113. Synthesis and Structure-Activity Relationships of Juvenoids Derived from 2-(4-Hydroxybenzyl)cycloalkan-1-ones

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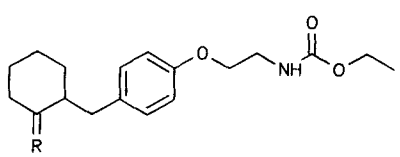
(17.I.94)

Juvenoids **16**–**30**, **32**, **36**, **38**–**41**, **44**–**46**, and **49**–**56** containing carbamate, carbonate, and urea moieties in the molecule were synthesized and subjected to a biological screening (*Schemes 2–7*, *Table 2*). Carbamate juvenoids **1**–**4** were used as reference compounds for a detailed structure-activity study of their analogues. A clear relationship between the nature of the side chain functional group and the biological activity was found. Surprisingly, not only the juvenoids **1**–**4** but also **38**–**41**, the compounds with a reversed carabamate *N,O*-substitution pattern, showed very promising biological activity. In contrast, the carbonate and urea derivatives displayed a remarkably low activity. The relationship between the size and substitution at atoms C(2) and C(3) of the saturated ring and the biological activity is very complex and is still not completely understood.

Introduction. – Compounds imitating the action of the natural juvenile hormones (juvenoids) [1] are representatives of biorational pesticides [2]. In contrast to the classical insecticides, their use in the practice is desirable mainly from the ecological point of view. This work is aimed at a group of juvenoids containing two carbocyclic subunits [3]. *Wimmer et al.* [4] published a series of carbamate juvenoids **1**–**4** that showed excellent biological activity on a broad spectrum of insect pests [2]; in particular, **2** is interesting also from the toxicological point of view [2]. Accordingly, we decided to study the synthetic analogues **16**–**30**, **32**, **36**, **38**–**41**, **44**–**46**, and **49**–**56** of these compounds, in order to investigate the structure-activity relationships more thoroughly. Concerning the design of these analogues, our attention focused on the nature of the side chain's functional group and on the size of the saturated ring as well as on its substitution on the atoms C(2) and C(3), because these factors were believed to be of biological signifi-

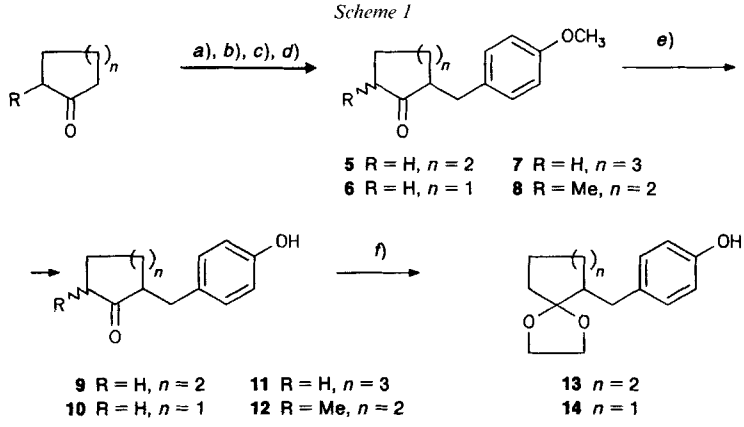


1 R = O
2 R = OCH_2CH_2O
3 R = OH, H, *cis*
4 R = OH, H, *trans*

cance. In particular, the presence of the secondary OH function at C(2) of compounds **3** and **4** serves for the synthesis of juvenogens [5], which are, *per definitionem*, complex substances capable of liberating the biologically active juvenoid by means of biotic or abiotic factors [5].

Results and Discussion. – The key intermediates, 2-(4-hydroxybenzyl)cycloalkan-1-ones **9**–**12** (*Scheme 1*) were prepared by the *Storck* [6] alkylation of pyrrolidine enamines of the corresponding cycloalkanones and 4-methoxybenzyl chloride (→ **5**–**8**), and by a subsequent demethylation. The resulting ketones **9** and **10** were converted to the ethylene acetals **13** and **14**, respectively, by standard procedures.

Scheme 1



5 R = H, *n* = 2 **7** R = H, *n* = 3
6 R = H, *n* = 1 **8** R = Me, *n* = 2

9 R = H, *n* = 2 **11** R = H, *n* = 3 **13** *n* = 2
10 R = H, *n* = 1 **12** R = Me, *n* = 2 **14** *n* = 1

a) Pyrrolidine, TsOH, benzene. *b*) $MeOC_6H_4CH_2Cl$, 1,4-dioxane, reflux. *c*) H_2O. *d*) Separation. *e*) HBr, Ac_2O. *f*) Ethylene glycol, TsOH, benzene.

The ketones **10**–**12** were alkylated by *N*-(2-halogenoethyl)carbamate **15**, easily available [7] from 2-aminoethanol (*Scheme 2*). The resulting carbamate juvenoids **16**–**18** were converted by known procedures into the acetals **19**–**21** and into alcohol mixtures **22**/**23**, **24**/**25**, and **26**/**27** which were separated.

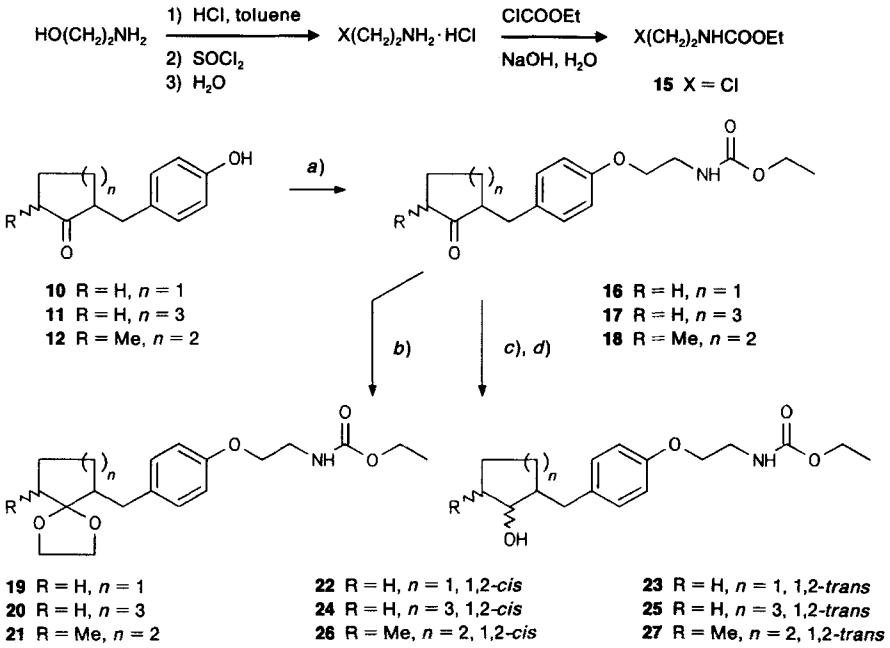
The isomeric methoxy derivatives **28** and **29** were obtained by methylation of the corresponding alcohols **3** and **4** using diazomethane [8] in the presence of boron trifluoride etherate, acetal **30** was accessible from **1**, and thioacetal **32** was synthesized from ketone **9** *via* **31** (*Scheme 3*).

The carbamate **36** was prepared to investigate whether the absence of functional groups in the cyclohexyl moiety is of biological significance. The synthesis of **36** was straightforward starting from **5** *via* **33**–**35**, the demethylation being achieved with monochloroborane-dimethyl sulfide complex [9] [10] (*Scheme 4*).

The carbamates **38**–**41** were obtained from the phenolic compound **9** by *O*-alkylation using ethylene carbonate [11] *via* intermediate **37** (*Scheme 5*). The latter was treated with ethyl isocyanate [12] to yield the juvenoid **38**, from which the ethylene acetal **39** and the isomeric alcohols **40** and **41** were obtained by known procedures.

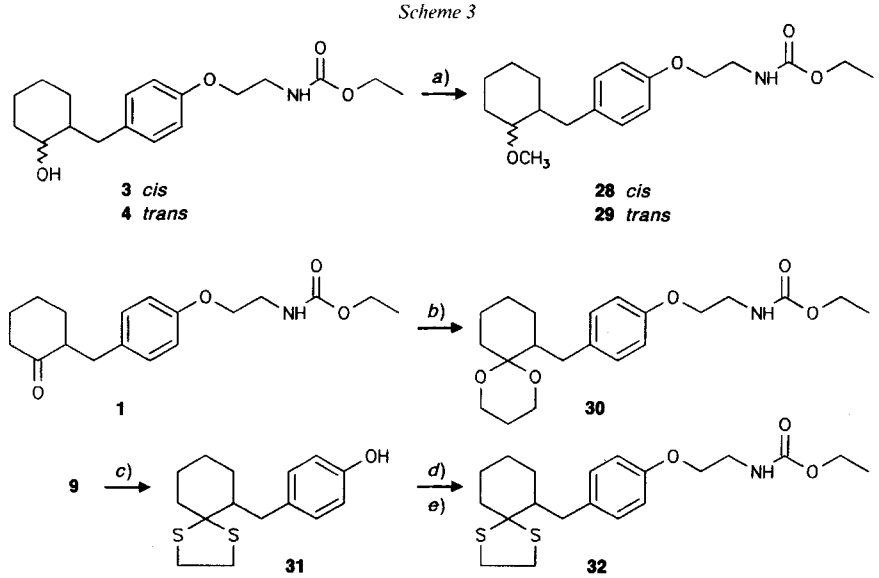
The synthesis of the urea derivatives **44**–**46** started again from the phenolic compound **9** that was alkylated using 1,2-dibromoethane. The resulting bromo derivative **42** was

Scheme 2



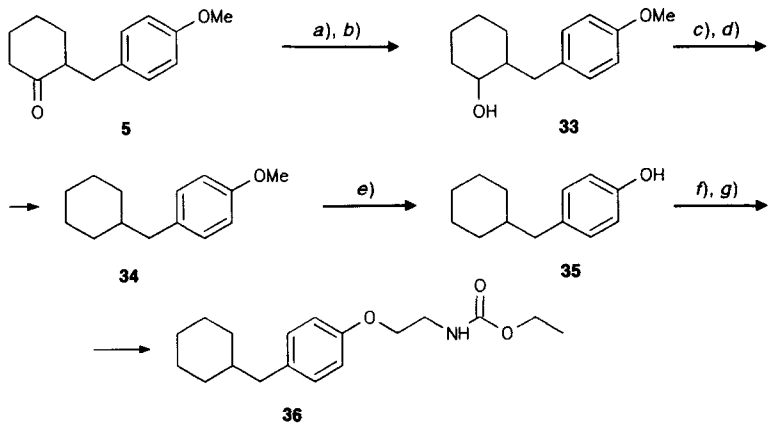
a) DMF, NaH, $Cl(CH_2)_2NHCOOEt$ (15). *b*) Ethylene glycol, TsOH, benzene. *c*) $NaBH_4$, MeOH. *d*) Separation.

Scheme 3



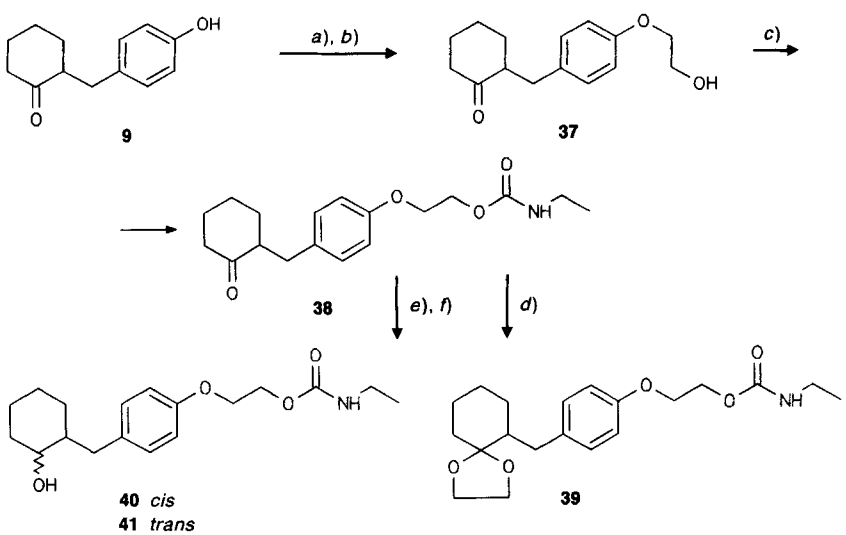
a) $BF_3 \cdot Et_2O$, CH_2N_2. *b*) Propane-1,3-diol, TsOH, benzene. *c*) $BF_3 \cdot Et_2O$, AcOH, $HS(CH_2)_2SH$. *d*) NaH, DMF. *e*) $Cl(CH_2)_2NHCOOEt$ (15).

