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Multicomponent Reactions. II [1]

Stereoselective Synthesis of 1(*S*)-Camphor-2-cis-methylidene-isocyanide and its Application in Passerini- and Ugi-Reaction

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Dedicated to Prof. Dr. Ekkehard Winterfeldt on the Occasion of his 65th Birthday

Abstract. The use of unsaturated isocyanides in multicomponent reactions leads to *N*-vinylamides, which can be cleaved to carboxylic acids or esters under mild conditions. The chiral 1(*S*)-camphor-2-*cis*-methylidene-isocyanide (**5**) can be prepared in two steps from camphor and methylisocyanide. Its application in the Passerini reaction generates α-acyloxyamides (**6**, **7**, **8**, **9**) with a diastereomeric excess of >92%, in the Ugi reaction α-acylaminoamides with a diastereomeric excess of 0% are formed.

Since a few years multicomponent reactions (MCRs) receive much attention as powerful tools for the generation of chemical libraries [2, 3, 4]. In MCRs three or more components react in a one-pot synthesis to one defined product. The Passerini three component reaction (P-3CR) [5] and the Ugi four component reaction (U-4CR) [6] are the classical MCRs operating with isocyanides. The three components to generate α-acyloxyamides **1** in the P-3CR are carboxylic acid, carbonyl compound and isocyanide. The U-4CR is enlarged by an amine as the fourth component and proceeds particularly well, when carbonyl compound and amine first condense to an imine. The latter subsequently reacts with a carboxylic acid and an isocyanide, yielding α-acylaminoamides **2**. In both reactions, input of prochiral carbonyl compounds produces amide derivatives with a new sterical centre (Figure 1).

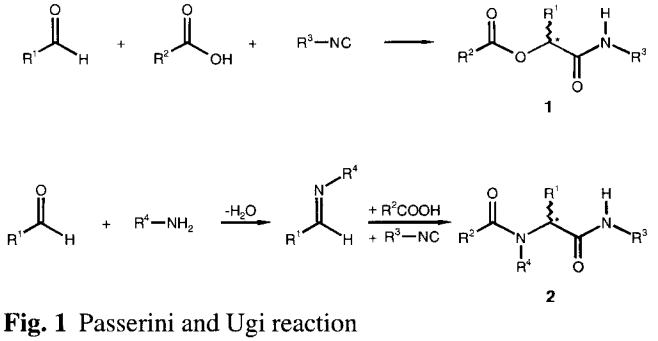


Fig. 1 Passerini and Ugi reaction

In the last decades, great efforts have been made to develop a stereoselective approach to these products. Using chiral α-ferrocenylalkylamines [7] and aminoglycosides [8] in the U-4CR, high degrees of diastereoselectivity could be obtained.

Armstrong demonstrated that the use of the unsaturated 1-isocyanocyclohexene in the U-4CR leads to *N*-vinylamides, that can be cleaved to carboxylic acids or esters in certain cases [9]. As a consequence, unsaturated, asymmetric isocyanides are potential chiral auxiliaries in the P-3CR and U-4CR. Hence the stereochemical features of 1(*S*)-camphor-2-*cis*-methylidene-isocyanide **5** in the P-3CR and Ugi-4CR were investigated.

The rigid, unsaturated **5** can be prepared from camphor in two steps (Figure 2).

The synthesis starts with the reaction of camphor with lithiated methylisocyanide. The *endo*-attack of the organolithium reagent and subsequent hydrolysis with MeOH at −50 °C generates camphor-2-*exo*-5'-spiro-2-oxazoline (**3**). Moreover, the basic methylisocyanide-lithium forms the camphorenolate anion, and camphor is regained after hydrolysis. Maximum yield of **3** (75%)

