

53. Carbamate Series of Juvenoids: Variation of the *O*-Alkyl Substituent

by Zdeněk Wimmer^{a)}*, David Šaman^{a)}, Václav Němec^{b)}, and Wittko Francke^{c)}

^{a)} Institute of Organic Chemistry and Biochemistry, Academy of Science of the Czech Republic,
Flemingovo náměstí 2, 166 10 Prague 6, Czech Republic

^{b)} Institute of Entomology, Academy of Science of the Czech Republic, Branišovská 31,
370 05 České Budějovice, Czech Republic

^{c)} Institute of Organic Chemistry, University of Hamburg, Martin-Luther-King-Platz 6, D-20146 Hamburg

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By changing the *O*-alkyl substituents of the carbamate moiety of alkyl *N*-{2-[4-[(2-oxocyclohexyl)-methyl]phenoxy]ethyl}carbamates and subsequent transformation of the oxo group in the cyclohexyl substituent, the juvenoids 1–20 were synthesized (*Scheme*). The methyl (1–4), propyl (9–12), isopropyl (13–16), and prop-2-ynylcarbamates (17–20) were subjected to biological screening on several non-related insect species (*Tenebrio molitor*, *Galleria mellonella*, *Dysdercus cingulatus*, and *Pyrrhocoris apterus*). Some of the juvenoids showed high biological activity and excellent selectivity with respect to target insect species (*Table 2*).

Since the early 1980's, a carbamate series of juvenoids (insect juvenile-hormone analogs; JHA's) was studied in our project of environmentally safe insect-pest control. Among other juvenoid series, carbamates were found to possess satisfactory biological activity against a number of economically important insect pests, and their toxicity values on vertebrates, and even on fish and small organisms living in the water (such as *Daphnia magna*), was found promising as well (*Table 1*).

Insects form the most numerous class of animals on Earth. Even if the majority of insect species are not harmful from a human point of view, many are considered to be serious food competitors with man and vectors of serious diseases. Methods of controlling the excessively spread insect pest populations are still one of the goals of common research in chemical and biological laboratories all over the world. Discovery of insect juvenile hormone (JH) [1], followed by discovery of juvabione, the first naturally occurring JH bioanalogue [2], have initiated a new period in the investigation of methods for insect-pest control. Since that time, thousands of compounds were synthesized showing juvenilizing activity on a broad variety of insect pests (*cf.*, *e.g.* [3–6]). Moreover, an important difference in the biological activity of geometrical isomers [3] [6], positional isomers [3], and even enantiomers [4] has been described.

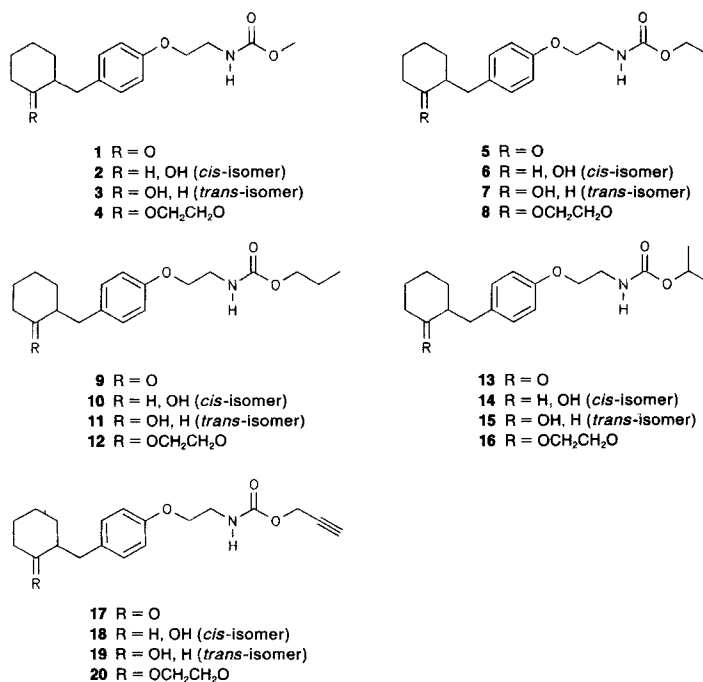
Some years ago, our first paper in the carbamate series of juvenoids appeared [7], concerning compounds 5–8. The method used for the synthesis of these juvenoid carbamates was recently improved in the key step [8]. For further investigations, the preparation of the carbamates has now been modified to enable the facile synthesis of juvenoid

Table 1. Selected Toxicity Data (*LD*₅₀ values) of 8

	Rat (feeding test)	Rabbit (eye test)	<i>Daphnia magna</i>
<i>LD</i> ₅₀	6 g · kg ⁻¹	0.1 g (no persistent effect)	> 6000 ppm

carbamates with different *O*-alkyl substituents. We needed these compounds for a comprehensive biological screening involving also a number of related compounds. The biological results are a contribution to the existing knowledge on the importance of the *O*-alkyl substituent of juvenoid carbamates on biological activity.

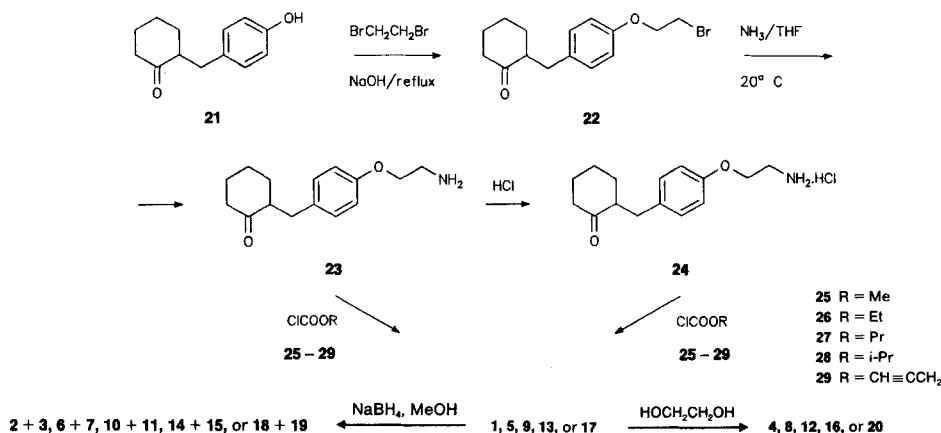
Thus, we prepared the juvenoids **1–20** in a modified way consisting in the use of alkyl chloroformates **25–29** as the key intermediates (*cf.* the *Scheme*). The 2-(4-hydroxybenzyl)cyclohexan-1-one (**21**) was easily converted into 2-[4-(2-bromoethoxy)benzyl]cyclohexan-1-one (**22**) [9] and the latter transformed to the corresponding 2-aminoethoxy derivative **23** and its hydrochloride **24** by treatment with liquid ammonia in tetrahydrofuran (THF) in a sealed metal container. The synthesis of the oxocyclohexyl-substituted carbamates **1, 5, 9, 13**, or **17** was completed by treatment of **23** or **24** with the corresponding alkyl chloroformates **25–29** in the presence of a strong base (quant. yields). The *cis/trans*-hydroxy-cyclohexyl derivatives **2/3, 6/7, 10/11, 14/15**, and **18/19** were then prepared by NaBH₄ reduction of **1, 5, 9, 13**, and **17**, respectively, and separated into the pure *cis*- and *trans*-isomers by column chromatography. Finally, the juvenoids **4, 8, 12, 16**, and **20** bearing the acetal moiety were obtained from **1, 5, 9, 13**, or **17**, respectively, and ethane-1,2-diol under azeotropic conditions (quant. yields).



