166. Copper (I)- and Copper (II)-catalyzed *Diels-Alder* Additions of α-Substituted Acrylonitrile to Furan. The Synthesis of 7-Oxa-bicyclo [2.2.1]hept-5-en-2-one

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Summary

The difficult *Diels-Alder* additions of α-acetoxy- and α-chloroacrylonitrile to furan can be run at 20–35° and atmospheric pressure in the presence of CuCl, $Cu(BF_4) \cdot 6\,H_2O$, $Cu(OOCCH_3)_2 \cdot H_2O$ or cupric tartrate $\cdot\, 3\,H_2O$. Under kinetic control, the *exo*-carbonitrile adducts **2** and **8**, respectively, are favoured. Saponification of the 2*endo*-acetoxy-7-oxabicyclo[2.2.1]hept-5-ene-2*exo*-carbonitrile (**2**) furnished the 7-oxabicyclo[2.2.1]hept-5-en-2-one (**4**). Basic hydrolysis of the adducts (**8**+**9**) of α-chloroacrylonitrile to furan and its 5*exo*, 6*exo*-isopropylidenedioxy derivatives did not give the corresponding ketones, the carboxamides **14**+**15** and **16**+**17**, respectively, were isolated.

Introduction. – Unless activated by electron-donating substituents [1], furans add to mono-activated dienophiles sluggishly giving mixtures of the *endo*- and *exo*-adducts in low yield [2]. Under very high pressure, the *Diels-Alder* additions can be accelerated [3]; in some cases, *Lewis* acids can be used as catalysts [4], although care must be taken to avoid the polymerization of the furans or/and rearrangement of the adducts [5]. Recently, *Kotsuki et al.* have reported the high-pressure *Diels-Alder* additions of **1** and **2** to furan, to 2,5-dimethylfuran and 2-substituted derivatives [6]. These reactions required 10–20 kbar at 30°. This work urges us to report our preliminary results on the Cu(I)- and Cu(II)-catalyzed *Diels-Alder* additions of furan to **1** and **7**. We disclose also an efficient synthesis of 7-oxabicyclo[2.2.1]hept-5-en-2-one[2]), a β,γ-unsaturated ketone of theoretical [10] and practical interest[3]) that had not been reported yet. This compound could become a useful starting material in the synthesis of various natural products, including the nucleosides[4]).

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[2]) The bicyclo[2.2.1]hept-5-en-2-one has been prepared by alcaline hydrolysis of the *Diels-Alder* adducts of cyclopentadiene to α-acetoxyacrylonitrile [7] or to α-chloroacrylonitrile [8]. Dry $Cu(BF_4)_2$ was shown to be a useful catalyst for the cycloadditions of the latter dienophile [9].

[3]) See *e.g.* the stereo- and regioselective electrophilic additions of bicyclo[2.2.1]hept-5-en-2-one, where the homoconjugated carbonyl group behaves as an electron-donating substituent [11].

[4]) For the syntheses of nucleosides starting with furan, see *e.g.* [12].

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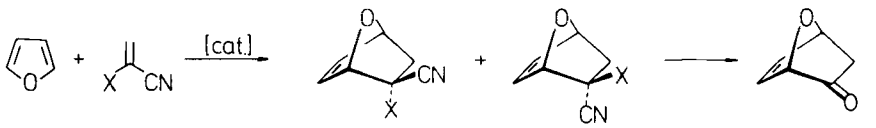
Results and discussion. – Furan added to α-acetoxyacrylonitrile (**1**) at 20° in the presence of 0.2 mol-equiv. of $Cu(OAc)_2 \cdot H_2O$ and 0.1 mol-equiv. of $Cu(BF_4)_2 \cdot 6\,H_2O$. Polymerization was slow when traces of hydroquinone and propylene oxide were added. After 5 days, the 2*endo*-acetoxy-7-oxabicyclo[2.2.1]hept-5-ene-2*exo*-carbonitrile (**2**) was isolated in 22% yield together with unreacted **1** (40%). The adduct **2** was contaminated by less than 10% of the *endo*-isomer **3**. Its structure was deduced from its ^{1}H- and ^{13}C-NMR. spectra and by comparison with those of 2*endo*- and 2*exo*-chloro-7-oxabicyclo[2.2.1]hept-5-ene-2-carbonitriles **8** and **9**, respectively (see below).



