

## Tricyclo[7.2.1.0<sup>2,7</sup>]dodec-2(7)-en-12-one. Synthesis and Some Reactions

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**Abstract**—Tricyclo[7.2.1.0<sup>2,7</sup>]dodec-2(7)-en-12-one was synthesized by dehydration of the corresponding hydroxy ketone and was brought into the Leuckart reaction. The resulting *N*-tricyclo[7.2.1.0<sup>2,7</sup>]dodec-2(7)-en-12-ylformamide was hydrolyzed to 12-aminotricyclo[7.2.1.0<sup>2,7</sup>]dodec-2(7)-ene and was converted into 2,7-epoxy derivative. The structure of the latter was determined by X-ray analysis. Hydrolysis of the amide group gave 12-amino-2,7-epoxytricyclo[7.2.1.0<sup>2,7</sup>]dodecane. The stereochemistry of hydroamination of the bridging carbonyl group is discussed.

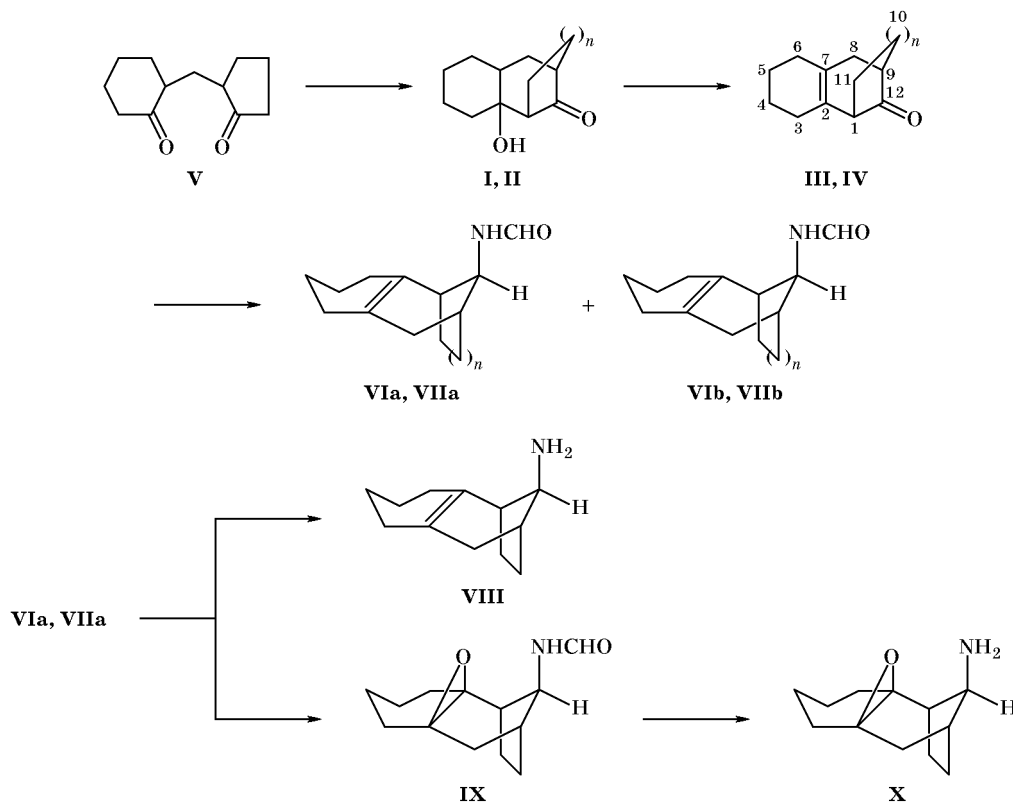
Tricyclotridecane systems attract attention due to their specific stereochemical behavior. The structure, configuration, and stereochemistry of some reactions of one of the most accessible compounds of this series, 2-hydroxytricyclo[7.3.1.0<sup>2,7</sup>]tridecan-13-one (**I**), were studied in [1–4]. Structurally related tricyclo[7.2.1.0<sup>2,7</sup>]dodecane derivatives remain almost not studied. An analog of **I**, 2-hydroxytricyclo[7.2.1.0<sup>2,7</sup>]dodecan-12-one (**II**) was synthesized relatively recently [5] by intramolecular aldol condensation of diketone **V** in basic medium. The five-membered ring in molecule **II** ensures its more rigid configuration which may be an essential factor determining the stereochemical behavior of compound **II**. In order to compare the stereochemical results of some transformations we performed a series of reactions with the dehydration product of **II**, tricyclo[7.2.1.0<sup>2,7</sup>]dodec-2(7)-en-12-one (**III**), under the conditions reported previously [4] for the same transformations of structurally related compound **IV**.

