N-Substituted tetrahydro-1,3-oxazines and oxazolidines
1. A new version of the Mannich reaction involving amino alcohols

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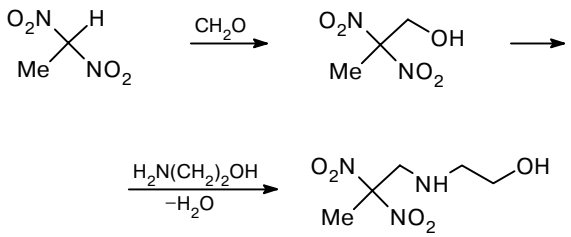
A new version of the Mannich reaction involving amino alcohols (3-aminopropan-1-ol and aminoethanol) was developed. These compounds react with formaldehyde and CH or NH acids to give N-substituted tetrahydro-1,3-oxazines or oxazolidines.

Key words: *C*-, *N*-, and *O*-aminomethylation, amino alcohols, tetrahydro-1,3-oxazines and oxazolidines, amides, imides, nitrogen heterocycles, 1,1-dinitroalkanes.

The Mannich reactions (*C*- and *N*-aminomethylation) with the use of amino alcohols are described in a comparatively small number of papers, all of them being concerned with *C*-aminomethylation, *e.g.*, of dinitromethane,[1] fluorodinitromethane,[2] trinitromethane,[3] and 1,1-dinitroethane[4,5] according to Scheme 1.

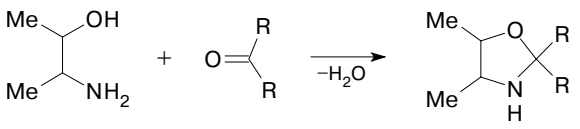
Scheme 1



In this version, amino alcohol functions only as an amino component, its second reaction center (the OH group) remaining inactive.

A much greater number of papers are devoted to reactions of amino alcohols with carbonyl compounds such as aldehydes or ketones[6] (Scheme 2).

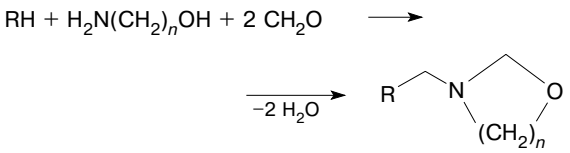
Scheme 2



This process is similar to the Mannich reaction and can be treated as intramolecular *O*-aminoalkylation that involves both reaction centers of amino alcohol, *i.e.*, the NH_2 and OH groups. Varying amino alcohols, aldehydes, and ketones, they obtained numerous tetrahydrooxazoles (oxazolidines), tetrahydro-1,3-oxazines, and 1,3-oxazepanes, depending on the mutual arrangement of the amino and hydroxy groups in the starting amino alcohol.[7]

In the present work, a new version of aminomethylation of CH and NH acids with the use of amino alcohols is described. The reaction involves a molecule of a CH or NH acid, a molecule of an amino alcohol, and two molecules of a carbonyl compound (formaldehyde). In this case, the NH_2 group of the amino alcohol is used twice for aminomethylation to give *N*-substituted tetrahydro-1,3-oxazine or oxazolidine as a final product (Scheme 3).

Scheme 3



RH = CH- or NH-acid, n = 2, 3

Results and Discussion

Initially, 1,1-dinitroethane, bromodinitromethane, and dinitromethane were used as CH acids in the new version of the reaction. Aminomethylation of the last two compounds was carried out in two steps. First, they reacted with formaldehyde to give 2-bromo-2,2-dinitroethanol and 2,2-dinitropropane-1,3-diol, respectively. These dinitroalkanols, which are more convenient in use than the starting nitroalkanes, then were mixed with amino alcohols and additional amounts of form-

