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Regioselective Synthesis of 3-*endo*-Hydroxymethyl-5-*exo*-phenylbicyclo[2.2.1]heptan-2-*endo*-amine and its Transformation into Saturated or Partially Saturated Di-*endo*-fused Heterocycles†

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$AlCl_3$-catalysed addition of benzene to di-*endo*-bicyclo[2.2.1]hept-5-ene-2,3-dicarboxylic acid (**1**) and subsequent treatment with acetic anhydride yields 5-*exo*-phenylbicyclo[2.2.1]heptane-2,3-di-*endo*-carboxylic anhydride (**2**). 3-*endo*-Hydroxymethyl-5-*exo*-phenylbicyclo[2.2.1]heptane-2-*endo*-amine (**4**) was prepared by LAH reduction of the β-amino acid **3** obtained by Hofmann degradation of the carboxy amide prepared from **2**. Reaction of **4** with ethyl chloroformate or with CS_2–NaOH–Pb^{2+} furnished the methylene-bridged hexahydro-3,1-benzoxazin-2(1*H*)-one (**5**) or -benzoxazine-2(1*H*)-thione (**6**). With ethyl chloroacetate or 2-chloropropionate, **4** gave the tricyclic oxazepinones **7** and **8**. The norbornane 1,3-amino alcohol **4** was transformed with phenyl isothiocyanate into the phenylimino-1,3-oxazine **9** and -thiazine **10**. The cyclizations of **4** with 2-(*p*-methylbenzoyl)benzoic acid or *cis*-2-*p*-chlorobenzoyl-1-cyclohexanecarboxylic acid led to the methylene-bridged isoindolo[2,1-*a*][3,1]benzoxazines **11** and **12**. With *p*-chlorobenzimidate, the di-*endo*-5,8-methano-4*H*-3,1-benzoxazine **13** was obtained, which was converted with dichloroacetic acid–triethylamine into the isomeric azetidinones **14** and **15**, or with benzonitrile oxide to the methano-1,2,4-oxadiazolo[4,5-*a*][3,1]benzoxazine (**16**). The stereostructures of the new compounds were elucidated by NMR spectroscopy and for **13** also by X-ray diffractometry.

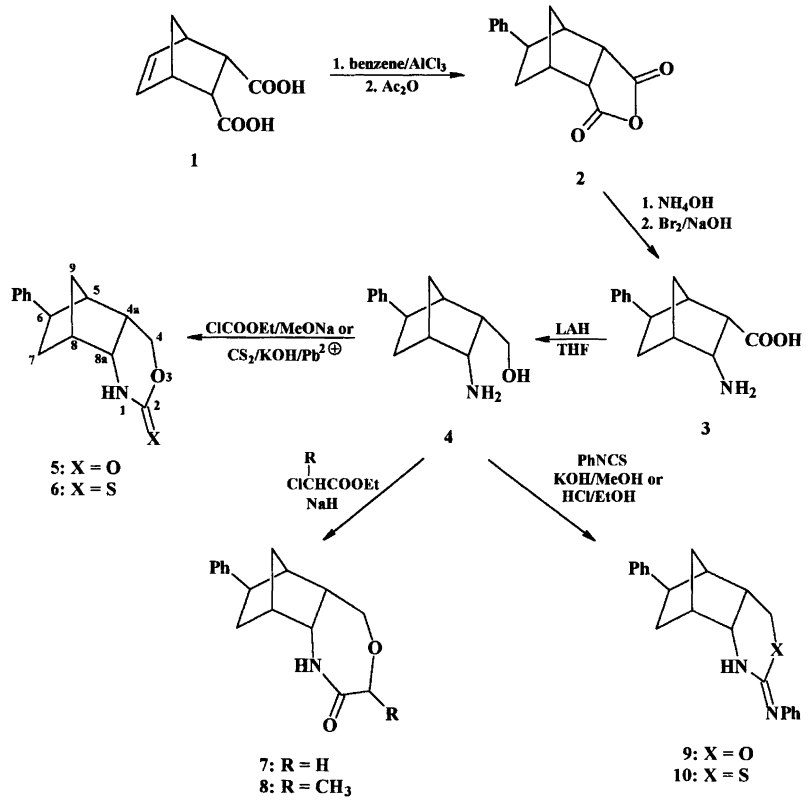
We earlier reported the syntheses of di-*exo*- and di-*endo*-3-hydroxymethylbicyclo[2.2.1]heptan- and -hept-5-en-2-amine and determination of the structures of fused-skeleton, saturated heterocyclic derivatives prepared from them.[1,2] Because of the theoretical and pharmacological importance of carbocycle-fused saturated heterocycles,[3,4] the synthesis and conformational study of various heterocycles have been our main research topics for several years.[5] A number of cycloalkane *cis*- or *trans*-fused 1,3-oxazine, thiazine and pyrimidinone derivatives and related bi-, tri-, tetra- and pentacyclic compounds have been synthesized and subjected to comparative stereochemical and conformational studies.[6–8]

Some of these compounds were used as synthons for further syntheses, e.g., the norbornane-fused 1,3-oxazines are suitable dipolarophiles for cycloadditions.[9,10]

Results

5-*exo*-Phenylbicyclo[2.2.1]heptane-2,3-di-*endo*-carboxylic anhydride (**2**) was obtained by a known method[11,12] (Scheme 1). Anhydride **2** has now been transformed into 3-*endo*-amino-6-*exo*-phenylbicyclo[2.2.1]heptane-2-*endo*-carboxylic acid (**3**) via the monocarboxy amide through Hofmann degradation with hypobromite. **3** was reduced, without isolation, with lithium aluminium hydride (LAH) to furnish 5-*exo*-phenyl-3-*endo*-hydroxymethylbicyclo[2.2.1]heptane-2-*endo*-amine (**4**). Though this pathway could result in both 5- and 6-phenyl analogues, we were able to isolate only the 5-phenyl derivative **4**.

† Saturated Heterocycles, Part 234. Part 233: Ref. 13.



Scheme 1.

The selective formation of **3** may be due to the conjugative effect of the phenyl group on **2**. This can act through three carbon atoms in the rigid norbornane skeleton by increasing the electron density on the nearer carbonyl carbon. Reaction of the more positive 2-carbonyl with ammonia yields the 2-carboxy amide isomer, which is converted into an amino group by Hofmann degradation.

Position 5 as the site of the phenyl substituent was proved by NMR spectroscopy and for **13**, also by X-ray measurements (see below).

The above $AlCl_3$-catalysed addition is a convenient method for substitution of the norbornane (and cyclohexane[13]) skeleton by an aryl group, i.e., formation of a new C–C bond on the functionalized norbornane moiety for the preparation of the bicyclic 1,3-amino alcohol (**4**).