The described synthesis of the juvenoids **1–20** is very effective with respect to the overall yield and also suitable for large-scale preparations.

The results of the biological screening of the juvenoids **1–20** are summarized in *Table 2*. The compounds were tested on several non-related insect species and their biological

Scheme



activities compared with those of to commercially available juvenoids, *i.e.* *Fenoxycarb* (Ciba-Geigy) and *Pyriproxyfen* (Sumitomo), commonly used as reference compounds in such tests. Excellent activities of several compounds, especially of **5–8** (some of them under field conditions as well), on all studied insect species are observed. The results also show important species selectivity for several juvenoids: Compound **2** in tests with *Tenebrio molitor* and *Dysdercus cingulatus*, compounds **16**, **17**, and **20** in tests with *Tenebrio molitor*, and finally compound **18** in tests with *Dysdercus cingulatus* and *Pyrrhocoris apterus*. On the other hand, there was no as generally active compound as *Fenoxycarb* within the studied series **1–20**. Comparing the toxicity data available for *Fenoxycarb* and those shown in Table 1 for **8**, the juvenoids **1–20** could eventually show more favourable toxicological properties. More biological results from laboratory and field studies with selected compounds of this series will be the subject of a forthcoming communication.

Table 2. Biological Activity (ID_{50} values) of the Juvenoids **1–20**^{a)}

	<i>Ten</i> ^{b)}	<i>Gal</i> ^{c)}	<i>Dys</i> ^{d)}	<i>Pyr</i> ^{e)}		<i>Ten</i> ^{b)}	<i>Gal</i> ^{c)}	<i>Dys</i> ^{d)}	<i>Pyr</i> ^{e)}
1	$5 \cdot 10^{-4}$	$1 \cdot 10^{-1}$	$5 \cdot 10^{-2}$	1	12	$1 \cdot 10^{-3}$	1	$1 \cdot 10$	$8 \cdot 10^{-1}$
2	$5 \cdot 10^{-4}$	1	$5 \cdot 10^{-4}$	$1 \cdot 10^{-2}$	13	$1 \cdot 10^{-3}$	1	$5 \cdot 10^{-1}$	$1 \cdot 10$
3	$5 \cdot 10^{-3}$	$1 \cdot 10^{-2}$	$5 \cdot 10^{-2}$	$5 \cdot 10^{-1}$	14	$5 \cdot 10^{-4}$	$1 \cdot 10$	$5 \cdot 10^{-3}$	$1 \cdot 10^{-2}$
4	$1 \cdot 10^{-5}$	$1 \cdot 10^{-1}$	$1 \cdot 10$	$8 \cdot 10^{-1}$	15	$5 \cdot 10^{-2}$	1	1	0
5	$1 \cdot 10^{-2}$	$1 \cdot 10^{-2}$	$1 \cdot 10^{-1}$	$2 \cdot 10^{-1}$	16	$5 \cdot 10^{-4}$	$5 \cdot 10^{-1}$	$1 \cdot 10$	1
6	$3 \cdot 10^{-2}$	$1 \cdot 10^{-2}$	$1 \cdot 10^{-3}$	$2 \cdot 10^{-4}$	17	$3 \cdot 10^{-4}$	1	$5 \cdot 10^{-1}$	$5 \cdot 10^{-1}$
7	$2 \cdot 10^{-4}$	$5 \cdot 10^{-4}$	$1 \cdot 10^{-4}$	$5 \cdot 10^{-2}$	18	$3 \cdot 10^{-2}$	$1 \cdot 10$	$5 \cdot 10^{-4}$	$1 \cdot 10^{-3}$
8	$1 \cdot 10^{-2}$	$1 \cdot 10^{-2}$	$1 \cdot 10^{-1}$	$2 \cdot 10^{-1}$	19	$5 \cdot 10^{-1}$	$1 \cdot 10$	$5 \cdot 10^{-3}$	$1 \cdot 10^{-2}$
9	$1 \cdot 10^{-2}$	1	$1 \cdot 10^{-3}$	$8 \cdot 10^{-1}$	20	$1 \cdot 10^{-4}$	1	1	$5 \cdot 10^{-1}$
10	$1 \cdot 10^{-1}$	$1 \cdot 10$	$1 \cdot 10^{-3}$	$1 \cdot 10^{-1}$	Fen.^{f)}	$5 \cdot 10^{-7}$	$5 \cdot 10^{-3}$	$5 \cdot 10^{-3}$	$5 \cdot 10^{-1}$
11	$1 \cdot 10^{-2}$	1	$1 \cdot 10^{-1}$	$1 \cdot 10^{-1}$	Pyr.^{g)}	–	–	$5 \cdot 10^{-1}$	$1 \cdot 10^{-1}$

^{a)} The ID_{50} values (in μg per individual) are given, which indicate the amount of a juvenoid to be used for obtaining a 50% inhibition of metamorphosis. ^{b)} *Tenebrio molitor*. ^{c)} *Galleria mellonella*. ^{d)} *Dysdercus cingulatus*. ^{e)} *Pyrrhocoris apterus*. ^{f)} *Fenoxycarb* (= ethyl *N*-[2-(4-phenoxyphenoxy)ethyl]carbamate; Ciba-Geigy, Switzerland). ^{g)} *Pyriproxyfen* (= 1-(4-phenoxyphenoxy)-2-(pyrid-2-yloxy)propane; Sumitomo, Japan).

Experimental Part

General. Methyl chloroformate (**25**) and ethyl chloroformate (**26**) were purchased from Aldrich. Column chromatography (CC): silica gel (Herrmann, Köln-Ehrenfeld, FRG). TLC: precoated silica-gel plates. HPLC: Hewlett-Packard-HP-1090 instrument, coupled with a HP-85-B microcomputer; detection at 200 nm using a UV DAD; integration at 250 nm using a DPU multichannel integrator; 3 columns connected in series, each 150 × 3 (i.d.) mm, filled with Separon SGX (particle size 5 µm); light petroleum ether/Et₂O 95:5, flow rate 0.5 ml · min⁻¹. IR Spectra: Hewlett-Packard instrument; CCl₄ solns.; in cm⁻¹. NMR Spectra: Varian-Unity-500 spectrometer (FT mode); for ¹H at 499.8 MHz in CDCl₃, δ in ppm rel. to Me₄Si as internal reference; ¹³C at 125.7 MHz in CDCl₃ using the central line of the solvent as internal reference (δ 77.0 ppm). GC/MS (EI): VG Anal. 70-250 SE mass spectrometer at 70 eV coupled with a Hewlett-Packard GC 5890 using a DB-5 capillary column (30 m × 0.25 mm × 0.25 µm), 60 → 200° (50°/min), 200–300° (10°/min), and then 300° for an unlimited time (manual processing). Elemental analyses were performed either on a Perkin-Elmer-240-C automatic analyzer (C, H, and N) or by manual analysis (other elements).