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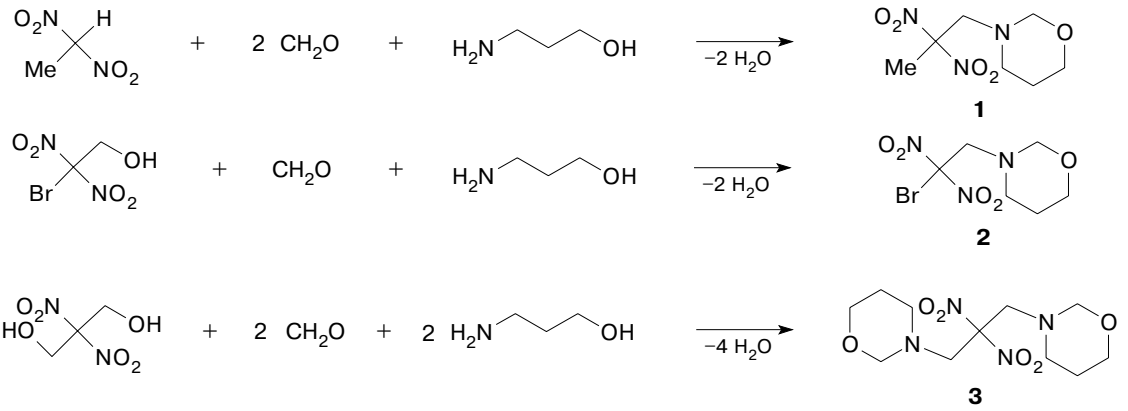
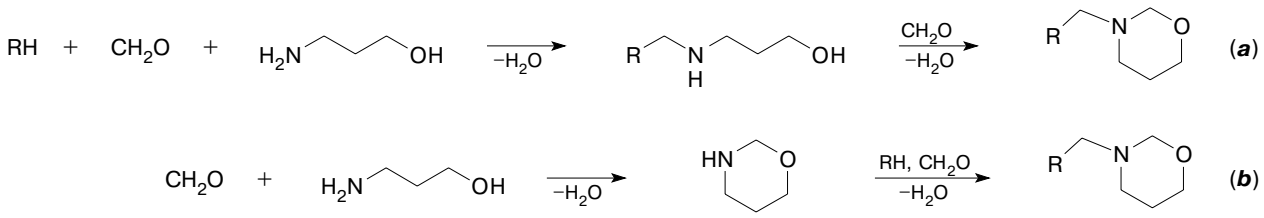
Scheme 4



Scheme 5



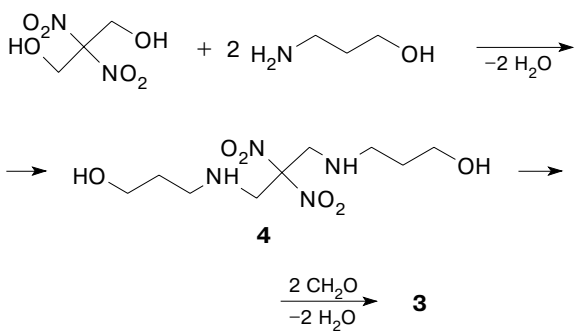
aldehyde. Reactions with 3-aminopropan-1-ol gave, in all three cases, tetrahydro-1,3-oxazines **1**—**3** in high yields (Scheme 4).

The reactions proceeded smoothly in an aqueous medium at room temperature, being completed within a short time. Crystalline products **1**—**3** were filtered off and recrystallized from organic solvents.

Presumably, these reactions can follow pathway ***a*** or ***b*** (Scheme 5).

When all reagents are mixed simultaneously, the reaction route is determined by the ratio between the rates of *C*- and *O*-aminomethylation. However, the reaction can be directed to each pathway by changing the order of mixing the reagents according to equations ***a*** or ***b***. For example, we managed to separate *C*- and *O*-aminomethylation of 2,2-dinitropropane-1,3-diol, *i.e.*, the *C*-aminomethylated product **4** was first isolated and then reacted with formaldehyde to give tetrahydro-1,3-oxazine **3** (Scheme 6).

Scheme 6



In the case of 1,3-oxazacyclic derivatives, the problem of competing *C*- and *O*-aminomethylation reactions is interesting only theoretically. However, if *C*-aminomethylation alone is desired (see Scheme 1), such a competition is of practical importance, because the occurrence of *O*-aminomethylation is always possible.

The proposed version of the reaction can also involve NH acids, namely, dicarboxamides (oxamide and succinamide), dicarboximides (succinimide and phthalimide), cyclic anhydrides of α-amino acids (piperazine-2,5-dione), and nitrogen-containing heterocycles (benzimidazole, benzotriazole, and isatin).

The reactions of all these compounds with 3-aminopropanol and formaldehyde afford the corresponding *N*-substituted tetrahydro-1,3-oxazines **5**—**12** (Scheme 7).

