81 (49), 69 (19), 41 (49)	1.04 (s, 3 H, 6-H_3), ≈1.06 (m, 1 H, 3-H), 1.15 (s, 3 H, 5-H_3), 1.49 (dd, *J* = 8.0, 8.0, 1 H, 7-H), 1.70 (d, *J* = 1.5, 3 H, 10-H_3 or 11-H_3), 1.73 (d, *J* = 1.5, 3 H, 11-H_3 or 10-H_3), 2.98 (dd, *J* = 13.0, 8.0, 1 H, 2-H^a), 3.06 (dd, *J* = 13.0, 6.5, 1 H, 2-H^b), 3.65 (dm, *J* = 6.0, 2 H, 1a-H_2), 4.90 (dqq, *J* = 8.0, 1.5, 1.5, 1 H, 8-H), 5.30 (ddt, *J* = 10.0, 1.5, 1.5, 1 H, 3a-H^a), 5.32 (ddt, *J* = 17.0, 1.5, 1.5, 1 H, 3a-H^b), 5.86 (ddt, *J* = 17.0, 10.0, 6.0, 1 H, 2a-H)	15.93 (q, C-6), 18.78 (q, C-10), 21.54 (s, C-4), 25.92 (d, C-7 or C-3), 27.34 (q, C-11), 27.46 (d, C-3 or C-7), 28.85 (q, C-5), 49.31 (t, C-2), 55.01 (t, C-1a), 118.84 (s, C-1), 119.55 (d, C-8), 120.05 (t, C-3a), 131.61 (d, C-2a), 136.79 (s, C-9)
24c	2200 (C≡N), 1580, 1485	268 (14, M^+), 267 (9), 253 (6), 225 (4), 136 (8), 123 (100), 95 (13), 91 (50), 81 (29), 41 (17)	0.93 (s, 3 H, 6-H_3), ≈1.0 (m, 1 H, 3-H), 1.11 (s, 3 H, 5-H_3), 1.42 (dd, *J* = 8.0, 8.0, 1 H, 7-H), 1.62 (d, *J* = 1.5, 3 H, 10-H_3 or 11-H_3), 1.65 (d, *J* = 1.5, 3 H, 11-H_3 or 10-H_3), 2.82 (dd, *J* = 13.0, 8.0, 1 H, 2-H^a), 2.90 (dd, *J* = 13.0, 6.5, 1 H, 2-H^b), 4.11 (s, 2 H, 1a-H_2), 4.72 (dqq, *J* = 8.0, 1.5, 1.5, 1 H, 8-H), ≈7.28 (m, 5 H, Ar-H)	15.20 (q, C-6), 18.26 (q, C-10), 20.28 (s, C-4), 25.43 (q, C-11), 25.89 (d, C-7 or C-3), 26.04 (d, C-3 or C-7), 28.18 (q, C-5), 47.60 (t, C-2), 55.35 (t, C-1a), 117.33 (s, C-1), 118.13 (d, C-8), 127.84 (d, 2 C, C-4a or C-5a), 128.01 (d, C-5a), 128.48 (d, 2 C, C-3a or C-4a), 134.93 (s, C-2a), 135.38 (s, C-8)
24e	2205 (C≡N), 1630, 1595 (C=C), 1480, 1370, 1030 (C−F)	304 (4, M^+), 285 (5), 261 (8), 137 (6847), 127 (100), 95 (19), 81 (33), 43 (72)	≈0.9 (m, 1 H, 3-H), 0.93 (s, 3 H, 6-H_3), 1.08 (s, 3 H, 5-H_3), 1.40 (dd, *J* = 8.0, 8.0, 1 H, 7-H), 1.62 (d, *J* = 1.5, 3 H, 10-H_3 or 11-H_3), 1.64 (d, *J* = 1.5, 3 H, 11-H_3 or 10-H_3), 2.92 (dd, *J* = 13.0, 8.0, 1 H, 2-H^a), 3.02 (dd, *J* = 13.0, 6.5, 1 H, 2-H^b), 4.11 (s, 2 H, 1a-H_2), 4.78 (dqq, *J* = 8.0, 1.5, 1.5, 1 H, 8-H), 6.75 (m ,2 H, 4a-H_2), 7.30 (m, 1 H, 5a-H)	15.05 (q, C-6), 18.24 (q, C-10), 20.35 (s, C-4), 25.35 (q, C-11), 25.60 (d, C-7 or C-3), 26.04 (d, C-3 or C-7), 28.03 (q, C-5), 42.39 (t, C-1a), 48.25 (t, C-2), 111.00 (s, $^2J_{CF}$ = 20.1, C-2a), 111.25 (d, $^2J_{CF}$ = 25.3, C-4a), 116.71 (s, C-1), 117.81 (d, C-8), 130.61 (d, $^3J_{CF}$ = 10.3, C-5a), 135.90 (s, C-9), 161.23 (s, $^1J_{CF}$ = 250.5, $^3J_{CF}$ = 7.3, C-3a)