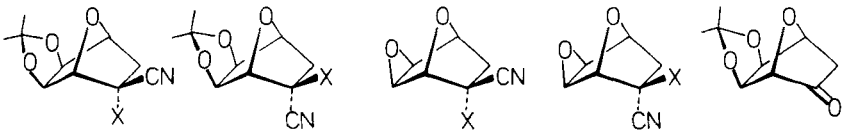
X = OAc	**1**	**2**	**3**	**4**
= Cl	**7**	**8**	**9**	

A slower reaction was observed in the presence of cupric tartrate $\cdot\, 3\,H_2O$; a product ratio **2/3** of 4:1 was obtained after 35 days at 20° (5% isolated yield). No cycloaddition of furan to **1** could be achieved without catalyst between 20° and 100° after prolonged reaction time (2 months).

Saponification of **2** gave 7-oxabicyclo[2.2.1]hept-5-en-2-one (**4**) whose spectral data were similar to those reported for bicyclo[2.2.1]hept-5-en-2-one [13]. As expected for a rigid β,γ-unsaturated ketone [13b], a relatively large absorbance was measured for the carbonyl chromophore ($\lambda_{max} = 312$ nm, $\varepsilon = 230$, in isooctane) and a charge-transfer band [10] [13b] was visible at $\lambda_{max} = 208$ nm ($\varepsilon = 3200$, in isooctane). Hydroxylation of **2** with H_2O_2 (acetone/OsO_4 [14]) followed by acidic treatment with 2,2-dimethoxypropane furnished the acetonide **5** which gave the ketone **6** upon saponification.

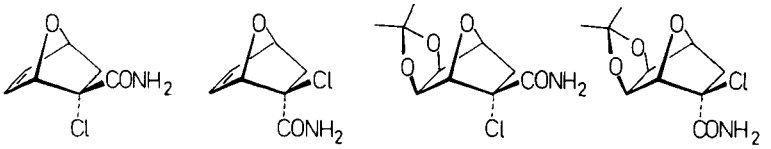
After prolonged (4–10 days) heating at 110° in a sealed pyrex tube, furan (5 mol-equiv.) and α-chloroacrylonitrile (1 mol-equiv.) could be 'equilibrated' with the corresponding adducts **8** and **9** (5%), accompanied by 10–40% of polymerization. Copper salts were also found to be catalysts of this cycloaddition (see the *Table* for a summary of our preliminary studies). $Cu(BF_4)_2 \cdot 6\,H_2O$ was found to be a better catalyst than CuCl or $Cu(OAc)_2 \cdot H_2O$, probably because of its stronger *Lewis* acid character and its greater solubility. The adduct ratio **8/9** was 50 ($\pm$ 10):50 ($\mp$ 10) under equilibrium conditions. For a low degree of conversion, the *exo*-carbonitrile **8** was the major product. The adduct ratio **8/9** was the largest when cupric tartrate was used as catalyst.

Hydroxylation of **8/9** (H_2O_2, OsO_4) followed by acetylation (2,2-dimethoxypropane) gave the acetonides **10**+**11**. Epoxydation of **8**+**9** with *m*-chloroperbenzoic acid furnished the epoxides **12**+**13** whose structures had been established by ^{1}H-NMR. and X-ray diffraction studies [15]. This allowed structural assignments for **8**–**11**.



X = OAc **5** **6**

= Cl **10** **11** **12** **13**



14 **15** **16** **17**

Saponification (DMSO, H_2O, KOH) of **8**+**9** and **10**+**11** did not give the corresponding ketones **4** and **6**. The carboxamide mixtures **14**+**15** and **16**+**17**, respectively, were formed instead. One can invoke retarded S_N1-heterolyses of the chlorides **8**–**11** compared with those of the bicyclo[2.2.1]heptane analogs [8] because of the inductive effect of the ethereal bridge. This renders the carbonitrile hydrolysis competitive and even faster than the chloride solvolysis. No significant kinetic selectivity was observed for the *exo*-carbonitrile *vs. endo*-carbonitrile hydrolysis.