Scheme 4



a) $LiAlH_4$. *b*) Separation. *c*) H_3PO_4 (85%), 100°. *d*) $Pd/CaCO_3$, H_2, hexane. *e*) $BClH_2 \cdot Me_2S$, benzene, reflux. *f*) NaH, DMF. *g*) $Cl(CH_2)_2NHCOOEt$ (15).

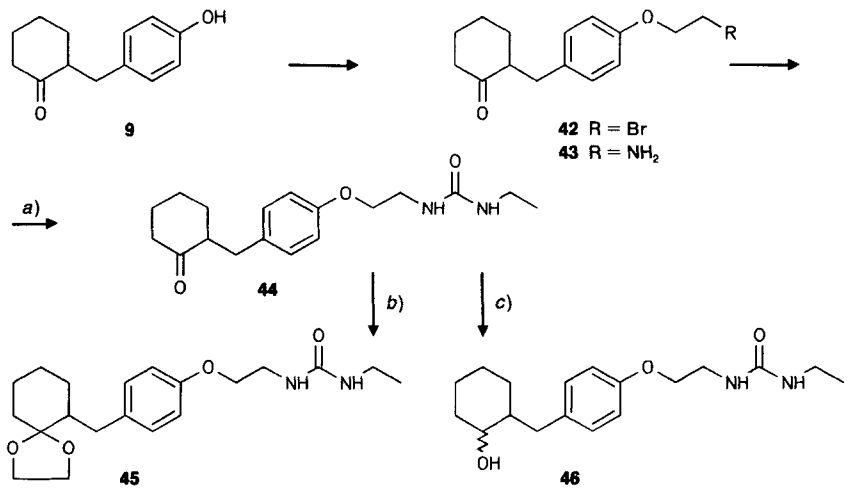
Scheme 5



a) NaOH, MeOH. *b*) Ethylene carbonate, toluene. *c*) EtNCO, Et_3N. *d*) Ethylene glycol, TsOH, benzene. *e*) $NaBH_4$, MeOH. *f*) Separation.

treated by liquid ammonia in THF to yield the primary amine **43** (*Scheme 6*). When the same reaction was carried out in the absence of THF, no product was obtained. Amine **43** reacted with ethyl isocyanate [13] to give the juvenoid **44** from which the ethylene acetal **45** and the alcohol mixture **46** were obtained in the usual way. Separation of **46** using column chromatography (silica gel) has so far been unsuccessful.

Scheme 6



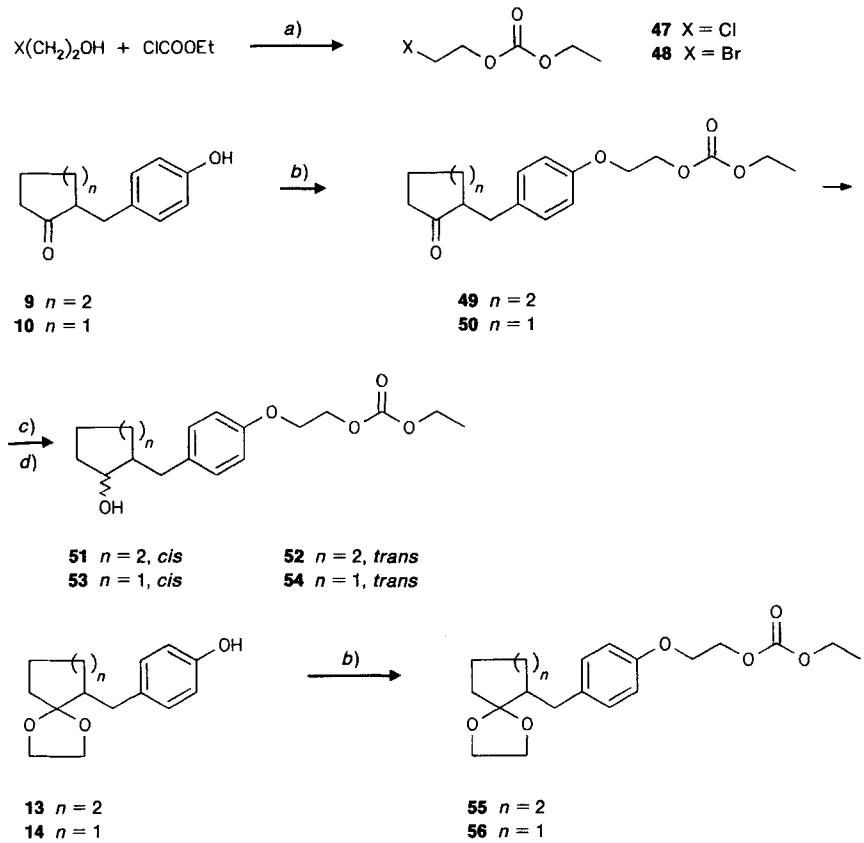
a) EtNCO, Et_3N. *b*) Ethylene glycol, TsOH, benzene. *c*) $NaBH_4$, MeOH.

The synthesis of the carbonate derivatives **49–56** started with the alkylation of **9** and **10** by 2-chloro- or 2-bromoethyl ethyl carbonate (**47** or **48**, resp.), easily available from 2-halogenoethanols (*Scheme 7*). The resulting juvenoids **49** and **50** were reduced using $NaBH_4$ in $EtOH/H_2O$ buffered by boric acid at 0° to yield the separable alcohol mixtures **51**/**52** and **53**/**54**. When the reduction was carried out in MeOH with no buffering, decomposition of the side chain was observed. The ethylene acetals **55** and **56** were also not prepared in the usual way starting from the corresponding ketones **49** and **50**, but rather from the ethylene acetals **13** and **14** (see *Scheme 1*) which were alkylated in the usual way (*Scheme 7*). The above described alkylations showed the same yields when chloro derivative **47** at 150° or bromo derivative **48** at 100° was used.

The yellow mealworm (*Tenebrio molitor*; *T.m.*) proved to be a suitable species for a fast and sensitive screening bioassay of compounds showing the juvenilizing activity [1]. The test of all compounds was carried out by a standard method described by *Sláma et al.* [1]. The results of the bioassays are summarized in *Tables 1* and *2*.

The relationship between the nature of the side chain's functional group and the biological activity is clearly established. The urea and the carbonate derivatives **44–46** and **49–56**, respectively, generally show a remarkable decrease of activity when compared with the standard carbamate derivatives **1–4**. The juvenoids **38–41** containing a carbamate moiety *N,O*-substituted in the opposite way exhibit a slightly lower activity compared to **1–4**. On the other hand, the biological activity is not significantly related to both the ring size and the substitution at C(2) of the cycloalkyl subunit. There is a slightly enhanced activity of the secondary alcohols with the *cis*-1,2 configuration of the substituents of the saturated ring in comparison with the *trans*-isomers. The biological activity of the isomeric methoxy derivatives **28** and **29** is practically comparable. The corresponding isomeric alcohols **3** and **4** show lower activity by one to two orders of magnitude when compared to **28** and **29**, and, moreover, the isomers **3** and **4** exhibit

Scheme 7



a) DMAP, pyridine. *b*) $X(CH_2)_2OCOOEt$, (X = Br for $n = 1$, X = Cl for $n = 2$), NaH, DMF. *c*) $NaBH_4$, EtOH, H_2O, H_3BO_3, 0°. *d*) Separation.

Table 1. *Biological Activity of Standards on Selected Insect Species*

Standard	*T.m.*[a])	*P.a.*[a])	*D.c.*[a])	*G.m.*[a])	*L.m.*[a])
JH I	$4.4 \cdot 10^{-5}$	–	–	–	–
JH II	$2.0 \cdot 10^{-3}$	$3.0 \cdot 10^{-1}$	$1.0 \cdot 10^{-1}$	–	–
ME	$3.2 \cdot 10^{-3}$	$1.0 \cdot 10^{-2}$	$1.0 \cdot 10^{-4}$	–	2.0
BPE	–	$1.0 \cdot 10^{-4}$	$1.0 \cdot 10^{-5}$	–	3.0
FE	$3.2 \cdot 10^{-6}$	$1.0 \cdot 10^{-1}$	$5.0 \cdot 10^{-3}$	$5.0 \cdot 10^{-3}$	5.0
PY	$7.9 \cdot 10^{-6}$	$1.0 \cdot 10^{-1}$	$1.0 \cdot 10^{-1}$	–	$5.0 \cdot 10^{-1}$
1	$1.2 \cdot 10^{-6}$	–	$1.0 \cdot 10^{-1}$	$1.0 \cdot 10^{-2}$	–
2	$2.7 \cdot 10^{-6}$	$1.0 \cdot 10^{-1}$	$1.0 \cdot 10^{-2}$	$1.0 \cdot 10^{-2}$	$5.0 \cdot 10^{-1}$
3	$5.3 \cdot 10^{-5}$	$1.0 \cdot 10^{-4}$	$1.0 \cdot 10^{-4}$	$1.0 \cdot 10^{-1}$	–
4	$1.2 \cdot 10^{-4}$	1.0	$5.0 \cdot 10^{-2}$	$1.0 \cdot 10^{-2}$	–

[a]) ID_{50} (μg/individual; ID_{50} is the dose of the active compound causing 50% of morphological changes of the treated individual).

Table 2. *Biological Activity of Prepared Juvenoids on Selected Insect Species*

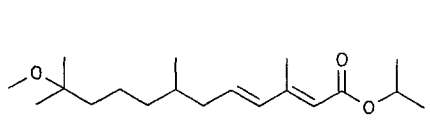
Juvenoid	*T.m.*[a])	*P.a.*[a])	*D.c.*[a])	*G.m.*[a])	*L.m.*[a])
16	$5.0 \cdot 10^{-5}$	$2.0 \cdot 10^{-1}$	$5.0 \cdot 10^{-3}$	–	–
19	$1.1 \cdot 10^{-5}$	2.0	2.0	$1.0 \cdot 10^{-2}$	–
22	$1.7 \cdot 10^{-4}$	$1.0 \cdot 10^{-3}$	$1.0 \cdot 10^{-4}$	$1.0 \cdot 10^{-2}$	–
23	$8.3 \cdot 10^{-5}$	$5.0 \cdot 10^{-2}$	$5.0 \cdot 10^{-3}$	–	–
17	$1.4 \cdot 10^{-5}$	$1.0 \cdot 10^{-2}$	$1.0 \cdot 10^{-1}$	$1.0 \cdot 10^{-2}$	–
20	$2.8 \cdot 10^{-5}$	$3.0 \cdot 10^{-1}$	$5.0 \cdot 10^{-1}$	$1.0 \cdot 10^{-1}$	–
24	$6.5 \cdot 10^{-6}$	$5.0 \cdot 10^{-3}$	$5.0 \cdot 10^{-4}$	$1.0 \cdot 10^{-3}$	$1.0 \cdot 10^{-3}$
25	$2.9 \cdot 10^{-5}$	$5.0 \cdot 10^{-3}$	$3.0 \cdot 10^{-4}$	$1.0 \cdot 10^{-2}$	$1.0 \cdot 10^{-2}$
18	$4.3 \cdot 10^{-5}$	2.0	$5.0 \cdot 10^{-1}$	–	–
21	$1.6 \cdot 10^{-5}$	0	0	–	–
26	$2.0 \cdot 10^{-5}$	$5.0 \cdot 10^{-3}$	$1.0 \cdot 10^{-3}$	–	–
27	$2.9 \cdot 10^{-6}$	$1.0 \cdot 10^{-2}$	$5.0 \cdot 10^{-3}$	–	–
28	$4.2 \cdot 10^{-6}$	$5.0 \cdot 10^{-2}$	$1.0 \cdot 10^{-4}$	–	–
29	$3.7 \cdot 10^{-6}$	$1.0 \cdot 10^{-1}$	$1.0 \cdot 10^{-1}$	–	–
30	$2.0 \cdot 10^{-5}$	1.0	1.0	–	–
32	$1.3 \cdot 10^{-4}$	$5.0 \cdot 10^{-5}$	$5.0 \cdot 10^{-5}$	–	–
36	$6.6 \cdot 10^{-5}$	$3.0 \cdot 10^{-1}$	$5.0 \cdot 10^{-2}$	$5.0 \cdot 10^{-3}$	–
38	$1.1 \cdot 10^{-5}$	$5.0 \cdot 10^{-3}$	$5.0 \cdot 10^{-5}$	$1.0 \cdot 10^{-3}$	$1.0 \cdot 10^{-2}$
39	$2.1 \cdot 10^{-6}$	1.0	$1.0 \cdot 10^{-5}$	$1.0 \cdot 10^{-6}$	–
40	$9.8 \cdot 10^{-5}$	$1.0 \cdot 10^{-3}$	$5.0 \cdot 10^{-5}$	$1.0 \cdot 10^{-4}$	1.0
41	$3.4 \cdot 10^{-5}$	$5.0 \cdot 10^{-3}$	$1.0 \cdot 10^{-5}$	$1.0 \cdot 10^{-4}$	–
44	$5.1 \cdot 10^{-4}$	0	0	–	–
45	$5.1 \cdot 10^{-4}$	0	1.0	–	–
46	$2.0 \cdot 10^{-1}$	$5.0 \cdot 10^{-2}$	$5.0 \cdot 10^{-2}$	–	–
49	$1.6 \cdot 10^{-3}$	0	10.0	–	–
55	$4.8 \cdot 10^{-3}$	10.0	10.0	–	–
51	$3.4 \cdot 10^{-2}$	$1.0 \cdot 10^{-2}$	$1.0 \cdot 10^{-1}$	–	–
52	$3.7 \cdot 10^{-2}$	5.0	5.0	–	–
50	$8.1 \cdot 10^{-2}$	5.0	10.0	–	–
56	$4.7 \cdot 10^{-3}$	0	0	–	–
53	$6.9 \cdot 10^{-3}$	0.5	0.1	–	–
54	$1.1 \cdot 10^{-2}$	1.0	1.0	5.0	–