Compound **III** was synthesized for the first time [1] by heating diketone **V** in acetic acid in the presence of *p*-toluenesulfonic acid without isolation of intermediate hydroxy ketone **II**. We have synthesized ketone **III** by dehydration of **II**. The reaction was carried out under various conditions: (a) hydroxy ketone **III** was heated in boiling benzene in the presence of P<sub>2</sub>O<sub>5</sub>; (b) heating on a water bath in a mixture of equal volumes of concentrated hydrochloric and acetic acids; heating in benzene in the presence of

(c) *p*-toluenesulfonic acid, (d) anhydrous oxalic acid, (e) 20% H<sub>2</sub>SO<sub>4</sub>, and (f) gaseous HCl; and (g) heating in boiling dioxane in the presence of KHSO<sub>4</sub>. In all cases, the formation of product **III** was accompanied by the reverse reaction, transformation of **II** into diketone **V**. The latter pathway prevailed in the reaction with oxalic acid. The best yields of ketone **III** were obtained following procedures *a* and *b* (67 and 48%, respectively). Taking into account that the double bond in such systems is capable of migrating from position 2(7) to 2(3) or 7(8) [3, 6], we recorded the <sup>1</sup>H NMR spectrum of **III** but revealed no vinyl proton signals therein. This means that the double bond in **III** is located in position 2(7).

The Leuckart reaction of ketone **III** gives rise to stereoisomeric compounds **VIa** and **VIb** with respect to the bridging carbon atom. The isomer ratio, determined by GLC, was 3:1. The major stereoisomer (**VIa**) was isolated by repeated recrystallizations, and it was brought into further transformations. Alkaline hydrolysis of **VIa** gave amine **VIII**. The reaction with monoperoxyphthalic acid resulted in formation of 2,7-epoxy derivative **IX**. The latter was hydrolyzed in alkaline medium to obtain epoxy amine **X** (Scheme 1). The structure of the products was confirmed by the IR, <sup>1</sup>H and <sup>13</sup>C NMR, and mass spectra (Tables 1, 2); the structure of **IX** was unambiguously proved by X-ray analysis (Figs. 1, 2; Tables 3, 4). According to the X-ray diffraction data, the hydrogen atom in position 1 of molecule **IX** is involved in both intra-

Scheme 1.



II, III, VI,  $n = 1$ ; I, IV, VII,  $n = 2$ .

( $N-H^1 \cdots O^1$ ) and intermolecular hydrogen bond ( $N-H^1 \cdots O^2$ ) with the following parameters:  $d(H \cdots O)$  2.750(2) and 3.048(3) Å and  $\angle NHO$  124(2) and 146(2)°, respectively. Molecules of **IX** in crystal form double bands along the  $b$  axis (Fig. 2).

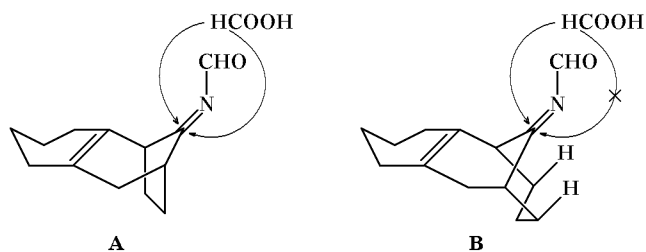
Leuckart hydroamination of tricyclo[7.3.1.0<sup>2,7</sup>]tridec-2(7)-en-13-one (**IV**) [4], which is a structural analog of **III**, also yielded a mixture of stereoisomeric products **VIIa** and **VIIb**. However, in this case the major product was isomer **VIIb**, i.e., the stereochemistry of hydroamination of the carbonyl group in ketones **IV** and **III** is the opposite. A possible reason is that the five-membered ring in **III** lacks 1,3-diaxial

interactions typical of six-membered rings; as a result, approach of hydride ion from the side of five-membered ring is less hindered. Scheme 2 shows that reducing agent ( $HCOOH$ ) can approach the double  $C=N$  bond in intermediate **A** at both sides, while one side of the same bond in intermediate **B** is shielded by axial hydrogen atoms.