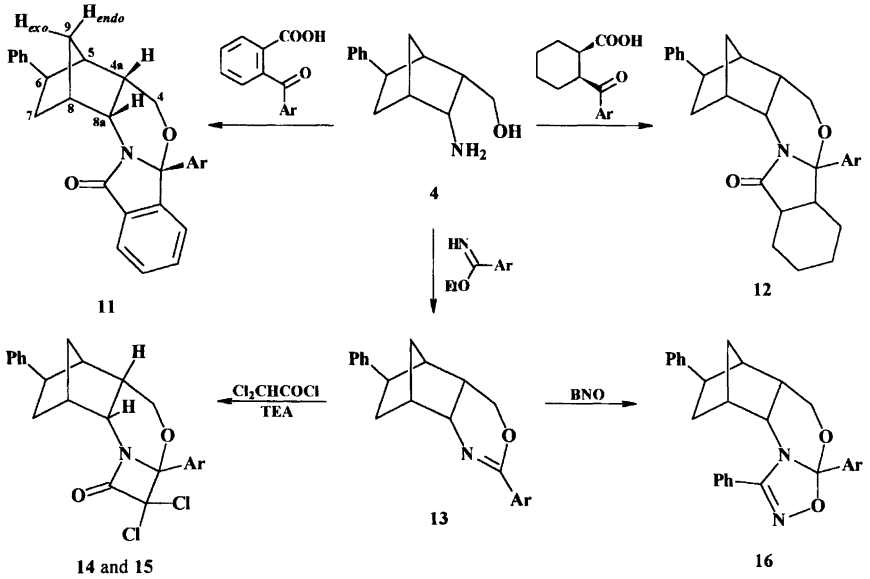
Synthon **4** was cyclized with ethyl chloroformate to yield a norbornane-condensed 1,3-oxazin-2(1*H*)-one (**5**), and the corresponding thione **6** was prepared by cyclization of the dithiocarbamate on treatment with Pb^{2+}. The norbornane-fused 1,4-oxazepinones **7** and **8** were obtained by reaction of **4** with chloroacetate or 2-chloropropionate.

Compound **4** was also reacted with phenyl isothiocyanate; the subsequent base- or acid-catalysed cyclization of the thiourea formed yielded the phenylimino-1,3-oxazine (**9**) and -thiazine (**10**), respectively. Because of its poor solubility, the structure of **10** could not be established by NMR methods. The reactions with 2-aroylbenzoic acid and *cis*-2-*p*-chlorobenzoyl-1-cyclohexanecarboxylic acid[14,15] led to **11** and **12**, respectively, containing five condensed rings (Scheme 2).

The interest in these compounds is due to their fairly complex stereochemistry. This stems in **12**, for example, from the mutual positions of the ring-junction aryl group and di-*exo*-ring-junction hydrogens or, in addition to the aryl group, the hydrogen atoms of the norbornane and cyclohexane ring junctions.

Compounds **14–16** were obtained by cycloaddition from the norbornane-condensed 1,3-dihydrooxazine **13**. The latter was prepared by the reaction of **4** with *p*-chlorobenzimidate, and its structure was established by X-ray diffractometry. With dichloroacetyl chloride and triethylamine (TEA), the azetidinone isomers **14** and **15** were formed from **13**, the arrangement of the ring-junction hydrogens and aryl group being *cis* in **14** and *trans* in **15**. Compounds of related structure have been prepared earlier.[9] The reaction of **4** and benzonitrile oxide (BNO), obtained *in situ* from benzhydroxamic chloride with TEA, yielded the methylene-bridged 1,2,4-oxadiazolo[4,5-*d*][3,1]benzoxazine (**16**).

As regards the regioselectivity, the cycloadditions result in the preferred formation of that heterocycle which contains a new carbon–hetero bond and not a hetero–hetero linkage at the hetero multiple bond.[16] ^1H and ^{13}C NMR studies revealed that BNO cycloaddition led to that of the two possible isomers which contains an *exo* aryl group on the carbon between the oxygen



Scheme 2.

and nitrogen atoms, i.e., the phenyl substituent and the *exo*-ring-junction hydrogens are *cis*.

It is noteworthy that from the reaction of the phenyl-unsubstituted dihydro-1,3-oxazine analogue of **13** and BNO, another isomer was isolated,[17] containing the aryl group *trans* to the ring-junction hydrogens. The present findings suggest that the 5-phenyl substituent modified the solubility favourably, and this allowed isolation of isomer **16** from the mixture (the presence of the other diastereomer could be detected by TLC, but it was not isolated).

Structure. The IR, ^{1}H and ^{13}C NMR data on the new compounds are listed in Tables 1 and 2. The structure elucidation is illustrated for **13**. The structures of **5**, **6** and **9** can be determined in a similar way.

From the ^{1}H NMR spectrum of **13**, the 4-OCH_2* and 8a-NC*H* hydrogens can be assigned unequivocally to the 4.36 ppm d (2 H) and 4.04 ppm dd (1 H) signals. The splits of the latter (10.7 and 4.4 Hz) prove the unaltered di-*endo* annelation of the norbornane moiety to the hetero ring.[9] Measurements support the origin of this signal: on saturation of the easily assignable H-4a signal in a double resonance (DR) experiment, the upfield one of the singlet-like H-5,8 signals became sharper, while its counterpart showed no change; the former is therefore assigned to H-5.

As the six-membered hetero ring has two possible distorted twist conformations, with the oxygen in either the *endo* or the *exo* position, the dihedral angles of the 4-CH_2 hydrogens and H-4a are ~30° and ~90° or ~180° and ~60°. For **13**, the average of the corresponding couplings is 4.2 Hz, which corresponds to the former conformation. (For the conformation in which the oxygen is *exo*, the average coupling would be higher because of the dihedral angle of 180°.[18]) For the analogue **6**, the couplings 2.7 and 5.5 Hz are obtained; their average is identical with that measured for **13**.

The location of the phenyl group at position 6 or 7 was established by means of DNOE.[19a,20] On irradiation of the H-5 signal at 2.50 ppm, assigned via DR measurements, the 3.36 ppm signal of the hydrogen geminal to the phenyl group became more intense, which is evidence that the phenyl substituent is at position 6. The NOE between H-6 and H-4*ax*(*endo*) proves the *exo* position of the 6-phenyl group (see below in connection with **8**).

The analogous stereostructures of the phenylnorbornane moieties in **8** and **13** follow from the very similar ^{13}C chemical shifts (Table 2) for the C-5–C-9 lines.

2D-HSC measurements[21] also indicate position 6 for the phenyl substituent, showing that the downfield of the C-5,8 lines relates to C-5, due to the α-effect of the vicinal tertiary C-6.[19b,22] Thus, the structure 4a*R**,5*R**,6*S**,8*R**,8a*S** (the other enantiomer is depicted in Fig. 1) is proved. The X-ray data support this structure (Fig. 2).

For **8**, it was also necessary to determine the position of the methyl group and the preferred conformation of the hetero ring. On saturation of the *O*-methine signal in a DNOE experiment, the H-4a and H-8a signals responded, which is proof of the *exo* position of the methine hydrogen, i.e., the methyl group and hydrogens H-4a,8a are *trans* to the hetero ring. From the steric proximity of these three hydrogens, it follows that the boat conformation is preferred for the hetero ring, in

* For comparison of the analogous spectroscopic data, the numbering in Schemes 1 and 2 is used in the text and Tables 1 and 2. See the Experimental for IUPAC nomenclature.