Table. *Preliminary studies on the* Diels-Alder *addition of furan* (5 mol) *to α-chloroacrylonitrile* (1 mol) *catalyzed by copper salts*[a]) (0.1 mol)

Catalyst	Temperature [°C]	Reaction time (d = days)	Isomeric ratio **8**/**9**[b])	Isolated yield
CuCl	31°	3 d	60:40	19%
$Cu(BF_4)_2 \cdot 6\,H_2O$	31°	1 d	55:45	50%
$Cu(OAc)_2 \cdot H_2O$	31°	5 d	70:30	24%
$Cu(OAc)_2 \cdot H_2O$	31°	10 d	60:40	34%
$Cu(OAc)_2 \cdot H_2O$	31°	15 d	50:50	36%
$Cu(OAc)_2 \cdot H_2O$	31°	35 d	50:50	62%
$Cu(OAc)_2 \cdot H_2O$	60°	2 d	60:40	34%
Cu(tartrate) · 3 H_2O[c])	31°	4 d	81:19[d])	19%
Cu(tartrate) · 3 H_2O[c])	31°	8 d	76:24	25%
Cu(tartrate) · 3 H_2O[c])	31°	12 d	70:30	28%
None	110°	4 d	50:50	5%

[a]) Only a fraction of the catalyst was solubilized in the reaction mixture (under Ar, vigorous stirring, in the dark).

[b]) By ^{1}H-NMR. (80 MHz), ± 5%.

[c]) Preparation, see *Exper. Part.*

[d]) $[\alpha]_D^{25°} \simeq 0$ for this adduct mixture.

We are currently exploring the possibility of inducing enantioselective *Diels-Alder* additions of acrylonitriles to furan in the presence of optically pure cupric salts. The application of 7-oxabicyclo[2.2.1]hept-5-en-2-one (**4**) and its derivative **6** to the synthesis of nucleosides is under study.

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Experimental Part

General Remarks. See [16]. None of the procedures given below has been optimized.

Synthesis of 2endo-*acetoxy-7-oxabicyclo[2.2.1]hept-5-ene-2*exo-*carbonitrile* (**2**). A mixture of furan (340 g, 5 mol), α-acetoxyacrylonitrile **1** (105 ml, 111.2 g, 1 mol), hydroquinone (1 g), propylene oxide (10 ml), $Cu(OAc)_2 \cdot H_2O$ (40 g, 0.1 mol) and $Cu(BF_4)_2 \cdot 6\,H_2O$ (34.5 g, 0.1 mol) was vigorously stirred under Ar at 31° for 5 days (in the dark). The catalyst removed by filtration and the organic mixture was washed with a sat. $NaHCO_3$-solution (100 ml), then with water (200 ml, 3–4 times). The unreacted cycloaddents were eliminated by fractional distillation i.V. (25°, 1 Torr); the residue yielded after column chromatography on silicagel (AcOEt/petroleum ether 1:5) 40.1 g (22.4%) of adduct **2** as a colorless oil (contaminated by less than 10% of the isomer **3**). – IR. (CCl_4): 3040, 2940, 2860, 2250, 1770, 1240, 1220, 1190, 1060, 1030. – ^{1}H-NMR. ($CDCl_3$): 6.65 (*d*×*d*, 1 H, $J(5,6)=5.8$, $J(4,5)=1.5$, H–C(5)); 6.21 (*d*×*d*, 1 H, $J(5,6)=5.8$, $J(1,6)=1.8$, H–C(6)); 5.55 (*d*, 1 H, $J(1,6)=1.8$, H–C(1)); 5.11 (*d*×*d*, 1 H, $J(3,4)=4.8$, $J(4,5)=1.5$, H–C(4)); 2.7 (*d*×*d*, 1 H, $J_{gem}=12$, $J(3,4)=4.8$, H_{exo}–C(3)); 2.04 (*s*, 3 H, CH_3COO); 1.73 (*d*, 1 H, $J_{gem}=12.8$, H_{endo}–C(3)). – ^{13}C-NMR. ($CDCl_3$, 90 MHz): 168.8 (*s*); 139.4 (*d*, $^1J(C,H)=178$); 130.3 (*d*, $^1J(C,H)=180$); 118.9 (*s*); 83.0 (*d*, $^1J(C,H)=175$); 78.4 (*d*, $^1J(C,H)=168$); 71.6 (*s*); 40.7 (*t*, $^1J(C,H)=141$); 19.9 (*qa*, $^1J(C,H)=131$).