## EXPERIMENTAL

The IR spectra were recorded on a Perkin-Elmer Spectrum BX-II spectrometer. The mass spectra were obtained on a Hewlett-Packard GC-MS system consisting of an HP 5972 mass-selective detector and an HP 5890 Series II gas chromatograph. GLC was performed on a Janaco G-1800 chromatograph with a flame-ionization detector (CPB-5 column, carrier gas helium, solvent 2-propanol, oven temperature 250°C). The  $^1H$  and  $^{13}C$  NMR spectra were measured from solutions in  $CDCl_3$  on a Bruker AC-250 instrument (250 MHz for  $^1H$  and 62.9 MHz for  $^{13}C$ ); tetramethylsilane was used as internal reference. Signals were assigned using off-resonance technique. The melting points were determined in a capillary.

Scheme 2.



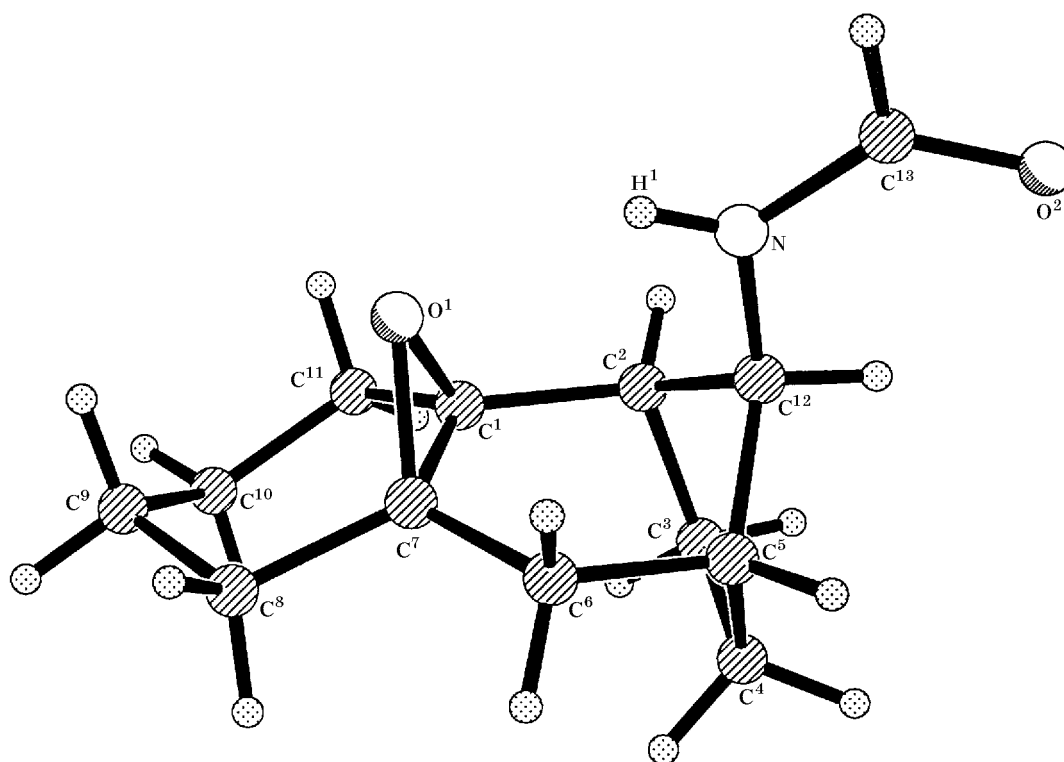


Fig. 1. Structure of the molecule of *N*-(12-oxatetracyclo[5.4.1.1<sup>2,5</sup>.0<sup>1,7</sup>]tridec-13-yl)methanamide (IX).