2-[4-(2-Bromoethoxy)benzyl]cyclohexan-1-one (22). A soln. of NaOH (0.56 g, 14.0 mmol) in H₂O (3.8 ml) was added to a mixture of 2-(4-hydroxybenzyl)cyclohexan-1-one [10] (**21**: 3.00 g, 14.7 mmol) and H₂O (20 ml). Then, 1,2-dibromoethane (3.32 g, 17.6 mmol) was added in several portions (neat) during 2 h. The mixture was refluxed with vigorous stirring for 6 h. Completion of reaction was indicated by a change in pH. After cooling, the org. layer was extracted with Et₂O, dried (Na₂SO₄), and evaporated, and the residue purified by CC (Et₂O/light petroleum ether 1:2): 3.0 g (80 %) of **22**. M.p. 68–71°. IR: 1712. ¹H-NMR: 1.30–2.04 (m, 6 H); 2.32 (dd, *J* = 1.2, 6.1, 13.5, 13.7, 1 H); 2.37 (dd, *J* = 8.5, 14.1, 1 H); 2.42 (dddd, *J* = 2.0, 2.7, 4.6, 13.7, 1 H); 2.50 (m, *J* = 1.2, 5.2, 5.2, 8.5, 12.1, 1 H); 3.15 (dd, *J* = 5.0, 14.1, 1 H); 3.62 (t, *J* = 5.1, 2 H); 4.27 (t, *J* = 5.1, 2 H); 6.82 (m, 2 H); 7.07 (m, 2 H). ¹³C-NMR: 25.00 (t); 28.00 (t); 29.19 (t); 33.34 (t); 34.53 (t); 42.12 (t); 52.58 (d); 67.92 (t); 114.62 (d); 130.14 (d); 133.21 (s); 156.36 (s); 212.58 (s). MS: 310 (30, *M*⁺), 211 (100), 133 (10), 107 (30). Anal. calc. for C₁₅H₁₉BrO₂ (311.22): C 57.89, H 6.15, Br 25.68; found: C 57.84, H 6.18, Br 25.61.

2-[4-(2-Aminoethoxy)benzyl]cyclohexan-1-one (23). In a metal vial, a soln. of **22** (11.5 g, 36.95 mmol) in THF (30 ml) was prepared. Liquid NH₃ (30 ml) was added at –78° and the vessel sealed and allowed to stand overnight at r.t. Addition of liquid NH₃ (30 ml each) was repeated twice (TLC monitoring). When all **22** had reacted, the excess of NH₃ was allowed to evaporate, the residue poured into a beaker, and the vial washed several times with 5% HCl soln./Et₂O 1:1. The acidified portion was filtered through a sintered glass, then saponified by solid NaOH. Finally the collected product was extracted with Et₂O and the extract dried (Na₂SO₄) and evaporated: 7.5 g (88%) of **23**. ¹H-NMR: 1.16–1.94 (m, 6 H); 2.24 (d, *J* = 14.2, 1 H); 2.50 (m, 3 H); 2.78 (t, *J* = 5.7, 2 H); 2.89 (d, *J* = 14.2, 1 H); 3.84 (t, *J* = 5.7, 2 H); 6.78 (m, 2 H); 7.02 (m, 2 H). ¹³C-NMR: 24.69 (t); 28.10 (t); 33.46 (t); 34.59 (t); 41.09 (t); 51.66 (d); 70.30 (t); 114.91 (d); 130.57 (d); 132.69 (s); 157.42 (s); 213.77 (s). MS: 247 (32, [*M* + H]⁺), 204 (50), 175 (4), 148 (4), 133 (4), 121 (15), 107 (100), 90 (10), 44 (70). Anal. calc. for C₁₅H₂₁NO₂ (247.33): C 72.84, H 8.56, N 5.66; found: C 72.81, H 8.59, N 5.71.

2-[4-(2-Aminoethoxy)benzyl]cyclohexan-1-one Hydrochloride (24). As described above, **22** was reacted with NH₃. After evaporation of the residue was treated with 5% HCl soln. until acidic, the soln. poured into a beaker, and the vessel washed several times with 5% HCl soln. The acidified portion was filtered through a sintered glass, and H₂O evaporated: crystalline **24** in 90% yield. ¹H-NMR: 1.25–1.99 (m, 6 H); 2.23 (m, 1 H); 2.30 (dd, *J* = 8.4, 14.0, 1 H); 2.38 (m, 1 H); 2.59 (m, 1 H); 2.97 (dd, *J* = 5.4, 14.0, 1 H); 3.16 (t, *J* = 5.3, 2 H); 4.15 (t, *J* = 5.3, 2 H); 6.87 (m, 2 H); 7.10 (m, 2 H); 8.33 (br. s, 2 H). ¹³C-NMR: 24.36 (t); 27.66 (t); 32.92 (t); 34.22 (t); 38.40 (t); 41.57 (t); 51.57 (d); 64.36 (t); 114.60 (d); 130.11 (d); 132.95 (s); 156.23 (s); 211.87 (s). MS: 247 (28, [*M* – HCl]⁺), 204 (48), 175 (5), 148 (4), 133 (4), 121 (12), 107 (100), 90 (12), 44 (70). Anal. calc. for C₁₅H₂₂ClNO₂ (283.79): C 63.48, H 7.82, Cl 12.49, N 4.94; found: C 63.54, H 7.78, Cl 12.55, N 4.90.

Alkyl Chloroformates 27–29: General Procedure. Through a soln. of the corresponding alcohol (10 ml) in Et₂O (50 ml), phosgene was bubbled for 1 h under cooling (0°). The mixture was then allowed to stand overnight at r.t. Excess phosgene was removed by saturation of the mixture with N₂. Et₂O was distilled off through a short column and the product distilled.

27: B.p. 115°. ¹H-NMR: 1.01 (t, *J* = 7.0, 3 H); 1.78 (m, 2 H); 4.30 (t, *J* = 7.0, 2 H).

28: B.p. 103°. ¹H-NMR: 1.39 (d, *J* = 6.0, 6 H); 5.09 (m, 1 H).

29: B.p. 120°. ¹H-NMR: 2.67 (t, *J* = 2.4, 1 H); 4.88 (d, *J* = 2.4, 2 H).

Alkyl N-[2-{4-[(2-Oxocyclohexyl)methyl]phenoxy}ethyl]carbamates 1, 5, 9, 13, and 17: General Procedure. A soln. of the corresponding alkyl chloroformate **25–29** (1.5 mmol) in benzene (3.5 ml) was added to a soln. of **23** or **24** (1.0 mmol) in H₂O (5 ml). A 45% soln. of NaOH was added dropwise to the mixture under vigorous stirring at r.t. Completion of the reaction was achieved by maintaining the pH at 12 for at least 10 min after the last drop of

NaOH soln. had been added. The product was extracted with benzene and the extract dried (Na_2SO_4) and evaporated. Yields 100%.