[a]) ID_{50} (μg/individual).

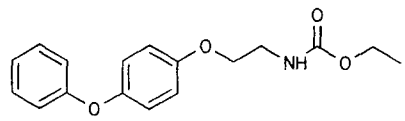
considerable difference in activity. In the series of carbamate juvenoids with different acetal groups, the biological activity declines in the following order: **2** > **30** > **32**. Complete absence of a substituent at C(2) of the saturated ring (see juvenoid **36**) does not lead to a considerable decrease of activity when compared with **1**–**4**. In comparison with **4**, compound **36** shows even better activity. When the biological activity of the standard juvenoids **1**–**4** are compared with that of the analogues **18**, **21**, **26**, and **27** (Me-substituted at C(3) of the saturated ring), the standard series is superior in case of the ketone (**1** and **18**) or the ethylene acetal (**2** and **21**). On the other hand, the 3-Me-substituted isomeric alcohols **26** and **27**, are more suitable active components for the preparation of juvenogens than the standard alcohols **3** and **4**.

From the practical point of view, it is interesting to compare the biological activity of commercially available or widely known juvenoids, as well as that of the native hormones, to that of the new juvenoids **16**–**30**, **32**, **36**, **38**–**41**, **44**–**46**, and **49**–**56**. Besides the

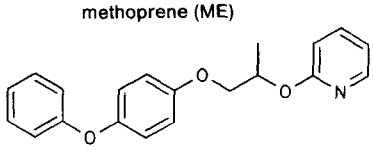
already mentioned standard series of juvenoids **1**–**4**, we used for this purpose methoprene (ME) [14], fenoxycarb (FE) [15], pyriproxyfene (PY) [16], BPE-epoxide (BPE) [17], and juvenile hormones I and II (JH I and JH II) [18] [19] as standards. These bioassays were performed on *Pyrrhocoris apterus* (*P.a.*), *Dysdercus cingulatus* (*D.c.*), *Galleria mellonella* (*G.m.*), and *Locusta migratoria migratorioides* (*L.m.*) which are economically important insect pests (with the exception of *P.a.* which was used as a reference testing species). *Tables 1* and *2* show that in the *P.a.* test, the new juvenoid **32** has the highest activity. In the *D.c.* test, the activity of the new juvenoids **39** and **41** is the same as that of the best standard compound BPE. The best results are obtained in the *G.m.* test. The already mentioned juvenoid **39** shows an activity increase by three orders of magnitude in comparison with the best standard compound FE and a four orders of magnitude increase in comparison with the standard compounds **1**–**4**. Similarly good results are obtained in the *L.m.* test. The cycloheptanol derivative **24** exhibits, surprisingly, a three orders of magnitude increase of activity in comparison with the standards ME, BPE, and FE and a two orders of magnitude increase of activity in comparison with PY and **2**.



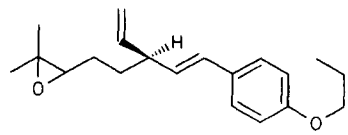
methoprene (ME)



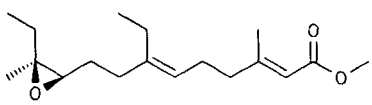
fenoxycarb (FE)



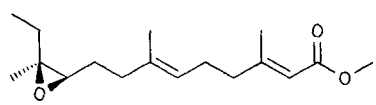
pyriproxyfene (PY)



BPE-epoxide (BPE)



juvenile hormone I (JH I)



juvenile hormone II (JH II)

Experimental Part

General. Solvents for extraction: technical grade, distilled. Solvents for reactions: distilled over $CaCl_2$ (CH_2Cl_2, pyridine), Na (THF, Et_2O), or molecular sieves 4 Å (DMF). NaH was used as a 50% dispersion in mineral oil. Column chromatography (CC): silica gel (*Gebr. Herrman*, Köln-Ehrenfeld), unless indicated otherwise. TLC: precoated silica gel TLC sheets *Silufol*® and *Silufol-UV 254*®. M.p.: *Kofler* hot stage; uncorrected. ^{1}H-NMR: FT-NMR *Varian Unity-200*; in ppm rel. to $SiMe_4$ as internal standard; in $CDCl_3$. IR: *FTIR Bruker IFS 88*; in CCl_4, $CHCl_3$, or as a liquid film between NaCl windows; in cm^{-1}. MS: *VG Analytical*, Manchester, *ZAB-EQ* (*BEQQ* config.). Microanalyses: *Perkin-Elmer 240c*.

2-(4-Methoxybenzyl)cycloalkanones **5**–**8**: *General Procedure.* An equimolar mixture of the appropriate cycloalkanone, and pyrrolidine was dissolved in benzene (300 ml for 1 mol of cycloalkanone), and a catalytic amount of TsOH was added. The mixture was heated and H_2O removed under azeotropic conditions. The volatiles were evaporated, and the residue was distilled *in vacuo*. B.p. of enamines and their yields: N-*(cyclohex-1-en-1-yl)pyrrolidine*, b.p. 113°/2.4 kPa, 64.2%; N-*(cyclopent-1-en-1-yl)pyrrolidine*, b.p. 93°/2.1 kPa, 64.7%; N-*(cyclo-*

hept-1-en-1-yl)pyrrolidine, b.p. 100°/2.1 kPa, 69.5%; N-*(6-methylcyclohex-1-en-1-yl)pyrrolidine*, b.p. 114°/2.0 kPa, 62.3%. To the soln. of the enamine (0.2 mol) in dioxane (30 ml), 4-methoxybenzyl chloride (0.22 mol) in dioxane (35 ml) was added. The mixture was refluxed at 120° for 5 h, H_2O (50 ml) added, and the mixture heated for an additional h. Dioxane was evaporated, the residue diluted with H_2O and extracted with Et_2O (10 × 100 ml), the combined org. extract washed with 5% HCl soln., sat. aq. $NaHCO_3$ soln., and H_2O until the mixture was neutral, dried (Na_2SO_4), and evaporated, and the residue purified by CC (light petroleum ether/Et_2O 1:1).

2-(4-Methoxybenzyl)cyclohexan-1-one (**5**): Yield 52.5%. IR (CCl_4): 2840, 1710, 1694, 1250. ^{1}H-NMR: 1.50–2.13 (*m*, 9 H); 2.36 (*dd*, *J* = 8.6, 13.5, 1 H); 3.16 (*dd*, *J* = 4.4, 13.5, 1 H); 3.78 (*s*, 3 H); 6.81 (*m*, 2 H); 7.07 (*m*, 2 H). MS: 218 (21, M^+), 121 (100). Anal. calc. for $C_{14}H_{18}O_2$ (218.28): C 77.03, H 8.31; found: C 77.11, H 8.29.

2-(4-Methoxybenzyl)cyclopentan-1-one (**6**): Yield 75.8%. IR (CCl_4): 2840, 1745, 1254. ^{1}H-NMR: 1.20–2.44 (*m*, 7 H); 2.51 (*dd*, *J* = 3.5, 13.5, 1 H); 3.06 (*dd*, *J* = 9.0, 13.5, 1 H); 3.78 (*s*, 3 H); 6.81 (*m*, 2 H); 7.09 (*m*, 2 H). MS: 204 (21, M^+), 147 (3), 121 (100), 108 (10), 91 (6), 77 (8). Anal. calc. for $C_{13}H_{16}O_2$ (204.26): C 76.44, H 7.90; found: C 76.41, H 7.89.

2-(4-Methoxybenzyl)cycloheptan-1-one (**7**): Yield 40.4%. IR (CCl_4): 1710, 1615, 1521, 1259. ^{1}H-NMR: 1.21–1.92 (*m*, 11 H); 2.50 (*dd*, *J* = 8.1, 13.4, 1 H); 3.00 (*dd*, *J* = 5.6, 13.4, 1 H); 3.81 (*s*, 3 H); 6.81 (*m*, 2 H); 7.07 (*m*, 2 H). MS: 232 (18, M^+), 135 (34), 121 (100), 77 (21). Anal. calc. for $C_{15}H_{20}O_2$ (232.31): C 77.55, H 8.68; found: C 77.59, H 8.69.

2-(4-Methoxybenzyl)-6-methylcyclohexan-1-one (**8**): Yield 36.6%. IR (CCl_4): 2838, 1712, 1612, 1584, 1250. ^{1}H-NMR: 1.02 (*d*, *J* = 6.3, 3 H); 1.31 (*m*, 2 H); 1.68 (*m*, 2 H); 2.07 (*m*, 2 H); 2.32–2.59 (*m*, 2 H); 2.34 (*dd*, *J* = 8.4, 13.6, 1 H); 3.15 (*dd*, *J* = 4.6, 13.6, 1 H); 3.76 (*s*, 3 H); 6.80 (*m*, 2 H); 7.07 (*m*, 2 H). MS: 232 (22, M^+), 121 (100). Anal. calc. for $C_{15}H_{20}O_2$ (232.31): C 77.55, H 8.68; found: C 77.51, H 8.67.

2-(4-Hydroxybenzyl)cycloalkanones **9–12**: *General Procedure*. To a mixture of methoxy derivative **5–8** (23.4 mmol) in Ac_2O (12 g), azeotropic HBr/H_2O (12 g) was added at r.t. After 4 h of heating to 140°, the mixture was cooled, H_2O (80 ml) added, the mixture neutralized by addition of powdered $CaCO_3$ (93.2 g), and the precipitate filtered off and washed with H_2O and Et_2O. The aq. layer was extracted with Et_2O (5 × 100 ml), the combined org. extract dried (Na_2SO_4), and evaporated, and the residue submitted to CC (light petroleum ether/Et_2O 1:2).

2-(4-Hydroxybenzyl)cyclopentan-1-one (**10**): Yield 39.4%. IR ($CHCl_3$): 3605, 1739, 1615, 1598, 1520, 1250. ^{1}H-NMR: 1.25–2.46 (*m*, 8 H); 2.51 (*dd*, *J* = 9.3, 13.6, 1 H); 3.03 (*dd*, *J* = 3.9, 13.6, 1 H); 6.46 (br. *s*, 1 H); 6.77 (*m*, 2 H); 7.07 (*m*, 2 H). MS: 190 (29, M^+), 107 (100), 94 (15). Anal. calc. for $C_{12}H_{14}O_2$ (190.23): C 75.76, H 7.42; found: C 75.80, H 7.43.

