# A New Versatile Synthesis of Ring-Substituted 2-Cyclopropylglycines and Related Amino Acids[1]☆

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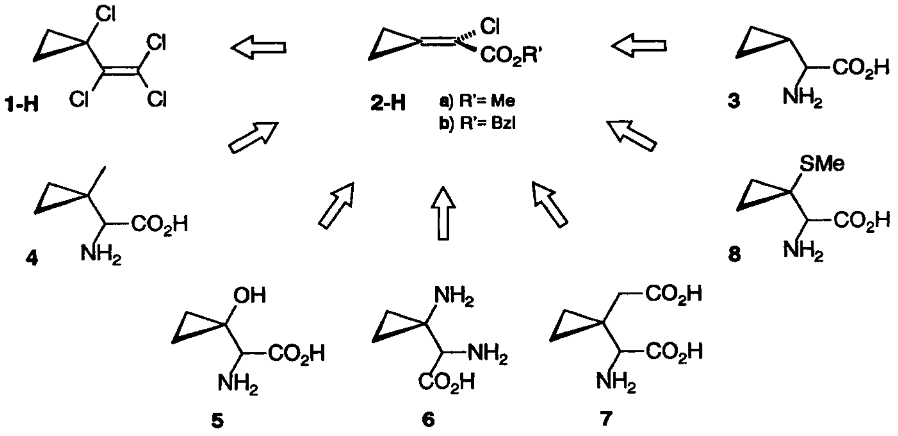
Alkyl 2-chloro-2-cyclopropylideneacetates **2** serve as universal starting materials for a new general synthesis of cyclopropylglycines by a simple three- to four-step methodology. 1,4-Addition of nucleophiles, substitution with azide ion, and mild catalytic deprotection lead to a variety of salt-free cyclopropyl-substituted amino acids in good yields, including the natural products 2-(1-methylcyclopropyl)glycine (**4**) and cleonin (**5**).

A variety of simple cyclopropane-containing compounds have been of synthetic interest due to their biological activities[3]. These include cyclopropylamines[4], cyclopropylmethanols[5], cyclopropanones[6], and more recently cyclopropane-derived amino acids, which also have attracted attention as phytochemical agents, enzyme inhibitors, or probes in metabolism studies[7]. In contrast to the other compounds, cyclopropyl-substituted amino acids are quite regularly found in plants or microorganisms. Formally, most of them are methano-bridged derivatives of proteinogenic amino acids. Synthetic efforts have mainly been directed towards 1-aminocyclopropanecarboxylic acid (ACC) and its 2-substituted derivatives. ACC is a biosynthetic precursor of the phytohormone ethylene. Thus, derivatives of ACC which enhance or preferably block the ethylene production in plants may conceivably find applications in agriculture[8].

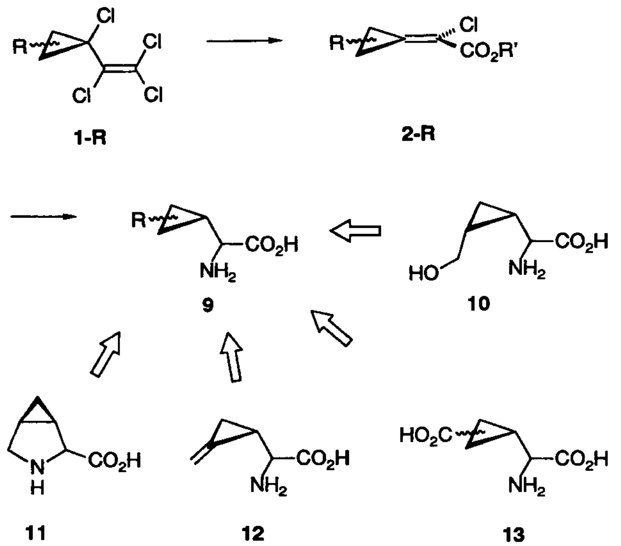
Cyclopropylglycines form the largest group of naturally occurring cyclopropane-derived amino acids, and some of them exhibit interesting biological properties. They have been used as probes for radical or cationic intermediates in studies of metabolic mechanisms[9]. The group of 1′-substituted derivatives consists of the antibacterial compound 2-(1-methylcyclopropyl)glycine (**4**)[10] and 2-(1-hydroxycyclopropyl)glycine (cleonin, **5**), a fragment of the macrocyclic antibiotic cleomycin[11].

The artificial 1′-amino compound **6** appears to be an interesting analogue of cleonin as well as of ACC. 2-[1-(Carboxymethyl)cyclopropyl]glycine (**7**) resembles glutamic acid[12]. A sulfur-containing acid like **8** and 2-cyclopropylglycine (**3**) have been envisaged as further targets of interest, which should be available along a general route from 2-chloro-2-cyclopropylideneacetates **2-H** (Scheme 1). The preparation of **3** from **2-H** would also prove the applicability of this methodology to 2′-substituted 2-cyclopropylglycines obtained from the correspondingly substituted precursors **2-R** (Scheme 2). They are represented by 2-(2-methylenecyclopropyl)- and 2-(2-carboxycyclopropyl)glycine (**12** and **13**), of which the first exhibits hypoglycemic activity. Cyclopropaproline **11** has been shown to be a gametocide[13].

Scheme 1. 1′-Substituted 2-cyclopropylglycines prepared from methyl 2-chloro-2-cyclopropylideneacetates **2-H**



Scheme 2. 2′-Substituted 2-chloro-2-cyclopropylideneacetates **2-R** as possible precursors of various 2′-substituted 2-cyclopropylglycines



## 1′-Substituted 2-Cyclopropylglycines

We have developed a methodology to prepare both types, 1′- and 2′-substituted, 2-cyclopropylglycines utilizing 2-chloro-2-cyclopropylideneacetates **2-H** and **2-R** as starting materials[14]. The unsubstituted methyl 2-chloro-2-cyclopropylideneacetate (**2a**) is easily accessible from commercial 1-chloro-1-(trichlorovinyl)cyclopropane (**1-H**) in over 80% yield[15]. To obtain the envisaged variety of 1′-substituted amino acids, the 1,4-addition of appropriate carbon, nitrogen, sulfur, and oxygen nucleophiles is required which allows mild deprotection in the last step. Thus, we have preferably used protecting groups which can be cleaved by mild catalytic hydrogenation. This has helped us to avoid the use of strongly acidic or basic conditions which often cause cleavage of the three-membered ring and/or provide charged amino acids only.

The addition of most nucleophiles to **2** occurs smoothly, as it is accelerated by the strain release upon conversion of the sp- to a sp$^2$-hybridized carbon[16] in the three-membered ring[14,17,18] (Scheme 3, Table 1).

Carbon nucleophiles add in a 1,4-fashion, when the usual soft reagents are applied. Thus, the reaction with LiCH$_2$CO$_2$*t*Bu in HMPA/THF yields 91% of **14a-CH$_2$CO$_2$*t*Bu**, whereas with lithium dimethylcuprate only 61% of **14a-Me** are obtained due to secondary reactions like coupling and 1,2-addition.

Some nitrogen nucleophiles cause problems. Primary amines add readily, but often give rise to side reactions either with the neighboring chloromethine group or the ester function. Less nucleophilic ammonia equivalents like acetamide or the classical phthalimide do not add or give low yields. Furthermore, the α-chlorine in **14a-NPhth** cannot be substituted nor can the phthalimido group be cleaved without destroying the ring. The latter is also true for the α-phthalimido derivatives **16-Nu** (Scheme 4). The (alkoxycarbonyl)amines (Boc)$_2$NH and (Moc)(Boc)NH add to **2a** in satisfactory yield, but the α-chlorine atom in **14a-N(Boc)$_2$** and even in the less bulky **14a-N(Boc)(Moc)** cannot be substituted, possibly due to steric hindrance.

These problems have been overcome by use of dibenzylamine or (diphenylmethylene)amine (DPMA-H)[18] as ammonia equivalents. Both compounds add quantitatively in a 1,4-fashion, and the corresponding products also give good results in the substitution reaction. The dibenzylamine adduct is easier to handle during the workup, but in some cases causes problems during deprotection to the amino function (see below).

Benzyl alkoxide has been chosen to introduce a protected hydroxy group, thus affording a precursor of cleonin (**5**). Although benzyl alcohol can be added without simultaneous transesterification of the methyl ester, it is easier to combine both steps to obtain 61% of the desired benzyl ester **14b-OBzl**.

Sulfur nucleophiles (e.g. NaSMe, NaSBzl) add smoothly at −78 °C, because at this temperature subsequent nucleophilic substitution of the chlorine is much slower.

The selective hydrogenation of the double bond is crucial for the synthesis of all natural 2′-substituted 2-cyclopropyl-

Scheme 3

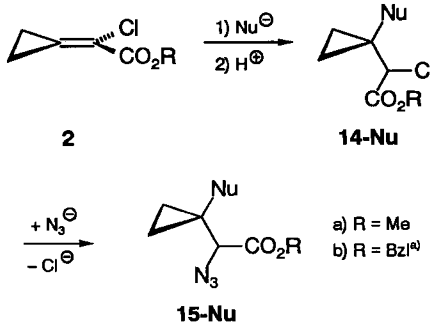


Table 1. 1,4-Addition of nucleophiles to 2-chloro-2-cyclopropylideneacetates (**2-H**) and substitution of the chlorine by azide

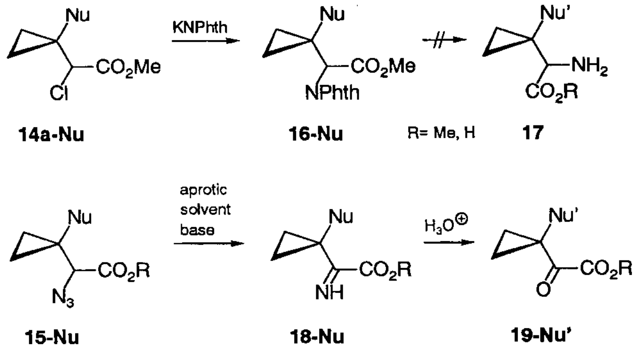
| Starting comp. | Reagent | Nu | Yield (%) **14a/b-Nu** | Method[b] | Yield (%) **15a/b-Nu** |
|---|---|---|---|---|---|
| **2a** | LiCH$_2$CO$_2$*t*Bu | CH$_2$CO$_2$*t*Bu | 91 | A | 94 |
| **2a** | LiCu(CH$_3$)$_2$ | CH$_3$ | 61 | A | 98 |
| **2a** | KNHCOCH$_3$ | NHCOCH$_3$ | 0 | – | – |
| **2a** | KNPhth[c] | NPhth | 18 | – | – |
| **2a** | KN(Boc)$_2$[d] | N(Boc)$_2$ | 69 | A/B | 0 |
| **2a** | KN(Boc)(Moc)[e] | N(Boc)(Moc) | 64 | A/B | 0 |
| **2a** | HNBzl$_2$[a] | NBzl$_2$ | 97 | B | 89 |
| **2b** | HNBzl$_2$ | NBzl$_2$ | 75 | B | 91 |
| **2a** | HN=CPh$_2$ | N=CPh$_2$ | 98 | A | 91 |
| **2b** | HN=CPh$_2$ | N=CPh$_2$ | 86 | A | 88 |
| **2a** | BzlOH/NEt$_3$ | OBzl | 60[f] | – | – |
| **2a** | KOBzl | OBzl | 61[g] | B | 66 |
| **2b** | NaOBzl | OBzl | 74 | B | 66 |
| **2a** | NaSMe | SMe | 77 | B | 96 |
| **2a** | NaSBzl | SBzl | 82 | B | 78 |
| **2a** | NaBH$_4$/*i*PrOH | H | 74 | A | 98 |

[a] Bzl = benzyl. – [b] A: NaN$_3$/DMF/(NaI)/20–80 °C; B: NaN$_3$/H$_2$O/Aliquat 336®/50 °C. – [c] Phth = phthaloyl. – [d] Boc = *tert*-butoxycarbonyl. – [e] Moc = methoxycarbonyl. – [f] According to $^1$H NMR and GC only. – [g] Includes transesterification to **14b-OBzl**.

glycines obtained from substituted cyclopropylideneacetates **2-R**. A yield of 74% of **14a-H**, the precursor of the parent cyclopropylglycine **3**, can be achieved by reduction of **2-H** with $NaBH_4$ in chloroform/2-propanol in the presence of silica gel[19]. The application of other methods affords only 45% or even less **14a-H**, contaminated with products of further reduction.

Once the desired substituents are placed on the ring, the α-chloro ester moiety in **14-Nu** has to be converted into a glycine moiety. The classical Gabriel phthalimide method has proved useless with respect to yields and deprotection conditions. Thus, at best a 41% yield of **16-Nu** has been obtained, and the phthalimido group can neither be hydrolyzed under basic or acidic conditions nor cleaved by reduction with $NaBH_4$ (Scheme 4). In contrast, azide can be introduced in good to mostly excellent yields either classically with sodium azide in DMF or by the phase-transfer technique with Aliquat 336® as catalyst (see Table 1). Other catalysts (e.g. benzyltriethylammonium chloride) or the recently described polymer-bound azide[20] give lower or no yields as do the sterically congested substrates **14a-N(Boc)$_2$** and **14a-N(Boc)(Moc)**.

Scheme 4



Interestingly, α-chloro esters **14a-Nu** bearing nucleophilic β-substituents (**14-Nu**, **Nu = SMe, SBzl, NBzl$_2$**, and **N=CPh$_2$**) are converted into α-imino esters **18-Nu** in good yields upon treatment with sodium azide in DMF at temperatures above ca. 50°C. With the sulfur compound **15a-SMe** up to 90% of α-imino ester **18a-SMe** are formed, which is easily hydrolyzed to the more stable α-keto ester **19a-SMe**, and both compounds can be isolated. The α-azido esters **15-Nu**, when treated with lithium methanolate in THF, preferentially under aprotic conditions, liberate nitrogen to furnish the imino esters **18-Nu** almost quantitatively (Scheme 4); in contrast, simple heating to 100°C even in the presence of acid does not cause considerable decomposition of **15a-SMe**. This suggests the influence of the non-bonding lone pair of the neighboring γ-hetero atom on the decomposition of the azido group as found by Hiyama et al.[21] in a similar case. This is also supported by the observation that the ease of imine formation is at least qualitatively correlated with the nucleophilicity of the neighboring group.

A special case of isomerism is encountered with diimine **18a-N=CPh$_2$**. Its spectroscopic data and properties, e.g. the insensitivity to hydrolysis, suggest that the compound in reality exists only as methyl 2′,2′-diphenylspiro[cyclopropane-1,4′-imidazolidine]-5′-carboxylate, resulting from the unusual *5-endo-trig* ring closure of the initial open chain by nucleophilic 1,2-addition of the α-imine NH to the other imine double bond.

The imine formation upon substitution of **14a-Nu** by the azide can be suppressed by lowering the reaction temperature and adding catalytic amounts of sodium or potassium iodide or more effectively by switching to the less basic phase-transfer conditions.

Free amino acids could be obtained by two general methods. The methyl esters **15a-H, -CH$_3$, -NBzl$_2$, -CH$_2$CO$_2$*t*Bu**, and **15a-SMe** can be hydrolyzed under basic conditions (1 N NaOH) to the corresponding azido acids **20-Nu′** upon acidification. These can be reduced preferably by catalytic hydrogenation over palladium (10% on charcoal) to give the respective isoelectric amino acids **3**, **4**, **6**, **7**, and **8** usually in good yields (Scheme 5, Table 2).

Scheme 5

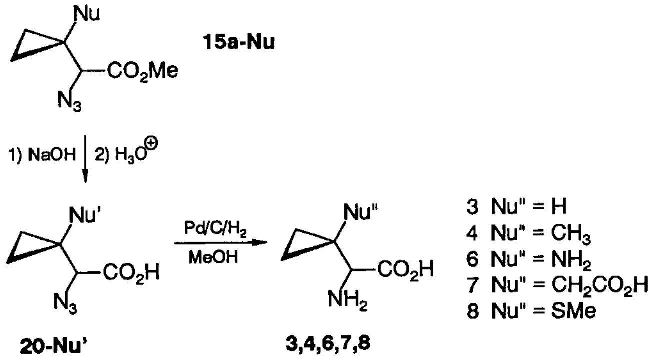
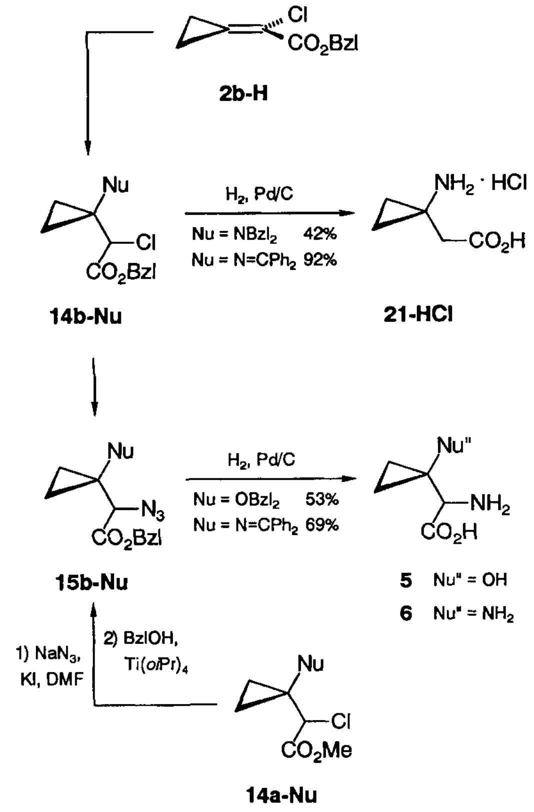


Table 2. Deprotection of α-azido esters **15a-Nu** in two steps to yield 1′-substituted 2-cyclopropylglycines (see Scheme 5)

| 15a-Nu (Nu) | 20-Nu′ (Nu′) | Yield (%) | Product amino acid | Nu″ | Yield (%) |
|---|---|---|---|---|---|
| H | H | 93 | **3** | H | 57 |
| $CH_3$ | $CH_3$ | 98 | **4** | $CH_3$ | 94 |
| $NBzl_2$ | $NBzl_2$ | 47 | **6** | $NH_2$ | 37 |
| $CH_2CO_2t$Bu | $CH_2CO_2H$ | 72 | **7** | $CH_2CO_2H$ | 98 |
| SMe | SMe | 92 | **8** | SMe | 73 |

Some precursor esters **15b-Nu** are outfitted with protecting groups (benzyl, diphenylmethylene, and azido groups) which potentially can be removed by catalytic hydrogenation in a single operation to yield the corresponding amino acids (Scheme 6). Thus, the benzyl esters **15b-OBzl** and **15b-N=CPh$_2$**, obtained by preceding titanium tetraisopropoxide-catalyzed transesterification of methyl esters[22] **2a-H** or **15a-Nu**, can be hydrogenated over palladium on charcoal to give the amino acids **5** and **6**, respectively (Scheme 6). The conversion of **15b-OBzl** to cleonin (**5**) proceeds readily (TLC, NMR) but after chromatography the isolated yield is only 53%. **15b-N=CPh$_2$** is converted into the somewhat instable α,β-diamino acid **6** in 69% yield. This route to **6** has turned out to be more advantageous than the two-step procedure described earlier. The attempted one-step conversion of **15b-NBzl$_2$** to **6** has failed. Although **15b-NBzl$_2$** is obtained in very good overall yield from **2b-H** (68%, see Table 1), it cannot be deprotected totally to the free amino acid **6** by catalytic hydrogenation over palladium at a hydrogen pressure of 1 bar.