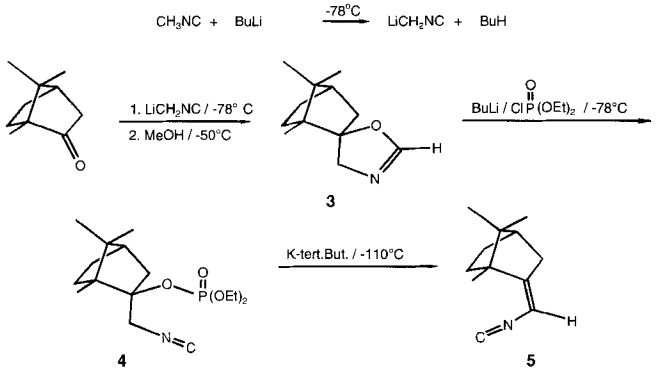


Fig. 2 Synthesis of 1(*S*)-camphor-2-*cis*-methylideneisocyanide (**5**)

is obtained when camphor is added to lithium-methylisocyanide at –78 °C in THF. Isolation of the oxazoline by column chromatography does not proceed successfully since **3** hydrolyses to the β-hydroxyformamide. However, **3** can be separated from camphor by sublimation. Final recrystallisation yields pure oxazoline as colourless crystals. In the next step, **3** is converted to the tertiary alcoholate anion by treatment with BuLi. Reaction with diethyl chlorophosphate forms the phosphate ester **4**, which is not isolated. **5** is obtained by elimination of the phosphate group in the presence of potassium *tert*-butoxide at –110 °C. The well known synthesis of unsaturated isocyanides with sulfonyl chlorides as eliminating reagents [10] is not successful in this case. Treatment of deprotonated **3** with methanesulfonyl chloride does not result in a oxygensulfur bond due to the steric hindrance of the tertiary alcoholate anion. In contrast, the strong oxophilic character of phosphorus leads to the formation of **4**.

The elimination temperature determines the ratio of *cis*- to *trans* isomers. 86% *cis*- and 14% *trans* isomer is formed, when potassium *tert*-butoxide is added at 25 °C. The amount of *trans* isomer turns to 2% at –78 °C and decreases below 1% at –110 °C.

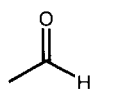
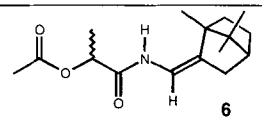
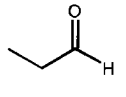
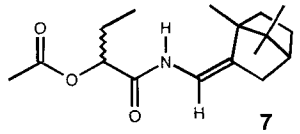
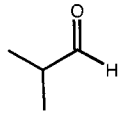
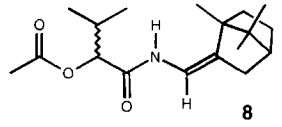
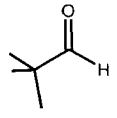
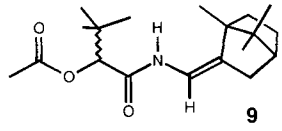
The *cis* isomer **5** is isolated by sublimation and recrystallisation from pentane, since column chromatography results in hydrolysis to the vinylformamide.

Because of the very similar sublimation properties of the unsaturated isocyanide and camphor, a one-pot synthesis of **5** can not be performed.

5 can also be prepared in a Wittig reaction [11]. Anyhow, the *cis-trans* selectivity in this reaction is not as good as in the two-step synthesis. The best ratio of 80% *cis* isomer is obtained, when camphor is added to the phosphorus ylid at –110 °C.

In order to investigate the stereochemical attributes of **5**, the P-3CR was first examined. Therefore, four different aldehydes, acetic acid and **5** were brought to reaction. The results are shown in table 1.

Table 1 Passerini reaction with **5** [a] [b]

starting aldehyde	Passerini product	*de* (%)
	 **6**	92
	 **7**	93
	 **8**	93
	 **9**	92

[a]) temperature 25 °C [b]) solvent THF

The diastereomeric access was determined by integration of the gas chromatography/mass spectra peaks (GC-MS). All products of the P-3CR show a diastereomeric excess > 90% at 25 °C. This confirms the mechanism first postulated in 1962 [12]. It was assumed that the P-3CR consists of an α-addition of the isocyanide to a hydrogen bridged adduct of carboxylic acid and