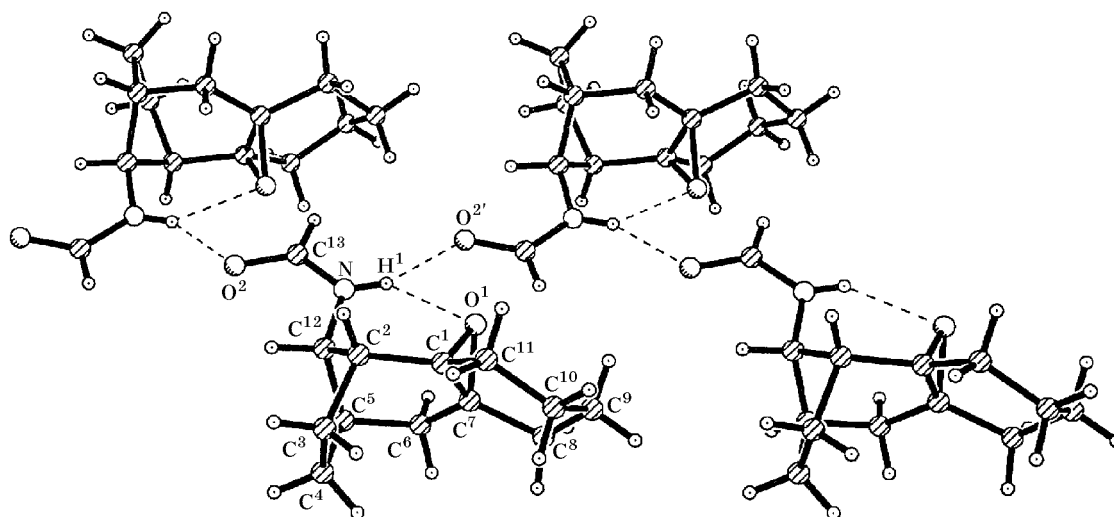


Fig. 2. Mutual arrangement of molecules IX in crystal.

X-Ray analysis of a single crystal (prism) of IX was performed on a SMART-1000 CCD diffractometer (Bruker). The structure was solved by the direct method and was refined by the least-squares procedure in anisotropic approximation for nonhydrogen atoms. The H<sup>1</sup> atom was localized by the difference synthesis and was refined with a fixed thermal parameter; the

other hydrogen atoms were localized on the basis of geometry considerations and were included in the refinement using the "rider" model. Experimental data were acquired and processed, and unit cell parameters were refined, using SMART and SAINT Plus programs [7]. All structural calculations were performed using SHELXTL/PC software [8]. The absorption of

**Table 1.** Melting points, IR spectra, and elemental analyses of compounds **VIa** and **VIII–X**

Comp. no.	mp, °C	IR spectrum, $\nu$ , $\text{cm}^{-1}$	Found, %			Formula	Calculated, %		
			C	H	N		C	H	N
<b>VIa</b>	101–103 <sup>a</sup>	KBr: 3285 (NH); 1670, 1653 (amide I), 1525 (amide II); 1219 CH <sub>2</sub> Cl <sub>2</sub> : 3419; 1682, 1503; 1275	76.29	9.47	6.97	C <sub>13</sub> H <sub>19</sub> NO	76.09	9.27	6.82
<b>VIII</b>	76–78 <sup>b</sup>	KBr: 3441, 3363, 3269 (NH <sub>2</sub> ); 1619, 1556; 1198 CH <sub>2</sub> Cl <sub>2</sub> : 3371, 3289, 3174, 3091, 3040; 1576; 1278, 1186	81.60	11.03	8.21	C <sub>12</sub> H <sub>19</sub> N	81.36	10.73	7.90
<b>IX</b>	73–75 <sup>c</sup>	KBr: 3318 (NH); 1679, 1652 (amide I), 1507 (amide II); 1300, 1230, 1209, 1191; 950, 868, 846 (C–O–C) CH <sub>2</sub> Cl <sub>2</sub> : 3394; 1676, 1503; 1302, 1274, 1230, 1192; 948, 864, 842	70.72	8.69	6.39	C <sub>13</sub> H <sub>19</sub> NO <sub>2</sub>	70.59	8.60	6.33
<b>X</b>	112–114 <sup>d</sup> (3 mm)	Neat: 3383, 3345 (NH <sub>2</sub> ); 1586, 1191; 948, 842 (C–O–C) CH <sub>2</sub> Cl <sub>2</sub> : 3391, 3319, 3170, 3043; 1592, 1264, 1192, 1089; 948, 856, 842	74.85	10.11	7.43	C <sub>12</sub> H <sub>19</sub> NO	74.61	9.84	7.25