Scheme 6

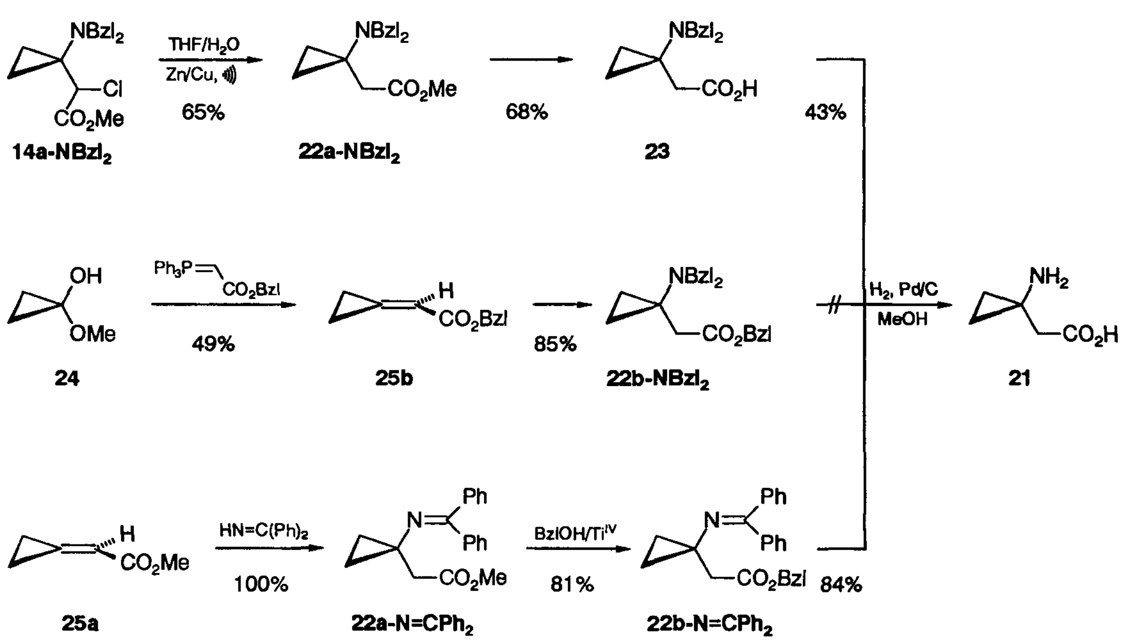


Hydrogenolysis of α-chloro esters **14b-NBzl$_2$** and **14b-N=CPh$_2$** in methanol/hydrochloric acid gives the new β-amino acid 3,3-ethylene-β-alanine hydrochloride **21 · HCl**[23] in 42 and 88% yield, respectively (Scheme 6). Hydrogenolysis of **14b-N=CPh$_2$** in methanol only gives product mixtures, e.g. of **21 · HCl** and 2-(1-aminocyclopropyl)-2-chloroacetic acid if the reaction is incomplete. Extended reaction times lead to complete dechlorination, but in addition to **21 · HCl** its methyl ester is formed in increasing amounts. Salt-free **21** is obtained by stepwise dechlorination and deprotection of **14a-NBzl$_2$** or from methyl (**25a**) and benzyl cyclopropylideneacetates (**25b**)[24], respectively (Scheme 7). Again cleavage of the (diphenylmethylene)amino group (84% yield including ester cleavage) proves to be superior to deprotection of the dibenzylamino group (43%).

## 2′-Substituted 2-Cyclopropylglycines

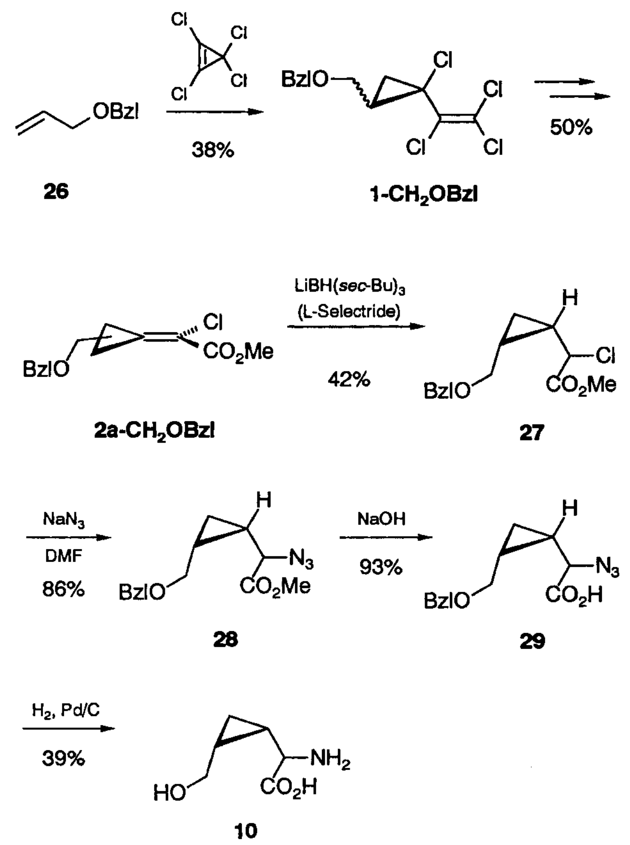
Further efforts have been directed towards the synthesis of 2′-substituted 2-cyclopropylglycines from the corresponding 2-cyclopropylideneacetates **2-R**. These can be obtained according to the same method as the unsubstituted compound **2-H**, yet from the correspondingly substituted 1-chloro-1-(trichlorovinyl)cyclopropanes **1-R** (Scheme 2). A first member of this group, 2-[2-(hydroxymethyl)cyclopropyl]glycine (**10**), has successfully been synthesized according to the route depicted in Scheme 8. Thus allyl benzyl ether (**26**) can be converted to the correspondingly substituted cyclopropylideneacetate **2a-CH$_2$OBzl** by means of our published standard procedure[15,17,25]. Reduction with lithium tri-*sec*-butylborohydride (L-selectride®) gives **27** in 42% yield, which is converted to **10** according to the previously described protocol (cf. Schemes 3 and 6). Although the yields will have to be improved, **10** is not only interesting by itself,

Scheme 7. Synthesis of 3,3-ethylene-β-alanine (**21**)



e.g. as a potential enzyme inhibitor[5,7], but may also serve as a precursor of the naturally occurring amino acids **11**–**13**.

Scheme 8. A route to 2-[2-(hydroxymethyl)cyclopropyl]glycine (**10**)



## Conclusion

This route to natural as well as new non-natural cyclopropane-containing α- and β-amino acids is the first general one to 1′-substituted 2-cyclopropylglycine derivatives. The 1′-substituent is introduced by a Michael addition, and subsequently the α-chloro substituent is converted to an α-amino group. The cyclopropyl group as well as the glycine part – which is intrinsic in the α-chloroacetate moiety – are both preformed in the starting material. Variation of only one step thus gives a large variety of cyclopropylglycines, whereas in former syntheses every amino acid required its own route[26]. Furthermore, appropriate choice of protecting groups permits deprotection to the salt-free isoelectric amino acids without the use of sometimes cumbersome ion exchange or dehydrochlorination procedures. Most steps proceed in good to excellent yields although most of them have not been optimized. In addition, the corresponding α-imino and α-keto acids have been made available. They are potential substrates for the perspective enantioselective syntheses of such cyclopropylgycines. The physiological properties of the new compounds are under current investigation.

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## Experimental

$^1$H NMR: Bruker AW 250, WH 270, WM 400 and Varian XL 300, EM 360 A. $\delta = 0$ for tetramethylsilane (TMS) and sodium 3-(trimethylsilyl)-1-propanesulfonate (DSS), 1.98 for acetonitrile ($CH_3CN$), 2.49 for [$D_5$]DMSO, 3.30 for $CHD_2OD$, 4.85 for HDO, and 7.26 for $CHCl_3$ (standards are given if necessary, otherwise the solvent is used as standard). $H_{cpr}$ = cyclopropylic H; $H_{ar}$ = aromatic H; *o,m,p*-$H_{ar}$ = H in *ortho, meta, para* position, respectively, of a phenyl group. Ambiguous assignments are marked with an asterisk (*); mc designates centrosymmetric multiplets. – $^{13}$C NMR: Bruker AW 250, WH 270, WM 400 and Varian XL 300. $\delta = 0$ for tetramethylsilane (TMS) and sodium 3-(trimethylsilyl)-1-propanesulfonate (DSS), 1.3 for $CD_3CN$, 1.7 for $CH_3CN$ in $D_2O$, 39.5 for [$D_6$]DMSO, 49.0 for [$D_4$]methanol, 77.0 for $CDCl_3$ (standards are given if necessary, otherwise the solvent is used as standard). $C_{cpr}$ = cyclopropylic C; $C_{ar}$ = aromatic C; *i,o,m,p*-$C_{ar}$ = *ipso, ortho, meta,* or *para* carbon, respectively, of a phenyl group. Assignments are usually confirmed by DEPT(135) spectra with complete DEPT (s, d, t, q stands for $CH_0$, $CH_1$, $CH_2$, and $CH_3$ respectively) or 2D- and/or long-range coupling when necessary. Ambiguous assignments are marked with an asterisk (*). – IR: Perkin-Elmer 399, 1310, 1720 X and Beckman instruments Acculab 4. – MS: Varian MAT CH7, MAT 311 A, Micromass 7070 F. – GC/MS: MAT 112 with Varian Aerograph 1400 (25-m capillary Oribond SE-54, helium). – GC: Siemens Sichromat 3 (25-m capillary CB SE-54, hydrogen), $R_t$ = relative retention time. – TLC: Silica 60 $F_{254}$ from Merck-Schuchardt. Detection: UV, iodine chamber, 3.5% alcoholic molybdatophosphoric acid; for imines, amines, and amino acids: 0.1% ninhydrin from Merck. – CC: Silica gel 60 (60–230 mesh, ca. 0.5 g/ml) was purchased from Merck, aluminum oxide from Woelm. For the preparation of impregnated "dry" silica gel see ref.[18]. – M.p.: uncorrected; apparatus from Wagner & Münz and Büchi (according to Dr. Tottoli). – U.S.: Ultrasonic bath Bandelin RK 225. – Microanalyses: Mikroanalytisches Labor des Instituts für Organische Chemie der Universität Hamburg and Mikroanalytisches Labor Beller, Göttingen. Some samples caused problems due to decomposition (e.g. some azides **15-Nu** liberate nitrogen when stored, amino acids have been found to contain nonstoichiometric solvent inclusions).

DMPA = (Diphenylmethylene)amino, PE = petroleum ether (b.p. < 70 °C), HMPA = hexamethylphosphoric triamide.

### *1-Chloro-1-(trichlorovinyl)cyclopropanes and Cyclopropylideneacetates* **1, 2, 25**

*1-Chloro-1-(trichlorovinyl)cyclopropane* (**1-H**) *and Methyl 2-Chloro-2-cyclopropylideneacetate* (**2a-H**) were obtained in 80–95 and 80% yield, respectively, and their 2′-derivatives are synthesized according to our published procedures[14,15,17,25].

*2-[(Benzyloxy)methyl]-1-chloro-1-(trichlorovinyl)cyclopropane* (**1-CH$_2$OBzl**): 60 g (0.34 mol) of tetrachlorocyclopropane and 100 g (0.68 mol) of allyl benzyl ether (**26**) in a glass autoclave (a thick-walled sealed glass ampoule) are agitated at 170 °C for 24 h. The crude product is separated from the polymers by a short-path distillation (> 150 °C) under vacuum ($10^{-2}$ Torr) followed by thorough distillation of the volatile compounds; thus 42 g (38%) of **1-CH$_2$OBzl** is obtained, b.p. 118–120 °C/0.05 Torr, *cis/trans* = 1.3:1 ($^1$H NMR). – IR (film): $\tilde{\nu}$ = 3100 cm$^{-1}$, 3060, 2960, 2900, 1730, 1590 (C=C), 1500, 1460, 1390, 1360, 1270, 1190, 1170, 1110, 1040, 950, 920, 900, 820, 750, 710, 680. – $^1$H NMR (270 MHz, $CDCl_3$):

δ = 1.30 (dd, 1H, 3-$H_c$), 1.53 (bs, 1H, 3-$H_t$), 1.62 (dd, 1H, 3-$H_c$), 1.71 (bs, 1H, 3-$H_t$), 1.83 (mc, 1H, 2-$H_c$), 2.02 (mc, 1H, 2-$H_t$), 3.29 (dd, 1H, 1″-$H_t$), 3.64–3.80 (3 dd, 3H, 1″-$H_t$, 2 × 1″-$H_c$), 4.48 (s, 2H, 2″-$H_t$), 4.61 (AB system, 2H, 2″-$H_c$), 7.26–7.40 (m, 10H, $H_{ar}$). – MS (70 eV): *m/z* (%) = 289 (0.5) [$M^+$ – Cl, 3 Cl], 259 (0.3), 223 (0.14), 163 (0.01) [$M^+$ – 2 Cl – Bzl], 146 (0.4) [$M^+$ – 2 Cl – BzlOH], 133 (0.8) [$M^+$ – 2 Cl – $CH_2OBzl$], 105 (1.6), 91 (100) [$Bzl^+$], 77 (2.5) [$Ph^+$].

$C_{13}H_{12}Cl_4O$ (326.1)
Calcd. C 47.89 H 3.71 Cl 43.49
Found C 47.75, 47.72 H 3.74, 3.69 Cl 43.61

*Benzyl 2-Chloro-2-cyclopropylideneacetate* (**2b-H**): 340 mg (1.2 mmol) of titanium tetraisopropoxide is added to 500 mg (3.42 mmol) of **2a-H** in 17 ml of benzyl alcohol. The mixture is stirred at 90°C for ≈18 h. The benzyl alcohol is distilled off (> 39°C/0.01 Torr) and the residue chromatographed on silica gel (100 g, 2.6 × 50 cm, PE/ethyl ether, 9:1). Yield 624 mg (73%) of **2b-H**, $R_f$ = 0.60. [A second fraction ($R_f$ = 0.51) predominantly contains **14b-OBzl** (v.i.).]; m.p. 49°C. – IR (KBr): ṽ = 3080 $cm^{-1}$, 3040, 2980, 1730 (C=O), 1500, 1450, 1380, 1270, 1110, 1060, 760, 740, 700. – $^1H$ NMR (270 MHz, $CDCl_3$): δ = 1.47 (ddd, 2H, $H_{cpr}$), 1.72 (ddd, 2H, $H_{cpr}$), 5.28 (s, 2H, $OCH_2$), 7.38 (mc, 5H, $H_{ar}$). – MS (70 eV): *m/z* (%) = 222 (0.1) [$M^+$], 141 (0.3), 128 (0.2), 115 (0.3) [$M^+$ – OBzl], 91 (100) [$Bzl^+$], 77 (2.2) [$Ph^+$], 65 (5.6), 51 (6.3).

$C_{12}H_{11}ClO_2$ (222.7)
Calcd. C 64.73 H 4.98 Cl 15.92
Found C 65.15, 65.06 H 5.07, 5.16 Cl 15.31

*Methyl 2-{2-[(Benzyloxy)methyl]cyclopropylidene}-2-chloroacetate* (**2a-$CH_2OBzl$**): A solution of 20.0 g (61.3 mmol) of **1-$CH_2OBzl$** in 30 ml of methanol is dropped to 40.0 g (0.7 mol) of KOH in 180 ml of methanol at 60°C. The solution is stirred at 80°C for an additional 18 h. 240 ml of water is then added, the organic phase separated, and the residue in turn extracted with 5 × 100 ml of ethyl ether. The combined ethereal extracts containing the orthoester are shortly dried with magnesium sulfate, the ethyl ether is removed and the residue taken up in 100 ml of methanol. The solution is stirred with 5 ml of diluted hydrochloric acid. The reaction is monitored by GC (200°C; $R_t$ = 1.00 and 1.70 for **2a-$CH_2OBzl$**; 2.25 and 3.56 for the corresponding orthoesters). After complete conversion (≈45 min) 100 ml of a sodium hydrogen carbonate solution is added. The mixture is extracted with 5 × 50 ml of ethyl ether, the combined extracts are dried, the solvent is removed and the residue chromatographed on silica gel (300 g, 4.8 × 45 cm, PE/*tert*-butyl methyl ether, 4:1). Yield 8.2 g (50%) of **2a-$CH_2OBzl$** (mixture of *cis/trans* isomers). – IR (film): ṽ = 3060 $cm^{-1}$, 3030, 2960, 2870, 1780, 1730 (C=O), 1450, 1430, 1370, 1270, 1200, 1150, 1100, 1070, 1040, 1010, 910, 760, 740, 700. – $^1H$ NMR (270 MHz, $CDCl_3$), isomer A: δ = 1.37 (dd, 1H, 3′-H), 1.62 (dd, 1H, 3′-H), 2.26 (mc, 1H, 2′-H), 3.07 (dd, 1H, 1″-H), 3.69 (s, 3H, $OCH_3$), 3.89 (dd, 1H, 1″-H), 4.45 (AB system, 2H, 2″-H), 7.25 (mc, 5H, $H_{ar}$). – Isomer B: δ = 1.56 (dd, 1H, 3′-H), 1.83 (dd, 1H, 3′-H), 2.08 (mc, 1H, 2′-H), 3.24 (dd, 1H, 1″-H), 3.71 (dd, 1H, 1″-H), 3.75 (s, 3H, $OCH_3$), 4.48 (AB system, 2H, 2″-H), 7.25 (mc, 5H, $H_{ar}$). – MS (70 eV): *m/z* (%) = 234 (0.2) [$M^+$ – MeOH], 231 (0.1) [$M^+$ – Cl], 213 (1.0), 160 (6.2) [$M^+$ – $CClCO_2Me$], 145 (2.0) [$M^+$ – $CH_2OBzl$], 125 (1.1), 107 (1.4), 91 (100) [$Bzl^+$], 77 (3.5), 65 (11), 59 (2.3) [$CO_2Me^+$], 51 (5.0).