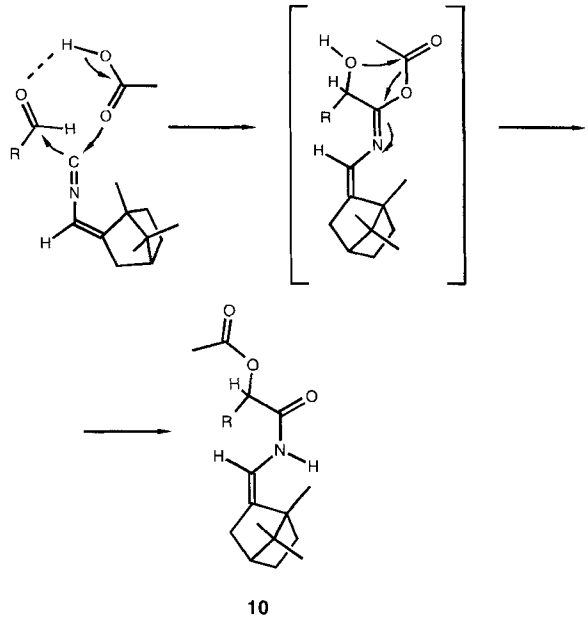


Fig. 3 Mechanism of the Passerini reaction

carbonyl compound, followed by an intramolecular rearrangement (Figure 3). The nucleophilic attack of the isocyanide onto the prochiral aldehyde defines the configuration of the new stereogenic centre in the final product **10**.

Next we investigated the Ugi reaction with **5**, using isobutyraldehyde, benzylamine and acetic acid as further components. The results are given in table 2.

Table 2 Ugi reaction with **5** [a])

solvent	complex salt	*de* (%)
THF	–	2
THF	$ZnCl_2$	3
THF	$CoCl_2$	3
MeOH	$LiClO_4$	3

[a]) temperature 25 °C

Unlike the P-3CR, the U-4CR shows particularly no diastereoselectivity at 25 °C. The use of complex salts like $ZnCl_2$ and $CoCl_2$ did not improve diastereoselectivity.

The reason is, that the protonated imine ion first is attacked by the carboxylic acid anion, generating a racemic mixture of **11** and **12**. The chiral isocyanide then substitutes the acyloxy anion in a pure S_N2 reaction. An irreversible rearrangement forms the diastereomers **13** and **14** in equal amounts (Figure 4).

The chiral isocyanide has no influence on the stereochemical procedure of the U-4CR by a nucleophilic attack at the prochiral imine ion. Even if the reaction is performed in MeOH with one equivalent $LiClO_4$ to stabilise a possible ion pair, the diastereomeric ratio does not change.

As a consequence, the difference between the P-3CR and Ugi-4CR corresponds to the sequence of the nucleophilic attack of isocyanide and carboxylic acid. The α-addition of the isocyanide in the P-3CR controls the configuration of the stereocentre, whereas the attack of the carboxylic acid anion at the protonated imine determines the stereochemical course of the U-4CR.