24f	2205 (C≡N), 1660, 1530 (C=C), 1360, 1130, 1025 (C−F)	358 (1, M^+), 340 (3), 315 (4), 301 (3), 181 (35), 139 (38), 123 (41), 95 (20), 81 (33), 43 (100)	1.00 (s, 3 H, 6-H_3), ≈1.1 (m, 1 H, 3-H), 1.15 (s, 3 H, 5-H_3), 1.46 (dd, *J* = 8.0, 8.0, 1 H, 7-H), 1.67 (d, *J* = 1.5, 3 H, 10-H_3 or 11-H_3), 1.71 (d, *J* = 1.5, 3 H, 11-H_3 or 10-H_3), 2.98 (dd, *J* = 13.0, 8.0, 1 H, 2-H^a), 3.02 (dd, *J* = 13.0, 6.5, 1 H, 2-H^b), 4.23 (br s, 2 H, 1a-H_2), 4.78 (dqq, *J* = 8.0, 1.5, 1.5, 1 H, 8-H)	15.69 (q, C-6), 18.65 (q, C-10), 23.05 (s, C-4), 27.11 (d, C-7 or C-3), 27.69 (q, C-11), 28.68 (d, C-3 or C-7), 28.98 (q, C-5), 43.51 (t, C-2a), 50.01 (t, C-2), 117.60 (s, C-1), 119.22 (d, C-8), 137.22 (s, C-9)
25a	3615 (OH), 2215 (C≡N)	210 (2, M^+), 195 (2), 155 (100), 81 (48), 69 (35), 43 (86)	0.75−0.90 (m, 2 H, 3-H and 7-H), 0.95 (s, 3 H, 6-H_3), 1.09 (s, 3 H, 5-H_3), 1.18 (s, 3 H, 10-H_3), 1.19 (s, 3 H, 11-H_3), 1.35 (dd, *J* = 14.0, 7.5, 1 H, 8-H^a), 1.42 (dd, *J* = 14.0, 5.0, 1 H, 8-H^b), 1.75 (br s, 1 H, OH), 2.78 (dd, *J* = 13.0, 8.5, 1 H, 2-H^a), 2.80 (s, 3 H, 1a-H_3), 2.95 (dd, *J* = 13.0, 6.0, 1 H, 2-H^b)	15.11 (q, C-6), 18.18 (s, C-4), 22.75 (d, C-7 or C-3), 23.17 (d, C-3 or C-7), 28.19 (q, C-11), 28.56 (q, C-10), 29.64 (q, C-5), 37.90 (t, C-8), 38.56 (q, C-1a), 50.07 (t, C-2), 70.55 (s, C-9), 118.54 (s, C-1)
25b	3615 (OH), 2215 (C≡N)	236 (8, M^+), 221 (9), 178 (26), 177 (59), 163 (37), 139 (18), 123 (27), 109 (20), 96 (47), 91 (25), 81 (83), 59 (100)	0.80−1.00 (m, 2 H, 3-H and 7-H), 1.06 (s, 3 H, 6-H_3), 1.17 (s, 3 H, 5-H_3), 1.23 (s, 3 H, 10-H_3), 1.24 (s, 3 H, 11-H_3), 1.48 (dd, *J* = 14.5, 7.0, 1 H, 8-H^a), 1.51 (dd, *J* = 14.5, 5.0, 1 H, 8-H^b), 2.95 (dd, *J* = 13.0, 8.5, 1 H, 2-H^a), 3.19 (dd, *J* = 13.0, 6.0, 1 H, 2-H^b), 3.73 (ddt, *J* = 6.5, 1.5, 1.0, 2 H, 1a-H_2), 5.39 (ddt, *J* = 10.0, 1.5, 1.0, 1 H, 3a-H^a), 5.42 (ddt, *J* = 17.0, 1.5, 1.0, 1 H, 3a-H^b), 5.93 (ddt, *J* = 17.0, 10.0, 6.5, 1 H, 2a-H)	15.69 (q, C-6), 19.36 (s, C-4), 24.42 (d, C-7 or C-3), 24.81 (d, C-3 or C-7), 28.79 (q, C-11), 29.02 (q, C-10), 29.72 (q, C-5), 38.90 (t, C-8), 49.46 (t, C-2), 55.16 (t, C-1a), 71.28 (s, C-9), 119.19 (s, C-1), 120.16 (t, C-3a), 132.80 (d, C-2a)