Table 1. Characteristic IR frequencies (in KBr, cm^{-1}) and ^1H NMR data (in $CDCl_3$, chemical shifts in ppm, $\delta_{TMS}=0$ ppm and coupling constants in Hz) on compounds **5–16** at 250.14 MHz.[a]

	$\nu_{C=X}$ band	$CH_2(9)$[b] 2 × d (2 × 1 H)		$CH_2(7)$ td (1 H)[c]	ddd (1 H)[d]	$OCH_2(4)$ 2 × dd (2 × 1 H)[e]		4a-H m (1 H)[f]	5-H ~s (1 H)[g]	6-H dd (1 H)[h]	8-H ~s (1 H)[i]	8a-H dd (1 H)[j]	ArH[k] 1–6 signal (5–14 H)
5	1683	1.45	1.82	1.69	2.22	~4.35		~2.5[l]	~2.5[l]	3.45	~2.5[l]	3.82	7.1–7.35
6	1554	1.50	1.87	1.75	2.20	~4.40		~2.55[l]	~2.55[l]	3.41	~2.55[l]	~3.8	7.2–7.4
7	1653	1.50	1.78[l]	~1.75[l]	2.30	~3.95[m]		~2.45[n]	2.60	2.96	~2.45[n]	~3.95[m]	7.15–7.35
8	1677	1.50	1.78[l]	~1.7[l]	2.20	3.88	4.08	2.35	2.58	2.95	2.53	3.98	~7.15, 7.30[o]
9	1676	1.38	1.72	1.64	~2.3[l]	~4.25		~2.4[l]	2.44[l]	3.40	2.37[l]	3.70	6.95[p], 7.1–7.3
10[q]	1618	1.45	1.73	1.55	~2.4[l]	~2.55	3.15[n]	~2.4[l]	2.55[m]	~3.15[n]	~2.4[l]	3.70	6.9–7.35
11	1697	1.45	1.65	1.40	1.75	3.85	4.25	~2.4[l]	2.38[l]	3.16	2.73	4.66	7.01[o], 7.10[r], ~7.2, 7.40[r], 7.88[s]
12	1697	~1.4[l]	~1.7[m]	~1.45[l]	~1.7[m]	3.85	4.00	2.45	2.28	2.65	2.80	4.15	6.95[o], 7.10, 7.20[r], 7.25–7.50[t]
13	1650	~1.6[l]	1.85	~1.6[l]	1.95	4.36		2.30	2.50	3.36	2.72	4.04	7.36[u], 7.90[u], 7.1–7.3
14	1786	1.27	1.80	~1.9[l]	2.15	3.93	4.13	~1.9[l]	2.43	3.31	2.99	3.80	7.20[v], 7.32[r]–7.40[o,t]
15	1805	1.37[l]	1.65[m]	1.37[l]	1.65[m]	4.17	4.58	~2.45[n]	~2.45[n]	3.10	2.58	4.40	6.95[o], 7.12[p], 7.23[r], ~7.45, 7.65[s]
16	1597	1.15	1.60[l]	1.55[l]	1.85	4.14	4.36	2.22	2.50	3.68	2.55	3.88	7.15, 7.30[o], 7.40[u], 7.55[w], 7.65[u] 7.82[z]

Further data, IR: νNH: 3500, 3420 and 3210 (**5**), 3175 (**6**), 3455 (**7**), 3200 (**8**), 3300–2700 (**9**, **10**); $\gamma C_{Ar}H$ and $\gamma C_{Ar}C_{Ar}$ (phenyl): 754 and 698 (**5**), 723 and 693 (**6**), 740 and 700 (**7**), 746 and 702 (**8**), 747 and 696 (**9**), 725 and 697 (**10**), 744 and 702 (**11**), 731 and 700 (**12**), 733 and 695 (**13**), 735 and 701 (**14**), 734 and 699 (**15**), 765 and 690 (**16**); $\gamma C_{Ar}H$ (*p*-disubst. phenyl): 892 (**11**), 825 (**12**), 835 (**13**, **16**), 861 (**14**), 854 (**15**); $\gamma C_{Ar}H$ (*o*-disubst. phenyl): 759 (**11**), νC–O: 1114 (**5**), 1197 and 1170 (split band pair, **6**), 1103 (**7**, **8**), 1107 (**9**), 1070 (**11**), 1088 (**12**, **14**), 1090 (**13**, **16**), 1094 (**15**); ^1H NMR: NH, (br s, 1 H): 5.92 (**5**), 8.35 (**6**), 6.75 (**7**), 6.00 (**8**), 6.60 (**9**), 5.85 (**10**); CH_3: 2.30 (s, 3 H) (**11**), 1.35 (d, $J=6.2$), (**8**); $COCH_2O$ (**7**); (2 × d, 2 × 1 H): 4.19 and 4.39 ($J=14.5$); OCH, (q, 1 H): 4.39 (**8**); CH (cyclohexyl, **12**), ~2.0 (m, 2 H); CH_2 (cyclohexyl, **12**): 0.25 (dq, H-5′*ax*), ~1.00 (tq, H-3′*ax*), ~1.2 (m, H-2′*ax*, H4′*ax*), ~1.7[m] (m, H-3′*eq*, H-4′*eq*, H-5′*eq*), 2.15 (td, H-2′*eq*), (see the numbering in Scheme 2). [a] Assignments were proved by DR (for **13**), DNOE and 2D-HSC measurements (except for **5**, **6** and **10**). [b] AB-type spectrum, $J(A,B)=10.6\pm0.1$, the upfield doublets originate from the *endo*, the downfield ones from the *exo* hydrogen. [c] *exo*-Hydrogen, the doublet splitting is about 13.5–14.0, the triplet ~4.0–4.5 Hz. [d] *endo*-Hydrogen, the splittings are about 13.5–14.0, 9 and 2.5 Hz. [e] A and B parts of a ABX spin-system ($\delta A \equiv Hax < \delta B \equiv Heq$), near to the A_2X limiting case for **5–7**, **9** and **13** (the eight AB lines are very close, for **13** coalesced to a d), $J(A,B)=11.5$ (**8**), 12.4 (**11**, **12**, **14**), 13.3 (**15**), 12.8 (**16**), $J(A,X)$ and $J(B,X)=2.7$ and 5.5 (**6**), 3.2 and 11.5 (**8**), 7.0 and 5.4 (**11**), 8.8 and 8.4 (**12**), 4.2 (**13**, mean value for the two couplings), 6.8 and 5.5 (**14**), 3.8 and 6.3 (**15**), <1 and 5.1 (**16**). [f] Multiplicity is dq for **13** (split by 10.7, 4.3, 4.3 and 4.3), td for **16** (split by 12.4, 4.0 and 4.0). [g] Triplet-like signal with coalesced lines for **7**, **8** and **14**, d for **12** ($J=4.0$), **13** ($J=3.3$) and **16** ($J=4.5$). [h] Split by 8.6 ± 0.2 and 5.0 ± 0.4. [i] Doublet for **8** ($J=4.1$) and **14** ($J=3.3$), triplet-like signal with coalesced lines for **11**, **12**, **13**, **15** and **16**. [j] Split by 10 and 3 (**8**, **10**), 12.1 and 4.0 (**11**), 12.5 and 2.2 (**12**), 10.8 and 4.2 (**13**, **14**), coalesced to a ~d (split by 10) for **5**, **6** and **9**, further split to ddd for **15** and **16** (split by 12.2, 4.3, 1.8 and 10, 2, 2). [k] Number of separated signals: 1 (**5**, **6**, **7** and **10**), 2 (**8** and **9**), 3 (**13** and **14**), 4 (**12**), 5 (**11** and **15**) and 6 (**16**), total intensity: 5 H (**5–8**), 9 H (**12–15**), 10 H (**9** and **10**), 13 H (**11**), 14 H (**16**). [l,m,n] Overlapping signals. [o] Separated signal (dd) of the *o*-hydrogens (2 H) in the 6-phenyl ring. [p] Separated signal (~t) of the *p*-hydrogen of the *N*-phenyl (**9**) or 6-phenyl (**15**) group. [q] Due to signal overlap and the poor quality of the spectrum (because of poor solubility), the assignments of overlapping signals are dubious. [r,v] Intensity: 2 H/1 H. [s] (dd, 1 H): H-2 (see the numbering in Scheme 2). [t] Aryl group (4 H). [u] H-3,5 and H-2,6 signals (A and B parts of an AA′BB multiplet) of the aryl group, $J^o=8.6$. [w/z] Conjugated phenyl group *m*-+*p*-/*o*-hydrogens.