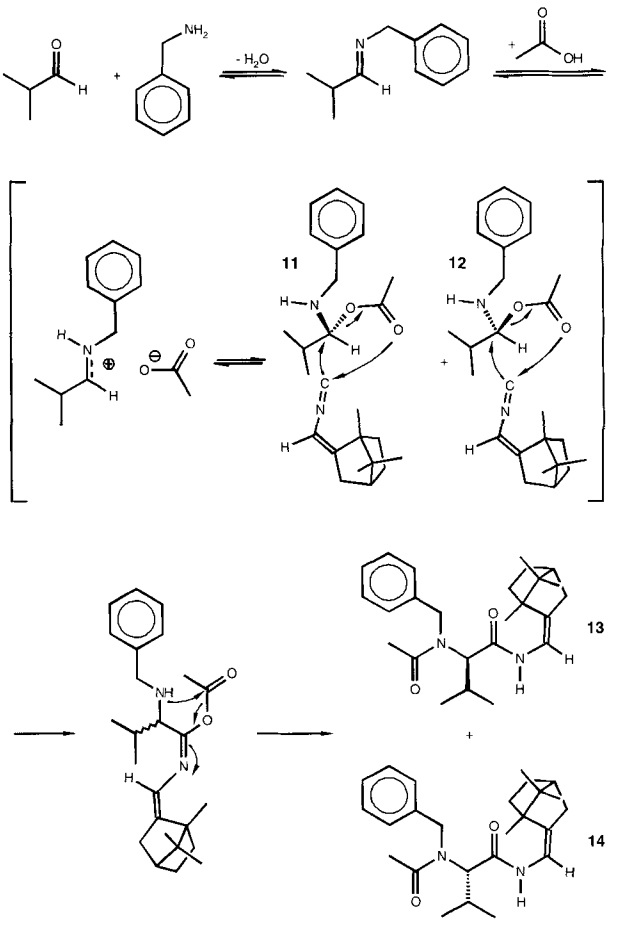


Fig. 4 Mechanism of the Ugi reaction

Experimental

Unless otherwise indicated all reactions were performed in oven dried glassware under argon atmosphere. THF was dried and distilled from sodium/benzophenone, MeOH from magnesium.

NMR spectra were recorded on Bruker spectrometers AM 360 or AC 200 with TMS as internal standard. The chemical shifts are reported in ppm downfield from TMS. The attribution of the different carbons (C, CH, CH_2, or CH_3) was determined by ^{13}C to ^1H polarisation transfer (DEPT). Elemental analyses were recorded by "Mikrochemisches Labor des Institutes für Organische Chemie und Biochemie der TU München".

GC-MS were performed on a varian MAT CH-5 apparatus coupled to a GC Carlo Erba 4160 column. All the commercial reagents were purchased from Aldrich, Merck and Fluka.

Camphor-2-exo-5'-spiro-2-oxazoline (**3**)

160 mmol (100ml, 1.6M) BuLi are added slowly to 165 mmol (9ml) methylisocyanide in 200 ml absolute THF at –78 °C. The suspension is stirred for 1 h at –78 °C, and 160 mmol (24.4 g) camphor is added in small portions. After 30 minutes the reaction is quenched with 222 mmol (9 ml) MeOH at –40 °C. The solution is diluted with ether, washed with water and brine and dried over anhydrous Na_2SO_4. Removal of the solvent yields a yellow oil, which is liberated from camphor by repeated sublimations at 40 °C and 0.05 torr. Crystallisation from pentane provides pure **3**.

Yield 14 g (45%) colourless crystals, *m.p.* 48–49 °C. – ^1H NMR: (360.1 MHz, $CDCl_3$): δ 6.77 (s_{br}, 1H, N=C<u>H</u>-O); 3.91 (dd, 1H, C-C<u>H</u>$_2$–N); 3.55 (dd, 1H, C-C<u>H</u>$_2$–N); 2.26 (dtr, 1H, C-C<u>H</u>$_2$-CH, ^2J = 14 Hz) 1.79 (m, 1H, C<u>H</u>); 1.70 (m, 1H, C<u>H</u>$_2$), 1.48 (d, 1H, C-C<u>H</u>$_2$-CH, ^2J = 14 Hz); 1.47 (m, 1H, C<u>H</u>$_2$); 1.31 (m, 1H, C<u>H</u>$_2$); 1.09 (m, 1H, C<u>H</u>$_2$); 1.04 (s, 3H, C<u>H</u>$_3$); 0.89 (s, 3H, C<u>H</u>$_3$); 0.78 (s, 3H, C<u>H</u>$_3$). – ^{13}C NMR: (90.6 MHz, $CDCl_3$): δ 154.5 (N=<u>C</u>H–O); 93.7 (O–<u>C</u>-CH_2); 62.1

(C-$\underline{C}H_2$–N); 51.7 ($\underline{C}$); 49.2 ($\underline{C}$); 48.3 (C-$\underline{C}H_2$-CH); 45.7 ($\underline{C}H$); 30.1 ($\underline{C}H_2$); 27.0 ($\underline{C}H_2$); 20.3 ($\underline{C}H_3$); 20.3 ($\underline{C}H_3$); 9.7 ($\underline{C}H_3$). – GC-MS (EI 70 eV): *m/e* (%):193 (4, M^+); 178 (6); 148 (7); 133 (15); 108 (55); 95 (100); 83 (48); 69 (33); 552); 43 (40).