$C_{14}H_{15}ClO_3$ (266.7)
Calcd. C 63.04 H 5.67 Cl 13.29
Found C 62.67, 62.95 H 5.75, 5.83 Cl 13.04

*Benzyl 2-Cyclopropylideneacetate* (**25b**) is synthesized according to the procedure described for **25a**[24]. Thus, a solution of 70.0 g (0.17 mol) of [(benzyloxycarbonyl)methylene]triphenylphosphorane in 600 ml of benzene is dropped to a solution of 15.0 g (0.17 mol) of 1-methoxycyclopropanol (**24**) and 5.0 g (0.04 mol) of benzoic acid in 600 ml of boiling benzene over a period of 5 h. The total volume is kept constant by distilling off the amount of benzene added during the reaction. After evaporation to dryness the residue is extracted with 4 × 300 ml of PE/ethyl ether (9:1), and the united extracts are chromatographed on silica gel (200 g, 4.3 × 42 cm, PE/ethyl ether, 9:1). Yield 15.8 g (49%) of **25b**; $R_f$ = 0.45. – IR (film): ṽ = 3080 $cm^{-1}$, 3050, 3000, 2970, 1720 (C=O), 1500, 1460, 1380, 1340, 1270, 1180, 1070, 1030, 970, 920, 830, 750, 700. – $^1H$ NMR (270 MHz, $CDCl_3$): δ = 1.23 (mc, 2H, $H_{cpr}$), 1.48 (mc, 2H, $H_{cpr}$), 5.22 (s, 2H, $OCH_2$), 6.32 (m, 1H, 2-H), 7.29–7.43 (m, 5H, $H_{ar}$). – $^{13}C$ NMR (67.9 MHz, $CDCl_3$): δ = 1.97, 4.57, 65.68 ($OCH_2$), 110.92 (C-2), 127.78, 128.29, 136.41, 145.14 (C-1′), 165.48 (C=O). – MS (70 eV): *m/z* (%) = 188 (0.7) [$M^+$], 143 (6.2), 128 (3.6), 107 (0.8) [$OBzl^+$], 91 (100) [$Bzl^+$], 81 (2.3) [$M^+$ – OBzl], 65 (5.1), 53 (5.2) [$M^+$ – $CO_2Bzl$], 40 (19) [$C_3H_4^+$].

### *1,4-Addition to Cyclopropylideneacetates* 14, 22

The syntheses and data of compounds **14a-Me**[17], **14a-N=CPh$_2$**[18], and **22a-N=CPh$_2$**[18] have already been reported.

*Methyl 2-{1-[(tert-Butoxycarbonyl)methyl]cyclopropyl}-2-chloroacetate* (**14a-$CH_2CO_2tBu$**): 16.2 g (140 mmol) of *tert*-butyl acetate is dropped to a solution of lithiumdiisopropylamide, obtained from 14.2 g (140 mmol) of diisopropylamine in 300 ml of THF and 93.3 ml (140 mmol, 1.5 N in hexane) of *n*-butyllithium at –78°C. After 1 h 17.1 ml (140 mmol) of HMPA is added, followed by 10 g (68.5 mmol) of methyl 2-chloro-2-cyclopropylideneacetate (**2a-H**) in 100 ml of THF. After 1 h at –78°C the yellow solution is poured onto 200 ml of saturated aqueous sodium hydrogen carbonate solution. The resulting mixture is extracted with three portions of 100 ml of ethyl ether, the extracts are combined, washed three times with 100 ml of water, dried with magnesium sulfate and filtered. Evaporation of the solvent and chromatography of the residue on silica gel (500 g, column 5 × 50 cm, PE/ethyl ether, 6:1, $R_f$ = 0.34) give 16.4 g (91%) of **14a-$CH_2CO_2tBu$**. – IR (film): ṽ = 1750 $cm^{-1}$ (CO), 1430, 1340, 1300, 1160, 1010. – $^1H$ NMR (270 MHz, $CDCl_3$): δ = 0.66–1.14 (m, 4H, $H_{cpr}$), 1.44 (s, 9H, *t*Bu-H), 2.36 and 2.56 (AB system, 2H, $^2J_{A,B}$ = 16.2 Hz, 1″-H), 3.77 (s, 3H, $CO_2CH_3$), 4.23 (s, 1H, 2-H). – $^{13}C$ NMR (67.9 MHz, $CDCl_3$): δ = 12.27, 13.33 (C-2′), 20.87 (C-1′), 28.06 [$(CH_3)_3C$], 39.01 (C-1″), 52.71 ($OCH_3$), 64.10 (C-2), 80.72 [$(CH_3)_3CO$], 168.51 (C-1), 170.51 (C-2″). – MS (CI, $NH_3$): *m/z* (%) = 280 (32) [$M^+$ + $NH_4$], 263 (11) [$M^+$ + H], 231 (15) [$M^+$ – OMe], 224 (26) [$M^+$ + H – $C_4H_8$], 214 (40), 209 (44), 207 (100) [$M^+$ + $NH_4$ – $C_4H_9O$], 171 (58), 161 (50), 153 (30), 126 (39).

$C_{12}H_{19}ClO_4$ (262.7) Calcd. C 54.86 H 7.29 Cl 13.49
Found C 54.78 H 7.29 Cl 13.49

*Methyl 2-Chloro-2-(1-phthalimidocyclopropyl)acetate* (**14a-NPhth**): 1.13 g (7.7 mmol) of **2a-H** and 1.45 g (7.8 mmol) of potassium phthalimide in 20 ml of DMF and 0.25 ml (14 mmol) of water are stirred at 100°C. After 4 h 100 ml of water is added followed by dil. hydrochloric acid until pH 6 is reached. Overnight 610 mg (27%) of **14a-NPhth** precipitates. Further purification of the product can be achieved by column chromatography on silica gel (1.2 × 58 cm, PE/acetone, 6:1). Yield 400 mg (18%) of **14a-NPhth**. White crystals, m.p. 144°C. – IR (film): ṽ = 1772 $cm^{-1}$ (C=O), 1725 (C=O), 1383, 1270, 1112, 718. – $^1H$ NMR (300 MHz, $CDCl_3$/TMS): δ = 1.395 (1.33–1.47, mc, 2H, $H_{cpr}$), 1.42 (1.20–1.65, mc, 2H, $H_{cpr}$), 3.80 (s, 3H, $CO_2CH_3$), 4.21 (s, 1H, CHCl), 7.79 (7.72–7.86, mc, 4H, $H_{ar}$). – $^{13}C$ NMR (75.4 MHz, $CDCl_3$/TMS): δ = 12.53 (t, $C_{cpr}$), 13.18 (t, $C_{cpr}$), 33.43 (s, $C_{cpr}$), 53.14 (q, $OCH_3$), 61.71 (d, CHCl), 123.24 (d, 2C, 3-, 6-$C_{ar}$), 131.18 (s, 2C, 1-, 2-$C_{ar}$), 134.08 (d, 2C, 4-, 5-$C_{ar}$), 167.47 (s, OC=O*), 167.70 (s, 2C*, NC=O*). – MS (70 eV): *m/z* (%) = 258 (91) [$M^+$ – Cl], 226 (100) [$M^+$ – Cl – MeOH], 198 (47) [$M^+$ – Cl – $HCO_2Me$], 186 (8) [$C_3H_4$=$NPhth^+$], 147 (22), 104 (58). – MS (CI: isobutane): *m/z* (%) = 294 (100) [$M^+$ + H], 258 (24) [$M^+$ – Cl].

$C_{14}H_{12}ClNO_4$ (293.7)
Calcd. C 57.25 H 4.12 Cl 12.07 N 4.77
Found C 57.36 H 4.19 Cl 11.89 N 4.78

*Methyl 2-{1-[Bis(tert-butoxycarbonyl)amino]cyclopropyl}-2-chloroacetate* [**14a-N(Boc)$_2$**]: 80 mg (0.37 mmol) of di-*tert*-butyl iminodicarboxylate, 250 mg (0.98 mmol) of the corresponding potassium salt and 70 mg (0.19 mmol) of dibenzo[18]crown-6 in 5 ml of dichloromethane are stirred with 150 mg (1.02 mmol) of **2a-H** at ambient temp. After complete conversion (≈2 d) the solvent is removed and the residue chromatographed on silica gel (80 g, 2.5 × 30 cm, pentane/ethyl ether, 4:1) to yield 257 mg (69%) of **14a-N(Boc)$_2$**, $R_f$ = 0.50. – IR (KBr): $\tilde{\nu}$ = 2960 $cm^{-1}$, 2920, 1760 (C=O), 1720 (C=O), 1480, 1450, 1420, 1340, 1250, 1160, 1120, 1030, 920, 850, 800, 760, 730. – $^1H$ NMR (270 MHz, $CDCl_3$): δ = 0.98–1.08 (m, 1H, $H_{cpr}$), 1.11–1.40 (2 m, 2H, $H_{cpr}$), 1.45–1.56 (m, 1H, $H_{cpr}$), 1.50 (s, 18H, $C(CH_3)_3$), 3.76 (s, 3H, $OCH_3$), 4.62 (s, 1H, 2-H). – MS (CI): *m/z* (%) = 364 (1.0) [$M^+$ + H], 308 (5.9), 264 (17), 252 (7.6), 2.25 (34), 208 (100), 196 (6.6), 179 (6.5), 164 (41), 130 (18), 98 (3.4), 72 (6.1).

$C_{16}H_{26}ClNO_6$ Calcd. 364.1527 Found 364.1491 (MS)

*Methyl 2-{1-[(tert-Butoxycarbonyl)(methoxycarbonyl)amino]cyclopropyl}-2-chloroacetate* [**14a-N(Boc)(Moc)**]: 200 mg (1.14 mmol) of methyl *tert*-butyl iminodicarboxylate, 500 mg (2.34 mmol) of the corresponding potassium salt, and 100 mg (0.28 mmol) of dibenzo[18]crown-6 in 7 ml of dichloromethane are stirred with 300 mg (2.05 mmol) of cyclopropylideneacetate **2a-H** at ambient temp. for 4 d. 10 ml of water is added, the organic phase is separated and the aqueous phase extracted three times with 10 ml of dichloromethane each. The combined organic phases are dried with magnesium sulfate, the solvent is removed and the residue chromatographed on silica gel (80 g, 4.5 × 20 cm, pentane/ethyl ether, 4:1). 32 mg (11%) of **2a-H** ($R_f$ = 0.62) is eluted followed by 420 mg (64%) of **14a-N(Boc)(Moc)**, $R_f$ = 0.30; m.p. 61 °C. – IR (KBr): $\tilde{\nu}$ = 3000 $cm^{-1}$, 2970, 1760 (C=O), 1750 (C=O), 1730 (C=O), 1440, 1370, 1350, 1280, 1170, 1130, 1100, 1040, 1020, 860, 790. – $^1H$ NMR (270 MHz, $CDCl_3$): δ = 0.96–1.06 (m, 1H, $H_{cpr}$), 1.13–1.22 (m, 1H, $H_{cpr}$), 1.32–1.42 (m, 1H, $H_{cpr}$), 1.45–1.57 (m, 1H, $H_{cpr}$), 1.48 [s, 9H, $C(CH_3)_3$], 3.73 (s, 3H, $OCH_3$), 3.78 (s, 3H, $OCH_3$), 4.58 (s, 1H, 2-H). – $^{13}C$ NMR (67.9 MHz, $CDCl_3$): δ = 15.07, 15.84, 27.97 [$C(\mathit{C}H_3)_3$], 39.88 (C-1′), 52.77 ($NHCO_2\mathit{C}H_3$), 53.47 ($CO_2\mathit{C}H_3$), 60.02 (C-2), 83.39 [$\mathit{C}(CH_3)_3$], 152.13 ($N\mathit{C}O_2CH_3$), 154.72 ($N\mathit{C}O_2C_4H_9$), 168.17 ($\mathit{C}O_2CH_3$). – MS (CI): *m/z* (%) = 339 (3.8) [$M^+$ + $NH_4$], 322 (0.7) [$M^+$ + H], 266 (2.9), 239 (31), 222 (100), 186 (10), 164 (3.5), 154 (2.4), 128 (4.2), 74 (1.8).

$C_{13}H_{20}ClNO_6$ Calcd. 322.1057 Found 322.1022 (MS)

*Methyl 2-Chloro-2-[1-(dibenzylamino)cyclopropyl]acetate* (**14a-NBzl$_2$**): 500 mg (3.41 mmol) of **2a-H** and 800 mg (4.06 mmol) of dibenzylamine in 20 ml of THF are stirred for 22 h. After evaporation of the solvent the residue is chromatographed on silica gel (90 g, 2.8 × 50 cm, PE/ethyl ether, 9:1, $R_f$ = 0.51). Yield 1.14 g (97%) of **14a-NBzl$_2$**. – IR (film): $\tilde{\nu}$ = 3070 $cm^{-1}$, 3040, 2960, 2850, 1760 (C=O), 1600, 1490, 1440, 1360, 1330, 1280, 1200, 1160, 1060, 1030, 1020, 970, 940, 910, 800, 750, 700. – $^1H$ NMR (270 MHz, $CDCl_3$): δ = 0.65 (mc, 1H, $H_{cpr}$), 0.78 (mc, 2H, $H_{cpr}$), 0.92 (mc, 1H, $H_{cpr}$), 3.67 (s, 3H, $OCH_3$), 3.67 and 3.85 (AB system, 4H, $NCH_2$), 4.76 (s, 1H, 2-H), 7.08–7.20 (m, 10H, $H_{ar}$). – $^{13}C$ NMR (67.9 MHz, $CDCl_3$): δ = 13.65, 16.66, 46.48 (C-1′), 52.55 ($OCH_3$), 56.72 ($NCH_2$), 59.67 (C-2), 126.89, 128.03, 128.92, 139.61, 169.17 (C=O). – MS (CI): *m/z* (%) = 344 (7.0) [$M^+$ + H], 308 (82) [$M^+$ – Cl], 276 (1.6) [$M^+$ – HCl – OMe], 266 (1.4) [$M^+$ – Ph], 252 (28) [$M^+$ – Bzl], 248 (2.8) [$M^+$ – HCl – $CO_2Me$], 236 (3.7) [$C_3H_4NBzl_2^+$], 216 (6.9) [$M^+$ – Bzl – HCl], 202 (3.6), 186 (4.4) [$M^+$ – Bzl – Cl – OMe], 184 (5.4), 156 (4.6), 145 (4.3) [$C_3H_4NBzl^+$], 130 (3.4), 121 (4.1), 105 (5.1) [$NBzl^+$], 91 (100) [$Bzl^+$], 65 (13).

*Benzyl 2-Chloro-2-[1-(dibenzylamino)cyclopropyl]acetate* (**14b-NBzl$_2$**): 2.51 g (11.3 mmol) of **2b-H** and 2.67 g (13.5 mmol) of dibenzylamine in 60 ml of THF are stirred for 22 h. 100 ml of water is added, and the mixture is extracted twice with 40 ml of ethyl ether and chloroform each. The united extracts are dried with magnesium sulfate, the solvent is removed and the resulting raw material chromatographed on silica gel (120 g, 3.2 × 55 cm, PE/ethyl ether, 9:1, $R_f$ = 0.52). Yield 1.14 g (75%) of **14b-NBzl$_2$**, m.p. 53 °C. – IR (film): $\tilde{\nu}$ = 3060 $cm^{-1}$, 3090, 2850, 1750 (C=O), 1490, 1450, 1380, 1360, 1320, 1270, 1240, 1150, 1030, 1000, 970, 910, 750, 700. – $^1H$ NMR (270 MHz, $CDCl_3$): δ = 0.63–0.81 (m, 3H, $H_{cpr}$), 0.90–1.06 (m, 1H, $H_{cpr}$), 3.74 and 3.91 (AB system, 4H, $NCH_2$), 4.89 (s, 1H, 2-H), 5.18 (s, 2H, $OCH_2$), 7.20 (s, 10H, $H_{ar}$), 7.38 (s, 5H, $H_{ar}$). – $^{13}C$ NMR (67.9 MHz, $CDCl_3$): δ = 13.46, 16.79, 46.42 (C-1′), 56.66 ($NCH_2$), 59.63 (C-2), 67.60 ($OCH_2$), 126.84, 128.00, 128.46, 128.60, 128.90, 135.0, 139.58, 168.48 (C=O). – MS (CI): *m/z* (%) = 420 (3.1) [$M^+$ + H, 1 Cl], 384 (97) [$M^+$ – Cl], 296 (38) [$M^+$ – O – OBzl], 294 (30), 292 (12), 277 (5.3) [$M^+$ – Cl – OBzl], 252 (22), 250 (30) [$M^+$ – Cl – $CO_2Bzl$], 198 (12), 196 (10) [$NBzl_2^+$], 162 (18), 160 (14), 108 (33) [$BzlOH^+$], 106 (64) [$NHBzl^+$], 91 (100) [$Bzl^+$], 78 (12), 65 (8.4), 58 (6.0).

$C_{26}H_{26}ClNO_2$ (419.95)
Calcd. C 74.36 H 6.24 N 3.34 Cl 8.44
Found C 74.12, 74.36 H 6.42, 6.45 N 3.41, 3.34 Cl 8.70

*Benzyl 2-Chloro-2-[1-(diphenylmethyleneamino)cyclopropyl]acetate* (**14b-N=CPh$_2$**): 0.64 g (2.87 mmol) of **2b-H** and 0.55 g (3.03 mmol) of (diphenylmethylene)amine (DPMA-H)[18] in 10 ml of dry methanol are stirred for 2 d. The solvent is evaporated and the residue chromatographed on "dry" silica gel[18] (column 1.5 × 50 cm, PE/ethyl ether, 6:1). Yield 995 mg (86%) of **14b-N=CPh$_2$**. – IR (film): $\tilde{\nu}$ = 3060 $cm^{-1}$, 3028, 1760 (C=O), 1640, 1450, 1275, 1169, 700. – $^1H$ NMR (270 MHz, $CDCl_3$/TMS): δ = 0.78 (0.67–0.87, mc, 2H, $H_{cpr}$), 1.11 (0.92–1.29, mc, 2H, $H_{cpr}$), 4.34 (s, 1H, CHCl), 5.21 and 5.32 (2 d, 2H, $OH_2CPh$), 7.18–7.42 (m, 13H, $H_{ar}$), 7.42–7.50 (m, 2H, $H_{ar}$). – $^{13}C$ NMR (67.9 MHz, $CDCl_3$/TMS): δ = 15.13 (t, $C_{cpr}H_2$), 16.86 (t, $C_{cpr}H_2$), 46.70 (s, $C_{cpr}$), 67.55 (t, $OCH_2$), 64.97 (d, CHCl), 127.90, 127.97, 128.20, 128.24, 128.49, 128.57, 128.61, 130.14 (all d, $C_{ar}$), 135.39 (s, *i*-$C_{ar}$–$CH_2O$*), 137.30 (s, *i*-$C^*_{ar}$), 140.21 (s, *i*-$C_{ar}$), 168.19 (2 C, s, C=O, C=N). – MS (CI, $NH_3$): *m/z* (%) = 406 (36), 404 (100) [$M^+$ + H], 370 (50) [$M^+$ + $H_2$ – Cl], 368 [$M^+$ – Cl], 328 (9).