2-(4-Hydroxybenzyl)cyclohexan-1-one (**9**): Yield 55.2%. M.p. 96–97°. IR ($CHCl_3$): 3605, 1795, 1706, 1258. ^{1}H-NMR: 1.20–2.65 (*m*, 10 H); 3.14 (*m*, 1 H); 5.83 (br. *s*, 1 H); 6.74 (*m*, 2 H); 6.97 (*m*, 2 H). MS: 204 (29, M^+), 175 (15), 107 (100), 94 (10). Anal. calc. for $C_{13}H_{16}O_2$ (204.26): C 76.44, H 7.90; found: C 77.18, H 8.11.

2-(4-Hydroxybenzyl)cycloheptan-1-one (**11**): Yield 50.2%. IR (CCl_4): 3611, 1700, 1659, 1615, 1516, 1259. ^{1}H-NMR: 1.25–1.38, 1.76–1.90 (2*m*, 8 H); 2.45 (*m*, 2 H); 2.78 (*m*, 1 H); 2.52 (*dd*, *J* = 8.0, 13.9, 1 H); 2.97 (*dd*, *J* = 6.3, 13.9, 1 H); 5.80 (br. *s*, 1 H); 6.73 (*m*, 2 H); 7.00 (*m*, 2 H). MS: 218 (34, M^+), 175 (23), 161 (18), 107 (100). Anal. calc. for $C_{14}H_{18}O_2$ (218.28): C 77.03, H 8.31; found: C 76.92, H 8.29.

2-(4-Hydroxybenzyl)-6-methylcyclohexan-1-one (**12**): Yield 31.1%. IR (CCl_4): 3611, 1712, 1703, 1614, 1596, 1515. ^{1}H-NMR: 1.02 (*d*, *J* = 6.4, 3 H); 1.20–1.47 (*m*, 2 H); 1.63 (*ddt*, *J* = 3.3, 3.3, 12.4, 13.4, 1 H); 1.80 (*m*, 1 H); 2.09 (*m*, 2 H); 2.33 (*dd*, *J* = 8.3, 13.7, 1 H); 2.46 (*m*, 2 H); 3.14 (*dd*, *J* = 4.8, 13.7, 1 H); 5.38 (br. *s*, 1 H); 6.75 (*m*, 2 H); 7.02 (*m*, 2 H). MS: 218 (40, M^+), 107 (100). Anal. calc. for $C_{14}H_{18}O_2$ (218.28): C 77.03, H 8.31; found: C 77.17, H 8.37.

Ethylene Acetals **13** *and* **14**: *General Procedure*. To the mixture of ketone **9** or **10** (9.8 mmol) and benzene (50 ml), ethylene glycol (2 ml) and a catalytic amount of TsOH were added. The mixture was heated 6 h under azeotropic removal of H_2O. Benzene was distilled off and the residue separated on CC (light petroleum ether/Et_2O 5:1).

2-(4-Hydroxybenzyl)cyclohexan-1-one Ethylene Acetal (**13**): Yield 90.5%. M.p. 86–88°. IR (CCl_4): 3612, 3400. ^{1}H-NMR: 1.50–3.15 (*m*, 11 H); 3.95 (*m*, 4 H); 6.68 (*m*, 2 H); 7.00 (*m*, 2 H). MS: 248 (35, M^+). Anal. calc. for $C_{15}H_{20}O_3$ (248.31): C 72.55, H 8.12; found: C 72.69, H 8.12.

2-(4-Hydroxybenzyl)cyclopentan-1-one Ethylene Acetal (**14**): Yield 97.4%. IR (CCl_4): 3615, 1260, 1226, 1175, 1110, 1048, 978. ^{1}H-NMR: 1.11–2.93 (*m*, 9 H); 3.90 (*m*, 4 H); 6.68 (*m*, 2 H); 7.00 (*m*, 2 H). MS: 234 (35, M^+), 205 (11), 190 (26), 146 (16), 133 (11), 107 (100), 99 (60). Anal. calc. for $C_{14}H_{18}O_3$ (234.28): C 71.77, H 7.74; found: C 71.68, H 7.71.

Ethyl N-*(2-Chloroethyl)carbamate* (**15**). To 2-aminoethanol (100 g, 1.64 mol), conc. HCl soln. (149 ml) was added under stirring and cooling to 0°. The mixture was diluted with toluene (290 ml), and H_2O was distilled off under azeotropic conditions. The mixture was cooled to 75° (crystallization at 70–74°) and $SOCl_2$ (136 ml) added under a reflux condenser. The mixture was refluxed for 1 h at 85°. Excess $SOCl_2$ was distilled off and a flow of N_2

passed for 4 h through the mixture under a reflux condenser at 90–100° (removal of excess SO_2). The mixture was cooled to 50°, and under stirring, H_2O (105 ml) was added until (2-chloroethyl)amino monohydrochloride was dissolved. Ethyl chloroformate (187 g, 1.72 mmol) was added in portions at 50°. Under cooling, NaOH (45% aq. soln.) was added to the mixture until the pH was 12 (H_2O layer). The org. layer was washed with brine (2 × 100 ml) and evaporated and the residue distilled *in vacuo*: 122.99 g (49.6%) of **15**. B.p. 115–120°/1.9 kPa. IR ($CHCl_3$): 3455, 3350, 1718, 1517, 1256. ^{1}H-NMR: 1.26 (*t*, *J* = 7.1, 3 H); 3.49–3.66 (*m*, 4 H); 4.13 (*q*, *J* = 7.1, 2 H); 5.23 (br. *s*, 1 H). MS: 151 (11, M^+), 102 (100). Anal. calc. for $C_5H_{10}ClNO_2$ (151.60): C 39.61, H 6.65, Cl 23.39, N 9.24; found: C 39.70, H 6.62, Cl 23.42, N 9.20.

Juvenoids **16–18**: *General Procedure*. To intermediate **10**, **11**, or **12** (11.0 mmol) in DMF (30 ml), NaH (0.6 g, 12.5 mmol) was added under cooling and stirring. After 1 h of stirring at r.t., **15** (4.3 g, 28.4 mmol) was added and the mixture heated to 150° for 5 h. The mixture was cooled, diluted with 5% HCl soln., and extracted with light petroleum ether/Et_2O 1:1 (5 × 100 ml). The combined org. layer was washed with H_2O, dried (Na_2SO_4), and evaporated and the residue submitted to CC (light petroleum ether/Et_2O 2:1).

Ethyl N-{*2-[4-(2-Oxocyclopent-1-ylmethyl)phenoxy]ethyl*}*carbamate* (**16**): Yield 57.5%. IR ($CHCl_3$): 3456, 1712, 1610, 1582, 1519, 1250. ^{1}H-NMR: 1.25 (*t*, *J* = 7.0, 3 H); 1.32–2.30 (*m*, 7 H); 2.52 (*dd*, *J* = 8.8, 13.9, 1 H); 3.06 (*dd*, *J* = 4.2, 13.9, 1 H); 3.57 (br. *q*, *J* = 5.5, 2 H); 4.01 (*t*, *J* = 5.4, 2 H); 4.13 (*q*, *J* = 7.0, 2 H); 5.14 (br. *s*, 1 H); 6.81 (*m*, 2 H); 7.08 (*m*, 2 H). MS: 305 (10, M^+), 259 (10), 176 (26), 133 (10), 116 (100), 107 (27), 88 (47). Anal. calc. for $C_{17}H_{23}NO_4$ (305.36): C 66.86, H 7.59, N 4.59; found: C 66.91, H 7.57, N 4.51.

Ethyl N-{*2-[4-(2-Oxocyclohept-1-ylmethyl)phenoxy]ethyl*}*carbamate* (**17**): Yield 73.8%. IR (CCl_4): 3464, 1726, 1705, 1612, 1585, 1510, 1243, 1220. ^{1}H-NMR: 1.17–1.38, 1.68–1.89 (2*m*, 8 H); 1.24 (*t*, *J* = 7.0, 3 H); 2.43 (*m*, 2 H); 2.51 (*dd*, *J* = 8.3, 13.9, 1 H); 2.76 (*m*, 1 H); 3.00 (*dd*, *J* = 5.9, 13.9, 1 H); 3.57 (br. *q*, *J* = 5.3, 2 H); 4.00 (*t*, *J* = 5.1, 2 H); 4.12 (br. *q*, *J* = 7.0, 2 H); 5.14 (br. *s*, 1 H); 6.80 (*m*, 2 H); 7.06 (*m*, 2 H). MS: 333 (16, M^+), 176 (11), 116 (100), 107 (24), 88 (65). Anal. calc. for $C_{19}H_{27}NO_4$ (333.42): C 68.44, H 8.16, N 4.20; found: C 68.35, H 8.12, N 4.22.

Ethyl N-{*2-[4-(3-Methyl-2-oxocyclohex-1-ylmethyl)phenoxy]ethyl*}*carbamate* (**18**): Yield 41.0%. IR ($CHCl_3$): 3455, 1709, 1611, 1584, 1520, 1512, 1245. ^{1}H-NMR: 1.02 (*d*, *J* = 6.3, 3 H); 1.16–1.85 (*m*, 6 H); 1.23 (*t*, *J* = 7.2, 3 H); 2.07 (*m*, 1 H); 2.34 (*dd*, *J* = 8.3, 13.6, 1 H); 2.46 (*m*, 1 H); 3.15 (*dd*, *J* = 4.9, 13.6, 1 H); 3.56 (br. *q*, *J* = 5.4, 2 H); 4.00 (*t*, *J* = 5.1, 2 H); 4.12 (*q*, *J* = 7.2, 2 H); 5.09 (br. *s*, 1 H); 6.79 (*m*, 2 H); 7.08 (*m*, 2 H). MS: 333 (8, M^+), 256 (11), 149 (16), 116 (100), 88 (50), 71 (32), 57 (48), 43 (61). Anal. calc. for $C_{19}H_{27}NO_4$ (333.42): C 68.44, H 8.16, N 4.20; found: C 68.49, H 8.20, N 4.15.

Juvenoids **19–21**: *General Procedure A*. A mixture of ketone **16**, **17**, or **18** (3.33 mmol), benzene (20 ml), ethylene glycol (1 ml, 17.95 mmol), and a catalytic amount of TsOH was heated for 12 h under azeotropic H_2O removal. The volatiles were evaporated, and the residue was purified by CC (light petroleum ether/Et_2O 5:1).

Ethyl N-{*2-{4-[2,2-(Ethylenedioxy)cyclopent-1-ylmethyl]phenoxy}ethyl*}*carbamate* (**19**): Yield 52.8%. IR (CCl_4): 3463, 1726, 1611, 1583, 1508, 1243, 1220, 1043. ^{1}H-NMR: 1.26–1.83 (*m*, 6 H); 1.24 (*t*, *J* = 7.1, 3 H); 2.18 (*m*, 1 H); 2.40 (*dd*, *J* = 10.5, 13.5, 1 H); 2.82 (*dd*, *J* = 4.3, 13.5, 1 H); 3.56 (br. *q*, *J* = 5.5, 2 H); 3.89 (*m*, 4 H); 4.00 (*t*, *J* = 5.2, 2 H); 4.12 (*q*, *J* = 7.1, 2 H); 5.16 (br. *s*, 1 H); 6.79 (*m*, 2 H); 7.10 (*m*, 2 H). MS: 349 (16, M^+), 116 (100), 99 (42), 61 (32). Anal. calc. for $C_{19}H_{27}NO_5$ (349.42): C 65.31, H 7.79, N 4.01; found: C 65.33, H 7.72, N 4.12.

Ethyl N-{*2-[4-[2,2-(Ethylenedioxy)cyclohept-1-ylmethyl]phenoxy}ethyl*}*carbamate* (**20**): Yield 73.6%. IR (CCl_4): 3462, 1725, 1612, 1585, 1510, 1244, 1220, 1152, 1102, 1047. ^{1}H-NMR: 1.21 (*t*, *J* = 7.0, 3 H); 1.24–1.70 (*m*, 10 H); 1.99 (*ddt*, *J* = 2.6, 2.6, 8.8, 11.4, 1 H); 2.25 (*dd*, *J* = 11.4, 13.6, 1 H); 2.92 (*dd*, *J* = 3.0, 13.6, 1 H); 3.56 (br. *q*, *J* = 5.1, 2 H); 3.89–4.02 (*m*, 4 H); 3.98 (*t*, *J* = 5.1, 2 H); 4.12 (*q*, *J* = 7.0, 2 H); 5.21 (br. *s*, 1 H); 6.80 (*m*, 2 H); 7.09 (*m*, 2 H). MS: 377 (8, M^+), 235 (13), 155 (13), 116 (61), 99 (35). Anal. calc. for $C_{21}H_{31}NO_5$ (377.47): C 66.82, H 8.28, N 3.71; found: C 66.89, H 8.23, N 3.70.