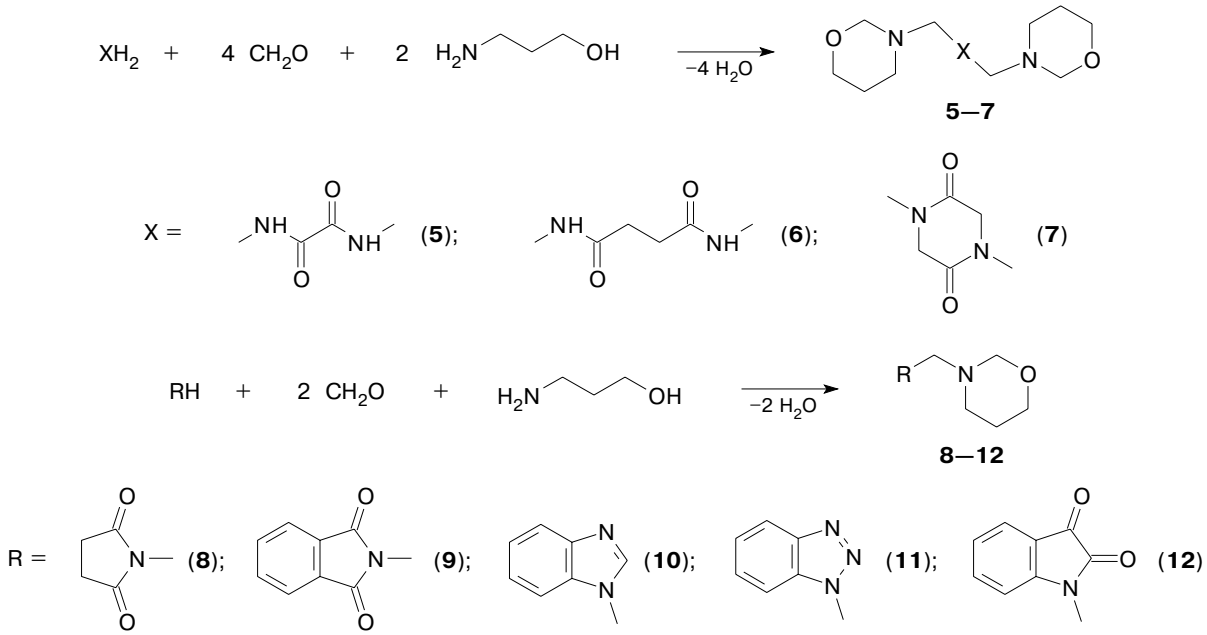
The reactions were mostly carried out in a water-alcohol (Pr^iOH) medium at 50—70 °C for 0.5—2.5 h. The product yields were 24—85%.

Worse results were obtained in the reactions of aminoethanol with the above CH and NH acids and formaldehyde. Only two tetrahydrooxazoles **13** and **14** (derived from piperazine-2,5-dione and benzotriazole, respectively) were isolated in a rather pure state (Scheme 8).

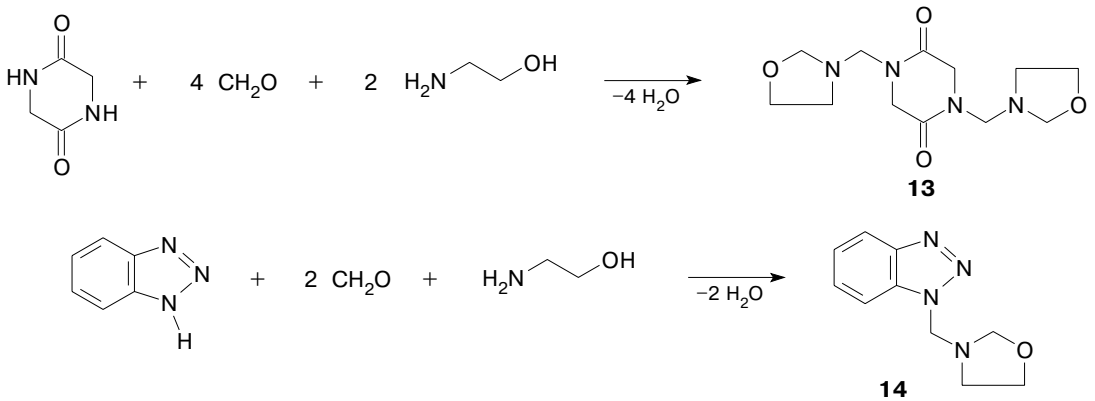
The compounds synthesized were identified by elemental analysis and NMR and IR spectroscopy (Table 1).