$C_9H_9NO_3$ (179.18) Calc. C 60.33 H 5.06% Found C 60.22 H 4.97%

Synthesis of 7-oxabicyclo[2.2.1]hept-5-en-2-one (**4**). The adducts **2**+**3** (1.79 g, 0.01 mol), CH_3ONa (2.16 g, 0.04 mol) and abs. CH_3OH (40 ml) were stirred at 20° for 3 h. After cooling to 0°, cold water was added (80 ml) and the mixture extracted with CH_2Cl_2 (80 ml, 3 times). The organic extract was washed with sat. NaCl-solution (50 ml, 2 times). After drying ($MgSO_4$), the solvent was removed by fractional distillation under atmospheric pressure. The residue was distilled under reduced pressure yielding 180 mg (16%), colorless oil, b.p. 79–80°/10 Torr, or purified by column chromatography on silicagel ($CHCl_3$) yielding 400 mg (36%) of **4**. – UV. (isooctane): 312 (230), 208 (3200). – UV. (C_2H_5OH/H_2O 95:5): 311 (200), 211 (3100). – IR. (CCl_4): 3030, 2950, 1775, 1615, 1060, 1020. – ^{1}H-NMR. ($CDCl_3$): 6.75 (*d*×*d*, 1 H, $J(5,6)=5.8$, $J(4,5)=1.5$, H–C(5)); 6.48 (*d*×*d*, 1 H, $J(5,6)=5.8$, $J(1,6)=1.8$, H–C(6)); 5.32 (*d*×*d*, 1 H, $J(3,4)=4.1$, $J(4,5)=1.5$, H–C(4)); 4.52 (*d*, 1 H, $J(1,6)=1.8$, H–C(1)); 2.15 (*d*×*d*, 1 H, $J_{gem}=16.0$, $J(3,4)=4.1$, H_{exo}–C(3)); 1.86 (*d*, 1 H, $J_{gem}=16.0$, H_{endo}–C(3)). – ^{13}C-NMR. ($CDCl_3$): 207.2 (*s*, CO); 142.1 (*d*, $^1J(C,H)=179$, C(5)); 130.5 (*d*, $^1J(C,H)=180$, C(6)); 82.0 (*d*, $^1J(C,H)=173$, C(1)); 78.9 (*d*, $^1J(C,H)=168$, C(4)); 33.9 (*t*, $^1J(C,H)=137$, C(3)). – MS. (70 eV): 110 (0.8, M^+), 94 (0.5), 82 (3.7), 81 (7.9), 68 (100).

$C_6H_6O_2$ (110.11) Calc. C 65.45 H 5.49% Found C 65.44 H 5.49%

Synthesis of 2endo-*acetoxy-5*exo,*6*exo-*isopropylidenedioxy-7-oxabicyclo[2.2.1]heptane-2*exo-*carbonitrile* (**5**). The adduct **2** (1.79 g, 0.01 mol) in acetone (20 ml) was added to a mixture of OsO_4 0.02M in *t*-BuOH (10 ml) and 30% H_2O_2-solution (10 ml). After stirring at 20° for 14 h (the yellow solution became colourless) the mixture was evaporated i.V. to dryness. The residue was dissolved in anh. acetone (10 ml); 2,2-dimethoxypropane (11.5 g, 13.5 ml, 0.11 mol) and *p*-toluenesulfonic acid (0.05 g) were added. After stirring at 20° for 3 days, the solvent was evaporated and the residue yields after column chromatography on silicagel ($CHCl_3$) 1.40 g (55%) of **5**, white crystals (50% after recrystallisation from Et_2O/hexane), m.p. 124–124.5°. – IR. (KBr): 3050, 3030, 3010, 2990, 2960, 2250, 1775, 1380, 1240, 1215, 1190, 1065. – ^{1}H-NMR. ($CDCl_3$): 4.88 (*s*, 1 H, H–C(1)); 4.53 and 4.30 (2*d*, 2 H, $J(5,6)=5.7$, H_{endo}–C(5,6)); 4.53 (*d*, 1 H, $J(3,4)=6.4$, H–C(4)); 2.70 (*d*×*d*, 1 H, $J_{gem}=14.2$, $J(3,4)=6.4$, H_{exo}–C(3)); 2.16 (*s*, 3 H, CH_3CO); 1.66 (*d*, 1 H, $J_{gem}=14.2$, H_{endo}–C(3)); 1.46 and 1.29 (2*s*, 6 H, 2 CH_3). – ^{13}C-NMR. ($CDCl_3$, 90 MHz): 168.5 (*s*); 117.8 (*s*); 112.0 (*s*); 82.9 (*d*, $^1J(C,H)=174$); 81.0