$C_{12}H_{19}NO$	calcd.:	C 74.57	H 9.91	N 7.25
(193.3)	found:	C 74.53	H 9.98	N 7.24.

Camphor-2-cis-methylidene-isocyanide (**5**)

64 mmol (12.4g) camphor-2-exo-5'-spiro-2-oxazoline (3) in 150 ml absolute THF are treated with 65 mmol (41ml, 1.6M) BuLi at –78 °C. The solution is stirred for 1 h at –78 °C and 65 mmol (9.4ml) diethyl chlorophosphate is added dropwise. The reaction mixture is allowed to warm to 25 °C and stirred for 12 h. After cooling to –110 °C, 90 mmol (10.1g) potassium *tert*-butoxide is added in small portions. The solution is allowed to warm to 25 °C, diluted with 400 ml of ether and washed three times with a saturated aqueous solution of $NaCO_3$, water and brine. The organic layer is dried over anhydrous Na_2SO_4 and concentrated to afford an orange oil. Sublimation at 25 °C and 0.05 torr and crystallisation from pentane provides pure **5**.

Yield 5 g (45%), colourless crystals, *m.p.*: 29–30 °C. – ^{1}H NMR: (360.1 MHz, $CDCl_3$): δ 5.58 (s_{br}, 1H, C=C$\underline{H}$–N); 2.44 (dd_{br}, 1H, =C-C$\underline{H}_2$-CH, ^2J = 16.8 Hz); 1.90 (d, 1H, =C-C$\underline{H}_2$-CH, ^2J = 16.8 Hz); 1.86–1.64 (m, 3H, C$\underline{H}_2$/C$\underline{H}_2$/C$\underline{H}$); 1.47 (m, 1H, C$\underline{H}_2$); 1.18 (m, 1H, C$\underline{H}_2$); 1.33 (s, 3H, C$\underline{H}_3$); 0.89 (s, 3H, C$\underline{H}_3$); 0.81 (s, 3H, C$\underline{H}_3$). – ^{13}C NMR: (90.6 MHz, $CDCl_3$): δ 164.7 (tr, N=$\underline{C}$); 156.2 (CH=$\underline{C}$); 103.2(tr, C=$\underline{C}$H–N); 53.5 ($\underline{C}$); 49.3 ($\underline{C}$); 43.9 ($\underline{C}H$); 36.2 (=C-$\underline{C}H_2$-CH); 34.3 ($\underline{C}H_2$); 27.5 ($\underline{C}H_2$); 19.9 ($\underline{C}H_3$); 18.3 ($\underline{C}H_3$); 13.0 ($\underline{C}H_3$). – GC-MS (EI, 70 eV): *m/e* (%):175 (27, M^+); 160 (56); 132 (64); 118 (54); 105 (47); 91 (83); 41(100).

$C_{12}H_{17}N$	calcd.:	C 82.21	H 9.80	N 7.99
(175.3)	found:	C 82.10	H 9.79	N 8.19.

General Procedure for the Passerini Reaction

2.28 mmol **5**, 4 mmol aldehyde and 4 mmol acetic acid are dissolved in 15 ml of THF and stirred for 40 h. After removal of the solvent, a GC-MS spectrum of the residue is carried out. The remaining product is solved in ether, washed with water and brine and dried over anhydrous Na_2SO_4. Evaporation of the solvent yields the Passerini products, that exist as a mixture of rotamers. Hence, some NMR peaks of protons and carbons appear twice. In this case, the average ppm-values are given.