Singlets from different methylene groups in nitro compounds **1** and **3** are close in chemical shifts and thus

Scheme 7



Scheme 8



difficult to assign. The problem was solved by taking into account a broadened singlet from a group attached to the dinitromethylene fragment and the influence of its electronegativity and magnetic anisotropy.[8] For compounds **2**, **7**, and **13**, assignment remains ambiguous.

The COC and $CN(C_2)$ stretching vibrations in the tetrahydrooxazine and tetrahydrooxazole rings are close in frequency to those in cyclic ethers and tertiary amines.[9]

In conclusion, it should be noted that the proposed version of the reaction opens the way to the synthesis of new *N*-substituted 1,3-oxazacyclic compounds.

Experimental

^{1}H NMR spectra were recorded on an NMR spectrometer with a superconducting magnet (294 MHz). This instrument was designed and manufactured at the Institute of Problems of Chemical Physics, Russian Academy of Sciences. IR spectra were recorded on a Specord M-82 spectrophotometer.

The starting CH acids and the products of their reactions with formaldehyde were prepared as described in Refs. 1 and 10. The starting NH acids and amino alcohols were commercial chemicals and used without additional purification. Formaldehyde was taken in the form of formalin (34%).

3-(2,2-Dinitropropyl)tetrahydro-1,3-oxazine (1). A solution of 3-aminopropanol (1.5 g, 20 mmol) in 4 mL water was added dropwise with stirring at room temperature to a mixture of 1,1-dinitroethane (2.4 g, 20 mmol) and 12 mL of water. Then formalin (4 mL, 45 mmol of CH_2O) was added, and the reaction mixture was kept for 2 h. An oily product crystallized upon trituration with a glass rod. The crystals were filtered off, washed with water, and dried. Yield 4.2 g (96%), m.p. 63—65 °C. Recrystallization from a mixture CCl_4—heptane gave the product with m.p. 63—65 °C.

3-(2-Bromo-2,2-dinitroethyl)tetrahydro-1,3-oxazine (2) was obtained as described for compound **1** from 2-bromo-2,2-dinitroethanol (4.3 g, 20 mmol), 3-aminopropanol (1.5 g,

Table 1. Physicochemical characteristics of *N*-substituted tetrahydro-1,3-oxazines and oxazolidines