1: M.p. 46–47°. IR: 3464, 3365, 3065, 3032, 2993, 1732, 1714, 1612, 1584, 1511, 1449, 1431, 1245. $^1\text{H-NMR}$: 1.30–2.09 (*m*, 6 H); 2.32 (*m*, 1 H); 2.37 (*dd*, $J = 8.8, 14.2$, 1 H); 2.43 (*m*, 1 H); 2.50 (*m*, 1 H); 3.15 (*dd*, $J = 4.9, 14.2$, 1 H); 3.57 (*br. q*, $J = 5.2, 2$ H); 3.68 (*s*, 3 H); 4.00 (*t*, $J = 5.1, 2$ H); 5.13 (*br. s*, 1 H); 6.79 (*m*, 2 H); 7.07 (*m*, 2 H). $^{13}\text{C-NMR}$: 25.03 (*r*); 28.03 (*r*); 33.37 (*r*); 34.55 (*r*); 40.62 (*r*); 42.15 (*r*); 52.17 (*q*); 52.64 (*d*); 66.92 (*r*); 114.27 (*d*); 130.13 (*d*); 132.91 (*s*); 156.76 (*s*); 157.01 (*s*); 212.63 (*s*). GC/MS: 305 (4, M^+), 284 (3), 256 (10), 213 (4), 176 (9), 149 (11), 129 (12), 107 (19), 102 (100). Anal. calc. for $\text{C}_{17}\text{H}_{23}\text{NO}_4$ (305.36): C 66.86, H 7.59, N 4.59; found: C 66.80, H 7.62, N 4.60.

5: IR: 3464, 3365, 3065, 3032, 2993, 1732, 1714, 1612, 1584, 1511, 1449, 1431, 1245. $^1\text{H-NMR}$: 1.21 (*t*, $J = 7.1, 3$ H); 1.50–2.35 (*m*, 8 H); 2.36 (*dd*, $J = 8.8, 13.4$, 1 H); 2.52 (*m*, 1 H); 3.15 (*dd*, $J = 4.5, 13.4$, 1 H); 3.56 (*q*, $J = 5.4, 1$ H); 4.00 (*t*, $J = 5.1, 2$ H); 4.12 (*br. q*, $J = 7.1, 2$ H); 5.11 (*br. s*, 1 H); 6.80 (*m*, 2 H); 7.07 (*m*, 2 H). $^{13}\text{C-NMR}$: 14.56 (*q*); 24.96 (*r*); 27.97 (*r*); 33.30 (*r*); 34.49 (*r*); 40.43 (*r*); 42.07 (*r*); 52.56 (*d*); 60.85 (*r*); 66.92 (*r*); 114.22 (*d*); 130.06 (*d*); 132.79 (*s*); 156.63 (*s*); 156.75 (*s*); 212.59 (*s*). GC/MS: 319 (3, M^+), 273 (22), 176 (100), 116 (61), 107 (55), 88 (27). Anal. calc. for $\text{C}_{18}\text{H}_{25}\text{NO}_4$ (319.39): C 67.69, H 7.89, N 4.39; found: C 67.72, H 7.87, N 4.41.

9: M.p. 47–48°. IR: 3464, 3392, 3366, 3064, 3033, 1725, 1714, 1612, 1584, 1511, 1449, 1430, 1245. $^1\text{H-NMR}$: 0.93 (*t*, $J = 7.4, 3$ H); 1.30–2.09 (*m*, 8 H); 2.32 (*m*, 1 H); 2.37 (*dd*, $J = 8.5, 14.0$, 1 H); 2.43 (*m*, 1 H); 2.50 (*m*, 1 H); 3.15 (*dd*, $J = 4.9, 14.0$, 1 H); 3.57 (*q*, $J = 5.3, 2$ H); 4.01 (*t*, $J = 5.3, 2$ H); 4.02 (*q*, $J = 7.1, 2$ H); 5.12 (*br. s*, 1 H); 6.80 (*m*, 2 H); 7.07 (*m*, 2 H). $^{13}\text{C-NMR}$: 10.31 (*q*); 22.34 (*r*); 25.03 (*r*); 28.03 (*r*); 33.37 (*r*); 34.55 (*r*); 40.51 (*r*); 42.15 (*r*); 52.64 (*d*); 66.61 (*r*); 67.00 (*r*); 114.28 (*d*); 130.13 (*d*); 132.89 (*s*); 156.81 (*s*); 156.81 (*s*); 212.62 (*s*). GC/MS: 333 (9, M^+), 273 (11), 256 (4), 204 (4), 176 (39), 149 (5), 130 (70), 126 (18), 107 (50), 88 (10). Anal. calc. for $\text{C}_{19}\text{H}_{27}\text{NO}_4$ (333.41): C 68.44, H 8.16, N 4.20; found: C 68.49, H 8.15, N 4.24.

13: M.p. 58–59°. IR: 3463, 3400, 3367, 3063, 3033, 1714, 1613, 1585, 1511, 1449, 1429, 1386, 1374, 1245, 1113. $^1\text{H-NMR}$: 1.23 (*d*, $J = 6.1, 6$ H); 1.53–2.07 (*m*, 6 H); 2.32 (*m*, 1 H); 2.37 (*dd*, $J = 8.5, 14.1$, 1 H); 2.42 (*m*, 1 H); 2.50 (*m*, 1 H); 3.15 (*dd*, $J = 4.9, 14.1$, 1 H); 3.56 (*br. q*, $J = 5.1, 2$ H); 4.00 (*t*, $J = 5.0, 2$ H); 4.91 (*m*, $J = 6.1, 1$ H); 5.06 (*br. s*, 1 H); 6.80 (*m*, 2 H); 7.07 (*m*, 2 H). $^{13}\text{C-NMR}$: 22.15 (*q*); 22.15 (*q*); 25.02 (*r*); 28.03 (*r*); 33.35 (*r*); 34.54 (*r*); 40.40 (*r*); 42.15 (*r*); 52.64 (*d*); 67.03 (*r*); 68.21 (*d*); 114.27 (*d*); 130.12 (*d*); 132.85 (*s*); 156.25 (*s*); 156.81 (*s*); 212.63 (*s*). GC/MS: 333 (6, M^+), 273 (3), 204 (3), 176 (18), 130 (35), 107 (37), 88 (100). Anal. calc. for $\text{C}_{19}\text{H}_{27}\text{NO}_4$ (333.41): C 68.44, H 8.16, N 4.20; found: C 68.48, H 8.20, N 4.15.