N-[11-(Camphor-2-cis-methylidene-yl)]-2-(acetoxy)-propanamide (**6**)

Yield 0.61 g (96%), yellow, sticky solid. – ^{1}H NMR: (360.1 MHz, $CDCl_3$): δ 8.11 (d, 1H, N$\underline{H}$, ^3J = 9.0 Hz); 6.48 (d, 1H, C=C$\underline{H}$–NH, ^3J = 9.0 Hz); 5.27 (q, 1H, O–C$\underline{H}$-CH_3, ^3J = 6.4 Hz); 2.44 (d_{br}, 1H, =C-C$\underline{H}_2$-CH, ^2J = 15.6 Hz); 2.15 (s, 3H, C$\underline{H}_3$-C=O); 1.88 (d, 1H, =C-C$\underline{H}_2$-CH, ^2J = 15.6 Hz); 1.84–1.71 (m, 2H, C$\underline{H}_2$/C$\underline{H}$); 1.65 (m, 1H, C$\underline{H}_2$); 1.50 (d, 1H, CH-C$\underline{H}_3$, ^3J = 6.4 Hz); 1.44 (m, 1H, C$\underline{H}_2$); 1.26 (s, 3H, C$\underline{H}_3$); 1.21 (m, 1H, C$\underline{H}_2$); 0.87 (s, 3H, C$\underline{H}_3$); 0.84 (s, 3H, C$\underline{H}_3$). – ^{13}C NMR: (90.6 MHz, $CDCl_3$): δ 168.9 ($\underline{C}$=O); 166.4 ($\underline{C}$=O); 132.1 (CH=$\underline{C}$); 112.6 (C=$\underline{C}$H–N); 70.5 (O–$\underline{C}$H-CH_3); 51.5 ($\underline{C}$); 48.9 ($\underline{C}$); 44.6 ($\underline{C}H$); 35.8 ($\underline{C}H_2$); 35.1 ($\underline{C}H_2$); 27.8 ($\underline{C}H_2$); 21.0 ($\underline{C}H_3$); 19.9 ($\underline{C}H_3$); 18.4 ($\underline{C}H_3$); 17.8 ($\underline{C}H_3$); 14.6 ($\underline{C}H_3$). – GC-MS (EI, 70 eV): *m/e* (%): 279 (13, M^+); 165 (13); 148 (24); 133 (16); 122 (18); 105 (26); 87 (22); 43(100); $C_{16}H_{25}NO_3$ (279.4).

N-[11-(Camphor-2-cis-methylidene-yl)]-2-(acetoxy)-butanamide (**7**)

Yield 0.63 g (94%), yellow, sticky solid. – ^{1}H NMR: (360.1 MHz, $CDCl_3$): δ 8.03 (s_{br}, 1H, N$\underline{H}$); 6.48 (m, 1H, C=C$\underline{H}$-NH); 5.23 (m, 1H, O–C$\underline{H}$-CH_2); 2.44 (d_{br}, 1H, =C-C$\underline{H}_2$-CH, ^2J = 15.5 Hz); 2.17 (s, 3H, C$\underline{H}_3$–C=O); 1.91 (m, 2H, C$\underline{H}_2$); 1.88 (d, 1H, =C-C$\underline{H}_2$-CH, ^2J = 15.5 Hz); 1.84–1.71 (m, 2H, C$\underline{H}_2$/C$\underline{H}$); 1.65 (m, 1H, C$\underline{H}_2$); 1.47 (m, 1H, C$\underline{H}_2$); 1.26 (s, 3H, C$\underline{H}_3$); 1.21 (m, 1H, C$\underline{H}_2$); 0.93 (m, 3H, CH_2-C$\underline{H}_3$); 0.87 (s, 3H, C$\underline{H}_3$); 0.84 (s, 3H, C$\underline{H}_3$). – ^{13}C NMR: (90.6 MHz, $CDCl_3$): δ 169.1 ($\underline{C}$=O); 165.9 ($\underline{C}$=O); 132.0 (CH=$\underline{C}$); 112.6 (C=$\underline{C}$H–N); 74.7 (O–$\underline{C}$H-CH_2); 51.4 ($\underline{C}$); 48.9 ($\underline{C}$); 44.5 ($\underline{C}H$); 35.7 ($\underline{C}H_2$); 35.1 ($\underline{C}H_2$); 27.8 ($\underline{C}H_2$); 25.0 ($\underline{C}H_2$); 20.8 ($\underline{C}H_3$); 19.9 ($\underline{C}H_3$); 18.3 ($\underline{C}H_3$); 14.7 ($\underline{C}H_3$); 8.8 ($\underline{C}H_3$). – GC-MS (EI, 70 eV): *m/e* (%): 293 (10, M^+); 165 (14); 148 (16); 133 (12); 122 (15); 105 (21); 101 (19); 43(100); $C_{17}H_{27}NO_3$ (293.4).