*Benzyl 2-[1-(Benzyloxy)cyclopropyl]-2-chloroacetate* (**14b-OBzl**) *and Methyl 2-[1-(Benzyloxy)cyclopropyl]-2-chloroacetate* (**14a-OBzl**) *from* **2a-H**: 146 mg (1.0 mmol) of **2a-H** in 3 ml of benzyl alcohol is stirred with some drops of freshly prepared potassium benzylate in benzyl alcohol. After 22 h 15 ml of water is added, and the product is extracted with 3 × 15 ml of ethyl ether. After drying of the united extracts with sodium sulfate and evaporation of the solvent the residual benzyl alcohol is removed at 60°C in vacuo (0.01 Torr). The residue is chromatographed on silica gel (60 g, 2.5 × 20 cm, pentane/ethyl ether, 9:1) to give 200 mg (61%) of **14b-OBzl**, $R_f$ = 0.51. – IR (film): $\tilde{\nu}$ = 3080 $cm^{-1}$, 3040, 2970, 2900, 1760 (C=O), 1500, 1460, 1380, 1340, 1280, 1170, 1070, 1030, 920, 810, 750, 700. – $^1$H NMR (270 MHz, CDCl$_3$): $\delta$ = 0.90–1.00 (m, 1H, H$_{cpr}$), 1.12–1.23 (m, 3H, H$_{cpr}$), 4.52 (s, 1H, 2-H), 4.61 and 4.81 (AB system, 2H, OCH$_2$), 5.30 (s, 2H, OCH$_2$), 7.22–7.43 (m, 10H, H$_{ar}$). – $^{13}$C NMR (67.9 MHz, CDCl$_3$): $\delta$ = 12.66, 13.97, 62.01 (C-2), 63.61 (C-1′), 67.63 (OCH$_2$), 71.13 (OCH$_2$), 127.23, 127.38, 128.11, 128.26, 135.13, 138.06, 167.22 (C=O). – MS (70 eV): $m/z$ (%) = 239 (3.0) [M$^+$ – Bzl], 185 (4.2), 147 (2.6), 145 (4.4), 104 (7.4), 91 (100) [Bzl$^+$]. – MS (CI): $m/z$ (%) = 348 (8.5) [M$^+$ + NH$_4$], 295 (3.7) [M$^+$ – Cl], 279 (4.2), 222 (10) [M$^+$ – BzlOH], 205 (35) [M$^+$ + H – Bzl – Cl], 189 (56) [M$^+$ + H – OBzl – Cl], 181 (14), 161 (10) [M$^+$ + H – CO$_2$Bzl – Cl], 108 (76) [BzlOH$^+$], 106 (63), 91 (100) [Bzl$^+$], 78 (10).

A second fraction at $R_f$ = 0.34 gives 24 mg (9.5%) of **14a-OBzl**. – $^1$H NMR (270 MHz, CDCl$_3$): $\delta$ = 0.88–0.96 (m, 1H, H$_{cpr}$), 1.08–1.20 (m, 3H, H$_{cpr}$), 3.81 (s, 3H, OCH$_3$), 4.44 (s, 1H, 2-H), 4.59 and 4.80 (AB system, 2H, $^2J$ = 11.8 Hz, OCH$_2$), 7.28 (mc, 5H, H$_{ar}$). – MS (70 eV): $m/z$ (%) = 219 (0.4) [M$^+$ – Cl], 187 (0.2) [M$^+$ – Cl – OMe], 163 (0.1) [M$^+$ – Bzl], 147 (1.1) [M$^+$ – OBzl], 104 (21), 91 (100) [Bzl$^+$], 65 (10). – MS (CI): $m/z$ (%) = 272 (3.0) [M$^+$ + NH$_4$], 255 (2.1) [M$^+$ + H], 221 (19), 219 (13) [M$^+$ – Cl], 206 (7.6), 189 (26), 161 (3.9), 143 (4.4), 113 (100), 108 (51), 106 (34), 91 (66) [Bzl$^+$].

In a series of experiments monitored by GC the best conditions with regard to solvent and base for the preferential production of **14a-Bzl** have been determined. The most suitable system tested is benzyl alcohol with a catalytic amount of triethylamine with no further solvent. After 20 h at 22°C 60% of **14a-Bzl** along with 11% of **2b-H** are formed.

*Benzyl 2-[1-(Benzyloxy)cyclopropyl]-2-chloroacetate* (**14b-OBzl**) *from* **2b-H**: 0.5 ml of a sodium benzylate solution in benzyl alcohol is added to 560 mg (2.51 mmol) of **2b-H** in 3 ml of benzyl alcohol and stirred at room temp. for 18 h. The reaction is worked up as described in the previous experiment. Chromatography on silica gel (120 g, 2.8 × 52 cm, PE/ethyl ether, 9:1) gives 610 mg (74%) of **14b-OBzl**. For data see preceding cxperiment.

*Methyl 2-Chloro-2-[1-(methylthio)cyclopropyl]acetate* (**14a-SMe**): A solution of 4.0 g (27.3 mmol) of **2a-H** in 20 ml of THF is dropped to a suspension of 2.1 g (30 mmol) of sodium methanethiolate in 40 ml of THF at –78°C under nitrogen. After 6 h the cooling is removed and the reaction is quenched with 100 ml of water after the temp. of the mixture has reached –20°C. The product is extracted with 3 × 80 ml of dichloromethane, and the combined extracts are dried with magnesium sulfate. The solvent is carefully removed and the residue distilled in vacuo to yield 4.07 g (77%) of **14a-SMe**; b.p. 70°C/0.05 Torr. – $^1$H NMR (270 MHz, CDCl$_3$): $\delta$ = 1.07 (m, 2H, H$_{cpr}$), 1.20 (m, 1H, H$_{cpr}$), 1.26 (m, 1H, H$_{cpr}$), 2.16 (s, 3H, SCH$_3$), 3.79 (s, 3H, OCH$_3$), 4.32 (s, 1H, 2-H).

$C_7H_{11}ClO_2S$ (194.7)
Calcd. C 43.18 H 5.69 Cl 18.21 S 16.47
Found C 43.15 H 5.76 Cl 18.23 S 16.28

*Methyl 2-[1-(Benzylthio)cyclopropyl]-2-chloroacetate* (**14a-SBzl**): 3.0 g (24.2 mmol) of phenylmethanethiol and 300 mg (3.0 mmol) of tricthylamine in 20 ml of THF are stirred under nitrogen for 1 h. Then the solution is cooled to –78°C, and 2.0 g (13.6 mmol) of **2a-H** in 5 ml of THF is added over a period of 30 min. After 20 h the solution is allowed to warm to –20°C and quenched with 100 ml of water. Extraction of the solution with 4 × 50 ml of ethyl ether, drying of the combined extracts with magnesium sulfate and evaporation of the solvent give 4.1 g of a yellow oil. Chromatography of this oil on silica gel (140 g, 4.3 × 30 cm, pentane/ethyl ether, 9:1) gives 3.03 g (82%) of **14a-SBzl**, a colorless oil. $R_f$ = 0.56. – IR (film): $\tilde{\nu}$ = 3070 cm$^{-1}$, 3040, 3000, 1740 (C=O), 1590 (arom.), 1480, 1420, 1310, 1250, 1150, 1000, 870, 840, 790, 760, 690. – $^1$H NMR (270 MHz, CDCl$_3$): $\delta$ = 0.96–1.07 (m, 2H, H$_{cpr}$), 1.16–1.27 (m, 2H, H$_{cpr}$), 3.76 (s, 3H, OCH$_3$), 3.84 and 3.86 (AB system, 2H, $^2J$ = 12 Hz, SCH$_2$), 4.22 (s, 1H, 2-H), 7.15–7.27 (m, 5H, H$_{ar}$). – MS (70 eV): $m/z$ (%) = 270 (3.3) [M$^+$], 235 (13) [M$^+$ – Cl], 234 (1.3), 203 (1.8) [M$^+$ – Cl – MeOH], 202 (2.7), 179 (2.0) [M$^+$ – Bzl], 175 (4.7) [M$^+$ – HCl – CO$_2$Me], 143 (3.2) [M$^+$ – HCl – Bzl], 123 (3.4) [SBzl$^+$], 121 (14), 91 (100) [Bzl$^+$], 77 (2.5) [Ph$^+$], 65 (14), 59 (7.1) [CO$_2$Me$^+$], 51 (3.3).

*Methyl 2-Chloro-2-cyclopropylacetate* (**14a-H**): To a suspension of 42 g of silica gel in a solution of 3.0 g (20 mmol) of **2a-H** in 250 ml of chloroform and 75 ml of 2-propanol at room temp. 3.9 g (103 mmol) of NaBH$_4$ is added with stirring in small portions over a period of 20 min. Stirring is continued for 1.5 h. 2 ml of glacial acetic acid is added, the solids are filtered off and thoroughly washed with 50 ml of chloroform. The filtrate is washed with 150 ml of water, which in turn is re-extracted with 3 × 50 ml of chloroform. The combined organic phases are monitored by GC/MS. They contain 2-cyclopropylethanol, 2-cyclopropylacetic acid and **14a-H** in 14, 0.7, and 83% relative intensity, respectively. After removal of the solvent vacuum distillation gives 2.25 g (74%) of **14a-H**; b.p. 74°C/17 Torr. – IR (film): $\tilde{\nu}$ = 3020 cm$^{-1}$, 2960, 1750 (C=O), 1440, 1310, 1280, 1200, 1170, 1030, 1010, 950, 840. – $^1$H NMR (270 MHz, CDCl$_3$): $\delta$ = 0.52 (mc, 2H, H$_{cpr}$), 0.76 (mc, 2H, H$_{cpr}$), 1.45 (mc, 1H, 1′-H), 3.64 (d, 1H, 2H), 3.81 (s, 3H, OCH$_3$). – GC/MS (70 eV): $m/z$ (%) = 148 (0.3) [M$^+$], 113 (100) [M$^+$ – Cl], 91 (13), 89 (45) [M$^+$ – CO$_2$Me], 81 (10) [M$^+$ – HCl – OMe], 71 (5.6), 59 (32) [CO$_2$Me$^+$], 53 (82).

$C_6H_9ClO_2$ (148.6) Calcd. C 48.50 H 6.11 Cl 23.86
Found C 48.66 H 6.31 Cl 23.84

*Methyl 2-[1-(Dibenzylamino)cyclopropyl]acetate* (**22a-NBzl$_2$**): To 710 mg (2.06 mmol) of **14a-Bzl$_2$** in 15 ml of THF and 190 µl of water an excess of freshly prepared zinc/copper pair is added, and the resulting mixture is kept in an ultrasonic bath at room temp. for 18 h and then at 65°C for 8 h. The solid components of the mixture are separated in a centrifuge and washed with 10 ml of chloroform followed by threefold centrifugation. The combined liquid organic phases are concentrated in vacuo, and the residue is chromatographed on silica gel (60 g, 2.6 × 37 cm, PE/ethyl ether, 9:1). Yield 414 mg (65%) of **22a-NBzl$_2$**, a colorless oil; $R_f$ (pentane/ethyl ether, 95:5) = 0.38. – IR (film): $\tilde{\nu}$ = 3080 cm$^{-1}$, 3060, 3020, 2840, 1730 (C=O), 1590, 1490, 1430, 1360, 1330, 1270, 1210, 1150, 1060, 1020, 960, 900, 860, 740, 700. – $^1$H NMR (270 MHz, CDCl$_3$): $\delta$ = 0.59 and 0.69 (superimposed AA′BB′ system, 4H, H$_{cpr}$), 2.69 (s, 2H, 2-H), 3.77 (s, 3H, OCH$_3$), 3.86 (s, 4H, NCH$_2$), 7.23–7.38 (m, 10H, H$_{ar}$). – $^{13}$C NMR (67.9 MHz, CDCl$_3$): $\delta$ = 14.97, 36.24 (C-2), 41.09 (C-1′), 51.17 (OCH$_3$), 56.33 (NCH$_2$), 125.53, 127.75, 128.76, 139.93, 172.64 (C=O). – MS (CI): $m/z$ (%) = 310 (100) [M$^+$ + H], 218 (29) [M$^+$ – Bzl], 91 (16) [Bzl$^+$].

$C_{20}H_{23}NO_2$ (309.4)
Calcd. C 77.64 H 7.49 N 4.53
Found C 77.59, 77.83 H 7.59, 7.58 N 4.34, 4.66

*Benzyl 2-[1-(Dibenzylamino)cyclopropyl]acetate* (**22b-NBzl$_2$**): 7.5 g (39.8 mmol) of benzyl 2-cyclopropylideneacetate (**25b**) in 10 ml of THF is added to 11.77 g (60 mmol) of dibenzylamine in 140 ml of THF. After 3 d the solvent is removed in vacuo and the residue chromatographed on silica gel (200 g, PE/ethyl ether, 9:1) to yield 13.0 g (85%) of **22b-NBzl$_2$**, a colorless oil; $R_f$ = 0.45. – IR (film): $\tilde{\nu}$ = 3080 cm$^{-1}$, 3040, 2950, 2840, 1740, 1500, 1460, 1380, 1340, 1270, 1220, 1160, 1030, 750, 700. – $^1$H NMR (270 MHz, CDCl$_3$): $\delta$ = 0.61 (m, 2H, H$_{cpr}$), 0.64 (m, 2H, H$_{cpr}$), 2.73 (s, 2H, 2-H), 3.80

(s, 4H, $NCH_2$), 5.22 (s, 2H, $OCH_2$), 7.30 (mc, 10H, $H_{ar}$), 7.47 (mc, 5H, $H_{ar}$). – $^{13}C$ NMR (67.9 MHz, $CDCl_3$): $\delta$ = 15.10, 36.79 (C-2), 41.38 (C-1′), 56.55 ($NCH_2$), 66.29 ($OCH_2$), 126.62, 127.85, 128.16, 128.37, 128.49, 128.89, 136.00, 140.08, 172.16 (C=O). – MS (70 eV): *m/z* (%) = 385 (0.4) [$M^+$], 294 [$M^+$ – Bzl], 236 (4.7) [$M^+$ – $CH_2CO_2Bzl$], 186 (1.2), 160 (1.3), 130 (1.7), 104 (2.2), 91 (100) [$Bzl^+$], 65 (2.9), 40 (6.0) [$C_3H_4^+$]. – MS (CI): *m/z* (%) = 386 (100) [$M^+$ + H], 294 (24) [$M^+$ – Bzl], 250 (1.0) [$M^+$ – $CO_2Bzl$], 160 (4.2), 108 (4.5), 91 (24) [$Bzl^+$].

$C_{26}H_{27}NO_2$ (385.5) Calcd. C 81.01 H 7.06 N 3.63
Found C 81.20 H 7.24 N 3.56

*Benzyl 2-[1-(Diphenylmethyleneamino)cyclopropyl]acetate* (**22b-N=CPh₂**): 2.20 g (7.5 mmol) of crude **22a-N=CPh₂** in 30 ml of dry benzyl alcohol and 0.3 ml of titanium tetraisopropoxide are heated to 90°C in a short-path distillation or a kugelrohr apparatus. After an initial evacuation to the boiling point of the mixture the apparatus is closed and left for 24 h. Higher temperatures (up to 160°C) may be employed to achieve faster conversions. After completion of the reaction the remaining benzyl alcohol is removed at 100°C/0.01 Torr. The residue is chromatographed on "dry" silica gel[18] (column 2 × 25 cm, PE/ethyl ether, 8:1) to give 2.25 g (81%) of **22b-N=CPh₂**; $R_f$ = 0.22 (*n*-pentane/ethyl ether, 4:1). – IR (film): $\tilde{\nu}$ = 3062 $cm^{-1}$, 3031, 1737 (C=O), 1617, 1446, 1162, 696. – $^1H$ NMR (270 MHz, $CDCl_3$/TMS): $\delta$ = 0.90 (0.80–1.00, mc, 4H, $H_{cpr}$), 2.33 (s, 2H, $CH_2C=O$), 5.10 (s, 2H, $OCH_2Ph$), 7.20–7.42 (m, 13H, $H_{ar}$), 7.49–7.55 (m, 2H, $H_{ar}$). – $^{13}C$ NMR (67.9 MHz, $CDCl_3$/TMS): $\delta$ = 16.39 (t, 2 C, $C_{cpr}H_2$), 40.55 (s, $C_{cpr}$), 42.76 (t, $\mathit{C}H_2C=O$), 66.04 (t, $O\mathit{C}H_2Ph$), 127.88, 127.97, 128.04, 128.19, 128.24, 128.41, 128.49, 129.88 (all d, $C_{ar}$), 136.09 (s, *i*-$C_{ar}$), 138.55 (s, *i*-$C_{ar}$), 140.75 (s, $C_{ar}$), 169.62 (s, C=N*), 171.20 (s, C=O*). – MS (70 eV): *m/z* (%) = 369 (3) [$M^+$], 341 (5) [$M^+$ – $C_2H_4$], 278 (5) [$M^+$ – Bzl], 234 (3) [$M^+$ – $CO_2Bzl$], 206 (23) [$M^+$ – $CO_2Bzl$ – $C_2H_4$], 184 (50), 165 (50).

*Methyl 2-{2-[(Benzyloxy)methyl]cyclopropyl}-2-chloroacetate* (**27**): To 1.24 g (4.65 mmol) of **2a-CH₂OBzl** and 760 mg of *tert*-butyl alcohol in 5 ml of dry THF at –78°C under nitrogen is dropped 5 ml (5 mmol) of 1 M L-selectride® ($LiBH\mathit{s}Bu_3$) in THF. After 30 min 15 ml of methanol is added to the solution which is concentrated in vacuo. Chromatography of the residue on silica gel (60 g, 2.6 × 25 cm, pentane/ethyl ether, 9:1) affords two fractions with a total of 520 mg (42%) of **27**:

Fraction I ($R_f$ = 0.21): 164 mg of **27**, isomer A.

II ($R_f$ = 0.21 and 0.12): 357 mg of **27**, isomer A and B. – IR (film): $\tilde{\nu}$ = 3070 $cm^{-1}$, 3040, 2960, 2870, 1750 (C=O), 1490, 1440, 1380, 1310, 1280, 1220, 1200, 1170, 1100, 1080, 1030, 840, 800. – $^1H$ NMR (270 MHz, $CDCl_3$), isomer A: $\delta$ = 0.55 (mc, 1H, 3′-H), 1.08 (mc, 1H, 3′-H), 1.53 (mc, 1H, 2′-H), 1.68 (mc, 1H, 1′-H), 3.31 (dd, 1H, 1″-H), 3.65 (s, 3H, $OCH_3$), 3.77 (dd, 1H, 1″-H), 4.00 (d, 1H, 2-H), 4.46 (AB system, 2H, 2″-H), 7.32 (mc, 5H, $H_{ar}$). – Isomer B: $\delta$ = 0.59 (mc, 1H, 3′-H), 1.02 (mc, 1H, 3′-H), 1.44 (mc, 1H, 2′-H), 1.61 (mc, 1H, 1′-H), 3.56 (dd, 1H, 1″-H), 3.71 (dd, 1H, 1″-H), 3.81 (s, 3H, $OCH_3$), 4.00 (d, 1H, 2-H), 4.57 (s, 2H, 2″-H), 7.32 (mc, 5H, $H_{ar}$). – $^{13}C$ NMR (67.9 MHz, $CDCl_3$), isomer A: $\delta$ = 10.47 (C-3′), 19.45 (C-2′), 20.26 (C-1′), 52.61 ($OCH_3$), 58.55 (C-2), 69.61 (C-1″), 72.89 (C-2″), 127.70 ($C_{ar}$), 128.35 ($C_{ar}$), 138.18 ($C_{ar}$), 169.49 (C-1). – Isomer B: $\delta$ = 10.28 (C-3′), 16.70 (C-2′), 20.47 (C-1′), 52.79 ($OCH_3$), 58.06 (C-2), 68.22 (C-1″), 73.08 (C-2″), 127.64 ($C_{ar}$), 128.41 ($C_{ar}$), 138.18 ($C_{ar}$), 169.61 (C-1). – MS (CI): *m/z* (%) = 286 [$M^+$ + $NH_4$], 269 [$M^+$ + H], 252, 235, 233 [$M^+$ – Cl], 219, 203, 185, 160, 144, 127 (100), 108 [$BzlOH^+$], 106, 94, 91 [$Bzl^+$]. – [A distinction of the NMR signals of the isomers has been made on the basis of C,H-COSY.]