Table 2 (continued)

Product	IR ($CHCl_3$)[a] ν (cm^{-1})	MS *m/z* (%)	^{1}H NMR[b] δ, *J*, $W_{1/2}$ (Hz)	^{13}C NMR[b,c] δ, *J* (Hz)
25e	3615 (OH), 2215 (C≡N), 1595 (C=C), 1480, 1370, 1030	322 (2, M^+), 307 (7), 264 (14), 245 (22), 209 (10), 169 (12), 155 (10), 139 (14), 127 (100), 96 (22), 81 (36), 59 (47)	0.75−0.90 (m, 2 H, 3-H and 7-H), 0.91 (s, 3 H, 6-H_3), 1.06 (s, 3 H, 5-H_3), 1.16 (s, 3 H, 10-H_3), 1.17 (s, 3 H, 11-H_3), 1.30 (dd, *J* = 14.5, 7.0, 1 H, 8-H[a]), 1.42 (dd, *J* = 14.5, 5.0, 1 H, 8-H[b]), 1.65 (br s, 1 H, OH), 2.85 (dd, *J* = 13.0, 8.5, 1 H, 2-H[a]), 3.03 (dd, *J* = 13.0, 6.0, 1 H, 2-H[b]), 4.24 (s, 2 H, 1a-H_2), 6.8−7.0 (m, 2 H, Ar-H), 7.2−7.4 (m, 1 H, Ar-H)	14.97 (q, C-6), 18.39 (s, C-4), 22.93 (d, C-7 or C-3), 23.07 (d, C-3 or C-7), 28.35 (q, C-11), 28.54 (q, C-10), 29.53 (q, C-5), 37.78 (t, C-8), 42.65 (t, C-1a), 48.21 (t, C-2), 70.53 (s, C-9), 111.14 (d, $^2J_{CF}$ = 25.3, C, C-4a), 111.40 (s, $^2J_{CF}$ = 20.0, C-2a), 116.88 (s, C-1), 130.76 (d, $^3J_{CF}$ = 10.3, C-5a), 161.48 (s, $^1J_{CF}$ = 250.5, $^3J_{CF}$ = 7.3, 2 C, C-3a)
25f	3615 (OH), 2215 (C≡N), 1545 (C=C), 1360, 1120, 1030	376 (1, M^+), 357 (1), 342 (2), 181 (40), 139 (42), 123 (29), 95 (25), 81 (45), 43 (100)	0.84−0.91 (m, 2 H, 3-H and 7-H), 0.99 (s, 3 H, 6-H_3), 1.11 (s, 3 H, 5-H_3), 1.18 (s, 3 H, 10-H_3), 1.23 (s, 3 H, 11-H_3), 1.41 (dd, *J* = 13.5, 8.0, 1 H, 8-H[a]), 1.48 (dd, *J* = 13.5, 6.0, 1 H, 8-H[b]), 2.99 (dd, *J* = 13.5, 8.0, 1 H, 2-H[b]), 3.21 (dd, *J* = 13.5, 6.0, 1 H, 2-H[a]), 4.41 (s, 2 H, 1a-H_2)	15.48 (q, C-6), 19.59 (s, C-4), 24.64 (d, C-3 or C-7), 24.65 (d, C-7 or C-3), 28.74 (q, C-11), 28.92 (q, C-10), 29.68 (q, C-5), 38.83 (t, C-8), 43.58 (t, C-1a), 50.16 (t, C-2), 71.27 (s, C-9), 117.77 (s, C-1)
26a	2220 (C≡N), 1720 (C=O), 1370, 1180	194 (4, M^+), 179 (2), 139 (100), 81 (48), 69 (35), 43 (86)	1.30−1.80 (m, 2 H, 7-H_2), 1.59 (s, 3 H, 6-H_3), 2.02 (s, 3 H, 10-H_3), 2.30 (m, 3 H, 3-H and 8-H_2), 2.77 (s, 3 H, 1a-H_3), 2.87 (m, 2 H, 2-H_2), 4.75 (br s, 1 H, 5-H[a]), 4.85 (br s, 1 H, 5-H[b])	17.89 (q, C-6), 23.35 (t, C-7), 29.72 (q, C-10), 38.58 (q, C-1a), 40.23 (t, C-8), 44.44 (d, C-30, 55.78 (t, C-2), 114.97 (t, C-5), 117.62 (s, C-1), 143.00 (s, C-4),206.19 (s, C-9)