(*d*, ^1J(C,H) = 160); 79.0 (*d*, ^1J(C,H) = 165); 77.3 (*d*, ^1J(C,H) = 160); 72.0 (*s*); 38.8 (*t*, ^1J(C,H) = 139); 25.6 and 25.0 (2 *qa*, ^1J(C,H) = 126); 20.2 (*qa*, ^1J(C,H) = 131). – MS. (200 eV): 253 (< 0.1, M^+), 238 (100).

$C_{12}H_{15}NO_5$ (253.26) Calc. C 56.91 H 5.97% Found C 56.67 H 6.17%

*Synthesis of 5*exo,*6*exo-*isopropylidenedioxy-7-oxabicyclo[2.2.1]heptan-2-one* (**6**). The acetonide **5** (0.76 g, 3 mmol), CH_3ONa (0.65 g, 12 mmol) and anh. CH_3OH (25–30 ml) were stirred at 20° for 3–3½ h. After the addition of ice-cold water (50 ml), the mixture was extracted with CH_2Cl_2 (50 ml, 3 times). The organic extract was washed with a sat. NaCl-solution (50 ml, 2 times). After drying ($MgSO_4$), the solvent was evaporated yielding 0.36 g (65%) of the ketone **6** pure at > 95%, m.p. 98–100°. Column chromatography on silicagel (petroleum ether/AcOEt 3:1) yielded 0.33 g (60%) of **6**, white crystals, m.p. 102–102.5°. – UV. (dioxane): 290 *S*, 303 (ε = 32), 313 (ε = 33), 325 *S* (ε = 20). – IR. (KBr): 3050, 3005, 2970, 2955, 1778, 1380, 1215, 1160, 1015. – ^{1}H-NMR. ($CDCl_3$): 4.79 (*d*, 1 H, J(3,4) = 6, H–C(4)); 4.6–4.4 (*m*, 2 H, H–C(5,6)); 4.25 (*s*, 1 H, H–C(1)); 2.39 (*d*×*d*, 1 H, J_{gem} = 18, J(3,4) = 6, H_{exo}–C(3)); 1.84 (*d*, 1 H, J_{gem} = 18, H_{endo}–C(3)); 1.51 and 1.32 (2*s*, 6 H, 2 CH_3). – ^{13}C-NMR. ($CDCl_3$, 90 MHz): 207.8 (*s*); 113.7 (*s*); 83.5 (*d*, ^1J(C,H) = 170); 82.0 (*d*, ^1J(C,H) = 158); 79.6 (*d*, ^1J(C,H) = 166); 78.2 (*d*, ^1J(C,H) = 158); 38.0 (*t*, ^1J(C,H) = 136); 25.6 and 25.0 (2 *qa*, ^1J(C,H) = 126). – MS. (200 eV): 184 (2, M^+), 169 (100).