Table 2. ^{13}C NMR chemical shifts ($\delta_{TMS}=0$) for compounds **5–9** and **11–16** in $CDCl_3$ solution at 62.9 MHz.[a]

										6-Phenyl group				Aryl group			
	C-2	C-4	C-4a	C-5	C-6	C-7	C-8	C-8a	C-9	C-1	C-2,6	C-3,5	C-4	C-1	C-2,6	C-3,5	C-4
5	157.2	67.0	36.5	46.6	39.8	29.6	43.6	53.4	36.2	145.8	126.9	128.2	125.6				
6	190.4	68.5	36.9	46.8	39.9	30.0	43.8	53.8	36.5	145.3	126.9	128.3	125.8				
7	171.9	66.7	44.7	45.8	38.7	30.2	42.3	53.6	35.9	145.5	126.8	128.3	125.8				
8	170.6	65.3	42.0	46.3	38.5	29.2	41.7	53.7	35.7	145.3	126.9	128.3	125.8				
9	153.0	66.2	37.5	46.4	39.9	29.6	43.3	52.5	35.7	146.1	127.0	128.4	125.4	145.0	122.0	128.5	121.7
11	92.4	61.6	34.9	46.0	39.2	31.8	43.1	54.2	35.7	146.4	126.9	128.0	125.0	137.7[b]	125.3	129.3	137.9[b]
12	93.2	60.5	33.8	44.7	38.8	30.6	42.1	52.3	34.9	145.7	126.9	128.3	125.4	136.3	127.9	128.7	134.1
13	155.7	65.4	37.5	48.4	40.0	30.9	43.3	53.4	36.8	146.5	126.9	128.4	125.4	136.5	128.2[c]	128.2[c]	132.3
14	91.9	64.8	33.0	47.8	38.3	30.2	40.9	52.9	34.7	144.5	127.5	128.2	126.0	133.5	128.9[b]	128.4[b]	135.7
15	93.5	63.3	35.4	46.1	38.6	32.2	41.8	52.9	35.9	145.4	126.6	128.3	125.7	134.2	128.7[e]	127.4[e]	135.7
16	115.1	59.7	35.1[c]	47.6	40.1	30.8	43.7	56.6	35.1[c]	146.2	127.0	128.4	125.4	139.9	127.7[d]	129.0	134.6

Further signals CH_3: 16.3 (**8**), 20.9 (**11**); $COCH_2O$ (**7**): 70.1; CHO (**8**): 69.9; CCl_2: 89.5 (**14**), 89.7 (**15**); C=O: 173.4 (**11**), 178.8 (**12**), 160.7 (**14**), 166.6 (**15**); NC=N (**16**): 159.9; carbon lines 1–6 of the condensed benzene (**11**) or cyclohexane (**12**) ring, C-1 is the carbonyl-substituted carbon in the ring: 129.4, 123.3, 122.5, 132.6, 129.0, 150.0 and 42.9, 25.4, 25.1,[b] 24.8,[b] 26.5, 54.9; 3-phenyl group on the oxadiazoline ring, C-1: 127.7,[d] C-2,6: 126.2, C-3,5: 128.1, C-4: 130.9. [a] Assignments were proved by DEPT (except for **5**) and 2D-HSC measurements (except for **5** and **6**). [b] Interchangeable assignments. [c,d] Two overlapping lines. [e] The signal pairs C-2,6 and C-3,5 are split (with the second line at 130.2 and 127.5, respectively) due to hindered rotation of the aryl group.

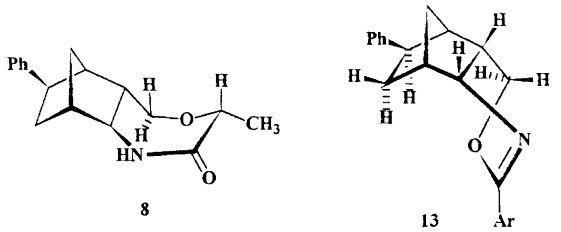


Fig. 1. Structures of compounds **8** and **13** (Ar = C_6H_4Cl-*p*).

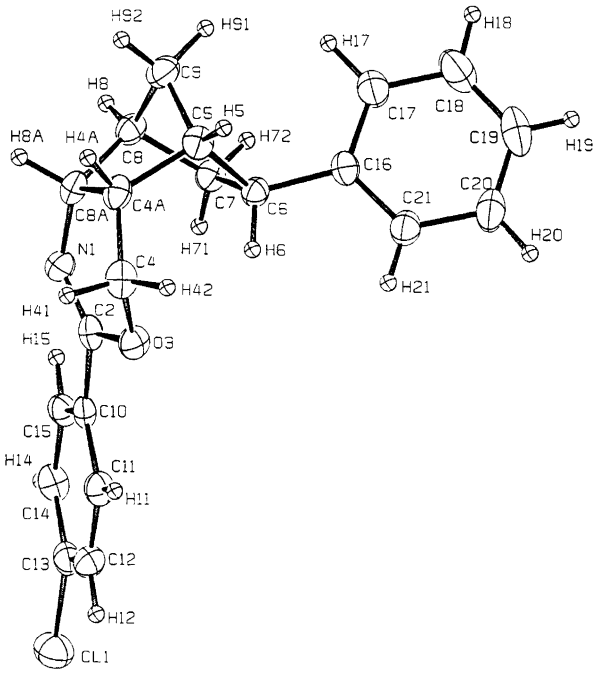


Fig. 2. ORTEP perspective view of **13** with atomic numbering.

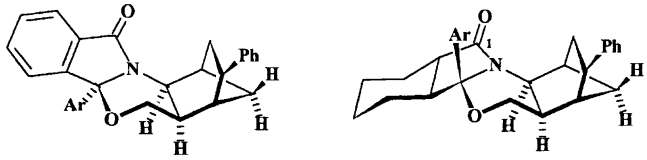
which the ring-junction carbons C-4a,8a and the carbon of the *O*-methine group lies on the same side of the plane fitted to the two hetero atoms, and the carbonyl and methylene carbons. Thus, with a *quasi-equatorial* methyl group, the molecule avoids the strong steric hindrance between the methyl group and the *endo* H-4,6,7 atoms, which would be the case in the other relatively stable conformation of the hetero ring.

The analogous stereostructure of the nor-compound **7** can be elucidated similarly.

For **8**, position 6 for the phenyl group and di-*endo* annelation can be established analogously as in the case of **13**. The relative configuration is 3*R**,4a*S**, 5*S**,6*R**,8*S**,8a*R** (Fig. 1).