17: M.p. 53–54°. IR: 3459, 3357, 3313, 3032, 2130, 1734, 1714, 1612, 1585, 1511, 1449, 1432, 1245. $^1\text{H-NMR}$: 1.30–2.09 (*m*, 6 H); 2.32 (*m*, 1 H); 2.37 (*dd*, $J = 8.6, 14.1$, 1 H); 2.43 (*m*, 1 H); 2.47 (*t*, $J = 2.4, 1$ H); 2.50 (*m*, 1 H); 3.15 (*dd*, $J = 5.0, 14.1$, 1 H); 3.59 (*br. q*, $J = 5.4, 2$ H); 4.01 (*t*, $J = 5.1, 2$ H); 4.69 (*d*, $J = 2.4, 2$ H); 5.27 (*br. s*, 1 H); 6.79 (*m*, 2 H); 7.07 (*m*, 2 H). $^{13}\text{C-NMR}$: 25.03 (*r*); 28.03 (*r*); 33.67 (*r*); 34.55 (*r*); 40.70 (*r*); 42.15 (*r*); 52.56 (*d*); 52.63 (*r*); 66.77 (*r*); 74.75 (*d*); 78.15 (*s*); 114.27 (*d*); 130.15 (*d*); 133.00 (*s*); 156.45 (*s*); 156.69 (*s*); 212.61 (*s*). GC/MS: 329 (6, M^+), 273 (9), 204 (2), 176 (33), 126 (100), 107 (31), 88 (6). Anal. calc. for $\text{C}_{19}\text{H}_{27}\text{NO}_4$ (329.38): C 69.28, H 7.04, N 4.25; found: C 69.31, H 7.01, N 4.28.

Alkyl N-[2-{4-[(*cis*/*trans*-2-Hydroxycyclohexyl)methyl]phenoxy}ethyl]carbamates 2/3, 6/7, 10/11, 14/15, and 18/19: General Procedure. NaBH_4 (0.25 g, 6.60 mmol) was added in 1 portion to a stirred and cooled (0°) soln. of 1, 5, 9, 13, or 17 (2.56 mmol) in MeOH (15 ml). The mixture was stirred at 0° for 45 min. Subsequently, MeOH was evaporated, sat. brine (10 ml) added to the residue, the product extracted with Et_2O , the extract dried (Na_2SO_4) and evaporated, and the residue separated by chromatography into pure *cis*- (40–45%) and *trans*-isomers (50–55%).

2: M.p. 68–70°. IR: 3615, 3454, 1721, 1520, 1241, 973. $^1\text{H-NMR}$: 0.96–1.76 (*m*, 9 H); 2.48 (*dd*, $J = 7.7, 13.5$, 1 H); 2.65 (*dd*, $J = 7.5, 13.5$, 1 H); 3.58 (*br. q*, $J = 5.4, 2$ H); 3.68 (*s*, 3 H); 3.78 (*dt*, $J = 2.6, 2.6, 4.4$, 1 H); 4.01 (*t*, $J = 5.1, 2$ H); 5.15 (*br. s*, 1 H); 6.80 (*m*, 2 H); 7.10 (*m*, 2 H). $^{13}\text{C-NMR}$: 20.29 (*r*); 25.20 (*r*); 26.27 (*r*); 33.19 (*r*); 37.63 (*r*); 40.58 (*r*); 43.62 (*d*); 52.11 (*q*); 66.89 (*r*); 68.41 (*d*); 114.18 (*d*); 130.03 (*d*); 133.59 (*s*); 156.57 (*s*); 157.05 (*s*). GC/MS: 307 (4, M^+), 275 (1), 257 (1), 206 (1), 188 (2), 176 (2), 159 (1), 107 (10), 102 (100). Anal. calc. for $\text{C}_{17}\text{H}_{25}\text{NO}_4$ (307.38): C 66.42, H 8.20, N 4.56; found: C 66.47, H 8.19, N 4.54.

3: M.p. 83–84°. IR: 3602, 3454, 1718, 1510, 1241, 979. $^1\text{H-NMR}$: 0.82–1.76 (*m*, 8 H); 1.98 (*m*, 1 H); 2.32 (*dd*, $J = 9.0, 13.5$, 1 H); 3.08 (*dd*, $J = 4.0, 13.5$, 1 H); 3.28 (*dt*, $J = 4.4, 9.9, 9.9$, 1 H); 3.58 (*br. q*, $J = 5.3, 2$ H); 3.68 (*s*, 3 H); 4.01 (*t*, $J = 5.1, 2$ H); 5.15 (*br. s*, 1 H); 6.80 (*m*, 2 H); 7.10 (*m*, 2 H). $^{13}\text{C-NMR}$: 24.89 (*r*); 25.43 (*r*); 29.95 (*r*); 35.82 (*r*); 38.00 (*r*); 40.63 (*r*); 47.07 (*d*); 52.16 (*q*); 66.92 (*r*); 74.43 (*d*); 114.17 (*d*); 130.36 (*d*); 133.27 (*s*); 156.65 (*s*); 157.07 (*s*). GC/MS: 307 (6, M^+), 275 (2), 257 (1), 206 (1), 188 (2), 176 (3), 159 (1), 107 (12), 102 (100). Anal. calc. for $\text{C}_{17}\text{H}_{25}\text{NO}_4$ (307.38): C 66.42, H 8.20, N 4.56; found: C 66.45, H 8.23, N 4.51.

6: M.p. 25°. IR: 3630, 3465, 1729, 1516, 1246, 979. $^1\text{H-NMR}$: 1.24 (*t*, $J = 7.2, 3$ H); 1.26–1.83 (*m*, 9 H); 2.47 (*dd*, $J = 7.5, 13.5$, 1 H); 2.66 (*dd*, $J = 7.3, 13.5$, 1 H); 3.56 (*q*, $J = 5.4, 2$ H); 3.78 (*dt*, $J = 2.5, 2.5, 4.3$, 1 H); 4.00 (*t*,

$J = 5.1, 2 \text{ H}$; 4.12 ($q, J = 7.2, 2 \text{ H}$); 5.21 (br. s, 1 H); 6.80 ($m, 2 \text{ H}$); 7.10 ($m, 2 \text{ H}$). $^{13}\text{C-NMR}$: 14.42 (q); 20.23 (r); 25.04 (r); 26.11 (r); 33.03 (r); 37.40 (r); 40.32 (r); 43.53 (d); 60.70 (r); 66.79 (r); 68.25 (d); 114.03 (d); 129.89 (d); 133.49 (s); 156.44 (s); 156.60 (s). GC/MS: 321 (4, M^+), 275 (15), 257 (48), 189 (10), 176 (48), 116 (100), 107 (60), 88 (42). Anal. calc. for $\text{C}_{18}\text{H}_{27}\text{NO}_4$ (321.39): C 67.26, H 8.47, N 4.36; found: C 67.30, H 8.44, N 4.35.