<sup>a</sup> From 70% ethanol.<sup>b</sup> From petroleum ether–methylene chloride, 1:4.<sup>c</sup> From diethyl ether–petroleum ether, 1:4.<sup>d</sup> Boiling point.**Table 2.** <sup>1</sup>H and <sup>13</sup>C NMR and mass spectra of compounds **VIa**, **VIII**, **IX**, and **X**

Comp. no.	<sup>1</sup> H NMR spectrum, $\delta$ , ppm	<sup>13</sup> C NMR spectrum, $\delta_{\text{C}}$ , ppm	Mass spectrum, $m/z$ ( $I_{\text{rel}}$ , %)
<b>VIa</b>	1.4–2.3 m (16H), 4.21 m (1H, 12-H), 5.9 br.m (1H, NH), 8.19 d.d (1H, CHO, $J_1 = 2$ , $J_2 = 0.9$ Hz)	22.7, 22.9, 29.04, 29.09, 29.6, 31.4, 36.8 (CH <sub>2</sub> ); 34.5 (C <sup>9</sup> ); 43.3 (C <sup>1</sup> ); 51.0 (C <sup>12</sup> ); 126.2, 131.6 (C <sup>2</sup> , C <sup>7</sup> ); 161.4 (CHO)	205 (67) [M] <sup>+</sup> , 177 (91), 160 (69), 132 (100), 117 (45), 104 (57), 91 (86), 79 (59), 56 (65)
<b>VIII</b>	1.3–1.95 m (15H), 2.46 m (2H, NH <sub>2</sub> ), 3.07 t (1H, 12-H, $J = 4.5$ Hz)	23.1, 23.2, 29.2, 29.6, 30.0, 32.0, 36.4 (CH <sub>2</sub> ); 37.0 (C <sup>9</sup> ); 45.9 (C <sup>1</sup> ); 55.4 (C <sup>12</sup> ); 125.0, 131.4 (C <sup>2</sup> , C <sup>7</sup> )	177 (15) [M] <sup>+</sup> , 160 (2), 148 (2.5), 132 (5), 91 (5), 77 (6), 56 (100)
<b>IX</b>	1.1–2.3 m (16H), 4.19 m (1H, 12-H), 7.57 br.m (1H, NH), 8.11 d.d (1H, CHO, $J_1 = 2$ , $J_2 = 0.9$ Hz)	19.7, 21.6, 24.3, 27.7, 28.0, 32.0, 35.8 (CH <sub>2</sub> ); 33.3 (C <sup>9</sup> ); 41.0 (C <sup>1</sup> ), 51.6 (C <sup>12</sup> ), 60.4 (C <sup>7</sup> ), 67.4 (C <sup>2</sup> ), 160.8 (CHO)	177 (21) [M–44] <sup>+</sup> , 160 (3, 5), 148 (5), 132 (10), 117 (3, 5), 106 (5), 91 (10), 77 (5), 56 (100)
<b>X</b>	1.1–2.1 m (15H), 2.9–3.1 m (3H, 12-H, NH <sub>2</sub> )	19.8, 21.8, 24.9, 27.6, 28.7, 32.2, 35.5 (CH <sub>2</sub> ); 35.8 (C <sup>9</sup> ); 42.4 (C <sup>1</sup> ); 57.7 (C <sup>12</sup> ), 59.8 (C <sup>7</sup> ), 67.2 (C <sup>2</sup> )	193 (6) [M] <sup>+</sup> , 176 (19), 148 (65), 133 (39), 120 (29), 105 (27), 91 (45), 82 (39), 70 (32), 56 (100)