For **11**, **12** and **14–16**, the relative positions of the *p*-tolyl group (C-2 configuration) also have to be elucidated. This is illustrated for **11**. The dd splitting of the NCH (H-8a) signal reveals the di-*endo* annelation. In the knowledge of the source of the H-8 signal, the assignment of H-5 is also possible. Saturation of the H-8a signal allows identification of the H-8 signal, due to its NOE response. The NOE between H-6 and H-5 is proof of position 6 for the phenyl substituent, while that on the *ortho* hydrogens of the phenyl group allows the assignment of H-6 dd. Irradiation of the H-9(*exo*) signal at 1.65 ppm in a further DNOE experiment results in an increased intensity of the signal of the phenyl *ortho* hydrogens, which is proof of the *exo* position of the 6-phenyl group.

The *cis* relative positions of the tolyl group and H-4a,8a were established from the NOE found between H-4*ax* and H-6. This can be proved directly for **16**, which has an analogous steric structure, by the NOE observed between H-4a,8a and H-2′,6′ of the *p*-chlorophenyl substituent. (For **11**, the same interaction cannot



11 12

Fig. 3. Structures of compounds **11** (Ar = $C_6H_4CH_3$-*p*) and **12** (Ar = C_6H_4Cl-*p*).

be observed because of the overlap of the signals of the condensed aromatic ring.) Hence, **11** has the structure 2*R**,4a*S**,5*S**,6*R**,8*S**,8a*R** (Fig. 3).

Because of the presence of further chiral centres in **12**, the conformation and *cis* or *trans* annelation of the cyclohexane ring and the mutual (*cis* or *trans*) positions of the ring-junction hydrogens of the cycloalkane ring and the aryl group have to be elucidated, too.

For the analogous parts of **12** and **11** and **16**, an analogous structure (di-*endo* annelation and 6-*exo*-phenyl substitution) can be concluded. Comparison of the carbon shifts for the perhydroisoindolone moiety with data on the previously investigated analogues[24] unambiguously demonstrates the *trans* annelation of the pyrrolidone–cyclohexane, the chair conformation of the latter, and the *cis* position of the *p*-tolyl group and the annelational hydrogen next to the carbonyl; only the mutual positions of the isoindolone- and oxazine-condensed norbornane moieties remain questionable.

The steric proximity of H-6 and H-2′,6′ of the *p*-chlorophenyl group and consequently the stereostructure 2*R**,4a*R**,5*R**,6*S**,8*R**,8a*S**,11*S**,16*S** of **12** (Fig. 3) follow from DNOE measurements. **12** contains the oxazine ring in the sofa conformation, with an out-of-plane oxygen.

For **14** and **15**, the β-lactam structure follows from the high IR carbonyl frequency characteristic for the β-lactams[24] and from the appearance of the ^{13}C NMR carbonyl line. The di-*endo* annelation of the norbornane and oxazine rings and the 6-*exo* position of the phenyl substituent can be proved similarly as for the former compounds. The two isomers differ in the positions of the aryl group and the ring-junction hydrogens H-4a,8a; the positions are *cis* (2*R**,4a*R**,5*R**,6*S**,8*R**,8a*S**) in **14** and *trans* (2*S**,4a*R**,5*R**,6*S**,8*R**,8a*S**) in **15**. The strong shielding ($\Delta\delta \approx 0.5$) of the 7-CH_2 hydrogens in **15** and the high increase of the H-4a,8a shielding (in **14** $\Delta\delta \approx 0.6$ relative to **15**) support these structures. (The shielding originates from the anisotropic effect,[19c] of the close-lying phenyl group.) Further supporting evidence is the NOE found between H-8a and the *ortho* hydrogens of the phenyl group for **14**, and the NOE observed on the signal of the *ortho* hydrogens on irradiation of H-6 for **15**.

Experimental

IR spectra were run for samples as KBr discs on a vacuum optic 113 v FT-spectrometer equipped with an Aspect 2000 computer. ^1H and ^{13}C NMR spectra were recorded for samples in $CDCl_3$ or DMSO-d_6 solution in 5 mm tubes at room temperature on a Bruker WM-250 FT-spectrometer controlled by an Aspect 2000 computer at 250.13 (^1H) and 62.89 (^{13}C) MHz, respectively, using the deuterium signal of the solvents as the lock and TMS as an internal standard. Conventional CW irradiation of ca. 0.15 W was used in the DR experiments. DEPT[25] spectra were run in the standard way,[26] using only the $\theta = 135°$ pulse to separate the CH/CH_3 and CH_2 lines phased up and down, respectively. For DNOE measurements,[19a,20] the standard Bruker microprogram DNOEMULT.AU to generate NOE was used. The 2D-HSC spectra[21] were obtained by using the standard Bruker pulse program XHCORRD.AU.

The X-ray data were collected at room temperature on a Rigaku AFC5S diffractometer with graphite-monochromatized Mo Kα ($\lambda = 0.71069$ Å) radiation. The intensity data were collected in an ω–2θ scan mode at an ω scan speed of 4.0° min^{-1} with the ω scan width = $1.52 + 0.30 \tan\theta$. A total of 2349 reflections were measured to $2\theta_{max} = 50°$, with 2195 unique reflections, and $R_{int} = 0.031$; 1432 reflections having $I > 2.00\sigma(I)$ were used. All data were corrected for Lorentz-polarization effects and for secondary extinction: coefficient = 0.2717E−05. The intensities of three representative check reflections showed only statistical fluctuations.

The structure was solved by direct methods, using SHELXS-86[27] followed by successive Fourier syntheses,[28] and refined by least-squares techniques to an *R* value of 0.068 [$R' = 0.079$, $w = 1/\sigma^2$ (F_o)], with heavy atoms anisotropic and hydrogen atoms with fixed isotropic displacement factors (1.2 × disp. factor of the host atom). Neutral atom scattering and dispersion factors were taken from *International Tables.*[29] All calculations were performed by using the TEXSAN[30] crystallographic software. The Figure was drawn with the program ORTEP.[31]

Bicyclo[2.2.1]hept-5-ene-2,3-di-endo-*carboxylic acid* (**1**). 164.1 g (1.0 mol) bicyclo[2.2.1]hept-5-ene-2,3-di-*endo*-carboxylic anhydride in 1200 ml 10% NaOH solution were refluxed for 3 h, then cooled to 10 °C and acidified with conc. HCl. The resulting white precipitate was filtered off by suction, washed with cold water, dried and crystallized from EtOH, m.p. 169–174 °C; yield 175.8 g (96.5%) **1**. Analytical data: found C 59.51; H 5.44. Calc. for $C_9H_{10}O_4$: C 59.34; H 5.53%.

5-exo-*Phenylbicyclo[2.2.1]heptane-2,3-di*-endo-*carboxylic anhydride* (**2**). To a solution of 70.5 g (0.53 mol) anhydrous $AlCl_3$ in 120 ml dry benzene, 40.0 g (0.22 mol) **1** was added in portions. After being stirred for 30 min at room temperature, the mixture was heated to 50 °C for 2 h, cooled, and then poured onto a mixture of 1000 ml crushed ice and 100 ml conc. HCl. The white precipitate was filtered off, washed with cold water, dried

at 100 °C and crystallized from AcOH, m.p. 167–172 °C; yield 44.4 g (77.5%) 5-*exo*-phenylbicyclo [2.2.1] cycloheptane-2,3-di-*endo*-carboxylic acid. Analytical data: found C 68.31; H 7.65. Calc. for $C_{15}H_{16}O_4$: C 69.22; H 6.20%.