7: M.p. 73–74°. IR: 3625, 3465, 1726, 1513, 1243, 1069, 1052. $^1\text{H-NMR}$: 1.25 ($t, J = 7.1, 3 \text{ H}$); 1.29–1.62 ($m, 9 \text{ H}$); 2.33 ($dd, J = 9.0, 13.5, 1 \text{ H}$); 3.08 ($dd, J = 4.0, 13.5, 1 \text{ H}$); 3.28 ($dt, J = 4.4, 9.5, 9.5, 1 \text{ H}$); 3.57 ($q, J = 5.4, 2 \text{ H}$); 4.01 ($t, J = 5.1, 2 \text{ H}$); 4.13 ($q, J = 7.1, 2 \text{ H}$); 5.12 (br. s, 1 H); 6.81 ($m, 2 \text{ H}$); 7.09 ($m, 2 \text{ H}$). $^{13}\text{C-NMR}$: 14.56 (q); 24.85 (r); 25.38 (r); 29.89 (r); 35.75 (r); 37.93 (r); 40.46 (r); 47.01 (d); 60.86 (r); 66.92 (r); 74.30 (d); 114.10 (d); 130.31 (d); 133.20 (s); 156.60 (s); 156.60 (s). GC/MS: 321 (4, M^+), 275 (13), 257 (34), 189 (8), 176 (38), 116 (100), 107 (54), 88 (39). Anal. calc. for $\text{C}_{18}\text{H}_{27}\text{NO}_4$ (321.39): C 67.26, H 8.47, N 4.36; found: C 67.29, H 8.50, N 4.41.

10: M.p. 70.5–72°. IR: 3616, 3454, 1714, 1518, 1241, 973. $^1\text{H-NMR}$: 0.93 ($t, J = 7.5, 3 \text{ H}$); 1.16–1.79 ($m, 11 \text{ H}$); 2.48 ($dd, J = 7.7, 13.5, 1 \text{ H}$); 2.65 ($dd, J = 7.5, 13.5, 1 \text{ H}$); 3.57 (br. $q, J = 5.3, 2 \text{ H}$); 3.78 ($dt, J = 2.6, 2.6, 4.4, 1 \text{ H}$); 4.01 ($t, J = 5.1, 2 \text{ H}$); 4.02 ($t, J = 7.2, 2 \text{ H}$); 5.13 (br. s, 1 H); 6.80 ($m, 2 \text{ H}$); 7.10 ($m, 2 \text{ H}$). $^{13}\text{C-NMR}$: 10.28 (q); 20.30 (r); 22.30 (r); 25.24 (r); 26.30 (r); 33.23 (r); 37.67 (r); 40.50 (r); 43.64 (d); 66.57 (r); 66.97 (r); 68.42 (d); 114.20 (d); 130.04 (d); 133.56 (s); 156.61 (s); 156.78 (s). GC/MS: 335 (6, M^+), 284 (4), 275 (1), 256 (7), 242 (1), 228 (2), 213 (3), 176 (8), 149 (10), 130 (90), 107 (23), 97 (17), 88 (100). Anal. calc. for $\text{C}_{19}\text{H}_{29}\text{NO}_4$ (335.53): C 68.01, H 8.71, N 4.17; found: C 67.97, H 8.69, N 4.21.

11: M.p. 94–95°. IR: 3604, 3454, 1714, 1517, 1242, 1026. $^1\text{H-NMR}$: 0.82–1.76 ($m, 10 \text{ H}$); 0.93 ($t, J = 7.5, 3 \text{ H}$); 1.98 ($m, 1 \text{ H}$); 2.33 ($dd, J = 9.0, 13.5, 1 \text{ H}$); 3.08 ($dd, J = 4.0, 13.5, 1 \text{ H}$); 3.28 ($dt, J = 4.2, 9.9, 9.9, 1 \text{ H}$); 3.57 (br. $q, J = 5.3, 2 \text{ H}$); 4.01 ($t, J = 5.1, 2 \text{ H}$); 4.02 ($t, J = 7.0, 2 \text{ H}$); 5.11 (br. s, 1 H); 6.81 ($m, 2 \text{ H}$); 7.09 ($m, 2 \text{ H}$). $^{13}\text{C-NMR}$: 10.26 (q); 22.27 (r); 24.86 (r); 25.38 (r); 29.89 (r); 35.76 (r); 37.93 (r); 40.48 (r); 47.01 (d); 66.55 (r); 66.94 (r); 74.30 (d); 114.11 (d); 130.21 (d); 133.21 (s); 156.61 (s); 156.77 (s). GC/MS: 335 (5, M^+), 284 (5), 275 (1), 256 (9), 242 (1), 228 (3), 213 (5), 176 (8), 149 (11), 130 (85), 107 (25), 97 (20), 88 (100). Anal. calc. for $\text{C}_{19}\text{H}_{29}\text{NO}_4$ (335.53): C 68.01, H 8.71, N 4.17; found: C 68.05, H 8.68, N 4.14.

14: M.p. 73–74°. IR: 3616, 3453, 1710, 1511, 1240, 973. $^1\text{H-NMR}$: 1.23 ($d, J = 6.3, 6 \text{ H}$); 1.28–1.78 ($m, 9 \text{ H}$); 2.48 ($dd, J = 7.6, 13.6, 1 \text{ H}$); 2.65 ($dd, J = 7.6, 13.6, 1 \text{ H}$); 3.56 (br. $q, J = 5.4, 2 \text{ H}$); 3.78 ($dt, J = 2.4, 4.6, 1 \text{ H}$); 4.01 ($t, J = 5.1, 2 \text{ H}$); 4.91 ($m, J = 6.3, 1 \text{ H}$); 5.08 (br. s, 1 H); 6.81 ($m, 2 \text{ H}$); 7.10 ($m, 2 \text{ H}$). $^{13}\text{C-NMR}$: 20.29 (r); 22.09 (q); 22.09 (q); 25.22 (r); 26.27 (r); 33.20 (r); 37.64 (r); 40.39 (r); 43.63 (d); 67.00 (r); 68.16 (d); 68.40 (d); 114.17 (d); 130.02 (d); 133.53 (s); 156.26 (s); 156.61 (s). GC/MS: 335 (5, M^+), 275 (1), 258 (3), 242 (1), 228 (1), 214 (1), 206 (1), 188 (10), 176 (10), 130 (40), 107 (23), 88 (100). Anal. calc. for $\text{C}_{19}\text{H}_{29}\text{NO}_4$ (335.53): C 68.01, H 8.71, N 4.17; found: C 68.00, H 8.67, N 4.19.

15: M.p. 87.5–88.5°. IR: 3604, 3453, 1710, 1510, 1241, 1025. $^1\text{H-NMR}$: 0.86–1.78 ($m, 8 \text{ H}$); 1.23 ($d, J = 6.4, 6 \text{ H}$); 1.97 ($m, 1 \text{ H}$); 2.33 ($dd, J = 9.0, 13.6, 1 \text{ H}$); 3.08 ($dd, J = 4.0, 13.6, 1 \text{ H}$); 3.28 ($dt, J = 4.4, 9.9, 9.9, 1 \text{ H}$); 3.57 (br. $q, J = 5.3, 2 \text{ H}$); 4.01 ($t, J = 5.0, 2 \text{ H}$); 4.91 ($m, J = 6.4, 1 \text{ H}$); 5.07 (br. s, 1 H); 6.81 ($m, 2 \text{ H}$); 7.09 ($m, 2 \text{ H}$). $^{13}\text{C-NMR}$: 22.10 (q); 22.10 (q); 24.86 (r); 25.39 (r); 29.90 (r); 35.77 (r); 37.94 (r); 40.40 (r); 47.02 (d); 66.99 (r); 68.16 (d); 74.31 (d); 114.11 (d); 130.31 (d); 133.19 (s); 156.26 (s); 156.63 (s). GC/MS: 335 (7, M^+), 275 (1), 258 (4), 242 (1), 228 (1), 214 (1), 206 (1), 188 (10), 176 (12), 130 (38), 107 (22), 88 (100). Anal. calc. for $\text{C}_{19}\text{H}_{29}\text{NO}_4$ (335.53): C 68.01, H 8.71, N 4.17; found: C 68.06, H 8.75, N 4.12.