N-[11-(Camphor-2-cis-methylidene-yl)]-2-(acetoxy)-3-methylbutanamide (**8**)

Yield 0.59 g (84%,) white, sticky solid. – ^{1}H NMR: (360.1 MHz, $CDCl_3$): δ 7.92 (m, 1H, N$\underline{H}$); 6.50 (m, 1H, C=C$\underline{H}$–NH); 5.18 (d, 1H, O–C$\underline{H}$-CH); 2.43 (d_{br}, 1H, =C-C$\underline{H}_2$-CH, ^2J = 15.6 Hz); 2.34 (m, 1H, CH-C$\underline{H}$-CH_3); 2.18 (s, 3H, C$\underline{H}_3$-C=O); 1.88 (d, 1H, =C-C$\underline{H}_2$-CH, ^2J = 15.6 Hz); 1.84–1.71 (m, 2H, C$\underline{H}_2$/C$\underline{H}$); 1.65 (m, 1H, C$\underline{H}_2$); 1.47 (m, 1H, C$\underline{H}_2$); 1.24 (s, 3H, C$\underline{H}_3$); 1.21 (m, 1H, C$\underline{H}_2$); 0.96 (m, 6H, C$\underline{H}_3$/C$\underline{H}_3$); 0.87 (s, 3H, C$\underline{H}_3$); 0.84 (s, 3H, C$\underline{H}_3$). – ^{13}C NMR: (90.6 MHz, $CDCl_3$): δ 169.3 ($\underline{C}$=O); 165.6 ($\underline{C}$=O); 132.0 (CH=$\underline{C}$); 112.6 (C=$\underline{C}$H–N); 77.8 (O–$\underline{C}$H-CH); 51.4 ($\underline{C}$); 48.9 ($\underline{C}$); 44.6 ($\underline{C}H$); 35.8 ($\underline{C}H_2$); 35.1 ($\underline{C}H_2$); 30.7 ($\underline{C}H$); 27.8 ($\underline{C}H_2$); 20.8 ($\underline{C}H_3$); 19.9 ($\underline{C}H_3$); 18.7 ($\underline{C}H_3$); 18.4 ($\underline{C}H_3$); 16.7 ($\underline{C}H_3$); 14.8 ($\underline{C}H_3$). – GC-MS (EI, 70 eV): *m/e* (%): 307 (8, M^+); 165 (23); 148 (17); 133 (10); 122 (16); 115 (21); 105 (18); 55 (9); 43(100); $C_{18}H_{29}NO_3$ (307.5).

N-[11-(Camphor-2-cis-methylidene-yl)]-2-(acetoxy)-3,3-dimethylbutanamide (**9**)