A solution of 20.0 g (77 mmol) of this dicarboxylic acid in 80 ml Ac_2O was refluxed for 3 h. The Ac_2O excess was removed by distillation and the residue was treated with 50 ml diethyl ether. The crystals were filtered off, washed with diethyl ether and dried; m.p. 106–108 °C; yield 16.0 g (86%) **2**. Analytical data: found C 74.60; H 5.88. Calc. for $C_{15}H_{14}O_3$: C 74.36; H 5.82%.

3-endo-*Amino*-*5*-exo-*phenylbicyclo[2.2.1]heptane*-*2*-endo-*carboxylic acid* (**3**). 12.1 g (0.05 mol) **2** were added in portions to 40 ml conc. NH_4OH under cooling with ice-water. The solution was stirred at room temp. for 30 min, cooled to 10 °C and acidified with conc. HCl. The white precipitate was filtered off, washed with 30 ml cold water and dried; m.p. 155–160 °C. 7.0 g (27 mmol) of this crude carboxy amide were added in portions to a solution of 1.7 ml (0.03 mol) bromine in 40 ml 25% NaOH at 0 °C. The solution was warmed quickly to 75 °C and was kept at this temperature for 2 min. The hot solution was filtered, and the filtrate was cooled to 10 °C and acidified with 14 ml conc. HCl and 6 ml glacial acetic acid. The white precipitate was filtered off, washed with 30 ml cold water and dried, m.p. 260–265 °C, yield 5.6 g (90%); the product was used for the preparation of **4**.

3-endo-*Hydroxymethyl*-*5*-exo-*phenylbicyclo[2.2.1]hept-an-2*-endo-*amine* (**4**). 4.2 g (0.11 mol) LAH were suspended in 200 ml dry THF at 0 °C. To the mixture, 9.25 g (0.04 mol) **3** were added in portions, with cooling. The mixture was refluxed for 8 h, and then cooled to 0 °C, and 9 ml water were added dropwise. The precipitate was filtered off, and the filtrate was dried (Na_2SO_4) and evaporated to dryness. The brown oily residue was distilled by fractions, to give a colourless oil, b.p. 123–129 °C/260 Pa, yield 5.8 g (67%).

6-exo-*Phenyl*-*5,8*-*methano*-*4ar,5t,6,7,8t,8ac*-*hexahydro*-*4H*-*3,1*-*benzoxazin*-*2(1H)*-*one* (**5**). 2.17 g (0.01 mol) of the amino alcohol **4** and 0.84 g (0.01 mol) $NaHCO_3$ were dissolved in 10 ml water, 1.1 g (0.01 mol) ethyl chloroformate was added dropwise, and the mixture was refluxed for 30 min. After being cooled, the solution was extracted with diethyl ether, the extract was dried (Na_2SO_4) and the solvent was evaporated off. On dissolution of the residue in a mixture of EtOAc and petroleum ether, and refrigeration of the solution, colourless crystals were formed. 2.89 g (0.01 mol) of this carbamate were heated with 50 mg MeONa in an oil bath at 200 °C for 1 h. The melt was extracted with EtOAc and the product obtained from the extract was crystallized from EtOH, m.p. 150–152 °C (58%). Analytical data: found C 74.04; H 7.23; N 5.90. Calc. for $C_{15}H_{17}NO_2$: C 74.05; H 7.04; N 5.76%.

6-exo-*Phenyl*-*5,8*-*methano*-*4ar,5t,6,7,8t,8ac*-*hexahydro*-*4H*-*3,1*-*benzoxazine*-*2(1H)*-*thione* (**6**). To a solution of 2.83 g (13 mmol) **4** in 8 ml 10% KOH, 1.0 g (13 mmol) CS_2 in 6.35 ml dioxane was added at 0 °C. The mixture was stirred for 5 min, and 8 ml 5% KOH and 5 g $Pb(NO_3)_2$ in 20 ml H_2O were added. After warming at 60 °C for 10 min, the mixture was filtered and the precipitate was washed with 50 ml hot water. The filtrate was evaporated to dryness, the residue was extracted with EtOH, and the solution was evaporated to dryness. The residue was purified by column chromatography (basic Al_2O_3, 50–200 μm, Janssen Woelm, EtOAc), the solvent was removed by evaporation and the residue was crystallized from EtOH, m.p. 204–206 °C (62%). Analytical data: found C 69.28; H 6.58; N 5.50. Calc. for $C_{15}H_{17}NOS$: C 69.46; H 6.61; N 5.40%.

7-exo-*Phenyl*-*6,9*-*methano*-*5ar,6t,7,8,9t,9ac*-*hexahydro*-*4,1*-*benzoxazepin*-*2(1H)*-*one* (**7**). To a solution of 2.17 g (0.01 mol) **4** in 20 ml dry benzene, 1.22 g (0.01 mol) ethyl chloroacetate and 0.3 g (12 mmol) NaH were added simultaneously. After being stirred for 10 min and refluxed for 1 h, the mixture was cooled, and 50 ml dry benzene were added. The organic phase was washed with 5% HCl, and then with 30 ml water, dried (Na_2SO_4) and evaporated to dryness. The residue was purified by column chromatography (Silica gel, 0.035–0.07 mm, Janssen), eluent: EtOAc. After evaporation, the product was crystallized from EtOH, m.p. 198–200 °C (55%). Analytical data: found C 74.48; H 7.44; N 5.21. Calc. for $C_{16}H_{19}NO_2$: C 74.68; H 7.44; N 5.44%.

3-*Methyl*-*7*-exo-*phenyl*-*6,9*-*methano*-*5ar,6t,7,8,9t,9ac*-*hexahydro*-*4,1*-*benzoxazepin*-*2(1H)*-*one* (**8**). To a solution of 2.17 g (0.01 mol) **4** in dry benzene, 1.37 g (0.01 mol) ethyl 2-chloropropionate and 0.3 g (12 mmol) NaH were added simultaneously. After being stirred for 10 min and refluxed for 1 h, the mixture was cooled to room temperature, and 50 ml benzene was added. The organic layer was washed with 5% HCl and water, dried (Na_2SO_4) and evaporated to dryness. The residue was purified by column chromatography (Al_2O_3 acidic, 50–200 μm, Janssen). After elution with EtOAc and evaporation of the eluate, the residue was crystallized from EtOAc, m.p. 158–160 °C (56%). Analytical data: found C 75.41; H 7.65; N 5.27. Calc. for $C_{17}H_{21}NO_2$: C 75.25; H 7.80; N 5.16%.

6-exo-*Phenyl*-*2*-*phenylimino*-*5,8*-*methano*-*4ar,5t,6,7,8t,8ac*-*hexahydro*-*4H*-*3,1*-*benzoxazine* (**9**). A mixture of 2.17 g (0.01 mol) **4** and 1.35 g (0.01 mol) phenyl isothiocyanate in 25 ml dry diethyl ether was left to stand for one day. The solid that separated out was filtered off by suction and crystallized from EtOH; m.p. 160–163 °C, yield 2.01 g (57%). A mixture of 3.52 g (0.01 mol) of this

2-*endo*-phenylaminothiocarbamoyl-3-*endo*-hydroxymethyl-5-*exo*-phenylbicyclo[2.2.1]heptane and 7.1 g (0.05 mol) MeI was stirred for 2 h, and the mixture was then evaporated to dryness. The residue was dissolved in 40 ml 3 M KOH–MeOH, stirred for 4 h and evaporated to dryness. To the residue, 5 ml water were added and the mixture was extracted with $CHCl_3$. After evaporation of the solvent, the residue was crystallized from EtOAc, m.p. 156–158 °C (52%). Analytical data: found C 79.03; H 6.77; N 8.75. Calc. for $C_{21}H_{22}N_2O$: C 79.21; H 6.96; N 8.80%.