18: M.p. 62–64°. IR: 3615, 3451, 3308, 2131, 1727, 1518, 1242, 973. $^1\text{H-NMR}$: 1.18–1.76 ($m, 9 \text{ H}$); 2.47 ($t, J = 2.4, 1 \text{ H}$); 2.47 ($dd, J = 7.7, 13.5, 1 \text{ H}$); 2.65 ($dd, J = 7.6, 13.5, 1 \text{ H}$); 3.59 (br. $q, J = 5.2, 2 \text{ H}$); 3.78 ($dt, J = 2.6, 2.6, 4.4, 1 \text{ H}$); 4.01 ($t, J = 5.2, 2 \text{ H}$); 4.69 ($d, J = 2.4, 2 \text{ H}$); 5.13 (br. s, 1 H); 6.80 ($m, 2 \text{ H}$); 7.10 ($m, 2 \text{ H}$). $^{13}\text{C-NMR}$: 20.30 (r); 25.23 (r); 26.30 (r); 33.22 (r); 37.67 (r); 40.68 (r); 43.63 (d); 52.52 (r); 66.74 (r); 68.43 (d); 74.63 (d); 78.15 (s); 114.20 (d); 130.06 (d); 133.67 (s); 156.46 (s); 156.50 (s). GC/MS: 331 (5, M^+), 275 (5), 257 (11), 188 (6), 176 (13), 149 (6), 126 (100), 107 (30), 84 (41). Anal. calc. for $\text{C}_{19}\text{H}_{25}\text{NO}_4$ (331.40): C 68.86, H 7.60, N 4.22; found: C 68.91, H 7.58, N 4.27.

19: M.p. 84.5–85.5°. IR: 3604, 3450, 3308, 2131, 1727, 1518, 1243, 1025. $^1\text{H-NMR}$: 0.82–1.76 ($m, 8 \text{ H}$); 1.97 ($m, 1 \text{ H}$); 2.33 ($dd, J = 9.0, 13.5, 1 \text{ H}$); 2.47 ($t, J = 2.4, 1 \text{ H}$); 3.08 ($dd, J = 4.0, 13.5, 1 \text{ H}$); 3.28 ($dt, J = 4.4, 9.9, 9.9, 1 \text{ H}$); 3.60 (br. $q, J = 5.3, 2 \text{ H}$); 4.02 ($t, J = 5.1, 2 \text{ H}$); 4.69 ($d, J = 2.4, 2 \text{ H}$); 5.27 (br. s, 1 H); 6.80 ($m, 2 \text{ H}$); 7.09 ($m, 2 \text{ H}$). $^{13}\text{C-NMR}$: 24.87 (r); 25.40 (r); 29.93 (r); 35.80 (r); 37.97 (r); 40.69 (r); 47.03 (d); 52.53 (r); 66.74 (r); 74.38 (d); 74.38 (d); 78.16 (s); 114.15 (d); 130.36 (d); 133.32 (s); 156.46 (s); 156.54 (s). GC/MS: 331 (6, M^+), 275 (7), 257 (10), 188 (10), 176 (15), 149 (6), 126 (100), 107 (32), 84 (38). Anal. calc. for $\text{C}_{19}\text{H}_{25}\text{NO}_4$ (331.40): C 68.86, H 7.60, N 4.22; found: C 68.81, H 7.64, N 4.20.

Alkyl N-[2-{4-[(2,2-(Ethylenedioxy)cyclohexyl]methyl}phenoxy]ethyl}carbamates 4, 8, 12, 16, and 20: General Procedure. A soln. of ketones **1**, **5**, **9**, **13**, or **17** (0.50 g, 1.499 mmol) in benzene (50 ml) was treated with ethane-1,2-diol (1 ml) under azeotropic distillation. After 4 h, the product was extracted with benzene and the extract dried (Na_2SO_4) and evaporated. Yields 98–100%.

4: M.p. 91–92°. IR: 3463, 3359, 3062, 3032, 2979, 2879, 1732, 1612, 1584, 1510, 1446, 1241. ¹H-NMR: 1.06–1.84 (*m*, 9 H); 2.20 (*dd*, *J* = 11.0, 13.4, 1 H); 2.98 (*dd*, *J* = 3.1, 13.4, 1 H); 3.57 (*br. q*, *J* = 5.3, 2 H); 3.68 (*s*, 3 H); 3.96–4.04 (*m*, 4 H); 5.14 (*br. s*, 1 H); 6.79 (*m*, 2 H); 7.07 (*m*, 2 H). ¹³C-NMR: 23.95 (*t*); 24.65 (*t*); 28.44 (*t*); 33.61 (*t*); 34.90 (*t*); 40.64 (*t*); 46.95 (*d*); 52.16 (*q*); 64.83 (*t*); 64.90 (*t*); 66.91 (*t*); 110.65 (*s*); 114.15 (*d*); 130.23 (*d*); 134.02 (*s*); 156.52 (*s*); 156.52 (*s*). GC/MS: 349 (12, *M*⁺), 331 (1), 317 (25), 306 (12), 274 (25), 255 (5), 221 (8), 207 (11), 189 (16), 176 (12), 141 (13), 128 (28), 107 (20), 102 (62), 99 (100). Anal. calc. for C₁₉H₂₇NO₅ (349.41): C 65.31, H 7.79, N 4.01; found: C 65.36, H 7.76, N 3.96.

8: M.p. 63–64°. IR: 3463, 3359, 3062, 3032, 2979, 2879, 1612, 1584, 1510, 1446, 1241. ¹H-NMR: 1.20–1.73 (*m*, 8 H); 1.24 (*t*, *J* = 7.1, 3 H); 1.78 (*m*, 1 H); 2.20 (*dd*, *J* = 11.0, 13.2, 1 H); 2.99 (*dd*, *J* = 3.1, 13.2, 1 H); 3.56 (*q*, *J* = 5.4, 2 H); 3.97–4.03 (*m*, 6 H); 4.12 (*q*, *J* = 7.1, 2 H); 5.12 (*br. s*, 1 H); 6.80 (*m*, 2 H); 7.07 (*m*, 2 H). ¹³C-NMR: 14.58 (*q*); 23.92 (*t*); 24.62 (*t*); 28.41 (*t*); 33.58 (*t*); 34.86 (*t*); 40.50 (*t*); 46.92 (*d*); 60.86 (*t*); 64.80 (*t*); 64.87 (*t*); 66.94 (*t*); 110.62 (*s*); 114.12 (*d*); 130.19 (*d*); 133.95 (*s*); 156.23 (*s*); 156.63 (*s*). GC/MS: 363 (4, *M*⁺), 317 (19), 274 (20), 189 (15), 176 (10), 141 (11), 128 (26), 116 (40), 107 (17), 99 (100). Anal. calc. for C₂₀H₂₉NO₅ (363.44): C 66.09, H 8.07, N 3.85; found: C 66.12, H 8.03, N 3.91.