### *2-Azido- and 2-Phthalimido-2-cyclopropylacetates* **15, 16, 28**

*General Procedures for the Conversion of 2-Chloro-2-cyclopropylacetates* **14** *into 2-Azido-2-cyclopropylacetates* **15**. – *Procedure A:* 10 mmol of chloride **14** in approximately 25 ml of dry DMF is stirred with 20 mmol of sodium azide. The reaction is accelerated by the addition of catalytic amounts of sodium iodide (0.1 mmol) and application of elevated temperatures (40–80°C). After the starting material has disappeared, 100 ml of water and 100 ml of ethyl ether are added. The ether phase is separated, washed twice with 50 ml of water and dried with magnesium sulfate. After evaporation of the solvent the crude product is purified by column chromatography on silica gel if necessary. A non-aqueous workup procedure is described for the isolation of **15-N=CPh₂** (see below).

*Procedure B:* 200 mg (3 mmol) of sodium azide and 200 mg (0.5 mmol) of methyltrioctylammonium chloride (Aliquat 336®) *in 3 ml* of water are vigorously stirred with 1 mmol of chloride **14** at ≈50°C. After complete conversion (≈16 h) 20 ml of water is added, and the azide **15** is extracted with three 20-ml portions of ethyl ether. These combined extracts are dried with magnesium sulfate, the ether is removed and the residue chromatographed to give **15**.

*Methyl 2-Azido-2-{1-[(tert-butoxycarbonyl)methyl]cyclopropyl}-acetate* (**15a-CH₂CO₂*t*Bu**): According to general procedure A, 3.56 g (13.56 mmol) of chloride **14a-CH₂CO₂*t*Bu** is allowed to react at 65°C for 14 h. Chromatography on silica gel (100 g, column 3 × 40 cm, PE/ethyl ether, 6:1, $R_f$ = 0.31) affords 3.26 g (94%) of **15a-CH₂CO₂*t*Bu** as a colorless oil. – IR (film): $\tilde{\nu}$ = 3010 $cm^{-1}$, 2950, 2130 ($N_3$), 1740 (CO), 1440, 1370, 1160, 1030. – $^1H$ NMR (270 MHz, $CDCl_3$): $\delta$ = 0.55–1.08 (m, 4H, $H_{cpr}$), 1.45 (s, 9H, *t*Bu), 2.31 and 2.42 (AB system, 2H, $^2J_{A,B}$ = 16 Hz, 1″-H), 3.78 (s, 3H, $CO_2CH_3$), 3.92 (s, 1H, 2-H). – $^{13}C$ NMR (67.9 MHz, $CDCl_3$): $\delta$ = 9.68, 10.50 (C-2′, C-3′), 19.50 (C-1′), 28.15 [$\mathit{C}(CH_3)_3$], 40.13 (C-1″), 52.22 ($OCH_3$), 66.70 (C-2), 80.79 [$(CH_3)_3\mathit{C}O$], 169.20 (C-1), 170.42 (C-2″). – MS (CI, $NH_3$): *m/z* (%) = 287 (20) [$M^+$ + $NH_4$], 270 (7) [$M^+$ + H], 242 (7), 231 (100), 214 (19), 186 (35), 170 (14).

*Methyl 2-Azido-2-(1-methylcyclopropyl)acetate* (**15a-CH₃**): 980 mg (6 mmol) of methyl 2-chloro-2-(1-methylcyclopropyl)acetate (**14a-CH₃**) and 1.37 g (21 mmol) of sodium azide in 10 ml of DMF are stirred at 55°C for 15 h. After the addition of 30 ml of water the mixture is extracted with three 15-ml portions of ethyl ether. The combined extracts are washed with 10 ml of satd. ammonium chloride solution and dried with magnesium sulfate. Evaporation of the solvent furnishes 1.11 g of crude **15a-CH₃** with a little DMF as sole impurity. Chromatography of a 300-mg portion on silica gel (column 1 × 40 cm, *n*-pentane/dichloromethane/ethyl ether, 40:7:1) gives 270 mg of **15a-CH₃** (i.e. 1.00 g for the total amount of **15a-CH₃**, 98%); $R_f$ = 0.20. – IR (KBr): $\tilde{\nu}$ = 3070 $cm^{-1}$, 2998, 2950, 2100 ($N_3$), 1742 (C=O), 1433, 1196, 1022. – $^1H$ NMR (300 MHz, $CDCl_3$/TMS): $\delta$ = 0.50 (mc, 2H, $H_{cpr}$), 0.70 (0.58–0.82, mc, 2H, $H_{cpr}$), 1.12 (s, 3H, $CH_3$), 3.46 (s, 1H, $HCN_3$), 3.80 (s, 3H, $OCH_3$). – $^{13}C$ NMR (75.4 MHz, $CDCl_3$/TMS): $\delta$ = 11.24 ($C_{cpr}H_2$), 12.02 ($C_{cpr}H_2$), 18.10 ($C^*_{cpr}$), 19.01 ($CH_3^*$), 51.11 ($OCH_3$), 69.03 ($HCN_3$), 169.28 (C=O). – MS (CI, isobutane): *m/z* (%) = 170 (1.2) [$M^+$ + H], 142 (23) [$M^+$ + H – $N_2$], 127 (100) [$M^+$ + H – $N_2$ – Me], 110 (37) [$M^+$ – $CO_2Me$ or $M^+$ – $N_2$ – OMe], 82 (85) [$M^+$ – $N_2$ – $CO_2Me$]. – HRMS: Calcd. for $C_7H_{11}N_3O_2$ and found: 169.085126.

*Methyl 2-Azido-2-[1-(dibenzylamino)cyclopropyl]acetate* (**15a-NBzl₂**): According to general procedure B, 111 mg (0.32 mmol) of **14a-NBzl₂** is converted into 100 mg (89%) of **15a-NBzl₂** after chromatography on neutral aluminum oxide (activity grade III, 15 g, 1.6 × 26 cm, pentane/ethyl ether, 4:1). – IR (film): $\tilde{\nu}$ = 3080 $cm^{-1}$, 3060, 3020, 2950, 2840, 2100 ($N_3$), 1770 (C=O), 1520, 1480, 1460, 1370, 1350, 1290, 1240, 1200, 1060, 980, 930, 780, 730. – $^1$H NMR (270 MHz, $CDCl_3$): δ = 0.54 (ddd, 1 H, $H_{cpr}$), 0.75 (ddd, 1 H, $H_{cpr}$), 0.89 (ddd, 1 H, $H_{cpr}$), 1.06 (ddd, 1 H, $H_{cpr}$), 3.83 (s, 3 H, $OCH_3$), 3.89 and 4.02 (AB system, 4 H, $NCH_2$), 4.32 (s, 1 H, 2-H), 7.25–7.40 (m, 10 H, $H_{ar}$). – $^{13}$C NMR (67.9 MHz, $CDCl_3$): δ = 12.24, 14.35, 45.84 (C-1'), 52.20 ($OCH_3$), 56.66 ($NCH_2$), 63.87 (C-2), 120.87, 128.03, 128.90, 139.64, 169.78 (C=O). – MS (CI): *m/z* (%) = 351 (100) [$M^+$ + H], 323 (26) [$M^+$ + H – $N_2$], 308 (6.9) [$M^+$ – $N_3$], 291 (1.9) [$M^+$ – $N_2$ – OMe or $M^+$ – $CO_2Me$], 263 (8.6) [$M^+$ – $N_2$ – $CO_2Me$], 233 (14), 218 (8.7) [$M^+$ + H – $N_3$ – Bzl], 198 (3.9), 187 (1.6) [$M^+$ + H – OMe – $N_3$ – Bzl], 173 (3.2), 146 (3.3), 108 (4.9), 106 (6.9) [$NHBzl^+$], 91 (16) [$Bzl^+$], 59 (48).

*Benzyl 2-Azido-2-[1-(dibenzylamino)cyclopropyl]acetate* (**15b-NBzl₂**): According to general procedure B, 610 mg (1.45 mmol) of **14b-NBzl₂** affords 563 mg (91%) of **15b-NBzl₂** after chromatography on silica gel (30 g, 2.6 × 18 cm, PE/ethyl ether, 9:1), m.p. 59°C. – IR (film): $\tilde{\nu}$ = 3070 cm$^{-1}$, 3040, 2840, 2120 ($N_3$), 1740 (C=O), 1490, 1450, 1380, 1340, 1320, 1260, 1210, 1170, 1030, 910, 750, 730, 700. – $^1$H NMR (270 MHz, $CDCl_3$): δ = 0.40 (mc, 1 H, $H_{cpr}$), 0.58 (mc, 1 H, $H_{cpr}$), 0.76 (mc, 1 H, $H_{cpr}$), 0.97 (mc, 1 H, $H_{cpr}$), 3.78 and 3.89 (AB system, 4 H, $NCH_2$), 4.28 (s, 1 H, 2-H), 5.13 and 5.20 (superimposed AB system, 2 H, $OCH_2$), 7.20 (s, 10 H, $H_{ar}$), 7.38 (s, 5 H, $H_{ar}$). – $^{13}$C NMR (67.9 MHz, $CDCl_3$): δ = 12.05, 14.33, 45.89 (C-1'), 56.66 ($NCH_2$), 63.80 (C-2), 67.37 ($OCH_2$), 126.81, 127.93, 128.55, 128.89, 134.99, 139.61, 169.05 (C=O).

| $C_{26}H_{26}N_4O_2$ (426.5) | | | |
|---|---|---|---|
| Calcd. | C 73.22 | H 6.14 | N 13.14 |
| Found | C 73.82, 73.58 | H 6.34, 6.32 | N 12.25, 12.36 |

*Methyl 2-Azido-2-[1-(diphenylmethyleneamino)cyclopropyl]acetate* (**15a-N=CPh₂**): 2.1 g (6.4 mmol) of crude **14a-N=CPh₂**, 1.5 g (23 mmol) of sodium azide, and 30 mg (0.2 mmol) of potassium iodide in 70 ml of DMF are stirred at 45°C. After 2.5 d the mixture is filtered, and most of the DMF is removed by kugelrohr distillation at 50°C under vacuum ($10^{-2}$ Torr). Chromatography of the residue on "dry" silica gel[18] (column 2.5 × 38 cm, PE/ethyl ether, 8:1) gives 1.95 g (91%) of **15a-N=CPh₂** as an oil which crystallizes. Recrystallization from hexane/ethyl ether by partial evaporation of the solvent gives clear crystals with very little loss of material; m.p. 60°C. – IR (film): $\tilde{\nu}$ = 3050 cm$^{-1}$, 3010, 2948, 2095 ($N_3$), 1740 (C=O), 1625 (C=N), 1440, 1262, 1215, 683. – $^1$H NMR (270 MHz, $CDCl_3$): δ = 0.69–0.91 (m, 3 H, $H_{cpr}$), 1.08–1.16 (m, 1 H, $H_{cpr}$), 3.48 (s, 1 H, $CHN_3$), 3.85 (s, 3 H, $OCH_3$), 7.21–7.41 (m, 5 H, $H_{ar}$), 7.44–7.50 (m, 3 H, $H_{ar}$), 7.54–7.60 (dd, 2 H, $H_{ar}$). – $^{13}$C NMR (67.9 MHz, $CDCl_3$): δ = 14.65 (t, $C_{cpr}$), 15.85 (t, $C_{cpr}$), 46.27 (s, $C_{cpr}$), 52.42 (q, $OCH_3$), 69.16 (d, $CN_3$), 127.89 (d, 4 C, o-$C^*_{ar}$), 128.25 (d, 2 C, m-$C^*_{ar}$), 128.43 (d, 2 C, m-$C^*_{ar}$), 128.59 (d, p-$C_{ar}$), 130.10 (d, p-$C_{ar}$), 137.35 (s, i-$C_{ar}$), 140.14 (s, i-$C_{ar}$), 167.17 (s, C=N$^{*1}$), 169.60 (s, C=O$^{*1}$). – MS (70 eV): *m/z* (%) = 306 (1.6) [$M^+$ – $N_2$], 292 (14) [$M^+$ – $N_2$ – $CH_2$], 247 (14) [$M^+$ – $N_2$ – $CO_2Me$], 182 (41), 165 (46), 105 (100).

| $C_{19}H_{18}N_4O_2$ (334.4) | | | |
|---|---|---|---|
| Calcd. | C 68.25 | H 5.43 | N 16.76 |
| Found | C 68.07, 68.44 | H 5.33, 5.43 | N 16.61, 16.56 |

*Benzyl 2-Azido-2-[1-(diphenylmethyleneamino)cyclopropyl]acetate* (**15b-N=CPh₂**)

a) *By Transesterification of* **15a-N=CPh₂**: To 0.2 ml of titanium tetraisopropoxide and 30 µl of titanium tetrachloride in 10 ml of dry benzyl alcohol is added 500 mg (1.5 mmol) of **15a-N=CPh₂**. After 24 h at 80°C the solvent is evaporated by kugelrohr distillation at the same temperature. The residue is chromatographed on "dry" silica gel[18] (column 2.5 × 23 cm, PE/ethyl ether, 8:1 + 0.1% triethylamine). Yied 465 mg (76%) of **15b-N=CPh₂**. – IR (film): $\tilde{\nu}$ = 3063 cm$^{-1}$, 2106 ($N_3$), 1746 (C=O), 1633, 1447, 1268, 1216, 1174, 696. – $^1$H NMR (250 MHz, $CDCl_3$/TMS): δ = 0.64–0.88 (m, 3 H, $H_{cpr}$), 1.04–1.12 (m, 1 H, $H_{cpr}$), 3.45 (s, 1 H, $CHN_3$), 5.27 (dd, 2 H, $OH_2CPh$), 7.08–7.14 (m, 2 H, $H_{ar}$), 7.18–7.30 (m, 6 H, $H_{ar}$), 7.32–7.38 (m, 5 H, $H_{ar}$), 7.47–7.51 (m, 2 H, $H_{ar}$). – $^{13}$C NMR (62.9 MHz, $CDCl_3$/TMS): δ = 14.86 (t, $C_{cpr}H_2$), 15.99 (t, $C_{cpr}H_2$), 46.46 (s, $C_{cpr}$), 67.23 (t, $OCH_2$), 69.29 (d, $CHN_3$), 127.90, 128.24, 128.50, 128.55, 130.08 (all d, $C_{ar}$), 135.38 (s, i-$C_{ar}$–$CH_2O$), 137.25 (s, i-$C_{ar}$), 140.10 (s, i-$C_{ar}$), 167.01 (s, C=O*), 169.12 (s, C=N*). – MS (70 eV): *m/z* (%) = 410 (0.1) [$M^+$], 382 (4) [$M^+$ – $N_2$], 368 (55), 247 (58) [$M^+$ – $N_2$ – Ph – $CO_2Me$], 165 (88), 91 (100).

| $C_{25}H_{22}N_4O_2$ (410.5) | | | |
|---|---|---|---|
| Calcd. | C 73.15 | H 5.40 | N 13.65 |
| Found | C 73.60 | H 5.56 | N 12.80 |

The reaction is very sensitive to temperature, the quality of the benzyl alcohol and the amount of titanium tetrachloride. The latter can successfully be replaced by tin tetrachloride (50 µl), but the formation of stannate gels complicates the workup [yield 400 mg (65%) of **15b-N=CPh₂**]. Titanium tetrachloride or the basic catalysts titanium tetraisopropoxide or sodium benzylate (from sodium hydride) alone are less effective due to the formation of more decomposition products (e.g. α-imino ester). The isolated product loses nitrogen more rapidly than the methyl ester!

b) *By Chloride-Azide Exchange of* **14b-N=CPh₂**: 960 mg (2.38 mmol) of **14b-N=CPh₂** and 300 mg (4.6 mmol) of sodium azide are allowed to react in DMF according to general procedure A (at room temp. for ca. 14 d). Complete consumption of the starting material is necessary, because its $R_f$ value is almost identical with that of the product. The reaction mixture is then filtered and the DMF removed by kugelrohr distillation at ca. 0.01 Torr and low temp. Chromatography of the residue on "dry" silica gel[18] (column 2 × 32 cm, PE/ethyl ether, 8:1) gives 0.86 g (88%) of **15b-N=CPh₂**.

*Benzyl 2-Azido-2-[1-(benzyloxy)cyclopropyl]acetate* (**15b-OBzl**): According to general procedure B 123 mg (0.37 mmol) of **14b-OBzl** gives after chromatography on silica gel (20 g, 1.6 × 15 cm, pentane/ethyl ether, 9:1) 82 mg (66%) of **15b-OBzl** as a colorless oil; $R_f$ = 0.54. – IR (film): $\tilde{\nu}$ = 3070 cm$^{-1}$, 3040, 2960, 2120 ($N_3$), 1740 (C=O), 1490, 1450, 1380, 1320, 1260, 1220, 1170, 1020, 910, 740, 700. – $^1$H NMR (270 MHz, $CDCl_3$): δ = 0.78–0.85 (m, 1 H, $H_{cpr}$), 1.00–1.15 (m, 3 H, $H_{cpr}$), 3.84 (s, 1 H, 2-H), 4.52 and 4.63 (AB system, 2 H, $OCH_2$), 5.26 and 5.33 (AB system, 2 H, $CO_2CH_2$), 7.20–7.45 (m, 10 H, $H_{ar}$).

| $C_{19}H_{19}N_3O_3$ (337.4) | | | |
|---|---|---|---|
| Calcd. | C 67.64 | H 5.68 | N 12.45 |
| Found | C 68.15, 67.89 | H 5.90, 5.80 | N 11.93, 11.78 |

*Methyl 2-Azido-2-[1-(methylthio)cyclopropyl]acetate* (**15a-SMe**): According to general procedure B 98 mg (1.51 mmol) of sodium azide, 50 mg of Aliquat 336®, and 194 mg (1.0 mmol) of **14a-SMe** in 1 ml of water are allowed to react at 50°C for 16 h. Chromatography on basic aluminum oxide (20 g, 1.7 × 14 cm, pentane/ethyl ether, 9:1) gives 193 mg (96%) of **15a-SMe**; $R_f$ = 0.54. – IR (film): $\tilde{\nu}$ = 3000 cm$^{-1}$, 2950, 2920, 2100 ($N_3$), 1740 (C=O), 1430, 1300, 1250 (C–O), 1020. – $^1$H NMR (270 MHz, $CDCl_3$): δ = 1.05 (mc, 3 H, $H_{cpr}$), 1.20 (mc, 1 H, $H_{cpr}$), 2.16 (s, 3 H, $SCH_3$), 3.68 (s, 1 H, 2-H), 3.80 (s, 3 H, $OCH_3$). – MS (70 eV): *m/z* (%) = 201 [$M^+$], 173 [$M^+$ – $N_2$], 159 [$M^+$ – $N_3$], 158, 127, 126 [$M^+$ – $N_2$ – SMe], 114 (100) [$M^+$ – $N_2$ – $CO_2Me$], 99, 87 [$C_4H_7S^+$], 74, 72, 71, 59 [$CO_2Me^+$], 53, 47 [$SMe^+$].

| $C_7H_{11}N_3O_2S$ (201.3) | | | | |
|---|---|---|---|---|
| Calcd. | C 41.78 | H 5.51 | N 20.88 | S 15.93 |
| Found | C 42.56, 42.80 | H 5.65, 5.85 | N 20.00, 20.65 | S 15.93, 16.25 |

*Methyl 2-Azido-2-[1-(benzylthio)cyclopropyl]acetate* (**15a-SBzl**): 94 mg (0.35 mmol) of **14a-SBzl**, 100 mg (1.54 mmol) of sodium azide, and 10 mg (0.07 mmol) of sodium iodide in 2 ml of dry DMSO are stirred at 50°C for 2.5 h. After the mixture is cooled to room temp., 20 ml of water is added, then it is extracted with 3 × 15 ml of ethyl ether. The combined organic phases are washed with 2 × 10 ml of water and dried with sodium sulfate. After removal of the solvent chromatography of the residue on basic aluminum oxide (12 g, activity III, 1.5 × 20 cm, pentane/ethyl ether, 4:1) gives 75 mg (78%) of **15a-Bzl**; $R_f$ = 0.40. – $^1$H NMR (270 MHz, $CDCl_3$): δ = 0.95–1.03 (m, 3H, $H_{cpr}$), 1.13–1.20 (m, 1H, $H_{cpr}$), 3.67 (s, 1H, 2-H), 3.80 (s, 3H, $OCH_3$), 3.91 (s, 2H, $SCH_2$), 7.30 (mc, 5H, $H_{ar}$). – MS (70 eV): *m/z* (%) = 249 (40) [$M^+ - N_2$], 216 (15) [$M^+ - N_2 - OMe$], 190 (100) [$M^+ - N_2 - CO_2Me$], 188 (16), 156 (11), 144 (19) [$M^+ - N_3 - Bzl$], 140 (11), 121 (14), 117 (44), 112 (52) [$M^+ - N_3 - SBzl$], 106 (61), 104 (34), 91 (28) [$Bzl^+$], 85 (26), 79 (11), 77 (21) [$Ph^+$], 71 (11), 63 (7.7), 59 (22) [$CO_2Me^+$], 51 (11).