Ethyl N-{*2-{4-[2,2-(Ethylenedioxy)-3-methylcyclohex-1-ylmethyl]phenoxy}ethyl*}*carbamate* (**21**): Yield 68.9%. IR (CCl_4): 3462, 1726, 1612, 1585, 1510, 1243, 1258, 1095. ^{1}H-NMR: 0.89 (*d*, *J* = 6.4, 3 H); 1.24 (*t*, *J* = 7.1, 3 H); 1.24–1.80 (*m*, 8 H); 2.11 (*dd*, *J* = 11.0, 12.9, 1 H); 2.96 (*dd*, *J* = 2.9, 12.9, 1 H); 3.56 (br. *q*, *J* = 5.3, 2 H); 4.00 (*t*, *J* = 5.1, 2 H); 4.10 (*m*, 4 H); 4.14 (br. *q*, *J* = 7.1, 2 H); 5.10 (br. *s*, 1 H); 6.75 (*m*, 2 H); 7.02 (*m*, 2 H). MS: 377 (24, M^+), 320 (32), 155 (14), 116 (71), 113 (100), 107 (14), 88 (32). Anal. calc. for $C_{21}H_{31}NO_5$ (377.47): C 66.82, H 8.28, N 3.71; found: C 66.78, H 8.21, N 3.62.

Juvenoids **22–27**: *General Procedure B*. To a soln. of ketone **16**, **17**, or **18** (4.38 mmol) in MeOH (40 ml), $NaBH_4$ (0.7 g, 18.48 mmol) was added at 0° under stirring (TLC monitoring). The mixture was diluted with brine (25 ml) and extracted with Et_2O (5 × 100 ml), the combined org. layer dried (Na_2SO_4) and evaporated and the isomer mixture separated by CC (light petroleum ether/Et_2O 1:1).

cis-*Ethyl* N-{*2-[4-(2-Hydroxycyclopent-1-ylmethyl)phenoxy]ethyl*}*carbamate* (**22**): Yield 23.4%. IR (CCl_4): 3617, 3465, 1728, 1521, 1244, 1112, 987. ^{1}H-NMR: 1.24 (*t*, *J* = 7.3, 3 H); 1.38–1.62 (*m*, 7 H); 2.61 (*dd*, *J* = 7.6, 13.7,

1 H); 2.79 (*dd*, *J* = 7.8, 13.7, 1 H); 3.57 (br. *q*, *J* = 5.4, 2 H); 4.01 (*t*, *J* = 5.1, 2 H); 4.07 (*m*, 1 H); 4.13 (*q*, *J* = 7.3, 2 H); 5.12 (br. *s*, 1 H); 6.81 (*m*, 2 H); 7.14 (*m*, 2 H). MS: 307 (10, M^+), 116 (100), 107 (16), 88 (44). Anal. calc. for $C_{17}H_{25}NO_4$ (307.38): C 66.42, H 8.20, N 4.56; found: C 66.39, H 8.15, N 4.49.

trans-*Ethyl* N-{*2-[4-(2-Hydroxycyclopent-1-ylmethyl)phenoxy]ethyl*}*carbamate* (**23**): Yield 68.2%. IR (CCl_4): 3611, 3470, 1731, 1523, 1249, 1112, 1071. ^{1}H-NMR: 1.25 (*t*, *J* = 7.2, 3 H); 1.40–1.86 (*m*, 7 H); 2.47 (*dd*, *J* = 8.1, 13.7, 1 H); 2.70 (*dd*, *J* = 6.9, 13.7, 1 H); 3.56 (br. *q*, *J* = 5.3, 2 H); 3.88 (br. *q*, *J* = 6.9, 6.9, 6.9, 1 H); 4.01 (*t*, *J* = 5.4, 2 H); 4.12 (*q*, *J* = 7.2, 2 H); 5.16 (br. *s*, 1 H); 6.81 (*m*, 2 H); 7.14 (*m*, 2 H). MS: 307 (8, M^+), 116 (100), 107 (18), 88 (40). Anal. calc. for $C_{17}H_{25}NO_4$ (307.38): C 66.42, H 8.20, N 4.56; found: C 66.38, H 8.26, N 4.57.

cis-*Ethyl* N-{*2-[4-(2-Hydroxycyclohept-1-ylmethyl)phenoxy]ethyl*}*carbamate* (**24**): Yield 66.0%. IR (CCl_4): 3616, 3461, 1725, 1612, 1585, 1510, 1242, 1070, 924. ^{1}H-NMR: 1.25 (*t*, *J* = 7.0, 3 H); 1.30–1.84 (*m*, 11 H); 2.51 (*dd*, *J* = 8.3, 13.7, 1 H); 2.72 (*dd*, *J* = 7.1, 13.7, 1 H); 3.56 (br. *q*, *J* = 5.3, 2 H); 3.86 (*dt*, *J* = 2.6, 5.3, 5.3, 1 H); 4.00 (*t*, *J* = 5.1, 2 H); 4.11 (*q*, *J* = 7.0, 2 H); 5.21 (br. *s*, 1 H); 6.80 (*m*, 2 H); 7.10 (*m*, 2 H). MS: 335 (20, M^+), 202 (11), 176 (19), 133 (11), 116 (100), 107 (20), 88 (30). Anal. calc. for $C_{19}H_{29}NO_4$ (335.43): C 68.03, H 8.71, N 4.18; found: C 67.99, H 8.68, N 4.20.

trans-*Ethyl* N-{*2-[4-(2-Hydroxycyclohept-1-ylmethyl)phenoxy]ethyl*}*carbamate* (**25**): Yield 10.7%. IR (CCl_4): 3615, 3460, 1725, 1711, 1612, 1585, 1510, 1244, 1225, 1008. ^{1}H-NMR: 1.20–1.84 (*m*, 11 H); 1.24 (*t*, *J* = 7.0, 3 H); 2.38 (*dd*, *J* = 9.0, 13.5, 1 H); 2.96 (*dd*, *J* = 4.7, 13.5, 1 H); 3.53 (*ddd*, *J* = 3.9, 6.8, 8.3, 2 H); 3.57 (br. *q*, *J* = 5.1, 2 H); 4.01 (*t*, *J* = 5.1, 2 H); 4.12 (br. *q*, *J* = 7.1, 2 H); 5.14 (br. *s*, 1 H); 6.81 (*m*, 2 H); 7.11 (*m*, 2 H). MS: 335 (24, M^+), 202 (10), 176 (19), 133 (10), 116 (100), 107 (23), 88 (34). Anal. calc. for $C_{19}H_{29}NO_4$ (335.43): C 68.03, H 8.71, N 4.18; found: C 68.10, H 8.72, N 4.08.

Ethyl N-{*2-[4-(*c*-2-Hydroxy-3-methylcyclohex-*r*-1-ylmethyl)phenoxy]ethyl*}*carbamate* (**26**): Yield 67.9%. IR ($CHCl_3$): 3629, 3620 (sh), 3455, 1713, 1612, 1585, 1521, 1510, 1241, 972. ^{1}H-NMR: 0.92 (*d*, *J* = 6.3, 3 H); 1.18–1.46 (*m*, 6 H); 1.24 (*t*, *J* = 7.1, 3 H); 1.69 (*m*, 1 H); 1.77 (*m*, 1 H); 2.51 (*dd*, *J* = 6.9, 13.4, 1 H); 2.66 (*dd*, *J* = 8.1, 13.4, 1 H); 3.57 (br. *q*, *J* = 5.2, 2 H); 3.59 (br. *t*, *J* = 2.0, 1 H); 4.01 (*t*, *J* = 5.1, 2 H); 4.12 (br. *q*, *J* = 7.1, 2 H); 5.09 (br. *s*, 1 H); 6.81 (*m*, 2 H); 7.10 (*m*, 2 H). MS: 335 (5, M^+), 279 (8), 256 (11), 149 (24), 116 (100), 88 (37). Anal. calc. for $C_{19}H_{29}NO_4$ (335.43): C 68.03, H 8.71, N 4.18; found: C 68.09, H 8.80, N 4.19.

Ethyl N-{*2-[4-(*t*-2-Hydroxy-3-methylcyclohex-*r*-1-ylmethyl)phenoxy]ethyl*}*carbamate* (**27**): Yield 25.3%. IR ($CHCl_3$): 3631, 3596, 3455, 1713, 1611, 1585, 1519, 1510, 1242, 1035. ^{1}H-NMR: 0.86–1.66 (*m*, 8 H); 1.02 (*d*, *J* = 6.6, 3 H); 1.23 (*t*, *J* = 7.1, 3 H); 2.32 (*dd*, *J* = 9.0, 13.4, 1 H); 2.84 (*t*, *J* = 9.7, 1 H); 3.10 (*dd*, *J* = 3.9, 13.4, 1 H); 3.56 (br. *q*, *J* = 5.1, 2 H); 4.01 (*t*, *J* = 5.1, 2 H); 4.12 (*q*, *J* = 7.1, 2 H); 5.08 (br. *s*, 1 H); 6.80 (*m*, H); 7.09 (*m*, 2 H). MS: 335 (6, M^+), 279 (10), 256 (6), 149 (24), 116 (100), 88 (35). Anal. calc. for $C_{19}H_{29}NO_4$ (335.43): C 68.03, H 8.71, N 4.18; found: C 68.15, H 8.75, N 4.24.

cis- *and* trans-*Ethyl* N-{*2-[4-(2-Methoxycyclohex-1-ylmethyl)phenoxy]ethyl*}*carbamates* **28** *and* **29**. To a soln. of *cis*-alcohol **3** (926.8 mg, 2.9 mmol) or *trans*-alcohol **4** (513.1 mg, 1.6 mmol) in Et_2O (20 ml), $BF_3 \cdot Et_2O$ (0.1 ml) and subsequently diazomethane (350 ml of Et_2O soln.) were added under stirring and cooling to 0°. After 4 h, the mixture was washed with sat. aq. $NaHCO_3$ soln. (2 × 20 ml), the org. layer dried ($MgSO_4$) and evaporated, and the residue separated by CC (light petroleum ether/Et_2O 10:1) to yield **28** or **29**, resp.

28: 48.5 mg (5.0%). IR (CCl_4): 3462, 3358, 3062, 3032, 2823, 1726, 1612, 1585, 1511, 1243, 1221, 1176, 1097, 1089, 1047, 1014, 890. ^{1}H-NMR: 1.05–2.01 (*m*, 9 H); 1.24 (*t*, *J* = 7.1, 3 H); 2.46 (*dd*, *J* = 7.3, 13.4, 1 H); 2.66 (*dd*, *J* = 7.6, 13.4, 1 H); 3.16 (*dt*, *J* = 2.5, 2.5, 4.9, 1 H); 3.29 (*s*, 3 H); 3.57 (br. *q*, *J* = 5.4, 2 H); 4.01 (*t*, *J* = 5.1, 2 H); 4.13 (*q*, *J* = 7.1, 2 H); 5.15 (br. *s*, 1 H); 6.80 (*m*, 2 H); 7.08 (*m*, 2 H). MS: 335 (7, M^+), 116 (100), 88 (31). Anal. calc. for $C_{19}H_{29}NO_4$ (335.43): C 68.03, H 8.71, N 4.18; found: C 68.12, H 8.73, N 4.21.

29: 59.5 mg (11.1%). IR (CCl_4): 3463, 3360, 3062, 3032, 2820, 1726, 1612, 1585, 1509, 1242, 1219, 1176, 1119, 1103, 1097, 1048, 1014, 906, 892, 879. ^{1}H-NMR: 0.80–1.80 (*m*, 8 H); 1.24 (*t*, *J* = 7.1, 3 H); 2.13 (*m*, 1 H); 2.26 (*dd*, *J* = 9.0, 13.4, 1 H); 2.78 (*dt*, *J* = 9.4, 9.4, 4.4, 1 H); 3.09 (*dd*, *J* = 3.2, 13.4, 1 H); 3.39 (*s*, 3 H); 3.57 (br. *q*, *J* = 5.3, 2 H); 4.01 (*t*, *J* = 5.6, 2 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). MS: 335 (7, M^+), 116 (100), 88 (35). Anal. calc. for $C_{19}H_{29}NO_4$ (335.43): C 68.03, H 8.71, N 4.18; found: C 67.98, H 8.69, N 4.10.