12: M.p. 87–88°. IR: 3463, 3365, 3062, 3032, 2879, 1725, 1612, 1585, 1510, 1447, 1242. ¹H-NMR: 0.93 (*t*, *J* = 7.3, 3 H); 1.06–1.84 (*m*, 9 H); 2.20 (*dd*, *J* = 11.0, 13.4, 1 H); 2.98 (*dd*, *J* = 3.2, 13.4, 1 H); 3.57 (*br. q*, *J* = 5.1, 2 H); 3.96–4.05 (*m*, 4 H); 5.12 (*br. s*, 1 H); 6.80 (*m*, 2 H); 7.07 (*m*, 2 H). ¹³C-NMR: 10.32 (*q*); 22.34 (*t*); 23.95 (*t*); 24.65 (*t*); 28.44 (*t*); 33.61 (*t*); 34.90 (*t*); 40.54 (*t*); 46.95 (*d*); 64.83 (*t*); 64.90 (*t*); 66.59 (*t*); 66.98 (*t*); 110.65 (*s*); 114.14 (*d*); 130.22 (*d*); 133.97 (*s*); 156.54 (*s*); 156.78 (*s*). GC/MS: 377 (15, *M*⁺), 334 (6), 317 (6), 274 (6), 249 (5), 176 (10), 141 (13), 130 (98), 107 (18), 99 (100), 88 (70). Anal. calc. for C₂₁H₃₁NO₅ (377.47): C 66.82, H 8.28, N 3.71; found: C 66.85, H 8.24, N 3.73.

16: M.p. 76–77°. IR: 3464, 3366, 3062, 3033, 1722, 1612, 1585, 1510, 1477, 1386, 1374, 1245. ¹H-NMR: 1.02–1.89 (*m*, 9 H); 1.23 (*d*, *J* = 6.2, 6 H); 2.20 (*dd*, *J* = 10.9, 13.3, 1 H); 2.98 (*dd*, *J* = 3.0, 13.3, 1 H); 3.56 (*br. q*, *J* = 5.5, 2 H); 3.96–4.03 (*m*, 6 H); 4.92 (*m*, *J* = 6.2, 1 H); 5.05 (*br. s*, 1 H); 6.80 (*m*, 2 H); 7.07 (*m*, 2 H). ¹³C-NMR: 22.12 (*q*); 22.12 (*q*); 23.92 (*t*); 24.62 (*t*); 28.41 (*t*); 33.58 (*t*); 34.86 (*t*); 40.42 (*t*); 46.91 (*d*); 64.79 (*t*); 64.86 (*t*); 67.00 (*t*); 68.16 (*d*); 110.62 (*s*); 114.12 (*d*); 130.18 (*d*); 133.92 (*s*); 156.25 (*s*); 156.55 (*s*). GC/MS: 377 (11, *M*⁺), 355 (4), 334 (4), 317 (19), 281 (20), 274 (21), 207 (48), 189 (15), 176 (17), 141 (15), 130 (50), 107 (27), 99 (100), 88 (63). Anal. calc. for C₂₁H₃₁NO₅ (377.47): C 66.82, H 8.28, N 3.71; found: C 66.80, H 8.31, N 3.75.

20: M.p. 80–81°. IR: 3458, 3352, 3314, 3033, 2130, 1736, 1612, 1585, 1510, 1446, 1242. ¹H-NMR: 1.34–1.84 (*m*, 9 H); 2.20 (*dd*, *J* = 11.0, 13.5, 1 H); 2.47 (*t*, *J* = 2.4, 1 H); 2.98 (*dd*, *J* = 3.2, 13.5, 1 H); 3.59 (*br. q*, *J* = 5.3, 2 H); 3.95–4.04 (*m*, 6 H); 4.69 (*d*, *J* = 2.4, 2 H); 5.27 (*br. s*, 1 H); 6.79 (*m*, 2 H); 7.07 (*m*, 2 H). ¹³C-NMR: 23.95 (*t*); 24.65 (*t*); 28.44 (*t*); 33.61 (*t*); 34.90 (*t*); 40.73 (*t*); 46.94 (*d*); 52.55 (*t*); 64.83 (*t*); 64.90 (*t*); 66.74 (*t*); 74.63 (*d*); 78.17 (*s*); 110.65 (*s*); 114.14 (*d*); 130.24 (*d*); 134.09 (*s*); 155.45 (*s*); 156.43 (*s*). GC/MS: 373 (7, *M*⁺), 355 (1), 330 (5), 317 (23), 274 (23), 245 (5), 207 (13), 189 (17), 176 (11), 141 (12), 128 (29), 126 (28), 107 (20), 99 (100). Anal. calc. for C₂₁H₂₇NO₅ (373.44): C 67.54, H 7.29, N 3.75; found: C 67.60, H 7.26, N 3.79.

Laboratory Testing with Topical Application of Juvenoids 1–20. Tests were based on evaluation of the morphogenetic effect of the juvenoid studied. The effect of the compounds results in the inhibition of metamorphosis. The juvenoid dissolved in acetone was applied to the insect-body surface using a microapplicator or a fully automated pipette. The effect of the juvenoid was evaluated after completion of the following molt. Evaluation of the effectivity of the juvenoid was based either on the number of affected insect individuals or on the level of inhibition of the metamorphosis and on that of formation of the selected body parts. The evaluation of the effect of the juvenoids is given as *ID*₅₀ (in µg per individual), *i.e.* the amount of juvenoid causing a 50% inhibition of metamorphosis of the insect organism [3].

***Tenebrio molitor*:** Pupae were used for screening tests, which were younger than 12–24 h after completion of the preceding molt. The juvenilizing effect of a test compound was evaluated 2 days after maturation of the reference (non-treated) beetles.

***Galleria mellonella*:** An acetone soln. of the juvenoid was applied on last larval instar individuals at the end of the feeding period (*i.e.* during the 5th or 6th day of the 8-days-long last larval instar). The larval-pupal intermediate forms occur as a response to the juvenilizing effect of the compound tested.

***Dysdercus cingulatus* and *Pyrrhocoris apterus*:** Freshly molted last larval instar individuals (younger than 24 h) were used. The concentration of the acetone soln. of a juvenoid was adjusted to enable the topical application of no more than 1–2 µl of the soln. per individual. The juvenilizing effect of the compound reflected evoking of the larval-adult intermediate forms.

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