**Table 3.** Crystallographic data and parameters of X-ray diffraction experiment

Parameter	Value
Formula	C <sub>13</sub> H <sub>19</sub> NO <sub>2</sub>
Molecular weight	221.29
Temperature, K	293(2)
Wavelength, MoK $\alpha$ , Å	0.71073
Space group	<i>P</i> 2 <sub>1</sub> / <i>c</i>
<i>a</i> , Å	10.083(3)
<i>b</i> , Å	8.732(2)
<i>c</i> , Å	13.843(3)
$\alpha$ , deg	98.882(5)
<i>V</i> , Å <sup>3</sup>	1204.2(5)
<i>Z</i>	4
<i>d</i> <sub>calc</sub> , g/cm <sup>3</sup>	1.221
$\mu$ , mm <sup>-1</sup>	0.082
<i>F</i> (000)	480
Crystal habit	Prism, 0.20 × 0.12 × 0.10 mm
Range of acquired data $\theta$ , deg	2.04–24.04
Reflection index range	–11 ≤ <i>h</i> ≤ 11, –8 ≤ <i>k</i> ≤ 10, –15 ≤ <i>l</i> ≤ 15
Total number of reflections	5562
Independent reflections	1889 ( <i>R</i> <sub>int</sub> = 0.033)
Reflections with <i>I</i> > 2 $\sigma$ ( <i>I</i> )	1281
Refinement procedure	Full-matrix least-squares method with respect to <i>F</i> <sup>2</sup>
Refined variables	148
<i>S</i>	1.018
<i>R</i> -Factors in <i>I</i> > 2 $\sigma$ ( <i>I</i> )	<i>R</i> 1 = 0.061, <i>wR</i> 2 = 0.1755
<i>R</i> -Factors in all reflections	<i>R</i> 1 = 0.087, <i>wR</i> 2 = 0.1927
Extinction coefficient	Not refined
Residual electron density (min/max), e/Å <sup>3</sup>	–0.252/0.416

X-rays by the sample was not taken into account. Table 3 contains the crystallographic data and the results of structure refinement. The coordinates of atoms are given in Table 4. The atoms were numbered in accordance with its IUPAC name: *N*-(12-oxatetracyclo[5.4.1.1.2<sup>5</sup>.0<sup>1,7</sup>]tridec-13-yl)methanamide.

**Tricyclo[7.2.1.0<sup>2,7</sup>]dodec-2(7)-en-12-one (III).**  
*a.* A mixture of 2 g (0.01 mol) of hydroxy ketone **II**, 20 ml of dry benzene, and 50 mg of P<sub>2</sub>O<sub>5</sub> was heated for 30 min under reflux. The solution was filtered and evaporated, and the residue (1.78 g) was distilled

under reduced pressure. Yield 1.2 g (67%), bp 92–93°C (1 mm), *n*<sub>D</sub><sup>20</sup> 1.5200. IR spectrum (KBr),  $\nu$ , cm<sup>-1</sup>: 1755 (C=O). <sup>1</sup>H NMR spectrum,  $\delta$ , ppm (*J*, Hz): 1.2–2.3 m (15H), 2.75 br.d (1H, 1-H, 4). Published data [1]: bp 142°C (13 mm), *n*<sub>D</sub><sup>17</sup> 1.5244.

*b.* Hydroxy ketone **II**, 5 g (0.025 mol), was added to a mixture of 5 ml of concentrated hydrochloric acid and 5 ml of glacial acetic acid. The mixture was heated on a water bath while stirring for 20 min at 70–80°C. It was then cooled and neutralized with a saturated solution of Na<sub>2</sub>CO<sub>3</sub>, and the products were extracted into ether. The extract was washed with water, dried over MgSO<sub>4</sub>, and evaporated, and the residue was distilled under reduced pressure. Yield 2.1 g (47%).

***N*-Tricyclo[7.2.1.0<sup>2,7</sup>]dodec-2(7)-en-12-ylmethanamide (VI).** Formamide, 79.5 g (0.177 mol), was heated to 170°C, and a mixture of 28 g (0.159 mol) of ketone **III** and 25 ml of 85% formic acid was added at a rate of one drop per second. The mixture was then heated for 5 h under reflux (170–180°C) until liquid no longer distilled off (16 ml), cooled, and diluted with water. The products were extracted into benzene, the extract was evaporated, and the residue (30.4 g) was distilled under reduced pressure. The major fraction (26.3 g, 81%) had bp 146–149°C (3 mm); it was a colorless liquid which crystallized on cooling. According to the GLC data, it contained two components at a ratio of 3:1 (retention times 3.05 and 3.2 min). The mass spectrum of the major stereoisomer (**VIa**) is given in Table 2. Mass spectrum of **VIb**, *m/z* (*I*<sub>rel</sub>, %): 205 [*M*]<sup>+</sup> (55), 177 (18.5), 160 (100), 132 (68), 117 (34), 104 (25), 91 (58), 79 (41), 56 (32). Pure stereoisomer **VIa** was isolated by recrystallization from petroleum ether, followed by repeated recrystallizations from 70% ethanol.