$C_9H_{12}O_4$ (184.19) Calc. C 58.69 H 6.57% Found C 58.83 H 6.59%

Synthesis of 2-chloro-7-oxabicyclo[2.2.1]hept-5-ene-2-carbonitriles (**8**+**9**). A mixture of furan (340 g, 5 mol), *a*-chloroacrylonitrile (**7**) (87.5 g, 1 mol), $Cu(OAc)_2 \cdot H_2O$ (20 g, 0.1 mol) and hydroquinone (1 g) was heated under reflux and stirring for 35 days. The catalyst was removed by filtration and the solution washed with water (100 ml, 2 times). After drying ($MgSO_4$), the unreacted furan and dienophile **7** were eliminated by fractional distillation i.V. (25°, 10 Torr). The residue contained more than 90% of the adducts **8**+**9** 1:1 (96.5 g, 62%), yellowish oil that could be purified by column chromatography on silicagel ($CHCl_3$). – IR. ($CHCl_3$): 3040, 2240, 1615, 1045, 1020. – ^{1}H-NMR. ($CDCl_3$) of **8**: 6.63 and 6.41 (2 *d*×*d*, 2 H, J(5,6) = 6.0, J(5,4) = J(1,6) = 1.9, H–C(5,6)); 5.30 (*m*, 1 H, J(1,6) = 1.9, J(1,4) = 0.9, H–C(1)); 5.18 (*m*, 1 H, J(3,4) = 4.6, J(4,5) = 1.9, J(1,4) = 0.9, H–C(4)); 2.85 (*d*×*d*, 1 H, J_{gem} = 11, J(3,4) = 4.6, H_{exo}–C(3)); 1.82 (*d*, 1 H, J_{gem} = 11, H_{endo}–C(3)). – ^{1}H-NMR. ($CDCl_3$) of **9**: 6.68 and 6.52 (2 *d*×*d*, 2 H, J(5,6) = 5.7, J(1,6) = J(4,5) = 1.8, H–C(5,6)); 5.22 (*m*, 1 H, J(3,4) = 4.2, J(4,5) = 1.8, J(1,4) = 0.9, H–C(4)); 5.15 (*m*, 1 H, J(1,6) = 1.8, J(1,4) = 0.9, H–C(1)); 2.48 (*d*×*d*, 1 H, J_{gem} = 11, J(3,4) = 4.2, H_{exo}–C(3)); 2.35 (*d*, 1 H, J_{gem} = 11, H_{endo}–C(3)). – ^{13}C-NMR. ($CDCl_3$) of **8**: 138.1 and 131.7 (2*d*, ^1J(C,H) = 180, C(5,6)); 119.8 (*s*, CN); 84.6 (*d*, ^1J(C,H) = 172, C(1)); 79.1 (*d*, ^1J(C,H) = 166, C(4)); 51.1 (*s*, C(2)); 43.9 (*t*, ^1J(C,H) = 142, C(3)). – ^{13}C-NMR. ($CDCl_3$) of **9**: 140.3 and 132.1 (2*d*, ^1J(C,H) = 180, C(5,6)); 118.1 (*s*, CN); 87.2 (*d*, ^1J(C,H) = 175, C(1)); 79.3 (*d*, ^1J(C,H) = 166, C(4)); 53.7 (*s*, C(2)); 45.3 (*t*, ^1J(C,H) = 142, C(3)). – MS. (70 eV) of **8**+**9**: 158 (1.7), 156 (5.6), 146 (19), 144 (58), 132 (11), 130 (35), 90 (6.5), 88 (21), 68 (100).

*Synthesis of 2-chloro-5*exo,*6*exo-*isopropylidenedioxy-7-oxabicyclo[2.2.1]heptane-2-carbonitriles* (**10**+**11**). A (1:1)-mixture of the adducts **8**+**9** (9.36 g, 0.06 mol) in acetone (100 ml), of a solution of 0.02 M OsO_4 in *t*-BuOH (10 ml) and of 30% H_2O_2-solution (10 ml) was stirred at 20° for 14 h. After evaporation i.V. to dryness, the residue was treated with anh. acetone (50 ml), 2,2-dimethoxypropane (6.88 g, 0.066 mol) and *p*-toluenesulfonic acid (0.1 g). The mixture was stirred at 20° for 3 days. The mixture was then introduced into a separatory funnel containing 200 ml of ether. The organic phase was washed successively with sat. $NaHCO_3$-solution (50 ml) and water (2 times, 50 ml). After drying ($MgSO_4$), the solvent was evaporated and the residue was purified by column chromatography on silicagel ($CHCl_3$) and recrystallized from Et_2O/hexane: a white powder was obtained (10.1 g, 72%, (1:1)-mixture of **10**+**11**). – IR. (KBr): 3020, 2860, 2240, 1470, 1450, 1385, 1215, 1160, 1090, 1055, 1015. – ^{1}H-NMR. ($CDCl_3$, 80 MHz) of **10**: 4.93 and 4.32 (2*d*, 2 H, J = 6, H–C(5,6)); 4.7 and 4.4 (2*m*, H–C(1,4)); 2.82 (*d*×*d*, 1 H, J_{gem} = 14, J(3,4) = 6, H_{exo}–C(3)); 1.80 (*d*, 1 H, J_{gem} = 14, H_{endo}–C(3)); 1.47 and 1.30 (2*s*, 2 CH_3). – ^{1}H-NMR. ($CDCl_3$, 80 MHz) of **11**: 4.73 and 4.30 (2*d*, 2 H, J = 6, H–C(5,6)); 4.7–4.4 (*m*, H–C(1,4)); 2.3–2.6 (*m*, 2 H–C(3)); 1.47 and 1.30 (2*s*, 2 CH_3). – ^{13}C-NMR. ($CDCl_3$) of **10**: 118.7 (*s*, CN); 112.1 (*s*, $C(CH_3)_2$); 84.3 (*d*, ^1J(C,H) = 168, C(1)); 80.9, 79.7 and 78.2 (3*d*, ^1J(C,H) = 160, C(4,5,6)); 51.8 (*s*, C(2)); 42.6 (*t*, ^1J(C,H) = 140, C(3)); 24.9 (*qa*, ^1J(C,H) = 126 Hz, $C(CH_3)_2$). – ^{13}C-NMR. ($CDCl_3$) of **11**: 116.7 (*s*, CN); 112.8 (*s*, $C(CH_3)_2$); 87.4 (*d*, ^1J(C,H) = 172, C(1)); 80.7, 79.5 and 78.4 (3*d*, ^1J(C,H) = 160, C(4,5,6)); 52.9 (*s*, C(2)); 44.2 (*t*, ^1J(C,H) = 140, C(3)); 25.5 (*qa*, ^1J(C,H)