*Methyl 2-Azido-2-cyclopropylacetate* (**15a-H**): 1.0 g (6.73 mmol) of **14a-H** and 650 mg (10 mmol) of sodium azide in 8 ml of dry DMF are stirred at 50°C for 14 h. Then 20 ml of water is added to the mixture which is subsequently extracted with 3 × 15 ml of ethyl ether. The united extracts are washed with 2 × 10 ml of water and dried with magnesium sulfate. Evaporation of the solvent gives 1.02 g (98%) of **15a-H**, which is pure according to GC and $^1$H-NMR analysis. – IR (film): ṽ = 3010 $cm^{-1}$, 2960, 2120 ($N_3$), 1750 (C=O), 1440, 1340, 1270, 1240, 1210, 1180, 1160, 1030, 830. – $^1$H NMR (270 MHz, $CDCl_3$): δ = 0.50 (mc, 2H, $H_{cpr}$), 0.72 (mc, 2H, $H_{cpr}$), 1.38 (mc, 1H, 1′-H), 3.20 (d, 1H, 2-H), 3.80 (s, 3H, $OCH_3$). – MS (70 eV): *m/z* (%) = 155 (0.3) [$M^+$], 113 (1.7) [$M^+ - N_3$], 96 (72) [$M^+ - N_2 - OMe$], 82 (7.1) [$M^+ - N_3 - OMe$], 68 (88) [$M^+ - N_2 - CO_2Me$], 59 (100) [$CO_2Me^+$], 53 (23).

*Methyl 2-[1-(Methylthio)cyclopropyl]-N-phthaloylglycinate* (**16-SMe**): A mixture of 505 mg (2.59 mmol) of **14a-SMe** in 40 ml of dry DMF and 580 mg (3.08 mmol) of potassium phthalimide is stirred at 90°C for 26 h. After the mixture has been cooled down to room temp., 80 ml of water is added, and the mixture is extracted with 4 × 50 ml of chloroform. After drying with magnesium sulfate, evaporation of the solvent and chromatography of the residue on silica gel (80 g, 2.5 × 42 cm, PE/ethyl ether, 3:2) 310 mg (39%) of **16-SMe** is isolated as second fraction; $R_f$ (pentane/ethyl ether, 1:1) = 0.48; m.p. 116°C. – IR (KBr): ṽ = 3200 $cm^{-1}$, 3000, 1750 (C=O), 1710 (C=O), 1460, 1420, 1390, 1220, 1180, 1170, 1110, 1030, 910, 870, 790, 710. – $^1$H NMR (270 MHz, $CDCl_3$): δ = 0.95 (mc, 1H, $H_{cpr}$), 1.19 (mc, 2H, $H_{cpr}$), 1.30 (mc, 1H, $H_{cpr}$), 2.13 (s, 3H, $SCH_3$), 3.70 (s, 3H, $OCH_3$), 4.72 (s, 1H, 2-H), 7.70 (mc, 2H, $H_{ar}$), 7.82 (mc, 2H, $H_{ar}$). – MS (70 eV): *m/z* (%) = 305 (30) [$M^+$], 273 (13) [$M^+ - MeOH$], 257 (8.7), 246 (12) [$M^+ - CO_2Me$], 230 (9.2) [$M^+ - MeOH - CO - Me$], 226 (1.5), 199 (7.4) [$M^+ - CO_2Me - SMe$], 198 (38), 158 (100) [$M^+ - HPhth$], 130 (25), 126 (50) [$M^+ - HPhth - MeOH$], 111 (34), 104 (90) [$C_7H_5O^+$], 99 (26) [$C_5H_7S^+$], 87 (98) [$C_4H_7S^+$], 76 (55) [$C_6H_4^+$], 59 (17) [$CO_2Me^+$], 50 (28).

$C_{15}H_{15}NO_4S$ (305.4)
Calcd. C 59.00 H 4.95 N 4.59 S 10.50
Found C 59.07 H 4.94 N 4.57 S 10.54

*Methyl (1-Methoxycyclopropyl)-N-phthaloylglycinate* (**16-OMe**), *One-Pot Procedure from* **2a-H**: 1.0 g (6.8 mmol) of **2a-H** and 1.37 g (7.4 mmol) of potassium phthalimide are stirred in 10 ml of methanol. After 1 h 10 ml of DMF is added to the mixture, the temp. of which is raised to 60°C. After the starting material has disappeared (ca. 1 h) the temp. is raised to 100°C and the methanol allowed to distill off. After ca. 6 h the mixture is allowed to cool to room temp., and 60 ml of water is added. The precipitate is filtered off and recrystallized from acetone/water. Yield 0.81 g (41%) of **16-OMe**. Alternatively, chromatography on silica gel may be applied (dichloromethane/ethyl ether, 15:1, $R_f$ = 0.36); m.p. 128°C. – IR (KBr): ṽ = 2942 $cm^{-1}$, 2912, 1753 (C=O), 1716 (C=O), 1390, 1202, 1116, 717. – $^1$H NMR (300 MHz, $CDCl_3$/TMS): δ = 0.82–1.14 (m, 4H, $H_{cpr}$), 3.38 (s, 3H, $OCH_3$), 3.76 (s, 3H, $CO_2CH_3$), 4.92 (s, 1H, 2-H), 7.82 (7.74–7.90, mc, 4H, $H_{ar}$). – $^{13}$C NMR (75.4 MHz, $CDCl_3$/TMS): δ = 11.98 (t, $C_{cpr}$), 12.34 (t, $C_{cpr}$), 52.34 (q, $CO_2CH_3$), 54.45 (d, C-2), 55.41 (q, $OCH_3$), 61.15 (s, $C_{cpr}$), 123.30 (d, 2 C, 3-, 6-$C_{ar}$), 131.60 (s, 2 C, 1-, 2-$C_{ar}$), 133.92 (d, 2 C, 4-, 5-$C_{ar}$), 167.03 (s, 2 C, NC=O*), 167.50 (s, OC=O*). – MS (70 eV): *m/z* (%) = 289 (0.6) [$M^+$], 257 (100) [$M^+ - MeOH$], 230 (25) [$M^+ - CO_2Me$], 198 (27) [$M^+ - MeOH - CO_2Me$], 160 [$CH_2=NPhth^+$], 142 (80), 111 (64), 104 (68).

$C_{15}H_{16}NO_5$ (289.3) Calcd. C 62.28 H 5.23 N 4.84
Found C 61.72 H 5.37 N 4.79

*Methyl 2-Azido-2-{2-[(benzyloxy)methyl]cyclopropyl}acetate* (**28**): 330 mg (1.23 mmol) of **27** is allowed to react according to general procedure A. After workup the crude product (319 mg) is chromatographed on silica gel (10 g, 1.4 × 16 cm, pentane/ethyl ether, 7:3). Yield 291 mg (86%) of **28**; $R_f$ = 0.46 and 0.42. – IR (film): ṽ = 3070 $cm^{-1}$, 3040, 3010, 2960, 2870, 2110 ($N_3$), 1740 (C=O), 1490, 1450, 1430, 1340, 1250, 1200, 1180, 1090, 1030, 900, 840, 740, 700. – $^1$H NMR (270 MHz, $CDCl_3$): δ = 0.55–0.65 (m, 2H, 3′-$H_A$, 3′-$H_B$), 0.90–1.10 (m, 2H, 3′-$H_A$, 3′-$H_B$), 1.34–1.50 (m, 4H, 1′-$H_A$, 1′-$H_B$, 2′-$H_A$, 2′-$H_B$), 3.41–3.69 (m, 6H, 2 × 1″-$H_A$, 2 × 1″-$H_B$, 2-$H_A$, 2-$H_B$), 3.71 (s, 3H, $OCH_3$), 3.80 (s, 3H, $OCH_3$), 4.50 and 4.56 (AB system, 2H, 2″-H), 7.34 (mc, 10H, $H_{ar}$). – $^{13}$C NMR (67.9 MHz, $CDCl_3$): δ = 7.90 (C-3′), 8.39 (C-3′), 15.61, 15.77, 16.44, 16.77, 52.10 ($OCH_3$), 52.16 ($OCH_3$), 61.90 (C-2), 68.50 (C-1″), 69.04 (C-1″), 72.54 (C-2″), 72.69 (C-2″), 126.45, 127.33, 127.38, 128.08, and 138.00 (all $C_{ar}$), 169.92 (C-1), 170.40 (C-1). – MS (70 eV): *m/z* (%) = 247 (0.09) [$M^+ - N_2$], 233 (0.06) [$M^+ - N_3$], 216 (0.5) [$M^+ - N_2 - OMe$], 188 (1.7) [$M^+ - CO_2Me - N_2$], 156 (1.5) [$M^+ - Bzl - N_2$], 140 (1.3) [$M^+ - OBzl - N_2$], 126 (1.0) [$M^+ - OBzl - N_3$], 107 (3.2) [$OBzl^+$], 91 (100) [$Bzl^+$], 82 (27), 65 (8.8), 59 (5.9) [$CO_2Me^+$].

### *2-Imino- and 2-Oxo-2-cyclopropylacetates* **18**, **19**

*Methyl 2-[1-(Diphenylmethyleneamino)cyclopropyl]-2-iminoacetate* (**18a-N=CPh₂**), *{Methyl 2′,2′-Diphenylspiro[cyclopropane-1,5′-imidazolidine]-4′-carboxylate}*: To 0.50 g (1.5 mmol) of **15a-N=CPh₂** in 10 ml of THF is added a solution of approximately 0.5 mmol of lithium methanolate prepared from 25 µl (0.6 mmol) of methanol and 350 µl (0.5 mmol) of 1.5 M *n*-butyllithium in hexane. After stirring for 2 d the solvent is removed and the residue chromatographed on "dry" silica gel[18] (column 1 × 30 cm, PE/ethyl ether, 8:1). Yield 260 mg (57%) of **18a-N=CPh₂**. Clear crystalline threads, m.p. 133°C. – IR (KBr): ṽ = 3265 $cm^{-1}$ (NH), 3055, 3000, 2950, 1723 (C=O), 1618 (C=N), 1263, 690. – $^1$H NMR (250 MHz, $CDCl_3$): δ = 1.34 (1.15–1.53, mc, 4H, $H_{cpr}$), ≈2.5 (bs, 1H, NH), 3.84 (s, 3H, $OCH_3$), 7.24–7.35 (m, 6H, *m*-, *p*-$H^*_{ar}$), 7.52–7.57 (m, 4H, *o*-$H^*_{ar}$). – $^{13}$C NMR (62.9 MHz, $CDCl_3$): δ = 13.91 (t, 2 C, $C_{cpr}$), 51.93 (s, $C_{cpr}$), 52.58 (q, $OCH_3$), 95.88 (s, N/N-acetal, 'C=N′), 126.61 (d, 4 C, *o*-$C^*_{ar}$), 127.53 (d, 2 C, *p*-$C_{ar}$), 128.26 (d, 4 C, *m*-$C^*_{ar}$), 144.39 (s, 2 C, *i*-$C_{ar}$), 161.89 (s, C=O*), 165.16 (s, C=N*). – MS (70 eV): *m/z* (%) = 306 (2.2) [$M^+$], 247 (100) [$M^+ - CO_2Me$], 229 (6) [$M^+ - Ph$], 206 (11) [$DPMA^+ - C_2H_2$], 165 (53), 105 (12).

| $C_{19}H_{18}N_2O_2$ (306.4) | | |
|---|---|---|
| Calcd. C 74.49 | H 5.92 | N 9.14 |
| Found C 74.35, 74.28 | H 5.86, 5.92 | N 9.04, 9.10 |

*Methyl 2-[1-(Methylthio)cyclopropyl]-2-oxoacetate* (**19-SMe**): In a flame-dried reaction flask 16 µl (0.4 mmol) of dry methanol is treated with 160 µl (0.24 mmol) of 1.5 M *n*-butyllithium in hexane. 1 ml of dry THF is added, followed by 171 mg (0.85 mmol) of **15a-SMe**. The mixture is stirred at room temp. for 2.5 h. The intermediate methyl 2-[1-(methylthio)cyclopropyl]-2-iminoacetate (**18-SMe**) can be detected by GC/MS (70 eV): *m/z* (%) = 173 [M$^+$], 158 [M$^+$ − Me], 127 [M$^+$ − Me − OMe], 126 [M$^+$ − SMe], 114 [M$^+$ − CO$_2$Me], 113, 112, 98, 87 (100) [$C_4H_7S^+$], 71, 59 [CO$_2$Me$^+$], 53, 47 [SMe$^+$]. 1 ml of dil. hydrochloric acid is added followed by 5 ml of water after 30 min. The product is extracted with 3 × 5 ml of ethyl ether. The united extracts are washed with sodium hydrogen carbonate solution and dried. After evaporation of the solvent chromatography of the residue (103 mg) on silica gel (10 g, 1.5 × 11 cm, pentane/ethyl ether, 9:1) yields 96 mg (65%) of **19-SMe**; $R_f$ (pentane/ethyl ether, 95:5) = 0.39. − $^1$H NMR (270 MHz, CDCl$_3$): $\delta$ = 1.36−1.42 (m, 2H, H$_{cpr}$), 1.69−1.75 (m, 2H, H$_{cpr}$), 2.12 (s, 3H, SCH$_3$), 3.84 (s, 3H, OCH$_3$). − $^{13}$C NMR (67.9 MHz, CDCl$_3$): $\delta$ = 16.33, 22.21, 32.80 (C-1′), 52.14, 165.26 (C-1), 196.68 (C-2). − MS (70 eV): *m/z* (%) = 174 [M$^+$], 141, 115 [M$^+$ − CO$_2$Me], 114, 87 (100) [$C_4H_7S^+$], 72, 71, 59 [CO$_2$Me$^+$], 53, 47 [SMe$^+$].

### *2-Azido-2-cyclopropylacetic acids* **20**, **29**, *2-Cyclopropylacetic Acid* **23**

*General Procedure C for the Hydrolysis of Methyl 2-Azido-2-cyclopropylacetates* **15a-Nu** *to the Corresponding Acids* **20-Nu′**: 1 mmol of ester **15a-Nu** in 5 ml of methanol is stirred with 1.5 ml (1.5 mmol) of 1 N NaOH at room temp. until a clear solution results. After additional 2−3 h, 20 ml of water is added. The solution is washed with 10 ml of ethyl ether, the aqueous phase then acidified with citric acid or diluted hydrochloric acid and extracted twice with 20 ml of chloroform. The combined chloroform extracts are washed with 2 × 10 ml of water, dried, and the chloroform is evaporated to give **20-Nu′**.

*2-Azido-2-cyclopropylacetic Acid* (**20-H**): 457 mg (2.95 mmol) of **15a-H** dissolved in 5 ml of dioxane and 2 ml (4.0 mmol) of a 2 N NaOH are stirred at room temp. for 19 h. Then 15 ml of water is added to this mixture which is washed with 2 × 10 ml of ethyl ether. The aqueous phase is acidified with dil. hydrochloric acid to pH ≈ 4 and extracted with 3 × 10 ml of dichloromethane. The united organic extracts are washed with 2 × 5 ml of water, and the solvent is removed in vacuo to leave 387 mg (93%) of **20-H** as a colorless oil. − IR (film): $\tilde{\nu}$ = 3500−2400 cm$^{-1}$, 2140 (N$_3$), 1730 (C=O), 1430, 1250, 1030, 980, 920, 880, 830. − $^1$H NMR (270 MHz, CDCl$_3$): $\delta$ = 0.55 (mc, 2H, H$_{cpr}$), 0.73 (mc, 2H, H$_{cpr}$), 1.30 (mc, 1H, 1′-H), 3.23 (d, 1H, 2-H), 11.60 (bs, 1H, CO$_2$H). − MS (70 eV): *m/z* (%) = 123 (0.3) [M$^+$ − H$_2$O], 96 (0.7) [M$^+$ − N$_2$ − OH], 68 (100) [M$^+$ − N$_2$ − CO$_2$H], 54 (4.2) [$C_4H_6^+$].

*2-Azido-2-(1-methylcyclopropyl)acetic Acid* (**20-Me**): 200 mg (1.18 mmol) of **15a-Me** dissolved in 5 ml of methanol and 2 ml of water is stirred with 0.15 g (2.6 mmol) of powdered potassium hydroxide at 65°C for 1.5 h. The methanol is removed in a rotary evaporator to afford 2 ml of a residue which is treated with 0.1 ml of conc. sulfuric acid in 5 ml of water and extracted with 15 ml of ethyl ether. The aqueous phase is acidified (pH 0) and extracted a second time. The combined extracts are washed with 10 ml of a conc. ammonium chloride solution and dried with magnesium sulfate. Evaporation of the solvent gives 180 mg (98%) of **20-Me**, the NMR spectrum of which reveals no impurities. It can thus be used for the following step without further treatment. TLC: $R_f$ = 0.18 (chloroform/methanol, 10:1). − IR (KBr): $\tilde{\nu}$ = 2960 cm$^{-1}$ (very broad, OH, CH), 2105 (N$_3$), 1720 (C=O), 1425, 1238, 1022, 941. − $^1$H NMR (60 MHz, CDCl$_3$/TMS): $\delta$ = 0.40−0.90 (m, 4H, H$_{cpr}$), 1.16 (s, 3H, CH$_3$), 3.45 (s, 1H, HCN$_3$), 11.19 (bs, 1H, CO$_2$H). − MS (CI, isobutane): *m/z* (%) = 156 (2.1) [MH$^+$], 138 (1.3) [M$^+$ − OH], 126 (3), 113 (32) [M$^+$ − N$_3$], 110 (5) [M$^+$ − CO$_2$H], 100 (15) [MH$^+$ − N$_2$ − CO], 84 (100) [MH$^+$ − N$_2$ − CO$_2$], 82 (52) [MH$^+$ − N$_2$ − HCO$_2$H]. − HRMS: Calcd. for $C_6H_9N_3O_2$ and found 155.069476.