Ethyl N-{*2-*{*4-*{*2,2-[(Propane-1,3-diyl)dioxy]cyclohex-1-ylmethyl*}*phenoxy*}*ethyl*}*carbamate* (**30**). A mixture of **1** (269.2 mg, 0.843 mmol), propane-1,3-diol (128.2 mg, 1.68 mmol), benzene (20 ml), and a catalytic amount of TsOH was heated under azeotropic removal of H_2O for 2 h. The volatiles were evaporated, and the residue was purified by CC (light petroleum ether/Et_2O 6:1): **30** (122.1 mg, 38.4%). IR (CCl_4): 3461, 1726, 1612, 1585, 1509, 1243, 1219, 1150, 1108, 1055. ^{1}H-NMR: 1.25 (*t*, *J* = 7.1, 3 H); 1.26–2.10 (*m*, 8 H); 1.83 (*m*, *J* = 5.5, 5.5, 5.5, 5.5, 2 H); 2.36 (*dd*, *J* = 8.7, 13.3, 1 H); 2.45 (*m*, 1 H); 3.15 (*dd*, *J* = 4.4, 13.3, 1 H); 3.20–3.40 (*m*, 4 H); 3.57 (*q*, *J* = 5.0, 2 H); 4.01 (*t*, *J* = 5.0, 2 H); 4.13 (*q*, *J* = 7.1, 2 H); 5.11 (br. *s*, 1 H); 6.80 (*m*, 2 H); 7.07 (*m*, 2 H). MS: 377 (17, M^+), 331 (21), 288 (16), 155 (19), 116 (60), 113 (100), 88 (20). Anal. calc. for $C_{21}H_{31}NO_5$ (377.47): C 66.82, H 8.28, N 3.71; found: C 66.78, H 8.26, N 3.69.

2-(4-Hydroxybenzyl)cyclohexan-1-one Ethylene Thioacetal (**31**). To a soln. of **9** (1.051 g, 5.1 mmol) in AcOH (20 ml) heated shortly to the boiling point, ethanedithiol (0.485 g, 5.1 mmol) and $BF_3 \cdot Et_2O$ (1 ml) were added through a septum. The mixture was stirred for 4 h, then diluted with H_2O (50 ml) and neutralized by addition of powdered K_2CO_3. The solid phase was filtered off and the filtrate extracted with Et_2O (3 × 30 ml). The combined org. layer was washed with H_2O, dried (Na_2SO_4), and evaporated and the residue purified by CC (light petroleum ether/Et_2O 2:1): 1.43 g (99.1%) of **31**. IR (CCl_4): 3611, 2931, 2858, 1614, 1596, 1513, 1254, 1224. ^{1}H-NMR: 1.00–2.05 (*m*, 9 H); 2.34 (*dd*, *J* = 10.7, 13.3, 1 H); 3.27–3.31 (*m*, 4 H); 3.30 (*dd*, *J* = 10.7, 13.3, 1 H); 6.75 (*m*, 2 H); 7.05 (*m*, 2 H). MS: 280 (73, M^+), 252 (16), 187 (39), 160 (16), 131 (68), 107 (100), 77 (16). Anal. calc. for $C_{15}H_{20}OS_2$ (280.43): C 64.24, H 7.19, S 22.86; found: C 64.28, H 7.23, S 22.91.

Ethyl N-{2-{4-[2,2-(Ethylenedithio)cyclohex-1-ylmethyl]phenoxy}ethyl}carbamate (**32**). To a soln. of **31** (1.43 g, 5.1 mmol) in DMF (20 ml), NaH (0.3 g, 6.3 mmol) was added under stirring and cooling to 0°. After 1 h, **15** (1.56 g, 10.3 mmol) was added and the mixture heated to 150° for 8 h. The mixture was diluted with 5% HCl soln. (50 ml) and extracted with light petroleum ether/Et_2O 1:1 (3 × 50 ml). The combined org. layer was washed with H_2O, dried (Na_2SO_4), and evaporated and the residue purified by CC (light petroleum ether/Et_2O 6:1): 1.020 g (50.1%) of **32**. B.p. 84–88°. IR (CCl_4): 3462, 3358, 1728, 1612, 1585, 1507, 1242, 1219. ^{1}H-NMR: 1.25 (*t*, *J* = 7.1, 3 H); 1.26–2.10 (*m*, 9 H); 2.35 (*dd*, *J* = 10.8, 13.3, 1 H); 3.20–3.40 (*m*, 4 H); 3.35 (*dd*, *J* = 2.5, 13.3, 1 H); 3.57 (br. *q*, *J* = 5.3, 2 H); 4.01 (*t*, *J* = 5.3, 2 H); 4.13 (br. *q*, *J* = 7.1, 2 H); 5.12 (br. *s*, 1 H); 6.80 (*m*, 2 H); 7.10 (*m*, 2 H). MS: 395 (19, M^+), 349 (8), 173 (15), 116 (100), 88 (20). Anal. calc. for $C_{20}H_{29}NO_3S_2$ (395.56): C 60.72, H 7.39, N 3.54, S 16.21; found: C 60.79, H 7.37, N 3.50, S 16.24.

cis-*2-(4-Methoxybenzyl)cyclohexan-1-ol* (**33**). To a stirred suspension of $LiAlH_4$ (1.9 g, 50.1 mmol) in Et_2O (25 ml), a soln. of **5** (4.1 g, 18.8 mmol) in Et_2O (25 ml) was added dropwise. After 4 h of stirring at r.t., H_2O (1.9 ml), 5% NaOH soln. (1.9 ml), and H_2O (5.7 ml) were added subsequently. The solid was filtered off and the filtrate extracted with Et_2O (3 × 50 ml). The combined layer was dried (Na_2SO_4) and evaporated and the residue separated by CC (light petroleum ether/Et_2O 5:1): 1.290 g (31.2%) of **33** (the corresponding *trans*-isomer was a by-product, not identified). IR (CCl_4): 3630, 1615, 1521, 1253. ^{1}H-NMR: 1.28–1.82 (*m*, 9 H); 2.48 (*dd*, *J* = 7.4, 13.5, 1 H); 2.66 (*dd*, *J* = 7.4, 13.5, 1 H); 3.78 (*m*, 1 H); 3.78 (*s*, 3 H); 6.82 (*m*, 2 H); 7.10 (*m*, 2 H). MS: 220 (26, M^+), 202 (34), 134 (11), 121 (100). Anal. calc. for $C_{14}H_{20}O_2$ (220.30): C 76.32, H 9.15; found: C 76.29, H 9.11.

4-(Cyclohexylmethyl)phenol (**35**). A mixture of **33** (5.717 g, 26.0 mmol) and 85% H_3PO_4 soln. (5.0 ml) was heated to 100° under stirring for 4 h. The mixture was cooled and diluted with Et_2O/H_2O 1:1 (100 ml), and powdered $NaHCO_3$ (19 g) was added. The solid was filtered off and the filtrate washed with H_2O and dried (Na_2SO_4). The volatiles were evaporated to give 3.91 g of crude olefins. This crude mixture in hexane (20 ml) was added to $Pd/CaCO_3$ (0.226 g). After 12 h of hydrogenation (H_2 consumption 433 ml), the mixture was diluted with Et_2O and filtered. The volatiles were distilled off using a classical distillation apparatus, and the residue was purified by CC (light petroleum ether/Et_2O 20:1): 5.126 g (96.7%) of 1-(cyclohexylmethyl)-4-methoxybenzene (**34**). The mixture of **34** (5.973 g, 29.2 mmol) and $BClH_2 \cdot Me_2S$ (3.23 g, 29.2 mmol) in benzene (60 ml) was refluxed under Ar for 24 h. The mixture was cooled, diluted with sat. aq. NH_4Cl soln. (100 ml), and extracted with Et_2O (3 × 100 ml), the combined org. layer washed with brine, dried (Na_2SO_4), and evaporated, and the residue purified by CC (light petroleum ether/Et_2O 20:1): 2.159 g (38.8% from **33**) of **35**. IR (CCl_4): 3612, 1614, 1597, 1515, 1224. ^{1}H-NMR: 1.20–1.75 (*m*, 11 H); 2.40 (*d*, *J* = 7.0, 2 H); 6.74 (*m*, 2 H); 7.00 (*m*, 2 H). MS: 190 (29, M^+), 145 (11), 107 (100). Anal. calc. for $C_{13}H_{18}O$ (190.27): C 82.06, H 9.53; found: C 82.17, H 9.52.

Ethyl N-{2-[4-(Cyclohexylmethyl)phenoxy]ethyl}carbamate (**36**). To a soln. of **35** (1.954 g, 10.27 mmol) in DMF (40 ml), NaH (0.493 g, 10.27 mmol) was added. After 1 h of stirring at r.t., **15** (3.157 g, 20.8 mmol) in DMF (10 ml) was added and the mixture heated to 150° for 4 h. The cooled mixture was diluted with 5% HCl soln., extracted with light petroleum ether/Et_2O 1:1, the combined org. layer washed with H_2O, dried (Na_2SO_4), and evaporated, and the residue purified by CC (light petroleum ether/Et_2O 6:1): 0.3 g (9.6%) of **36**. IR (CCl_4): 3462, 1726, 1612, 1585, 1510, 1243, 1220, 1070. ^{1}H-NMR: 0.80–1.62 (*m*, 11 H); 1.24 (*t*, *J* = 7.0, 3 H); 2.41 (*d*, *J* = 7.1, 2 H); 3.56 (br. *q*, *J* = 5.2, 2 H); 4.01 (*t*, *J* = 5.0, 2 H); 4.12 (*q*, *J* = 7.0, 2 H); 5.14 (br. *s*, 1 H); 6.79 (*m*, 2 H); 7.04 (*m*, 2 H). MS: 305 (5, M^+), 259 (35), 176 (92), 116 (100), 107 (52), 102 (24), 88 (37). Anal. calc. for $C_{18}H_{27}NO_3$ (305.41): C 70.78, H 8.91, N 4.59; found: C 70.72, H 8.89, N 4.61.

2-[4-(2-Hydroxyethoxy)benzyl]cyclohexan-1-one (**37**). A mixture of **9** (5.032 g, 24.6 mmol), MeOH (50 ml), and NaOH (1.085 g, 27.1 mmol) was stirred and refluxed for 1 h at 70°. MeOH was evaporated, and toluene (60 ml) and ethylene carbonate (6.435 g, 73.1 mmol) were added. The mixture was refluxed for 12 h, then cooled and washed with sat. aq. $NaHCO_3$ soln. and H_2O. The org. layer was dried (Na_2SO_4) and evaporated and the residue purified by CC (light petroleum ether/Et_2O 1:1): 5.432 g (88.8%) of **37**. IR (CCl_4): 3613, 1713, 1613, 1585, 1513, 1246, 1043. ^{1}H-NMR: 1.24–2.10 (*m*, 6 H); 2.36 (*dd*, *J* = 8.8, 13.4, 1 H); 2.46 (*m*, 3 H); 3.15 (*dd*, *J* = 4.4, 13.4, 1 H);

3.94 (*m*, 2 H); 4.06 (*m*, 2 H); 6.83 (*m*, 2 H); 7.07 (*m*, 2 H). MS: 248 (39, M^+), 151 (100), 107 (84). Anal. calc. for $C_{15}H_{20}O_3$ (248.31): C 72.55, H 8.12; found: C 72.57, H 8.14.