= 126 Hz, $C(CH_3)_2$). – MS. (70 eV): 216 (36), 214 (100). – MS. (CI, isobutane): 232 (37, $M^+ + 1$), 230 (100).

*Synthesis of 2-chlorb-5*exo,*6*exo*-epoxy-7-oxabicyclo[2.2.1]heptane-2-carbonitriles* (**12**+**13**). A (1:1)-mixture of the adducts **8**+**9** (3.12 g, 0.02 mol), *m*-chloroperbenzoic acid (10.4 g, 0.06 mol) in $CHCl_3$ (70 ml) was heated to 40° and under stirring for 2 days. After staying overnight at 0°, the precipitate was removed by filtration. The solution was evaporated to dryness i.V. and the residue was purified by column chromatography on silicagel ($CHCl_3$). The main fraction gave a (1:1)-mixture of **12**+**13** that was recrystallized from $CHCl_3$/hexane yielding 2.74 g (80%) of a white solid. Using a (4:1)-mixture of **8**+**9** prepared by Cu(tartrate) · 3 H_2O catalyzed cycloaddition of furan to *α*-chloroacrylonitrile (31°, 4 days), a (4:1)-mixture of **12**+**13** was obtained. – IR. (KBr): 3100, 2250, 1455, 1025. The other characteristics of **12** and **13** were identical to those reported [15].

$C_7H_6ClNO_2$ (171.58) Calc. C 49.00 H 3.52 N 8.16% Found C 48.85 H 3.50 N 8.17%