Compound	Molecular formula	Found / Calculated (%) C	H	N	T_m/°C	^{1}H NMR (solvent) (Me_4Si, δ, *J*/Hz)	IR (KBr), ν/cm^{-1}
1	$C_7H_{13}N_3O_5$	38.03 38.36	5.64 5.98	19.19 19.17	63—65	(CD_2Cl_2) 1.64 (br.m, 2 H, $CH_2\underline{CH_2}CH_2$); 2.11 (s, 3 H, CH_3); 2.94 (t, 2 H, $N\underline{CH_2}CH_2$, *J* = 5.0); 3.80 (s, 2 H, CH_2N); 3.82 (t, 2 H, OCH_2, *J* = 4.0); 4.21 (s, 2 H, NCH_2O)	2966, 2946, 2921, 2851, 1458, 1452, 1440, 1346 (CH_3, CH_2); 1561, 1320 (NO_2); 1221, 1200, 1046, 966, 888 (oxazacycle)
2	$C_6H_{10}BrN_3O_5$	25.47 25.37	3.60 3.55	14.54 14.79	88—89	($CDCl_3$) 1.67 (quint, 2 H, $CH_2\underline{CH_2}CH_2$, *J* = 5.7); 3.04 (t, 2 H, $N\underline{CH_2}CH_2$, *J* = 5.7); 3.87 (t, 2 H, $O\underline{CH_2}CH_2$, *J* = 5.7); 4.17, 4.33 (both s, each 2 H, $Br(NO_2)_2CCH_2N$; NCH_2O)	2970, 2936, 2876, 1475, 1426, 1376, 1367, 1341 (CH_2); 1227, 1199, 1051, 974, 888 (oxazacycle); 775 (C—Br)
3	$C_{11}H_{20}N_4O_6$	43.51 43.42	6.58 6.62	18.22 18.41	87—88 (decomp.)	(CD_2Cl_2) 1.63 (br.m, 4 H, $CH_2\underline{CH_2}CH_2$); 2.90 (t, 4 H, $N\underline{CH_2}CH_2$, *J* = 5.0); 3.80 (t, 4 H, $CH_2\underline{CH_2}O$, *J* = 5.0); 3.82 (s, 4 H, $C(NO_2)_2CH_2N$); 4.15 (s, 4 H, NCH_2O)	2963, 2918, 2861, 1451, 1439, 1427 (CH_2); 1556, 1346 (NO_2); 1199, 1076, 1049, 992, 977, 878 (oxazacycle)
4*	$C_9H_{20}N_4O_6$	38.13 38.57	7.29 7.19	19.62 19.99	65—66	(CD_2Cl_2) 1.72 (quint, 4 H, $CH_2\underline{CH_2}CH_2$, *J* = 6.0, 5.4); 2.68 (t, 4 H, $NH\underline{CH_2}CH_2$, *J* = 6.0); 3.10, 3.39 (both br.s, each 2 H; OH; NH); 3.62 (s, 4 H, $C(NO_2)_2CH_2$); 3.66 (t, 4 H, $CH_2\underline{CH_2}OH$, *J* = 5.4)	3316, 1039 (OH); 3252 sh (NH); 2942, 2873, 1472, 1465, 1442, 1378, 1348 (CH_2); 1569, 1560, 1370 (NO_2); 3617 (OH); 1580 (NO_2), 1325**
5	$C_{12}H_{22}N_4O_4$	50.30 50.34	7.81 7.74	19.78 19.57	142—144	(CD_2Cl_2) 1.65 (m, 4 H, $CH_2\underline{CH_2}CH_2$); 2.94 (t, 4 H, $N\underline{CH_2}CH_2$, *J* = 5.5); 3.80 (t,4 H, $CH_2\underline{CH_2}O$, *J* = 5.5); 4.31 (s, 4 H, NCH_2O); 4.33 (d, 4 H, $NH\underline{CH_2}$, J_{CH-NH} = 5.5); 7.94 (br.t, 2 H, C(O)NH)	3335, 1505 (NH); 2945, 2927, 2861, 1448, 1385, 1370 (CH_2); 1673 (C=O); 1211, 1040, 1007, 971, 944, 878 (oxazacycle)
6	$C_{14}H_{26}N_4O_4$	52.74 53.00	8.69 8.34	17.91 17.82	122—124	(CD_2Cl_2) 1.65 (m, 4 H, $CH_2\underline{CH_2}CH_2$); 2.52 (s, 4 H, CH_2CO); 2.90 (t, 4 H, $N\underline{CH_2}CH_2$, *J* = 5.5); 3.78 (t, 4 H, $CH_2\underline{CH_2}O$, *J* = 5.2); 4.20 (d, 4 H, $NH\underline{CH_2}$, J_{NH-CH} = 5.5); 4.28 (s, 4 H, NCH_2O); 6.85 (br.t, 2 H, C(O)NH)	3248, 3080, 1550 (NH); 2966, 2957, 2927, 2801, 1481, 1463, 1415, 1376 (CH_2); 1652 (C=O); 1208, 1187, 1061, 1049, 971, 866 (oxazacycle)
7	$C_{14}H_{24}N_4O_4$	53.53 53.83	7.63 7.74	17.80 17.93	168—170	(CD_3CN) 1.59 (m, 4 H, $CH_2\underline{CH_2}CH_2$); 2.90 (t, 4 H, $N\underline{CH_2}CH_2$, *J* = 5.3); 3.78 (t, 4 H, $O\underline{CH_2}CH_2$, *J* = 5.3); 3.91 (s, 4 H, $NCH_2C(O)$); 4.29; 4.35 (both s, each 4 H, NCH_2N; NCH_2O)	2987, 2960, 2939, 2873, 2843, 1478, 1460, 1431, 1388, 1379, 1370 (CH_2); 1667 (C=O); 1220, 1205, 1052, 998, 980, 884 (oxazacycle)
8	$C_9H_{14}N_2O_3$	54.24 54.53	6.92 7.12	14.40 14.13	64—66	(CD_2Cl_2) 1.11 (quint, 2 H, $CH_2\underline{CH_2}CH_2$, *J* = 5.1; 4.8); 2.68 (s, 4 H, $CH_2C(O)$); 2.92 (t, 2 H, $N\underline{CH_2}CH_2$, *J* = 5.1); 3.73 (t, 2 H, $CH_2\underline{CH_2}O$, *J* = 4.8); 4.28 (s, 2 H, NCH_2O); 4.42 (s, 2 H, NCH_2N)	2987, 2969, 2954, 2924, 2864, 2810, 2750, 2726, 1442, 1418, 1409, 1388, 1367, 1349 (CH_2); 1763, 1697 (C=O); 1223, 1058, 983, 899 (oxazacycle)
9	$C_{13}H_{14}N_2O_3$	63.13 63.40	5.91 5.73	11.78 11.38	85—87	(CD_2Cl_2) 1.65 (quint, 2 H, $CH_2\underline{CH_2}CH_2$, *J* = 5.0); 3.00 (t, 2 H, $N\underline{CH_2}CH_2$, *J* = 5.0); 3.72 (t, 2 H, $CH_2\underline{CH_2}O$, *J* = 5.0); 4.38 (s, 2 H, NCH_2O); 4.70 (s, 2 H, NCH_2N); 7.60—7.90 (m, 4 H, CH, system AA′BB′)	3098, 3032, 2993, 1613, 1508, 1466, 728, 713 (Ar); 2960, 2924, 2876, 2843, 1451, 1409, 1358, 1334 (CH_2); 1772, 1706 (C=O); 1208, 1040, 980, 959, 884 (oxazacycle)