26c	2220 (C≡N), 1715 (C=O), 1380, 920	270 (5, M^+), 139 (77), 121 (14), 91 (100), 81 (16), 43 (66)	1.25−1.70 (m, 2 H, 7-H_2), 1.48 (s, 3 H, 6-H_3), 1.97 (s, 3 H, 10-C_3), 2.22 (t, *J* = 7.5, 2 H, 8-H_2), 2.30 (m, 1 H, 3-H), 2.77 (d, *J* = 7.5, 2 H, 2-H_2), 4.04 (s, 2 H, 1a-H_2), 4.71 (br s, 1 H, 5-H[a]), 4.81 (br s, 1 H, 5-H[b]), ≈7.22 (br s, 5 H, Ar-H)	17.66 (q, C-6), 23.15 (t, C-7), 29.49 (q, C-10), 40.04 (t, C-8), 44.19 (d, C-3), 52.63 (t, C-2), 55.18 (t, C-1a), 114.73 (t, C-5), 116.97 (s, C-1), 128.14 (d, 2 C, C-3a or C-4a), 128.15 (d, C-5a), 128.41 (d, 2 C, C-4a or C-3a), 134.34 (s, C-2a), 142.72 (s, C-4), 206.14 (s, C-9)
27a	2215 (C≡N), 1720 (C=O), 1640 (C=C)	262 (33, M^+), 247 (46), 219 (64), 205 (74), 201 (87), 187 (39), 173 (64), 159 (100), 145 (54), 133 (87)	0.99 (s, 6 H, 9-H_3 and 10-H_3), 1.37 (t, *J* = 10.5, 1 H, 7-H[a]), 1.60 (m, 2 H),1.80 (m, 2 H), 2.04 (s, 3 H, 15-H_3), 2.20−2.35 (m, 5 H), 2.80 (s, 3 H, 1a-H_3), 3.00 (t, *J* = 8.0, 2 H, 2-H_2), 4.72 (br s, 1 H, 5-H[a]), 4.81 (br s, 1 H, 5-H[b])	22.10 (q, C-9), 24.31 (t, C-12), 29.62 (q, C-15), 30.87 (q, C-10), 32.00 (t, C-3), 33.47 (s, C-8), 38.66 (q, C-1a), 39.66 (t, C-7), 41.18 (d, C-6), 41.64 (t, C-13), 47.70 (d, C-11), 51.41 (t, C-2), 109.38 (t, C-5), 118.02 (s, C-1), 147.96 (s, C-4), 208.17 (s, C-14)
27c	2220 (C≡N), 1715 (C=O), 1640 (C=C)	338 (63, M^+), 323 (34), 295 (57), 281 (69), 267 (37), 225 (51), 213 (97), 149 (100), 134 (29), 121 (66)	0.97 (s, 3 H, 9-H_3 or 10-H_3), 0.98 (s, 3 H, 10-H_3 or 9-H_3), 1.42 (t, *J* = 10.5, 1 H, 7-H[a]), 1.50-1.80 (m, 4 H), 2.05 (s, 3 H, 15-H_3), 2.20−2.35 (m, 5 H), 2.97 (t, *J* = 8.0, 2 H, 2-H_2), 4.14 (s, 2 H, 1a-H_2), 4.69 (br s, 1 H, 5-H[a]), 4.79 (br s, 1 H, 5-H[b]), 7.31 (m, 5 H, Ar-H)	22.03 (q, C-9), 24.24 (t, C-12), 29.61 (q, C-15), 30.80 (q, C-10), 32.11 (t, C-3), 33.39 (s, C-8), 39.44 (t, C-7), 41.05 (d, C-6), 41.61 (t, C-13), 47.58 (d, C-11), 48.74 (t, C-2), 55.65 (t, C-1a), 109.37 (t, C-5), 118.19 (s, C-1), 128.18 (d, 2 C, C-3a or C-4a), 128.30 (d, C-5a), 128.64 (d, 2 C, C-4a or C-3a), 134.52 (s, C-2a), 147.83 (s, C-4), 208.23 (s, C-14)
28a	2300−3300 (N^+−H), 1580 (C−N^+)	167 (1, M^+ − HCl), 152 (2), 98 (5), 95 (5), 93 (3), 81 (3), 72 (26), 67 (3), 44 (100), 36 (9)	1.01 (s, 3 H, 5-H_3), 1.13 (s, 3 H, 4-H_3), 1.13 (m, 1 H, 2-H), 1.45 (dd, *J* = 8.0, 8.0, 1 H, 6-H), 1.64 (d, *J* = 1.5, 3 H, 9-H_3), 1.68 (d, *J* = 1.5, 3 H, 10-H_3), 2.60 (s, 3 H, 1a-H_3), 2.88 (dd, *J* = 13.0, 8.0, 1 H, 1-H[a]), 2.94 (dd, *J* = 13.0, 6.5, 1 H, 1-H[b]), 4.74 (dqq, *J* = 8.0, 1.5, 1.5, 1 H, 7-H), 9.45 (br s, 2 H, $^+NH_2$)	15.28 (q, C-5), 18.43 (q, C-9), 20.32 (s, C-3), 23.72 (d, C-2), 25.56 (q, C-10), 25.83 (d, C-6), 27.93 (q, C-4), 31.54 (q, C-1a), 45.67 (t, C-1), 117.39 (d, C-7), 136.72 (s, C-8)