2-[4-(2-Oxocyclohex-1-ylmethyl)phenoxy]ethyl N-*Ethylcarbamate* (**38**). To a soln. of **37** (5.021 g, 20.2 mmol) in Et_3N (5 ml), ethyl isocyanate (2 g, 28.1 mmol) was added dropwise at r.t. and the stirred mixture heated to 50° for 4 h. Then, the mixture was cooled, diluted with $CHCl_3$ (10 ml), and washed with 5% HCl soln. and H_2O, the org. layer dried (Na_2SO_4) and evaporated, and the residue crystallized ($CHCl_2/Et_2O$): 3.28 g, (51.0%) of **38**. M.p. 101–102°. IR (CCl_4): 3458, 1731, 1714, 1615, 1585, 1511, 1245, 1223. ^{1}H-NMR: 1.15 (*t*, *J* = 7.3, 3 H); 1.22–2.13 (*m*, 6 H); 2.22–2.59 (*m*, 3 H); 2.36 (*dd*, *J* = 8.6, 13.4, 1 H); 3.15 (*dd*, *J* = 4.4, 13.4, 1 H); 3.22 (*dq*, *J* = 5.7, 7.3, 7.3, 7.3, 2 H); 4.22 (*m*, 2 H); 4.40 (*m*, 2 H); 4.81 (br. *s*, 1 H); 6.82 (*m*, 2 H); 7.07 (*m*, 2 H). MS: 319 (5, M^+), 248 (10), 116 (100). Anal. calc. for $C_{18}H_{25}NO_4$ (319.39): C 67.69, H 7.89, N 4.39; found: C 67.52, H 7.71, N 4.35.

2-{4-[2-(Ethylenedioxy)cyclohex-1-ylmethyl]phenoxy}ethyl N-*Ethylcarbamate* (**39**). From **38** (996.1 mg, 3.1 mmol) according to the *General Procedure A*: 681.6 mg (60.3%) of **39**. M.p. 93–94°. IR (CCl_4): 3459, 1730, 1613, 1585, 1511, 1245, 1224, 1156, 1088, 1054, 926. ^{1}H-NMR: 1.05–1.86 (*m*, 9 H); 1.14 (*t*, *J* = 7.3, 3 H); 2.20 (*dd*, *J* = 11.0, 13.4, 1 H); 2.98 (*dd*, *J* = 3.2, 13.4, 1 H); 3.22 (*m*, *J* = 6.8, 7.2, 7.2, 7.2, 2 H); 4.00 (*m*, 4 H); 4.13 (*m*, 2 H); 4.40 (*m*, 2 H); 4.75 (br. *s*, 1 H); 6.82 (*m*, 2 H); 7.07 (*m*, 2 H). MS: 363 (5, M^+), 116 (100), 99 (35). Anal. calc. for $C_{20}H_{29}NO_5$ (363.44): C 66.09, H 8.04, N 3.85; found: C 66.21, H 8.13, N 3.82.

cis- *and* trans-*2-[4-(2-Hydroxycyclohex-1-ylmethyl)phenoxy]ethyl* N-*Ethylcarbamates* (**40** and **41**, resp.). From **38** (1.9 g, 5.9 mmol) according to the *General Procedure B*. The isomeric alcohols were separated by CC: 0.771 g (40.6%) of **40** and 0.534 g (28.1%) of **41**.

40: M.p. 95–97°. IR ($CHCl_3$): 3616, 3453, 1718, 1612, 1584, 1511, 1235, 975. ^{1}H-NMR: 1.14 (*t*, *J* = 7.1, 3 H); 1.20–1.83 (*m*, 9 H); 2.48 (*dd*, *J* = 7.4, 13.7, 1 H); 2.66 (*dd*, *J* = 7.6, 13.7, 1 H); 3.23 (*m*, *J* = 5.5, 7.1, 2 H); 3.78 (*dt*, *J* = 2.2, 2.2, 4.2, 1 H); 4.13 (*m*, 2 H); 4.41 (*m*, 2 H); 4.72 (br. *s*, 1 H); 6.84 (*m*, 2 H); 7.10 (*m*, 2 H). MS: 321 (5, M^+), 116 (100). Anal. calc. for $C_{18}H_{27}NO_4$ (321.41): C 67.26, H 8.47, N 4.36; found: C 67.19, H 8.51, N 4.33.

41: M.p. 129–131°. IR ($CHCl_3$): 3609, 3451, 1718, 1612, 1584, 1522, 1511, 1029. ^{1}H-NMR: 0.82–1.69 (*m*, 8 H); 1.14 (*t*, *J* = 7.3, 3 H); 1.98 (*m*, 1 H); 2.32 (*dd*, *J* = 9.0, 13.5, 1 H); 3.08 (*dd*, *J* = 4.1, 13.5, 1 H); 3.23 (*m*, 2 H); 3.29 (*dt*, *J* = 9.5, 9.5, 4.2, 1 H); 4.13 (*m*, 2 H); 4.41 (*m*, 2 H); 4.78 (br. *s*, 1 H); 6.84 (*m*, 2 H); 7.10 (*m*, 2 H). MS: 321 (3, M^+), 116 (100). Anal. calc. for $C_{18}H_{27}NO_4$ (321.41): C 67.26, H 8.47, N 4.36; found: C 67.35, H 8.42, N 4.29.

2-[4-(2-Bromoethoxy)benzyl]cyclohexan-1-one (**42**). To a mixture of **9** (8.517 g, 41.7 mmol) and H_2O (57 ml), 1,2-dibromoethane (9.4 g, 50.0 mmol) and NaOH (1.59 g, 398 mmol) in H_2O (10 ml) were added. The stirred mixture was heated to 110° for 7 h. The mixture was cooled and extracted with Et_2O (4 × 100 ml), the combined org. extract dried (Na_2SO_4) and evaporated, and the residue purified by CC (light petroleum ether/Et_2O 3:1): 5.999 g (46.2%) of **42**. IR (CCl_4): 1713, 1612, 1584, 1512, 1241. ^{1}H-NMR: 1.15–2.15 (*m*, 6 H); 2.22–2.60 (*m*, 3 H); 2.37 (*dd*, *J* = 8.4, 13.4, 1 H); 3.16 (*dd*, *J* = 4.4, 13.4, 1 H); 3.62 (*t*, *J* = 6.3, 2 H); 4.27 (*t*, *J* = 6.3, 2 H); 6.83 (*m*, 2 H); 7.08 (*m*, 2 H). MS: 312 (25, $[M + 2]^+$), 310 (26, M^+), 215 (94), 213 (100), 133 (32), 121 (17), 109 (25), 107 (32). Anal. calc. for $C_{15}H_{19}BrO_2$ (311.22): C 57.89, H 6.15, Br 25.68; found: C 57.76, H 6.17, Br 25.71.

2-[4-(2-Aminoethoxy)benzyl]cyclohexan-1-one (**43**). To a soln. of **42** (10.46 g, 33.6 mmol) in THF (30 ml), liq. NH_3 (60 ml) was added and the mixture sealed in a vial. After 24 h standing at r.t., the vial was cooled and opened and NH_3 allowed to evaporate. The mixture was diluted with 5% HCl soln., then neutralized by addition of 5% aq. NaOH soln., and extracted with Et_2O (10 × 100 ml). The combined extract was dried (Na_2SO_4) and evaporated: 7.906 g (95.14%) of **43**. IR ($CHCl_3$): 3388, 1705, 1656, 1612, 1583, 1513, 1246. ^{1}H-NMR: 1.20–2.15 (*m*, 6 H); 2.27–2.59 (*m*, 3 H); 2.36 (*dd*, *J* = 8.5, 13.5, 1 H); 3.15 (*dd*, *J* = 4.5, 13.5, 1 H); 3.07 (*t*, *J* = 5.1, 2 H); 3.97 (*t*, *J* = 5.1, 2 H); 6.82 (*m*, 2 H); 7.07 (*m*, 2 H). MS: 247 (3, M^+), 107 (100). Anal. calc. for $C_{15}H_{21}NO_2$ (247.33): C 72.84, H 8.56, N 5.66; found: C 72.89, H 8.49, N 5.61.

N-*Ethyl* N′-{*2-[4-(2-Oxocyclohex-1-ylmethyl)phenoxy]ethyl*}*urea* (**44**). To a soln. of **43** (2.23 g, 9.0 mmol) in Et_3N (19 ml), ethyl isocyanate (0.96 g, 13.5 mmol) was added portionwise. The mixture was stirred at 50° for 2 h. The solid was dissolved in MeOH (10 ml), and $CHCl_3$ (10 ml) and the solvents were evaporated. The residue was purified by CC (Et_2O) and the product crystallized ($CHCl_3/Et_2O$): 0.895 g (31.2%) of **44**. M.p. 84–86°. IR ($CHCl_3$): 3446, 1706, 1663, 1649, 1612, 1562, 1540, 1512, 1244. ^{1}H-NMR: 1.13 (*t*, *J* = 7.2, 3 H); 1.25–2.15 (*m*, 6 H); 2.22–2.59 (*m*, 3 H); 2.36 (*dd*, *J* = 8.6, 13.7, 1 H); 3.15 (*dd*, *J* = 4.6, 13.7, 1 H); 3.20 (br. *q*, *J* = 7.1, 2 H); 3.58 (*t*, *J* = 5.0, 2 H); 4.00 (*t*, *J* = 5.0, 2 H); 4.55 (br. *s*, 1 H); 4.90 (br. *s*, 1 H); 6.79 (*m*, 2 H); 7.06 (*m*, 2 H). FAB-MS: 319 (39, $[M + 1]^+$), 115 (100). Anal. calc. for $C_{18}H_{26}N_2O_3$ (318.41): C 67.89, H 8.23, N 8.80; found: C 67.75, H 8.32, N 8.73.

N-*Ethyl* N′-{*2-{4-[2,2-(Ethylenedioxy)cyclohex-1-ylmethyl]phenoxy}ethyl*}*urea* (**45**). From **44** (297.6 mg, 0.9 mmol) according to the *General Procedure A*. The crude **45** was purified first by CC (3 g of Al_2O_3, act. IV, $CHCl_3$) and then by crystallization ($CHCl_3/Et_2O$): 263.9 mg (77.9%) of **45**. M.p. 153–156°. IR (CCl_4): 3448, 3381, 1666, 1648, 1560, 1538, 1240, 1156, 1086, 1055, 924. ^{1}H-NMR: 1.12 (*t*, *J* = 7.2, 3 H); 1.18–1.90 (*m*, 9 H); 2.20 (*dd*, *J* = 10.9, 13.4, 1 H); 2.98 (*dd*, *J* = 3.0, 13.4, 1 H); 3.20 (br. *q*, *J* = 7.2, 2 H); 3.57 (br. *t*, *J* = 4.9, 2 H); 4.00 (*m*, 6 H);

4.56 (br. *s*, 1 H); 4.94 (br. *s*, 1 H); 6.79 (*m*, 2 H); 7.06 (*m*, 2 H). MS: 362 (3, M^+), 115 (100), 99 (68). Anal. calc. for $C_{20}H_{30}N_2O_4$ (362.46): C 66.27, H 8.34, N 7.73; found: C 66.31, H 8.39, N 7.68.

cis/trans-N-*Ethyl* N'-{*2-[4-(2-Hydroxycyclohex-1-ylmethyl)phenoxy]ethyl*}*urea* (**46**). From **44** (1.533 g, 4.8 mmol) according to the *General Procedure B*. The mixture could be separated neither by TLC nor by CC. Crystallization (MeOH/Et_2O) yielded 0.538 g (34.9%) of **46**. M.p. 83–85°. IR ($CHCl_3$): 3614, 3446, 1665, 1649, 1611, 1562, 1511, 1243. ^{1}H-NMR: 0.83–1.78 (*m*, 16 H); 1.12 (*t*, *J* = 7.3, 6 H); 1.96 (*m*, 1 H); 1.98 (*m*, 1 H); 2.31 (*dd*, *J* = 9.0, 13.6, 1 H); 2.47 (*dd*, *J* = 7.6, 13.4, 1 H); 2.65 (*dd*, *J* = 7.9, 13.4, 1 H); 3.07 (*dd*, *J* = 3.9, 13.6, 1 H); 3.20 (br. *q*, *J* = 7.3, 4 H); 3.27 (*dt*, *J* = 4.1, 9.5, 9.5, 1 H); 3.78 (*m*, 1 H); 3.57 (*t*, *J* = 5.1, 4 H); 3.99 (*t*, *J* = 5.1, 4 H); 6.78 (*m*, 4 H); 7.07 (*m*, 4 H). FAB-MS: 321 (28, $[M + 1]^+$), 115 (100). Anal. calc. for $C_{18}H_{28}N_2O_3$ (320.43): C 67.47, H 8.81, N 8.74; found: C 67.32, H 8.92, N 8.71.