6-exo-*Phenyl-2-phenylimino-5,8-methano-4ar,5t,6,7,8t,8ac-hexahydro-4H-3,1-benzothiazine* (**10**). A mixture of 3.52 g (0.01 mol) 2-*endo*-phenylaminothiocarbamoyl-3-*endo*-hydroxymethyl-5-*exo*-phenylbicyclo[2.2.1]heptane in 25 ml EtOH containing 20% dry HCl was refluxed for 5 h. After evaporation of the mixture to dryness, the residue was neutralized with 10% Na_2CO_3 solution and extracted with 3×15 ml $CHCl_3$. After washing with water and drying, the solvent-free residue was crystallized from $CHCl_3$–MeOH, m.p. 229–230 °C (48%). Analytical data: found C 75.60; H 6.78; N 8.49. Calc. for $C_{21}H_{22}N_2S$: C 75.41; H 6.63; N 8.38%.

6a-p-*Methylphenyl-3*-exo-*phenyl-1,4-methano-1,3,4,4a,5,12a-hexahydro-2H-isoindolo[2,1-a][3,1]benzoxazin-11(6a-H)-one* (**11**). A solution of 2.17 g (0.01 mol) **4**, 2.4 g (0.01 mol) 2-(*p*-methylbenzoyl)benzoic acid and 1 crystal of *p*-TosOH in 50 ml dry toluene was refluxed for 6 h. After evaporation to dryness, the residue was purified by column chromatography (Al_2O_3 neutr., 50–200 μm, Janssen, eluent: benzene). The residue of the eluate was crystallized from EtOAc, m.p. 205–207 °C (56%). Analytical data: found C 82.72; H 6.45; N 3.25. Calc. for $C_{29}H_{27}NO_2$: C 82.63; H 6.46; N 3.32%.

6a-p-*Chlorophenyl-3*-exo-*phenyl-1,4-methanoperhydro-isoindolo[2,1-a][3,1]benzoxazin-11-one* (**12**). A solution of 2.17 g (0.01 mol) **4**, 2.66 g (0.01 mol) *cis*-2-*p*-chlorobenzoyl-1-cyclohexanecarboxylic acid and 1 crystal of *p*-TosOH as catalyst in 50 ml dry toluene was refluxed for 6 h. After evaporation to dryness, the residue was purified by column chromatography (Al_2O_3 neutr., 50–200 μm, Janssen, eluent: EtOAc). After evaporation of the eluate, the residue was crystallized from EtOH, m.p. 209–212 °C; (54%). Analytical data: found C 74.96; H 6.70; N 3.27. Calc. for $C_{28}H_{30}ClNO_2$: C 75.07; H 6.75; N 3.13%.

2-p-*Chlorophenyl-5,8-methano-4a,5,6,7,8,8a-hexahydro-4H-3,1-benzoxazine* (**13**). A mixture of 2.17 g (0.01 mol) **4**, 1.83 g (0.01 mol) ethyl *p*-chlorobenzimidate, 2 drops of 20% HCl in dry EtOH and 70 ml EtOH was refluxed for 5 h, and the solution was then evaporated to dryness. The residue was purified by column chromatography (Al_2O_3 neutr., 50–200 μm, Janssen, eluent: benzene). After evaporation of the eluate, the residue was crystallized from benzene, m.p. 122–123 °C (68%). Analytical data: found C 74.28; H 6.30; N 4.01. Calc. for $C_{21}H_{20}NClO$: C 74.66; H 5.97; N 4.15%.

X-Ray crystal data on **13**: triclinic, space group *P*-1 (No. 2), $a = 9.884(1)$, $b = 13.581(2)$, $c = 6.430(1)$ Å, $\alpha = 96.99(1)$, $\beta = 101.24(1)°$, $\gamma = 88.38(1)$, $U = 840.3(2)$ Å^3 [by least-squares refinement on setting angles ($29.2 < 2\theta < 36.8$) for 24 carefully centred reflections], $Z = 2$, $D_c = 1.335$ g cm^{-3}, $F(000) = 356$. Colourless prisms, dimensions $0.12 \times 0.14 \times 0.14$ mm, μ(Mo-Kα) = 2.31 cm^{-1}. Data on the position parameters for **13** are listed in Table 3.

Table 3. Positional parameters for **13** (with esds in parentheses).

Atom	*x*	*y*	*z*
Cl(1)	−0.0399(1)	0.27399(8)	0.3876(2)
O(3)	0.4102(2)	0.6351(2)	0.7836(4)
N(1)	0.3620(3)	0.5936(2)	1.1067(5)
C(2)	0.3468(3)	0.5829(2)	0.9054(6)
C(4)	0.5372(4)	0.6844(3)	0.8906(6)
C(4A)	0.5338(4)	0.7333(3)	1.1120(6)
C(5)	0.4748(4)	0.8398(3)	1.1453(6)
C(6)	0.3227(4)	0.8427(3)	1.0209(6)
C(7)	0.2460(4)	0.7900(3)	1.1669(6)
C(8)	0.3617(4)	0.7549(3)	1.3373(6)
C(8A)	0.4488(4)	0.6732(3)	1.2333(6)
C(9)	0.4598(4)	0.8434(3)	1.3785(6)
C(10)	0.2502(3)	0.5088(2)	0.7714(5)
C(11)	0.2559(4)	0.4781(3)	0.5590(6)
C(12)	0.1670(4)	0.4054(3)	0.4427(6)
C(13)	0.0710(4)	0.3653(3)	0.5343(6)
C(14)	0.0618(4)	0.3961(3)	0.7437(6)
C(15)	0.1509(4)	0.4677(3)	0.8604(6)
C(16)	0.2652(3)	0.9438(2)	0.9764(6)
C(17)	0.2535(5)	1.0206(3)	1.1356(7)
C(18)	0.1947(5)	1.1105(3)	1.088(1)
C(19)	0.1452(5)	1.1259(3)	0.879(1)
C(20)	0.1560(5)	1.0520(3)	0.7179(8)
C(22)	0.2158(4)	0.9621(3)	0.7675(7)
H(4A)	0.626(4)	0.740(2)	1.192(5)
H(5)	0.536(3)	0.888(2)	1.111(5)
H(6)	0.320(3)	0.803(2)	0.885(5)
H(8)	0.330(3)	0.738(2)	1.454(5)
H(8A)	0.509(3)	0.645(2)	1.356(5)
H(11)	0.322(4)	0.506(2)	0.495(5)
H(12)	0.172(3)	0.382(3)	0.301(6)
H(14)	−0.009(4)	0.371(3)	0.804(5)
H(15)	0.144(3)	0.492(2)	1.002(5)
H(17)	0.293(4)	1.008(3)	1.293(6)
H(18)	0.192(4)	1.161(3)	1.207(7)
H(19)	0.106(4)	1.186(3)	0.849(6)
H(20)	0.130(4)	1.062(3)	0.568(6)
H(21)	0.223(4)	0.911(3)	0.654(5)
H(41)	0.610(4)	0.629(3)	0.894(5)
H(42)	0.555(3)	0.732(3)	0.794(6)
H(71)	0.190(3)	0.736(2)	1.089(5)
H(72)	0.183(3)	0.839(2)	1.232(5)
H(91)	0.418(4)	0.908(3)	1.445(5)
H(92)	0.546(4)	0.835(3)	1.474(5)