Table 2 (continued)

Product	IR ($CHCl_3$)[a] ν (cm^{-1})	MS *m/z* (%)	^{1}H NMR[b] δ, *J*, $W_{1/2}$ (Hz)	^{13}C NMR[b,c] δ, *J* (Hz)
28c	2300−3300 (N^+−H), 1580 (C−N^+)	218 (1), 200 (1), 174 (3), 152 (2), 148 (19), 120 (42), 95 (5), 91 (100)	0.86 (s, 3 H, 5-H_3), 1.07 (s, 3 H, 4-H_3), 1.38 (m, 1 H, 2-H), 1.35 (t, *J* = 8.5, 1 H, 6-H), 1.58 (br s, 6 H, 9-H_3 and 10-H_3), 2.75 (m, 2 H, 1-H_2), 3.93 (AB-system: J_{AB} = 14.0, $\Delta\delta_{AB}$ = 12, 2 H, 1a-H_2), 4.57 (dqq, *J* = 8.0, 1.5, 1.5, 1 H, 7-H), 7.20−7.60 (m, 5 H, Ar-H), 9.80 (br s, 2 H, $^+NH_2$)	14.95 (q, C-5), 18.33 (q, C-9), 20.44 (s, C-3), 23.85 (d, C-6), 25.45 (q, C-10), 25.83 (d, C-6), 27.86 (q, C-4), 43.01 (t, C-1), 49.61 (t, C-1a), 117.34 (d, C-7), 128.74 (d, 2 C, C-4a), 128.96 (d, C-5a), 129.88 (d, C-3a), 130.49 (s, C-2a), 136.41 (s, C-8)
28g	2300−3300 (N^+−H), 1580 (C−N^+), 1575, 1485	335 (1), 320 (1), 266 (4), 240 (45), 212 (27), 200 (4), 198 (4), 183 (100), 171 (5), 169 (5), 168 (4), 152 (7)	0.91 (s, 3 H, 5-H_3), 1.10 (s, 3 H, 4-H_3), 1.25 (m, 1 H, 2-H), 1.42 (dd, *J* = 8.5, 8.0, 1 H, 6-H), 1.62 (br s, 3 H, 9-H_3 or 10-H_3), 1.63 (br s, 3 H, 10-H_3 or 9-H_3), 2.80 (m, 2 H, 1-H_2), 3.98 (AB-system: J_{AB} = 14.0, $\Delta\delta_{AB}$ = 10, 2 H, 1a-H_2), 4.72 (dqq, *J* = 8.0, 1.5, 1.5, 1 H, 7-H), 6.85−7.50 (m, 9 H, Ar-H), 9.90 (br s, 2 H, $^+NH_2$)	15.00 (q, C-5), 18.38 (q, C-9), 20.48 (s, C-3), 23.83 (d, C-2), 25.50 (q, C-10), 25.84 (d, C-6), 27.87 (q, C-4), 43.09 (t, C-1), 49.30 (t, C-1a), 117.34 (d, C-7), 118.92 (d, 2 C, C-9a), 120.23 (d, C-7a), 123.46 (d, C-3a or C-11a), 124.46 (d, C-11a or C- 3a), 129.62 (d, 2 C, C-10a), 130.30 (d, C-4a), 132.39 (s, C-2a), 136.54 (s, C-8), 156.36 (s, C-6a), 157.47 (s, C-8a)