Ethyl 2-Chloroethyl Carbonate (**47**) *and Ethyl 2-Bromoethyl Carbonate* (**48**): *General Procedure*. An equimolar mixture of ethyl chloroformate and 2-chloro- or 2-bromoethanol in pyridine (183 ml for 1 mol of ethyl chloroformate) was stirred at 0° in the presence of a catalytic amount of 4-(dimethylamino)pyridine for 4 h. The mixture was poured onto ice, and conc. HCl soln. (10 ml) was added. The mixture was extracted with benzene, the combined extract washed with 5% HCl soln., sat. aq. $NaHCO_3$ soln., and H_2O, dried (Na_2SO_4), and evaporated, and the residue distilled *in vacuo*: **47** (61.8%) or **48** (54.3%), resp.

47: B.p. 74–75°/1.9 kPa. IR (CCl_4): 1759, 1278. ^{1}H-NMR: 1.33 (*t*, *J* = 7.0, 3 H); 3.70 (*t*, *J* = 6.0, 2 H); 4.23 (*q*, *J* = 7.1, 2 H); 4.38 (*t*, *J* = 6.0, 2 H). MS: 152 (1, M^+), 117 (24), 79 (6), 63 (100), 45 (81). Anal. calc. for $C_5H_9ClO_3$ (152.58): C 39.36, H 5.95, Cl 23.24; found: C 39.42, H 5.86, Cl 23.31.

48: B.p. 87–88°/1.9 kPa. IR (CCl_4): 1759, 1273, 1018. ^{1}H-NMR: 1.32 (*t*, *J* = 9.0, 3 H); 3.53 (*t*, *J* = 6.0, 2 H); 4.22 (*q*, *J* = 9.0, 2 H); 4.42 (*t*, *J* = 6.0, 2 H). MS: 196 (1, M^+), 117 (100), 107 (84), 89 (51). Anal. calc. for $C_5H_9BrO_3$ (197.04): C 30.48, H 4.60, Br 40.55; found: C 30.52, H 4.53, Br 40.49.

Ethyl 2-[4-(2-Oxocyclohex-1-ylmethyl)phenoxy]ethyl Carbonate (**49**). To a stirred soln. of **9** (0.3 g, 1.0 mmol) in DMF (10 ml), NaH (43.4 mg, 1.0 mmol) was added at 0°. After 1 h stirring at 0°, **47** (0.7 g, 4.0 mmol) was added and the mixture heated to 150° for 4 h. The mixture was diluted with 5% HCl soln. and extracted with light petroleum ether/Et_2O 1:1. The combined extract was dried (Na_2SO_4) and evaporated and the residue purified by CC (Al_2O_3 (*Woelm* neutral, act. I), light petroleum ether/Et_2O 3:1): 0.1 g (21.3%) of **49**. M.p. 56–58°. IR (CCl_4): 1753, 1718, 1613, 1516, 1270, 1245. ^{1}H-NMR: 1.17–2.13 (*m*, 9 H); 1.32 (*t*, *J* = 7.1, 3 H); 2.37 (*dd*, *J* = 8.6, 13.5, 1 H); 3.16 (*dd*, *J* = 4.4, 13.5, 1 H); 4.17 (*m*, 2 H); 4.22 (*q*, *J* = 7.1, 2 H); 4.47 (*m*, 2 H); 6.82 (*m*, 2 H); 7.07 (*m*, 2 H). MS: 320 (11, M^+), 149 (15), 117 (100), 89 (84). Anal. calc. for $C_{18}H_{24}O_5$ (320.37): C 67.48, H 7.55; found: C 67.56, H 7.61.

Ethyl 2-[4-(2-Oxocyclopent-1-ylmethyl)phenoxy]ethyl Carbonate (**50**). To a stirred soln. of **10** (0.922 g, 5.0 mmol) in DMF (22 ml), NaH (0.22 g, 5.0 mmol) was added at 0°. After 1 h stirring at 0°, **48** (1.97 g, 10.0 mmol) was added and the mixture heated to 100° for 6.5 h. The mixture was diluted with 5% HCl soln. and extracted with light petroleum ether/Et_2O 1:1. The combined extract was dried (Na_2SO_4) and evaporated and the residue purified by CC (Al_2O_3 (*Woelm* neutral, act. I), light petroleum ether/Et_2O 2:1): 0.488 g (32.9%) of **50**. IR (CCl_4): 1756, 1740, 1613, 1520, 1409, 1273, 1246. ^{1}H-NMR: 1.32 (*t*, *J* = 7.1, 3 H); 1.48–2.17 (*m*, 7 H); 2.52 (*dd*, *J* = 9.0, 13.7, 1 H); 3.06 (*dd*, *J* = 4.2, 13.7, 1 H); 4.17 (*m*, 2 H); 4.22 (*q*, *J* = 7.1, 2 H); 4.47 (*m*, 2 H); 6.82 (*m*, 2 H); 7.07 (*m*, 2 H). MS: 306 (15, M^+), 190 (10), 149 (10), 117 (97), 107 (44), 89 (100). Anal. calc. for $C_{17}H_{22}O_5$ (306.35): C 66.65, H 7.24; found: C 66.73, H 7.19.

Juvenoids **55** *and* **56**: *General Procedure*. An equimolar mixture of phenol **13** or **14** and NaH in DMF (10 ml for 1.0 mmol of **13** or **14**, resp.) was stirred at 0° for 1 h. Then, 5 equiv. of **47** or **48**, resp., were added, and the stirred mixture was heated to 150° or 100°, resp., for 5 h. The mixture was cooled, diluted with 5% HCl soln., and extracted with light petroleum ether/Et_2O (1:1), the combined extract dried (Na_2SO_4) and evaporated, and the residue purified by CC (light petroleum ether/Et_2O 5:1).

Ethyl 2-{4-[2,2-(Ethylenedioxy)cyclohex-1-ylmethyl]phenoxy}ethyl Carbonate (**55**): Yield 40.1%. M.p. 49–52°. IR (CCl_4): 1757, 1615, 1520, 1270, 1248, 1160, 1102, 1091, 1056, 930. ^{1}H-NMR: 1.03–1.87 (*m*, 9 H); 1.31 (*t*, *J* = 7.2, 3 H); 2.20 (*dd*, *J* = 11.0, 13.4, 1 H); 2.98 (*dd*, *J* = 3.1, 13.4, 1 H); 3.99 (*m*, 4 H); 4.17 (*m*, 2 H); 4.21 (*q*, *J* = 7.2, 2 H); 4.46 (*m*, 2 H); 6.82 (*m*, 2 H); 7.09 (*m*, 2 H). MS: 364 (35, M^+), 321 (21), 236 (26), 141 (15), 117 (69), 99 (100). Anal. calc. for $C_{20}H_{28}O_6$ (364.42): C 65.91, H 7.74; found: C 66.02, H 7.83.

Ethyl 2-{4-[2,2-(Ethylenedioxy)cyclopent-1-ylmethyl]phenoxy}ethyl Carbonate (**56**): Yield 40.8%. IR (CCl_4): 1760, 1613, 1520, 1267, 1244, 1178, 1156, 1111, 1046, 948. ^{1}H-NMR: 1.30–1.82 (*m*, 7 H); 1.31 (*t*, *J* = 7.1, 3 H); 2.40 (*dd*, *J* = 10.6, 13.6, 1 H); 2.81 (*dd*, *J* = 4.5, 13.6, 1 H); 3.88 (*m*, 4 H); 4.16 (*m*, 2 H); 4.21 (*q*, *J* = 7.1, 2 H); 4.46 (*m*, 2 H); 6.81 (*m*, 2 H); 7.09 (*m*, 2 H). MS: 350 (15, M^+), 262 (19), 190 (10), 135 (32), 107 (100), 89 (21). Anal. calc. for $C_{19}H_{26}O_6$ (350.40): C 65.12, H 7.48; found: C 65.08, H 7.52.

Juvenoids **51–54**: *General Procedure.* To a soln. of containing EtOH (10 ml), H_2O (0.6 ml), and H_3BO_3 (1 g), **49** or **50** (1.6 mmol) was added. The mixture was cooled to 0° and $NaBH_4$ (1.6 mmol, 0.06 g) added. After 0.5 h, the mixture was diluted with 5% HCl soln. and extracted with Et_2O (3 × 100 ml). The combined extract was washed with H_2O, dried (Na_2SO_4), and evaporated and the residue purified by CC (light petroleum ether/Et_2O 6:1).

cis-*Ethyl 2-[4-(2-Hydroxycyclohex-1-ylmethyl)phenoxy]ethyl Carbonate* (**51**): Yield 36.6%. IR (CCl_4): 3629, 1756, 1615, 1520, 1280, 1240, 975. ^{1}H-NMR: 0.80–1.78 (*m*, 9 H); 1.31 (*t*, *J* = 7.1, 3 H); 2.47 (*dd*, *J* = 7.6, 13.4, 1 H); 2.66 (*dd*, *J* = 7.6, 13.4, 1 H); 3.78 (*m*, *w* = 9.5, 1 H); 4.16 (*m*, 2 H); 4.21 (*q*, *J* = 7.1, 2 H); 4.47 (*m*, 2 H); 6.83 (*m*, 2 H); 7.09 (*m*, 2 H). MS: 322 (6, M^+), 188 (34), 117 (82), 107 (100), 89 (58). Anal. calc. for $C_{18}H_{26}O_5$ (322.39): C 67.05, H 8.13; found: C 66.93, H 8.06.

trans-*Ethyl 2-[4-Hydroxycyclohex-1-ylmethyl)phenoxy]ethyl Carbonate* (**52**): Yield 28.9%. IR (CCl_4): 3624, 1758, 1612, 1517, 1260, 1240, 1031. ^{1}H-NMR: 0.76–1.78 (*m*, 9 H); 1.32 (*t*, *J* = 7.1, 3 H); 2.32 (*dd*, *J* = 8.5, 13.4, 1 H); 3.07 (*dd*, *J* = 3.2, 13.4, 1 H); 3.28 (*dt*, *J* = 4.4, 9.8, 9.8, 1 H); 4.17 (*m*, 2 H); 4.22 (*q*, *J* = 7.1, 2 H); 4.47 (*m*, 2 H); 6.83 (*m*, 2 H); 7.09 (*m*, 2 H). MS: 322 (10, M^+), 188 (2), 117 (100), 107 (20), 89 (68). Anal. calc. for $C_{18}H_{26}O_5$ (322.39): C 67.05, H 8.13; found: C 69.93, H 8.13.

cis-*Ethyl 2-[4-(2-Hydroxycyclopent-1-ylmethyl)phenoxyethyl Carbonate* (**53**): Yield 6.3%. IR (CCl_4): 3630, 1756, 1614, 1520, 1270, 1250, 1035, 991. ^{1}H-NMR: 1.15–2.07 (*m*, 7 H); 1.31 (*t*, *J* = 7.1, 3 H); 2.62 (*dd*, *J* = 7.5, 13.8, 1 H); 2.79 (*dd*, *J* = 8.0, 13.8, 1 H); 4.13 (*m*, *w* = 11.0, 1 H); 4.17 (*m*, 2 H); 4.22 (*q*, *J* = 7.2, 2 H); 4.47 (*m*, 2 H); 6.83 (*m*, 2 H); 7.14 (*m*, 2 H). MS: 308 (11, M^+), 117 (100), 107 (37), 89 (92). Anal. calc. for $C_{17}H_{24}O_5$ (308.36): C 66.21, H 7.84; found: C 66.15, H 7.78.

trans-*Ethyl 2-[4-(2-Hydroxycyclopent-1-ylmethyl)phenoxy]ethyl Carbonate* (**54**): Yield 45.1%. IR (CCl_4): 3625, 1755, 1614, 1520, 1270, 1244, 1077, 1040. ^{1}H-NMR: 1.16–2.08 (*m*, 7 H); 1.32 (*t*, *J* = 7.1, 3 H); 2.49 (*dd*, *J* = 8.0, 13.5, 1 H); 2.69 (*dd*, *J* = 7.0, 13.5, 1 H); 3.89 (br. *q*, *J* = 5.7, 5.7, 5.7, 1 H); 4.17 (*m*, 2 H); 4.22 (*q*, *J* = 7.1, 2 H); 4.47 (*m*, 2 H); 6.84 (*m*, 2 H); 7.11 (*m*, 2 H). MS: 308 (10, M^+), 117 (100), 107 (24), 89 (92). Anal. calc. for $C_{17}H_{24}O_5$ (308.36): C 66.21, H 7.84; found: C 66.32, H 7.95.

We thank the *Grant Agency of the Academy of Sciences of the Czech Republic* (grant No. 65541) for the generous financial support of the biological part of this work.

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