*2-Azido-2-[1-(dibenzylamino)cyclopropyl]acetic Acid* (**20-NBzl$_2$**): According to general procedure C, 400 mg (1.14 mmol) of **15a-NBzl$_2$** is converted into 352 mg of crude **20-NBzl$_2$**. Two additional base/acid cycles (extraction of the product into sodium hydrogen carbonate solution, acidification with citric acid, re-extraction with chloroform) give 178 mg (47%) of **20-NBzl$_2$** as a white solid; $R_f$ (chloroform/methanol, 9:1) = 0.46. − $^1$H NMR (270 MHz, CDCl$_3$): $\delta$ = 0.78 (mc, 1H, H$_{cpr}$), 0.98 (mc, 2H, H$_{cpr}$), 1.10 (mc, 1H, H$_{cpr}$), 3.70 and 3.95 (AB system, 4H, $^2J$ = 13.2 Hz, NCH$_2$), 3.98 (s, 1H, 2-H), 7.27 (s, 10H, H$_{ar}$), 10.20 (bs, 1H, CO$_2$H). − $^{13}$C NMR (67.9 MHz, CDCl$_3$): $\delta$ = 11.10, 12.93, 46.02 (C-1′), 56.69 (NCH$_2$), 63.44 (C-2), 127.26, 128.24, 129.09, 138.38, 173.28 (C=O).

*Methyl 2-Azido-2-[1-(carboxymethyl)cyclopropyl]acetate* (**15a-CH$_2$CO$_2$H**): 538 mg (2 mmol) of **15a-CH$_2$CO$_2$*t*Bu** dissolved in 2 ml of dichloromethane and 2 ml of trifluoroacetic acid is stirred at room temp. for 20 h. The solvents are removed in vacuo, and the residue is chromatographed on silica gel (3 × 40 cm, PE/ethyl ether, 3:1, $R_f$ = 0.14) to give 357 mg (84%) of **15a-CH$_2$CO$_2$H**, white crystals, m.p. 53°C. − IR (KBr): $\tilde{\nu}$ = 3500−2500 cm$^{-1}$ (CO$_2$H), 2130 (N$_3$), 1750 (CO), 1720, 1440, 1230, 1210, 1030. − $^1$H NMR (270 MHz, CDCl$_3$): $\delta$ = 0.58−1.07 (m, 4H, H$_{cpr}$), 2.34 and 2.62 (AB system, 2H, $J_{A,B}$ = 16.9 Hz, 1″-H), 3.78 (s, 3H, CO$_2$CH$_3$), 3.88 (s, 1H, 2-H), 10.78 (s, 1H, CO$_2$H). − $^{13}$C NMR (67.9 MHz, CDCl$_3$): $\delta$ = 9.90, 11.05 (C-2′/3′), 19.06 (C-1′), 38.55 (C-1″), 52.31 (OCH$_3$), 66.73 (C-2), 169.40 (C-1), 178.52 (C-2″). − MS (EI, 70 eV): *m/z* (%) = 186 (0.5) [M$^+$ + H − N$_2$], 167 (2.5), 154 (17.1) [M$^+$ − N$_2$ − OMe], 126 (100) [M$^+$ − N$_2$ − CO$_2$CH$_3$], 110 (12.5), 108 (16.9), 99 (16.2), 98 (29.4), 82 (11.4), 81 (43.6), 80 (50.3) [$C_5H_6N^+$].

$C_8H_{11}N_3O_4$ (213.0) Calcd. C 45.07 H 5.20 N 19.79
Found C 45.07 H 5.20 N 19.50

*2-Azido-2-[1-(carboxymethyl)cyclopropyl]acetic Acid* (**20-CH$_2$CO$_2$H**): 10.0 g (37 mmol) of **15a-CH$_2$CO$_2$*t*Bu** is suspended in 400 ml of 2 N NaOH until the starting material is dissolved (≈24 h). The solution is then brought to pH 1 with conc. hydrochloric acid and stirred for 1 h. The mixture is extracted three times with 150 ml of ethyl ether, and the combined extracts are dried with sodium sulfate. After evaporation of the solvent recrystallization from ethyl acetate/PE furnishes 5.31 g (72%) of **20-CH$_2$CO$_2$H**, m.p. 131°C. − IR (KBr): $\tilde{\nu}$ = 3500−2450 cm$^{-1}$ (OH), 2140 (N$_3$), 1720 (C=O), 1430, 1400, 1330, 1300, 1280, 1240, 900, 730, 680. − $^1$H NMR (400 MHz, CD$_3$OD): $\delta$ = 0.61−0.77 (m, 3H, H$_{cpr}$), 0.93 (mc, 1H, H$_{cpr}$), 2.41 and 2.48 (AB system, 2H, $J_{A,B}$ = 15.9 Hz, 1″-H), 3.99 (s, 1H, 2-H). − $^{13}$C NMR (67.9 MHz, CD$_3$OD): $\delta$ = 10.86 (C-2′/3′), 19.99 (C-1′), 39.44 (C-1″), 67.71 (C-2), 172.12, 175.20 (CO).

$C_7H_9N_3O_4$ (199.2) Calcd. C 42.21 H 4.55 N 21.10
Found C 42.29 H 4.54 N 21.09

*2-Azido-2-[1-(methylthio)cyclopropyl]acetic Acid* (**20-SMe**): According to general procedure C, 210 mg (1.04 mmol) of **15a-SMe** is converted into 180 mg (92%) of **20-SMe**. − IR (KBr): $\tilde{\nu}$ = 3200 cm$^{-1}$ (OH), 2100 (N$_3$), 1700 (C=O), 1400, 1240, 1200, 1020, 950, 880, 740. − $^1$H NMR (270 MHz, CDCl$_3$): $\delta$ = 1.02−1.17 (m, 3H, H$_{cpr}$), 1.20−1.30 (m, 1H, H$_{cpr}$), 2.21 (s, 3H, SCH$_3$), 3.73 (s, 1H, 2-H), 11.1 (bs, 1H, CO$_2$H). − $^{13}$C NMR (67.9 MHz, CDCl$_3$): $\delta$ = 15.31, 15.41, 15.78, 28.03 (C-1′), 69.26, 173.66 (C-1). − MS (70 eV): *m/z* (%) = 187 (25) [M$^+$], 145 (14) [M$^+$ − N$_3$], 127 (5.8) [M$^+$ − N$_3$ − H$_2$O], 126 (7.7), 115 (18), 114 (25) [M$^+$ − N$_2$ − CO$_2$H], 100

(100) [$M^+ - N_3 - CO_2H$], 98 (16), 87 (47) [$C_4H_7S^+$], 71 (32), 67 (54), 58 (10) [$C_2H_2O_2^+$], 47 (33.3) [$SMe^+$], 45 [$CO_2H^+$].

$C_6H_9N_3O_2S$ (187.2) Calcd. C 38.49 H 4.85 N 22.44
Found C 38.27 H 4.91 N 21.28

*[1-(Dibenzylamino)cyclopropyl]acetic Acid* (**23**): According to general procedure C, 390 mg (1.26 mmol) of **22a-NBzl$_2$** is hydrolyzed to 359 mg of crude **23** after acidification. This should be carried out carefully to avoid a large excess of acid and thus the formation of the water-soluble ammonium salt. Another cycle of base/citric acid treatment gives 253 mg (68%) of **23**, a white solid of m.p. 114°C. – IR (KBr): $\tilde{\nu}$ = 3200–2600 $cm^{-1}$ (peaks at 3080, 3040, 2940, 2820), 1700 (C=O), 1490, 1450, 1420, 1360, 1340, 1320, 1290, 1270, 1240, 1170, 1130, 1050, 1030, 1020, 1000, 970, 950, 940, 910, 750, 730, 700, 630. – $^1H$ NMR (270 MHz, $CDCl_3$): $\delta$ = 0.62 (bs, 2H, $H_{cpr}$), 0.75 (bs, 2H, $H_{cpr}$), 2.57 (s, 2H, 2-H), 3.80 (s, 4H, $NCH_2$), 7.30 (s, 10H, $H_{ar}$), 12.50 (bs, 1H, $CO_2H$). – $^{13}C$ NMR (67.9 MHz, $CDCl_3$): $\delta$ = 14.46, 37.28 (C-2), 41.34 (C-1′), 56.43 ($NCH_2$), 126.67, 128.02, 128.99, 139.47, 178.08 (C=O). – MS (CI): *m/z* (%) = 296 (1.3) [$M^+ + H$], 278 (3.1) [$M^+ - OH$], 252 (100), 250 (15) [$M^+ - CO_2H$], 198 (12), 196 (5.2) [$NBzl_2^+$], 187 (1.5) [$M^+ - OH - Bzl$], 173 (1.6) [$M^+ - Ph - CO_2H$], 162 (21), 160 (35) [$M^+ - CO_2 - Bzl$], 146 (2.4), 108 (13), 106 (24) [$NHBzl^+$], 91 (25) [$Bzl^+$], 74 (5.9), 72 (7.5), 65 (2.2), 58 (3.6), 46 (4.4).

$C_{19}H_{21}NO_2$ (295.4) Calcd. C 77.26 H 7.17 N 4.74
Found C 76.72 H 7.13 N 4.72

*2-Azido-2-[2-(benzyloxymethyl)cyclopropyl]acetic Acid* (**29**): 230 mg (0.84 mmol) of **28** in 2 ml of methanol is stirred with 0.9 ml (0.9 mmol) of 1 N NaOH at room temp. for 23 h. Then 20 ml of water and sodium hydroxide are added to the mixture until pH 12 is reached, the solution is then washed twice with 15 ml of ethyl ether. The aqueous phase is acidified with citric acid to pH 3–4 and extracted with 3 × 15 ml of ethyl ether. The combined ethereal extracts are dried with magnesium sulfate, and the solvent is removed in vacuo. Yield 203 mg (93%) of **29**. – IR (film): $\tilde{\nu}$ = 3600–2500 $cm^{-1}$ (peaks at 3020, 2860), 2100 ($N_3$), 1730, 1710, 1440, 1370, 1230, 1200, 1080, 1060, 740, 700. – $^1H$ NMR (270 MHz, $CDCl_3$): $\delta$ = 0.52–0.64 (m, 2H, 2 × 3′-H), 0.91–1.10 (m, 2H, 2 × 3′-H), 1.31–1.55 (m, 4H, 2 × 2′-H, 2 × 1′-H), 3.30–3.69 (m, 5H, 3 × 1″-H, 2 × 2-H), 3.89 (dd, 1H, 1″-H), 4.56 (AB system, 4H, 2″-H), 7.22–7.38 (m, 10H, $H_{ar}$), 10.75 ($CO_2H$). – $^{13}C$ NMR (67.9 MHz, $CDCl_3$): $\delta$ = 8.20 (C-3′), 9.07 (C-3′), 15.77, 15.83, 16.95, 17.15, 61.79 (C-2), 68.66 (C-1″), 69.88 (C-1″), 72.83 (C-2″), 73.18 (C-2″), 127.62, 127.67, 128.03, 128.15, 128.28, and 128.49 (all $C_{ar}$), 136.4 ($C_{ar}$), 137.69 ($C_{ar}$), 171.96 (C-1), 174.65 (C-1).

### *Amino Acids* **3–10, 21**

*General Procedure D for the Hydrogenative Deprotection of Cyclopropylglycine Precursors* **20** *and* **15b**: 1 mmol of azide **20** or **15b** and ≈30 mg of palladium catalyst (10% on charcoal) in approximately 20 ml of methanol are stirred under hydrogen by utilizing a rubber balloon. Some sulfur and nitrogen compounds may require another catalyst or its reactivation by ultrasonics after some hours. After the starting material has disappeared (TLC) the catalyst is filtered off with the help of Celite, thoroughly washed (>20 ml of methanol), and the solution is concentrated in vacuo. The obtained amino acid is then either crystallized by adding an appropriate less polar solvent (e.g. acetone or ether) or, after evaporation to dryness, isolated by chromatography. Further purification may be accomplished by recrystallization from water/acetone or methanol/acetonitrile. Solvent inclusions cannot be avoided totally and lead to deviations in the microanalytical data with $\Delta$C values of ≈1–2% for new as well as known compounds[11,12,23].

*2-Cyclopropylglycine* (**3**): 140 mg (0.99 mmol) of **20-H** in 2 ml of methanol is hydrogenated over 10% palladium on charcoal for 3 h at a hydrogen pressure of 1.5 bar. Then 20 ml of methanol is added to the mixture which is subsequently filtered through Celite and further washed with 20 ml of water. Partial evaporation of the solvent leads to crystallization of 65 mg (57%) of **3**. $R_f$ (methanol/chloroform, 7:3, + ca. 0.5% acetic acid) = 0.28; m.p. 249°C (dec.). – IR (KBr): $\tilde{\nu}$ = 3550 $cm^{-1}$, 3440, 3385, 3200–2550, 1625 (C=O), 1580, 1490, 1420, 1390, 1340, 1260, 1030, 710. – $^1H$ NMR (270 MHz, $D_2O$): $\delta$ = 0.36 (mc, 1H, $H_{cpr}$), 0.43 (mc, 1H, $H_{cpr}$), 0.56 (mc, 2H, $H_{cpr}$), 0.94 (mc, 1H, 1′-H), 2.92 (d, 1H, 2-H). – $^{13}C$ NMR (67.9 MHz, $D_2O/CH_3CN$): $\delta$ = 4.04 ($C_{cpr}H_2$), 4.77 ($C_{cpr}H_2$), 12.96 (C-1′), 60.49 (C-2), 174.90 (C=O). – MS (CI): *m/z* (%) = 116 (4.7) [$M^+ + H$], 70 (45) [$M^+ - CO_2H$], 58 (100) [$CHCO_2H^+$], 54 (4.0) [$C_4H_6^+$], 43 (41), 41 (45) [$C_3H_5^+$].

The mother liquid contains a further product which is subjected to chromatography on silica gel (20 g, 1.6 × 16 cm, methanol/chloroform, 7:3, + 1% acetic acid) to give 107 mg of hydroacetate **3 · *n*HOAc**.

*2-(1-Methylcyclopropyl)glycine* (**4**): 180 mg (1.16 mmol) of **20-Me** and 40 mg of palladium catalyst (10% on charcoal) in 7 ml of methanol and 1 ml of water are vigorously stirred under hydrogen ($p \approx$ 1 bar, balloon) for ca. 45 min. The mixture is controlled by TLC (ethanol/chloroform/13% ammonia, 7:4:1, $R_f$ = 0.25, detection by ninhydrin or molybdatophosphate reagent). Filtration with thorough washing of the residues and evaporation of the solvent from the filtrate give 140 mg of **4** (94%, 92% based on **15a-Me**) as sole product. All data are in good agreement with those documented in ref.[10]. – IR (KBr): $\tilde{\nu}$ = 3100–2900 $cm^{-1}$ (NH, CH), 1590 (C=O), 1490, 1410, 1363, 1316, 1237, 1027, 1020, 719. – $^1H$ NMR (300 MHz, $D_2O$, [$D_6$]DMSO/$CD_3OD$): $\delta$ = 0.70 (mc, 2H, $H_{cpr}$), 0.79 (0.58–1.00, mc, 2H, $H_{cpr}$), 1.15 (s, 3H, $CH_3$), 3.13 (s, 1H, NCH). – $^{13}C$ NMR (75.4 MHz, $D_2O$, [$D_6$]DMSO/$CD_3OD$): $\delta$ = 12.91 ($C_{cpr}H_2$), 14.74 ($C_{cpr}H_2$), 17.76 ($C_{cpr}$), 18.88 ($CH_3$), 64.25 ($HC-NH_2$), 173.89 (C=O). – MS (70 eV): *m/z* (%) = 111 (1.2) [$M^+ - H_2O$], 84 (100) [$M^+ - HCO_2$], 74 (14), 57 (18), 55 (15), 42 (22).

$C_6H_{11}NO_2$ (129.2) Calcd. C 55.80 H 8.58 N 10.84
Found C 55.78 H 8.33 N 10.67

*2-(1-Hydroxycyclopropyl)glycine* (*Cleonin*, **5**): 120 mg (0.36 mmol) of **15b-OBzl** in 15 ml of dry methanol is hydrogenated according to general procedure D. The reaction needs more than 16 h for completion. After filtration and removal of the solvent from the filtrate 75 mg of crude product is obtained. This is dissolved in as little methanol as possible for crystallization (5 mg). The mother liquid is then chromatographed on silica gel (10 g, 1.4 × 18 cm, methanol/chloroform/toluene/water, 12:4:4:1). The main fraction ($R_f$ = 0.24) gives 20 mg of cleonin, i.e. a total yield of 25 mg (53%) **5** is obtained. The data are in good accordance with those given in ref.[11], m.p. 255–258°C (dec.). – IR (KBr): $\tilde{\nu}$ = 3520 $cm^{-1}$, 3440, 3380 ($NH_2$), 3100, 3020, 2960, 1630 (C=O), 1510, 1410, 1280, 1120, 960, 720. – $^1H$ NMR (270 MHz, $D_2O$): $\delta$ = 0.57–0.68 (m, 1H, $H_{cpr}$), 0.72–0.87 (m, 3H, $H_{cpr}$), 3.23 (s, 1H, 2-H). – $^{13}C$ NMR (67.9 MHz, $D_2O$/DMSO): $\delta$ = 13.48, 13.91, 55.61 (C–1′), 62.91 (C-2).

For mass spectroscopy two small crystals of **5** in 0.1 ml of dichloromethane are stirred under nitrogen with 10 µl of *N,N*-bis(trimethylsilyl)trifluoroacetamide (BSTFA) at room temp. for 14 h. Only Bis(trimethylsilyl)cleonine is detected by GC/MS (70 eV): *m/z* (%) = 275 (3.0) [$M^+$], 260 (3.4) [$M^+ - Me$], 258 (5.9) [$M^+ - OH$], 247 (1.7) [$M^+ - C_2H_4$], 243 (8.4) [$M^+ - Me - OH$], 232 (17) [$M^+ - C_2H_4 - Me$], 218 (42) [$M^+ - C_3H_5O$], 185 (1.5) [$M^+ - SiMe_3 - OH$], 158 (32) [$M^+ - CO_2SiMe_3$], 147 (44), 142 (31) [$C_4H_5OSiMe_3^+$], 129 (6.0), 100 (6.5), 75 (26), 73 (100) [$SiMe_3^+$], 57 (18) [$C_3H_4OH^+$], 45 (19).