[a] The NMR spectra were recorded for solutions in the following solvents: $CDCl_3$ for compounds **9**, **11**, **12**, **15**, **20a**, **20b**, **20c**, **20d**, **22a**, **22c, 23a, 23b, 23c, 23e, 23f, 24e, 25a, 25e, 27a, 27c, 28a, 28c, 28g**), $CDCl_3$:CCl_4= 1:1 v/v for compounds **19b, 19c, 24a, 24c, 26a, 26c**), CD_3OD for compounds **14, 18a, 18b, 18c, 19a, 21a, 21b, 21c, 22b, 24b, 24f, 25b, 25f**). Signal assignments are given in accordance with the numbering shown in Schemes 2, 4 and 6.

[b] ^{19}F NMR spectra were recorded for the following fluorine containing compounds. **23e**: δ = 47.90; **23f**: δ = 1.44 (2 F, 4a-F_2), 10.27 (1 F, 5a-F), 20.33 (2 F, 3a-F_2); **24e**: δ = 48.10; **24f**: δ = 0.95 (2 F, 4a-F_2), 9.48 (5a-F), 21.29 (2F, 3a-F_2); **25e**: δ = 48.37; **25f**: δ = 0.75 (2 F, 4a-F_2), 9.08 (5a-F), 21.89 (2 F, 3a-F_2).

[c] Multiplicity of the carbon resonances are given in accordance with the off-resonance proton-decoupled spectra. For the 2,6 difluorobenzyl derivatives **23e**, **24e** and **25e** values of J_{C-F} couplings are given in brackets. In the spectra of pentafluorobenzyl derivatives **23f**, **24f** and **25f** chemical shifts of the aromatic carbons were not determined because of their low intensities due to plural carbon-fluorine couplings.

amide **(25b)**, (2,6-difluorobenzyl)[(1*R*,3*S*)-3-(2-hydroxy-2-methylpropyl)-2,2-dimethylcyclopropylmethyl]cyanamide **(25e)**, [(1*R*,3*S*)-3-(2-hydroxy-2-methylpropyl)-2,2-dimethylcyclopropylmethyl]pentafluorophenylmethylcyanamide **(25f)**, [(1*R*,3*S*)-3-(2-hydroxy-2-methylpropyl)-2,2-dimethylcyclopropylmethyl]-(3-phenoxybenzyl)cyanamide (**25g**, yield 74%, described earlier[17]), (±)-methyl[3-methyl-2-(3-oxobutyl)but-3-enyl]cyanamide **(26a)**, (±)-benzyl[3-methyl-2-(3-oxobutyl)but-3-enyl]cyanamide **(26c)**, {3-[(1*S*,2*R*)-3,3-dimethyl-2-(3-oxobutyl)cyclobutyl]but-3-enyl}-methylcyanamide **(27a)**, benzyl{3-[(1*S*,2*R*)-3,3-dimethyl-2-(3-oxobutyl)cyclobutyl]but-3-enyl}cyanamide **(27c)** (Tables 1 and 2).

Reduction of *N*-Cyanamides 24a, 24 c and 24g

Zinc powder (0.30 g, 4.6 mmol) was added portionwise to a stirred solution of the cyanamides **24a**, **24c**, or **24g** (2.0 mmol) in AcOH (3 mL). The reaction mixture was stirred under reflux for 8 h, diluted with H_2O (2 mL) and extracted with Et_2O (2 × 2 mL). The aqueous phase was treated with an excess of aq NaOH and extracted with $CHCl_3$ (3 × 2 mL). The combined $CHCl_3$ extracts were dried (Na_2SO_4) and concentrated at reduced pressure. The residue was dissolved in anhyd Et_2O and treated with gaseous HCl to afford the corresponding hydrochlorides: [(1*R*,3*S*)-2,2-dimethyl-3-(2-methylpropenyl)cyclopropylmethyl]methylamine hydrochloride **(28a)**, benzyl[(1*R*,3*S*)-2,2-dimethyl-3-(2-methylpropenyl)cyclopropylmethyl]amine hydrochloride **(28c)**, and [(1*R*,3*S*)-2,2-dimethyl-3-(2-methylpropenyl)cyclopropylmethyl]-(3-phenoxybenzyl)-amine hydrochloride **(28g)**.

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[#] Present address: Chemistry department, University of Idaho, Moscow, Idaho, USA
[†] Present address: Department of chemistry, University of Oregon, Oregon, USA
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