Synthesis of 2-chloro-7-oxabicyclo[2.2.1]hept-5-ene-2-carboxamides (**14**+**15**). A solution of KOH (2.24 g, 0.04 mol) in H_2O (4 ml) was added dropwise to a stirred solution of a (1:1)-mixture of **8**+**9** (1.56 g, 0.01 mol) in DMSO (40 ml) cooled to 0°. After the end of the addition, the mixture was stirred at 20° for 2 h. Then it was added to ice/water (100 ml) under vigorous stirring and was neutralized with 2 N HCl. The mixture was extracted with CH_2Cl_2 (100 ml, 4 times). The organic extract was washed with a sat. NaCl-solution (100 ml, 4 times). After drying ($MgSO_4$), the solvent was evaporated i.V. The crude **14**+**15** (0.66 g, 38%) was recrystallized from $CHCl_3$/hexane yielding 0.60 g (35%) of **14**+**15** ((1:1)-mixture of *exo*- and *endo*-carboxamides as a white powder). No trace of the ketone **4** was detected. – IR. (KBr): 3525, 3415, 1705, 1590. – ^{1}H-NMR. ($CDCl_3$, 360 MHz) of **14**: 6.7–6.4 and 6.2–5.9 (2 br. *m*, 2 H, NH_2); 6.58 and 6.51 (2 *d*×*d*, 2 H, $J(5,6)=5.7$, $J(5,4)=J(1,6)=1.8$, H–C(5,6)); 5.18 (*m*, 1 H, $J(1,6)=1.8$, $J(1,4)=0.8$, H–C(1)); 5.15 (*m*, 1 H, $J(3,4)=4.8$, $J(4,5)=1.8$, $J(1,4)=0.8$, H–C(4)); 2.86 (*d*×*d*, 1 H, $J_{gem}\approx 12$, $J(3,4)=4.8$, H_{exo}–C(3)); 1.75 (*d*, $J_{gem}\approx 12$ Hz, H_{endo}–C(3)). – ^{1}H-NMR. ($CDCl_3$, 360 MHz) of **15**: 6.7–5.8 (2 br. *m*, 2 H, NH_2); 6.66 (*d*×*d*, 1 H); 6.33 (*d*×*d*, 1 H); 5.17 (*d*×*d*, 1 H); 4.97 (*d*, 1 H); 2.44 (*d*, 1 H); 2.34 (*d*×*d*, 1 H, H_{exo}–C(3)). – ^{13}C-NMR. ($CDCl_3$, 90 MHz) of **14**: 172.6 (*s*, CO), 136.9 (*d*, $^1J(C,H)=178$, C(5)); 134.3 (*d*, $^1J(C,H)=180$, C(6)); 83.8 (*d*, $^1J(C,H)=170$, C(4)); 79.2 (*d*, $^1J(C,H)=166$, C(1)); 67.5 (*s*, C(2)); 42.3 (*t*, $^1J(C,H)=140$, C(3)). – MS. (70 eV): 158 (0.7), 156 (1.9), 138 (3.6), 68 (100).

$C_7H_8ClNO_2$ (173.60) Calc. C 48.43 H 4.65% Found C 48.36 H 4.68%

*Synthesis of 2-chloro-5*exo,*6*exo*-isopropylidenedioxy-7-oxabicyclo[2.2.1]heptane-2-carboxamides* (**16**+**17**). Same procedure as for the synthesis of **14**+**15** using a (1:1)-mixture of the acetonides **10**+**11**. A (1:1)-mixture of **16**+**17** was obtained (60%) as a white powder. – IR. (KBr): 3440, 3340, 2990, 1665, 1065. – ^{1}H-NMR. ($CDCl_3$, 360 MHz) of **16**: 6.5–6.2 and 5.9–5.6 (2 br. *m*, 2 H, NH_2); 5.09 and 4.43 (2*d*, 2 H, $J(5,6)=5.6$, H–C(5,6)); 4.62 (*s*, 1 H, H–C(1)); 4.53 (*d*, 1 H, $J(3,4)=6.3$, H–C(4)); 2.88 (*d*×*d*, 1 H, $J_{gem}=14.0$, $J(3,4)=6.3$, H_{exo}–C(3)); 1.71 (*d*, 1 H, $J_{gem}=14.0$, H_{endo}–C(3)); 1.48 and 1.33 (2*s*, 6 H, $C(CH_3)_2$). – ^{13}C-NMR. ($CDCl_3$) of **16**: 171.4 ($CONH_2$); 117.7 ($C(CH_3)_2$); 84.0, 81.3, 80.0 and 79.5 (C(1,4,5,6)); 71.5 (C(2)); 40.2 (C(3)); 25.0 ($C(CH_3)_2$). – ^{13}C-NMR. ($CDCl_3$) of **17**: 169.9 ($CONH_2$); 118.8 ($C(CH_3)_2$); 87.4, 81.1, 80.6 and 78.1 (C(1,4,5,6)); 66.5 (C(2)); 40.7 (C(3)); 25.7 ($CH_3)_2$). – MS. (70 eV): 234 (36), 232 (100).

Preparation of Cu-tartrate · 3 H_2O [17]. (+)-L-Tartaric acid (15 g, 0.1 mol) was dissolved in water (500 ml) containing NaOH (8 g, 0.2 mol). A solution of $CuSO_4$ (25 g, 0.1 mol) in water (500 ml) was added. After staying overnight at 20°, the clear-blue precipitate was collected and washed with acetone. After drying i.V. 26.4 g (93%) of $Cu(C_4H_4O_6) \cdot 3\ H_2O$ were obtained.

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