Yield 0.65 g (89%), white, sticky solid. – ^{1}H NMR: (360.1 MHz, $CDCl_3$): δ 7.80 (m, 1H, N$\underline{H}$); 6.50 (m, 1H, C=C$\underline{H}$–NH); 4.94 (s, 1H, O–C$\underline{H}$-C); 2.43 (d_{br}, 1H, =C-C$\underline{H}_2$-CH, ^2J = 14.2 Hz); 2.17 (s, 3H, C$\underline{H}_3$-C=O); 1.87 (d, 1H, =C-C$\underline{H}_2$-CH, ^2J = 14.2 Hz); 1.84-1.71 (m, 2H, C$\underline{H}_2$/C$\underline{H}$); 1.65 (m, 1H, C$\underline{H}_2$); 1.45 (m, 1H, C$\underline{H}_2$); 1.23 (s, 3H, C$\underline{H}_3$); 1.21 (m, 1H, C$\underline{H}_2$); 1.03 (s, 9H, C$\underline{H}_3$); 0.87 (s, 3H, C$\underline{H}_3$); 0.84 (s, 3H, C$\underline{H}_3$). – ^{13}C NMR: (90.6 MHz, $CDCl_3$): δ 169.1 ($\underline{C}$=O); 164.6 ($\underline{C}$=O); 131.5 (CH=$\underline{C}$); 112.6 (C=$\underline{C}$H); 80.5 (O–$\underline{C}$H-C); 51.3 ($\underline{C}$); 48.8 ($\underline{C}$); 44.5 ($\underline{C}H$); 35.7 ($\underline{C}H_2$); 35.1 ($\underline{C}H_2$); 34.4 ($\underline{C}$); 27.8 ($\underline{C}H_2$); 26.0 ($\underline{C}H_3$); 20.6 ($\underline{C}H_3$); 19.8 ($\underline{C}H_3$); 18.3 ($\underline{C}H_3$); 14.7 ($\underline{C}H_3$). – GC-MS (EI, 70 eV): *m/e* (%): 321 (12, M^+); 246 (13); 165 (42); 148 (21); 129 (20); 122 (20); 105 (21); 87 (35); 69 (13); 43(100); $C_{19}H_{31}NO_3$ (321.5).

General Procedure for the Ugi Reaction

4 mmol (0.37 ml) isobutyraldehyde, 4 mmol (0.44 ml) benzylamine (and 4 mmol complex salt) are stirred in 15 ml

of solvent. 4 mmol (0.5 g) **5** and 4 mmol (0.23 ml) acetic acid are added and the mixture is stirred for 40 h. After removal of the solvent, a GC-MS spectrum of the residue is carried out. The remaining product is solved in ether, washed with water and brine and dried over anhydrous Na_2SO_4. Evaporation of the solvent yields the Ugi product as a mixture of diastereomers and their rotamers. Hence, some NMR peaks of protons and carbons appear twice. In this case, the average ppm-values are given.

N-[11-(Camphor-2-cis-methylidene-yl)]-2-(N'-benzylaceta-mido)-3-methylbutanamide (**13/14**)

Yield 1.05 g (66%), white, sticky solid. – ^{1}H NMR: (360.1 MHz, $CDCl_3$): δ 8.30 (s_{br}, 1H, NH); 7.27 (m, 3H, =CH); 7.11 (d, 2H, =CH); 6.37 (m, 1H, C=CH–NH); 4.58 (m, 2H, =C-CH_2-N); 4.44 (m_{br}, 1H, N–CH-CH); 2.49 (m, 1H, CH-CH-CH_3); 2.42 (d_{br}, 1H, =C-CH_2-CH, ^2J = 16.8 Hz); 2.04 (s, 3H, CH_3-C=O); 1.86 (d, 1H, =C-CH_2-CH, ^2J = 16.8 Hz); 1.77 (m, 1H, CH_2); 1.72 (m, 1H, CH); 1.68 (m, 1H, CH_2); 1.45 (m, 1H, CH_2); 1.27 (s, 3H, CH_3); 1.22 (m, 1H, CH_2); 0.97 (s, 3H, CH_3); 0.84 (m, 9H, CH_3/CH_3/CH_3). – ^{13}C NMR: (90.6 MHz, $CDCl_3$): δ 173.4 (O=C–N); 166.6 (O=C–N); 136.8 (=C); 132.1 (=C); 128.5 (=CH); 127.2 (=CH); 126.2 (=CH); 112.9 (C=CH–N); 66.1 (N–CH-CH); 51.1 (C); 48.7 (C); 44.4 (CH); 36.0 (CH_2); 35.3 (CH_2); 34.9 (CH_2); 27.9 (CH_2); 26.3 (CH); 22.5 (CH_3); 19.9 (CH_3); 19.3 (CH_3); 19.0 (CH_3); 18.4 (CH_3); 14.3 (CH_3). – GC-MS (EI, 70 eV): *m/e* (%): 396 (3, M^+); 232 (60); 204 (47); 162 (45); 91 (100); 43(16). $C_{25}H_{36}N_2O_2$ (396.6).

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