*2-(1-Aminocyclopropyl)glycine* (**6**)

a) *From* **15b-N=CPh$_2$**: 615 mg (1.5 mmol) of **15b-N=CPh$_2$** in 30 ml of dry methanol is stirred with 70 mg of dry palladium catalyst (10% on charcoal) under hydrogen ($p \approx 1$ bar, balloon). After the starting material has disappeared (TLC, ca. 2.5 d) the mixture is filtered through Celite and concentrated to ca. 6 ml in a rotary evaporator at less than 35°C. 35 ml of ethyl ether is added, and within 1 h at −20°C 85 mg (44%) of white **6** precipitates. Further concentration and precipitation give a total of 135 mg (69%) of **6**. After some days or above 170°C diamino acid **6** becomes slightly brown. Rapid decomposition occurs above 200°C. TLC: $R_f = 0.11$ (ethanol/chloroform/25% ammonia, 10:5:2). – IR (KBr): $\tilde{\nu}$ = *3430* cm$^{-1}$, 3080–2500, 2250, 1630 (C=O), 1580, 1540, 1490, 1420, 1380, 1290, 1030, 1000, 830, 770. – $^1$H NMR (250 MHz, $D_2O/CH_3CN$): $\delta$ = 0.73–1.02 (m, 4H, $H_{cpr}$), 3.32 (s, 1H, NCH). – $^{13}$C NMR (62.9 MHz, $D_2O/CH_3CN$): $\delta$ = 12.33 (t, $C_{cpr}H_2$), 14.07 (t, $C_{cpr}H_2$), 34.73 (s, $C_{cpr}$), 62.14 (d, NCH), 170.81 (s, C=O).

b) *From* **20-NBzl$_2$**: 140 mg (0.42 mmol) of **20-NBzl$_2$** in 50 ml of methanol is hydrogenated over 10% palladium on charcoal for 18 h according to general procedure D. The catalyst is filtered off through Celite and washed with 200 ml of water. The solvents are removed from the filtrate in a rotary evaporator at 20°C. The residue is dissolved in 10 ml of dry methanol, and ethyl ether is added until the solution just becomes turbid. The mixture is allowed to stand overnight at −20°C after which time 11 mg of **6** has precipitated. Chromatography of the mother liquid on silica gel (10 g, 1.5 × 11 cm, methanol/chloroform/toluene/water, 12:4:4:1, $R_f$ = 0.08) gives 12 mg of less pure material which is subjected to column chromatography. Total yield 20 mg (37%) of **6**; m.p. 224–226°C (dec.).

For mass spectroscopy two small crystals of **6** dissolved in 0.1 ml of dichloromethane are stirred under nitrogen with 10 µl of *N,N*-bis(trimethylsilyl)trifluoroacetamide (BSTFA) at room temp. for 14 h. Two procucts are detected by GC/MS:

I: *2-(1-Aminocyclopropyl)-N-(trimethylsilyl)glycine:* MS (70 eV): *m/z* (%) = 202 (2.7) [$M^+$], 185 (34) [$M^+$ – OH], 170 (55) [$M^+$ – OH – Me], 157 (4.7) [$M^+ - CO_2H$], 142 (6.2) [$M^+ - CO_2H$ – Me], 128 (12), 126 (21) [$M^+ - CO_2H - NH_2$ – Me], 112 (4.1) [$M^+ - SiMe_3$ – OH], 99 (7.2), 96 (15) [$M^+ - SiMe_3 - NH_2$ – OH], 85 (88), 75 (59), 73 (100) [$SiMe_3^+$], 68 (46), 58 (21) [$CHCO_2H^+$], 56 (42) [$C_3H_6N^+$], 45 (22) [$CO_2H^+$].

II: *Trimethylsilyl 2-[(Trimethylsilyl)amino]-2-{1-[(trimethylsilyl)amino]cyclopropyl}acetate:* MS (70 eV): *m/z* (%) = 346 (1.8) [$M^+$], 331 (3.5) [$M^+$ – Me], 291 (5.6), 257 (2.4) [$M^+ - OSiMe_3$], 242 (16) [$M^+ - OSiMe_3$ – Me], 229 (42) [$M^+ - CO_2SiMe_3$], 218 (4.6), 214 (5.7) [$M^+ - CO_2SiMe_3$ – 2 Me], 204 (5.2), 147 (23), 141 (8.6) [$M^+ - CO_2SiMe_3 - NHSiMe_3$], 130 (29) [$CHCO_2SiMe_3^+$], 128 (100) [$C_3H_5NSiMe_3^+$], 102 (18), 73 (100) [$SiMe_3^+$], 57 (14), 45 (20).

*2-Amino-2-[1-(carboxymethyl)cyclopropyl]acetic Acid* (*3,3-Ethyleneglutamic Acid,* **7**): 3.0 g (15.1 mmol) of **20-CH$_2$CO$_2$H** in 400 ml of methanol/water (1:1) and 100 mg of palladium catalyst (10% on charcoal) are stirred under hydrogen ($p \approx 1$ bar, balloon) for 2 d. The catalyst is then filtered off through 3 g of Celite and the solvent evaporated under vacuum. Recrystallization from water/acetone gives 2.3 g (89%) of **7** as a white powder. According to general procedure D, smaller batches (≈1 mmol) give up to 98% yield. The analytical data are in good agreement with those reported in ref.[9a]. – IR (KBr): $\tilde{\nu}$ = 3600–2400 cm$^{-1}$ ($CO_2H$), 2000, 1680, 1600, 1500, 1400, 1340, 1300, 1220, 1150, 1040, 880. – $^1$H NMR (270 MHz, $D_2O$): $\delta$ = 0.56–1.02 [m, 4H, 2′(3′)-H], 2.08 and 2.84 (AB system, 2H, $^2J_{A,B}$ = 17.5 Hz, 1″-H), 3.14 (s, 1H, 2-H), 4.83 (s, 3H, $CO_2H$, $NH_2$). – $^{13}$C NMR (67.9 MHz, $D_2O$): $\delta$ = 10.67, 14.85 (C-2′/C-3′), 17.33 (C-1′), 40.68 (C-1″), 62.09 (C-2), 172.82 (C-1), 178.24 (C-2″). – MS (CI, $NH_3$): *m/z* (%) = 173 (44) [$M^+ + NH_4 - H_2O$], 156 (100) [$M^+$ – OH], 110 (40), 82 (7).

*2-[1-(Methylthio)cyclopropyl]glycine* (**8**): 75 mg (0.40 mmol) of **20-SMe** is hydrogenated according to general procedure D. Upon addition of chloroform 15 mg of the amino acid precipitates. The mother liquid is concentrated and the residue chromatographed on silica gel (15 g, 1.6 × 28 cm, chloroform/methanol, 7:3, $R_f$ = 0.14). The main fraction contains 32 mg of the amino acid giving a total yield of 47 mg (73%) of **8**. Further fractions contain another 5 mg of amino acid, but also some impurities. – IR (KBr): $\tilde{\nu}$ = 3600–2850 cm$^{-1}$ (peaks at 3540, 3400, 3380, 3240, 3015), 1650 (C=O), 1610, 1510, 1410, 1395, 1040. – $^1$H NMR (270 MHz, $D_2O$): $\delta$ = 0.82–0.92 (m, 2H, $H_{cpr}$), 0.98–1.10 (m, 1H, $H_{cpr}$), 1.13–1.23 (m, 1H, $H_{cpr}$), 1.95 (s, 3H, $SCH_3$), 3.11 (s, 1H, 2-H). – $^{13}$C NMR (67.9 MHz, $D_2O$/DMSO): $\delta$ = 15.27, 16.10, 16.28, 27.85 (C-1′), 62.22, 174.61 (C-1).

For mass spectroscopy two small crystals of **8** in 0.1 ml of dichloromethane are stirred under nitrogen with 10 µl of *N,N*-bis(trimethylsilyl)trifluoroacetamide (BSTFA) at room temp. for 14 h. The resulting 2-[1-(methylthio)cyclopropyl]-*N*-(trimethylsilyl)glycine is subjected to GC/MS (70 eV): *m/z* (%) = 233 (0.3) [$M^+$], 218 (0.9) [$M^+$ – Me], 201 (2.7) [$M^+$ – Me – OH], 173 (0.9) [$M^+$ – Me – $CO_2H$], 172 (2.7), 146 (4.6), 116 (100), 101 (24), 87 (3.2) [$C_4H_7S^+$], 75 (11), 73 (28) [$SiMe_3^+$], 68 (5.2), 45 (4.7).

*2-Amino-2-[2-(hydroxymethyl)cyclopropyl]acetic Acid* (**10**): 180 mg (0.69 mmol) of **29** is hydrogenated and worked up according to general procedure D. The crude product (135 mg) is recrystallized from methanol/ethyl ether. Yield 39 mg (39%) of **10**. Chromatography on silica gel (80 g, 4 × 18 cm, methanol/chloroform/water, 16:2:1) of the mother liquid yields further 32 mg of impure material. – IR (film): $\tilde{\nu}$ = 3600–2400 cm$^{-1}$, 1680, 1490, 1400, 1390, 1330, 1270, 1250, 1150, 1090, 1040, 1020, 900. – $^1$H NMR (270 MHz, $D_2O$): $\delta$ = 0.29 (mc, 1H), 0.50 (mc, 1H), 0.89–0.96 (m, 2H), 1.07–1.40 (m, 1H), 3.09–3.39 (2 dd, 2 d superimposed, 4H, 2-H, 1″-H), 3.75 (dd, 1H, 1″-H), 3.93 (dd, 1H, 1″-H). – $^{13}$C NMR (67.9 MHz, $D_2O/CH_3CN$): $\delta$ = 8.82 (C-3′), 10.45 (C-3′), 17.49 and 18.24 and 18.48 and 19.56 (C–1′, C-2′), 56.72 (C-2), 56.97 (C-2), 62.66 (C-1″), 63.08 (C-1″), 175.02 (C-1).

For mass spectroscopy 1–2 mg of **10** in 0.1 ml of dichloromethane is stirred under nitrogen with 10 µl of *N,N*-bis(trimethylsilyl)trifluoroacetamide (BSTFA) at room temp. for 18 h. Two products are detected by GC/MS:

I: *2-[Bis(trimethylsilyl)amino]-2-[2-(hydroxymethyl)cyclopropyl]acetic Acid:* MS (70 eV): *m/z* (%) = 274 (0.8) [$M^+$ – Me], 186 (6.4) [$M^+ - NHSiMe_3$ – Me], 172 (27) [$M^+ - CO_2SiMe_3$], 147 (3.9), 129 (1.9), 109 (2.6) [$M^+ - OSiMe_3 - SiMe_3 - H_2O$], 96 (3.6), 82 (31), 73 (49) [$SiMe_3^+$], 56 (100), 45 (20).

II: *Trimethylsilyl 2-{2-[(trimethylsiloxy)methyl]cyclopropyl}-2-[(trimethylsilyl)amino]acetate:* MS (70 eV): *m/z* (%) = 361 (0.3) [$M^+$], 346 (3.3) [$M^+$ – Me], 244 (100) [$M^+ - O_2SiMe_3$], 172 (5.4) [$M^+ - SiMe_3 - CO_2SiMe_3$], 147 (7.8), 128 (50), 73 (19) [$SiMe_3$], 56 (13), 45 (1.2).

*2-(1-Aminocyclopropyl)acetic Acid* (**21**)

a) *From* **26b-N=CPh$_2$**: 1.00 g (2.7 mmol) of **26b-N=CPh$_2$** in 30 ml of dry methanol is stirred with 80 mg of dry palladium catalyst (10% on charcoal) under hydrogen ($p \approx 1$ bar, balloon). After the starting material has been consumed (TLC, overnight) the mixture is filtered through Celite and the filtrate concentrated to 10 ml in a rotary evaporator at less than 35°C. Cooling to −20°C gives 59 mg of white crystalline **21**. Further cycles of concentration and cooling give a total of 262 mg (84%) of **21**. Alternatively, precipitation by addition of less polar solvents, e. g. acetonitrile or acetone, can be employed. The data obtained are in agreement with those of our independently synthesized **21** [see b) and ref.[23]]. TLC: $R_f$ = 0.19 (ethanol/chloroform/25% ammonia, 10:5:2). – IR (KBr): $\tilde{\nu}$ = ≈2940 $cm^{-1}$ (broad), 1650, 1585, 1392, 1030. – $^1H$ NMR (250 MHz, $D_2O/CD_3CN$): δ = 0.84 (0.71–0.97 mc, 4H, $H_{cpr}$), 2.41 (s, 2H, $CH_2$). – $^{13}C$ NMR (62.9 MHz, $D_2O/CH_3CN$): δ = 10.38 (t, 2 C, $C_{cpr}H_2$), 32.79 (s, $C_{cpr}$), 41.64 (t, $CH_2$), 179.27 (s, C=O). For further data see b) and ref.[23].

b) *From* **23**: 89 mg (0.30 mmol) of **23** is hydrogenated according to general procedure D. The Celite is washed with 50 ml of methanol and 20 ml of water. The solvents are evaporated, the residue is dissolved in ≈3 ml of dry methanol. Then ethyl ether is added until the solution gets cloudy. After 2 d at −20°C the precipitate formed is separated and dried in vacuo. Yield 15 mg (43%) of **21**. – IR (KBr): $\tilde{\nu}$ = 3500–2600 $cm^{-1}$, 2100, 1640, 1580, 1420, 1380, 1310, 1260, 1180, 1090, 1030, 980, 950, 890, 740, 680. – $^{13}C$ NMR (67.9 MHz, $D_2O/CH_3CN$): δ = 10.98, 33.12 (C-1′), 42.45 (C-2), 179.31 (C=O).

For mass spectroscopy two small crystals of **21** in 0.1 ml of dichloromethane are stirred under nitrogen with 10 µl of *N,N*-bis(trimethylsilyl)trifluoroacetamide (BSTFA) at room temp. for 6 h. Only *2-{1-[Bis(trimethylsilyl)amino]cyclopropyl}acetic acid* is found by GC/MS (70 ev): *m/z* (%) = 241 (2.7) [$M^+ - H_2O$], 187 (6.6) [$M^+ - SiMe_3$], 183 (6.2) [$M^+ - H_2O - CO - 2\ Me$], 172 (9.6) [$M^+ - SiMe_3 - Me$], 153 (2.6), 117 (11), 98 (6.0), 97 (18), 73 (100) [$SiMe_3^+$], 69 (24), 56 (3.6), 45 (9.6) [$CO_2H^+$].

*2-(1-Aminocyclopropyl)acetic Acid, Hydrochloride* (**21 · HCl**)

a) *From* **14b-N=CPh₂**: 0.50 g (1.24 mmol) of **14b-N=CPh₂** dissolved in 10 ml of methanol and 10 ml of 0.1 N HCl is vigorously stirred with 25 mg of palladium catalyst (10% on charcoal) under hydrogen ($p$ ≈ 1 bar, balloon). The reaction is controlled by TLC. After completion of the reaction the mixture is filtered through Celite, the filtrate is added to 5 ml of water and washed three times with 5 ml of ethyl ether. The aqueous phase is then evaporated to dryness at low temp. to give 165 mg (88%) of **21 · HCl**. TLC and NMR of the free amino acid **21** (see above) prove the identity with an authentic sample. – $^1H$ NMR (250 MHz, $D_2O$): δ = 1.05 (0.89–1.20, mc, 4H, $H_{cpr}$), 2.70 (s, 2H, $CH_2$). – $^{13}C$ NMR (62.9 MHz, $CD_3OD$): δ = 10.86 (t, 2 C, $C_{cpr}H_2$), 32.83 (s, $C_{cpr}$), 40.59 (t, $CH_2$), 176.0 (bs, C=O).

b) *From* **15b-NBzl₂**: 210 mg (0.5 mmol) of **15b-NBzl₂** is hydrogenated according to general procedure D. The crude product is purified by chromatography on silica gel (15 g, 1.5 × 25 cm, methanol, $R_f$ = 0.37) to give 32 mg (43%) of **21 · HCl** (for data see above).

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[*] Dedicated to Professor *Lars Skattebøl* on the occasion of his 65th birthday.

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CAS Registry Numbers

**1**-$CH_2OBzl$ (*cis*): 139132-01-7 / **1**-$CH_2OBzl$ (*trans*): 139132-02-8 / **2**-$CH_2OBzl$ (*cis*): 139132-03-9 / **2**-$CH_2OBzl$ (*trans*): 139132-04-0 / **2a**-H: 82979-45-1 / **2b**-H: 139132-05-1 / **3**: 5687-71-8 / **4**: 139132-43-7 / **5**: 139132-46-0 / **6**: 139166-30-6 / **7**: 139132-44-8 / **8**: 139132-45-9 / **10**: 139132-47-1 / **14a**-H: 139132-18-6 / **14a**-Me: 116588-56-8 / **14a**-SMe: 139132-16-4 / **14a**-SBzl: 139132-17-5 / **14a**-OBzl: 139132-14-2 / **14a-N**=CPhz: 125506-36-7 / **14a**-$CH_2CO_2$tBu: 139132-07-3 / **14a**-NPhth: 139132-08-4 / **14a**-N(BOC)$_2$: 139132-09-5 / **14a**-N(BOC)(MOC): 139132-10-8 / **14a**-$NBzl_2$: 139132-11-9 / **14b**-NBzlz: 139132-12-0 / **14b**-OBzl: 139132-15-3 / **14b**-N=$CPh_2$: 139132-13-1 / **15a**-H: 139132-28-8 / **15a**-$CH_2CO_2$tBu: 139132-21-1 / **15a**-$CH_3$: 139132-22-2 / **15a**-$NBzl_2$: 139132-23-3 / **15a**-N=$CPh_2$: 139132-25-5 / **15a**-SMe: 139132-26-6 / **15a**-SBzl: 139132-27-7 / **15a**-$CH_2CO_2H$: 139132-42-6 / **15b**-$NBzl_2$: 139132-24-4 / **15b**-N=$CPh_2$: 139132-48-2 / **15b**-OBzl: 139132-49-3 / **16**-SMe: 139132-29-9 / **16**-OMe: 139132-30-2 / **18**-SMe: 139132-33-5 / **18a**-N=$CPh_2$: 139132-32-4 / **19**-SMe: 139132-34-6 / **20**-H: 139132-35-7 / **20**-Me: 139132-36-8 / **20**-$NBzl_2$: 139132-37-9 / **20**-$CH_2CO_2H$: 139132-38-0 / **20**-SMe: 139132-39-1 / **21**: 133616-20-3 / **21** · HCl: 139132-50-6 / **22a**-$NBzl_2$: 133616-15-6 / **22a**-N=$CPh_2$: 125506-35-6 / **22b**-$NBzl_2$: 133616-14-5 / **22b**-N=$CPh_2$: 139132-19-7 / **23**: 139132-40-4 / **24**: 5009-28-9 / **25b**: 139132-06-2 / **26**: 14593-43-2 / **27**: 139132-20-0 / **28**: 139132-31-3 / **29**: 139132-41-5 / bis(trimethylsilyl)cleonine: 139132-51-7 / 2-(1-aminocyclopropyl)-*N*-(trimethylsilyl)glycine: 139132-52-8 / trimethylsilyl-2-[(trimethylsilyl)amino]-2-{1-[(trimethylsilyl)amino]cyclopropyl}acetate: 139132-53-9 / 2-[1-(methylthio)cyclopropyl]-*N*-(trimethylsilyl)glycine: 139132-54-0 / 2-[bis(trimethylsilyl)amino]-2-[2-hydroxymethyl)cyclopropyl]acetic acid: 139132-55-1 / trimethylsilyl-2-{2-[(trimethylsiloxy)methyl]cyclopropyl}-2-[(trimethylsilyl)amino]acetate: 139132-56-2 / 2-{1-[bis(trimethylsilyl)amino]cyclopropyl}acetic acid: 139132-57-3