**Tricyclo[7.2.1.0<sup>2,7</sup>]dodec-2(7)-en-12-amine (VIII).** A mixture of 4 g (0.0196 mol) of compound **VIa** and 20 ml of a 2 N alcoholic solution of NaOH was refluxed for 3 h. The solution was separated from the precipitate of sodium formate by decanting, the solvent was distilled off, and the residue was diluted with water and extracted with ether. The extract was washed with water, dried over MgSO<sub>4</sub>, and evaporated. The residue (3.2 g) was distilled under reduced pressure through a 7-cm column. Yield 2.4 g (69%), bp 72°C (2 mm), *n*<sub>D</sub><sup>20</sup> 1.5285. The product crystallized on cooling.

***N*-(2,7-Epoxytricyclo[7.2.1.0<sup>2,7</sup>]dodec-12-yl)-methanamide (IX).** A suspension of 5 g (0.0244 mol) of compound **VIa** in 15 ml of diethyl ether was mixed with 70 ml of a solution of 0.0247 mol of mono-

**Table 4.** Coordinates of atoms in the molecule of *N*-(12-oxatetracyclo[5.4.1.1<sup>2,5</sup>.0<sup>1,7</sup>]tridec-13-yl)methanamide (**IX**) ( $\times 10^3$  for H<sup>1</sup>,  $\times 10^4$  for the other atoms) and their isotropic equivalent temperature factors

Atom	<i>x</i>	<i>y</i>	<i>z</i>	<i>U</i> <sub>eq</sub>	Atom	<i>x</i>	<i>y</i>	<i>z</i>	<i>U</i> <sub>eq</sub>
O <sup>1</sup>	1360(1)	687(2)	1129(1)	0.056(1)	C <sup>7</sup>	2804(2)	810(2)	1297(2)	0.053(1)
O <sup>2</sup>	263(2)	6018(2)	2070(1)	0.087(1)	C <sup>8</sup>	3479(3)	-756(3)	1339(3)	0.094(1)
N	715(2)	3568(2)	1711(1)	0.058(1)	C <sup>9</sup>	2886(4)	-1772(4)	452(3)	0.132(1)
C <sup>1</sup>	2045(2)	1327(2)	377(2)	0.047(1)	C <sup>10</sup>	2778(4)	-973(4)	-469(3)	0.137(2)
C <sup>2</sup>	1888(2)	3067(3)	243(2)	0.059(1)	C <sup>11</sup>	1924(2)	391(3)	-538(2)	0.080(1)
C <sup>3</sup>	3207(2)	3713(3)	-9(2)	0.070(1)	C <sup>12</sup>	1830(2)	3902(2)	1207(2)	0.056(1)
C <sup>4</sup>	4106(2)	3874(3)	968(2)	0.072(1)	C <sup>13</sup>	48(2)	4654(3)	2113(2)	0.063(1)
C <sup>5</sup>	3224(2)	3548(3)	1749(2)	0.067(1)	H <sup>1</sup>	60(2)	267(3)	186(2)	0.075
C <sup>6</sup>	3335(3)	1921(3)	2088(2)	0.072(1)					

peroxyphthalic acid in diethyl ether. The homogeneous mixture was left to stand for 3 days at 20°C. The solution was separated from the precipitate of phthalic acid (by decanting), and the precipitate was washed twice with ether. The washings were combined with the ether solution, washed with a solution of Na<sub>2</sub>CO<sub>3</sub> until CO<sub>2</sub> no longer evolved, dried over MgSO<sub>4</sub>, and evaporated. Yield 5 g (92%).

**2,7-Epoxytricyclo[7.2.1.0<sup>2,7</sup>]dodecan-12-amine (X).** Compound **IX**, 4.2 g (0.019 mol), was dissolved in 10 ml of ethanol. The solution was mixed with a solution of 2.7 g (0.068 mol) of NaOH in 3.5 ml of water and 20 ml of ethanol, and the resulting mixture was refluxed for 1.5 h. The solvent was distilled off, and the residue (3.6 g) was distilled under reduced pressure through a 8.5-cm column. Yield 2.5 g (68%).

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