*2,2-Dichloro-2a-*p*-chlorophenyl-6-*exo*-phenyl-5,8-methano-perhydroazeto[1,2-*a*][3,1]benzoxazin-1-ones* (**14** and **15**). To a solution of 3.37 g (0.01 mol) **13** and 1.47 g (0.01 mol) dichloroacetyl chloride in 10 ml dry benzene, 1 g (0.01 mol) TEA was added dropwise, and the mixture was warmed up to 50 °C. After warming for a further 10 min, it was cooled and filtered, and the filtrate was evaporated to dryness. The residue was purified by column chromatography (Silica gel 0.035–0.07 mm, Janssen, eluent: benzene). After evaporation, the product was crystallized, and **15** was prepared (1.7 g, 38%). From the mother liquor, **14** (0.9 g, 21%) was obtained by fractional crystallization, with monitoring by TLC [DC Alufolien, Kieselgel 60 F254 Merck, 0.2 mm, solvent: benzene–EtOH–petroleum ether (b.p. 40–60 °C) 4:1:3; **15** (m.p. 134–136 °C, 38% from EtOAc) with higher R_f and **14** (m.p. 180–182 °C, 21% from benzene) with lower R_f]. Analytical data: found (for **14**) C 61.37; H 4.35; N 3.13 and (for **15**) C 61.30; H 4.28; N 3.20. Calc. for $C_{23}H_{20}Cl_3NO_2$: C 61.56; H 4.49; N 3.12%.

*3a-*p*-Chlorophenyl-1,7-*exo*-diphenyl-6,9-methano-5a,6,7,8,9,9a-hexahydro[1,2,4]oxadiazolo[4,5-*a*][3,1]-benzoxazine* (**16**). To a solution of 3.37 g (0.01 mol) **13** and 1.1 g (0.011 mol) TEA in 20 ml dry diethyl ether, 1.56 g (0.01 mol) chlorobenzaldoxime in 5 ml dry diethyl ether was added dropwise. The mixture was stirred for 3 h at room temperature, washed with water and extracted with EtOAc. The organic layer was dried (Na_2SO_4) and evaporated to dryness. The yellow oily residue was purified by column chromatography (Al_2O_3 neutr., 50–200 μm, Janssen, eluent: benzene). After evaporation of the eluate, the product was crystallized from EtOH, m.p. 231–233 °C (60%). Analytical data: found C 73.31; H 5.57; N 6.24. Calc. for $C_{28}H_{25}ClN_2O_2$: C 73.59; H 5.51; N 6.13%.

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References

1. Stájer, G., Szabó, A. E., Fülöp, F., Bernáth, G. and Sohár, P. *J. Heterocycl. Chem. 20* (1983) 1181.
2. Stájer, G., Szabó, A. E., Fülöp, F., Bernáth, G. and Sohár, P. *J. Heterocycl. Chem. 21* (1984) 1373.
3. Crabb, T. A. In: Lambert, J. B. and Takeuchi, Y., Eds., *Organonitrogen Stereodynamics,* Ch. 8, VCH, 1992, pp. 270–272.
4. Bernáth, G., Fülöp, F., Ecsery, Z., Blazsó, G. and Minker, E. *Pharmazie 38* (1983) 89.
5. Bernáth, G. *Bull. Soc. Chim. Belg. 103* (1994) 509.
6. Stájer, G., Szabó, A. E., Frimpong-Manso, S., Bernáth, G. and Sohár, P. *Tetrahedron 46* (1990) 6859.
7. Stájer, G., Szőke-Molnár, Zs., Bernáth, G. and Sohár, P. *Tetrahedron 46* (1990) 1943.
8. Sohár, P., Stájer, G., Szabó, A. E. and Bernáth, G. *Magn. Reson. Chem. 29* (1991) 706.
9. Sohár, P., Stájer, G. and Bernáth, G. *Org. Magn. Reson. 21* (1983) 512.
10. Sohár, P., Stájer, G. and Bernáth, G. *Magn. Reson. Chem. 25* (1987) 635.
11. Sugita, K. and Tamura, S. *Bull. Chem. Soc. Jpn. 44* (1971) 2866.
12. Sugita, K. and Tamura, S. *Bull. Chem. Soc. Jpn. 44* (1971) 3383.
13. Sohár, P., Stájer, G., Szabó, A. E. and Bernáth, G. *J. Mol. Struct.* Accepted for publication.
14. Fieser, L. F. and Novello, C. F. *J. Am. Chem. Soc. 64* (1942) 802.
15. Jucker, E. and Süss, R. *Helv. Chim. Acta 42* (1959) 2506.
16. Padwa, A. *1,3-Dipolar Cycloaddition Chemistry*, Wiley, New York, 1984, Vol. 1, pp. 128, 138.
17. Stájer, G., Szabó, A. E., Bernáth, G. and Sohár, P. *Tetrahedron 43* (1987) 1931.
18. Karplus, M. J. *J. Chem. Phys. 30* (1959) 11; *ibid 33* (1960) 1842.
19. Sohár, P. *Nuclear Magnetic Resonance Spectroscopy* CRC Press, Boca Raton, Florida, 1983 (a) Vol. 1, pp. 196, 197; (b) Vol. 2, pp. 152–154; (c) Vol. 2, pp. 25, 27; (d) Vol. 1, pp. 35, 38.
20. Sanders, J. K. M. and Mersh, J. D. *Prog. Nucl. Magn. Reson. 15* (1982) 353 and references cited therein.
21. Ernst, R. R., Bodenhausen, G. and Wokaun, A. *Principles of Nuclear Magnetic Resonance in One and Two Dimensions*, Calderon Press, Oxford, UK, 1987, pp. 471–479.
22. Mason, J. *J. Chem. Soc. A.* (1971) 1038.
23. Stájer, G., Csende, F., Bernáth, G. and Sohár, P. *Heterocycles 37* (1994) 883.
24. Holly, S. and Sohár, P. In: Láng, L. and Prichard, W. H., Eds., *Theoretical and Technical Introduction to the Series: Absorption Spectra in the Infrared Region*, Akadémiai Kiadó, Budapest, 1975, pp. 113, 114.
25. Pegg, D. T., Doddrell, D. M. and Bendall, M. R. *J. Chem. Phys. 77* (1982) 2745.
26. Bendall, M. R., Doddrell, D. M., Pegg, D. T. and Hull, W. E. *High Resolution Multipulse NMR Spectra Editing and DEPT*, Bruker, Karlsruhe, 1982.
27. Sheldrick, G. M. *Acta Crystallogr., Sect. A 46* (1990) 467.
28. Beurskens, P. T. *DIRDIF*, Technical Report 1984/1, Crystallography Laboratory, Toernooiveld, Nijmegen, Netherlands, 1984, p. 6525.
29. *International Tables for X-Ray Crystallography*, Kynoch Press, Birmingham, UK, 1974, Vol. 4, Table 2.2 A.
30. TEXSAN-TEXRAY, *Single Crystal Structure Analysis Package*, Version 5.0, Molecular Structure Corporation, The Woodlands, Texas, 1989.
31. Johnson, C. K. *ORTEP II.* Report ORNL-5138. Oak Ridge National Laboratory, Oak Ridge, Tennessee, 1976.

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