(*to be continued*)

Table 1 (*continued*)

Compound	Molecular formula	Found / Calculated (%)			T_m/°C	^{1}H NMR (solvent) (Me_4Si, δ, J/Hz)	IR (KBr), ν/cm^{-1}
		C	H	N			
10	$C_{12}H_{15}N_3O$	66.31 66.18	6.64 6.99	19.38 19.43	58—60	(CD_2Cl_2) 1.68 (br.m, 2 H, $CH_2\underline{CH_2}CH_2$); 3.02 (t, 2 H, $N\underline{CH_2}CH_2$, J = 4.8); 3.83 (t, 2 H, $CH_2\underline{CH_2}O$, J = 4.8); 4.41 (s, 2 H, NCH_2O); 5.15 (s, 2 H, NCH_2N); 7.30 (m, 2 H, CH(5), CH(6)); 7.51, 7.75 (both d, each 1 H, CH(7), J = 7.0; CH(4), J = 7.0); 7.95 (s, H, NCHN)	3095, 2984, 1613, 1502, 1454, 791, 749 (Ar); 2963, 2921, 2903, 2867, 1397, 1379, 1349, 1337 (CH_2); 1652 (C=N); 1202, 1193, 1046, 1019, 986, 950, 878 (oxazacycle)
11	$C_{11}H_{14}N_4O$	60.32 60.54	6.32 6.47	26.01 25.67	105—107	(CD_3CN) 1.60 (quint, 2 H, $CH_2\underline{CH_2}CH_2$, J = 5.0); 2.98 (t, 2 H, $N\underline{CH_2}CH_2$, J = 5.0); 3.70 (t, 2 H, $O\underline{CH_2}CH_2$, J = 5.0); 4.41 (s, 2 H, NCH_2O); 5.63 (s, 2 H, NCH_2N); 7.41, 7.55 (both dd, each 1 H, CH(6), J = 8.0; CH(5), J = 8.0); 7.75, 8.00 (both d, each 1 H, CH(7), J = 8.0; CH(4), J = 8.0)	3062, 3029, 1616, 1496, 1454, 800, 743 (Ar); 2973, 2951, 2930, 2870, 2837, 1382, 1367, 1340 (CH_2); 1205, 1181, 1046, 1001, 977, 950, 884 (oxazacycle)
12	$C_{13}H_{14}N_2O_3$	63.53 63.40	5.59 5.73	11.10 11.37	130—131	(CD_3CN) 1.70 (quint, 2 H, $CH_2\underline{CH_2}CH_2$, J = 4.8); 3.10 (t, 2 H, $N\underline{CH_2}CH_2$, J = 4.8); 3.80 (t, 2 H, $CH_2\underline{CH_2}O$, J = 4.8); 4.38 (s, 2 H, NCH_2O); 4.70 (s, 2 H, NCH_2N); 7.10, 7.55 (both d, each 1 H, CH(7), J = 8.0; CH(4), J = 8.0); 7.14, 7.63 (both t, each 1 H, CH(6), J = 8.0; CH(5), J = 8.0)	2978, 2954, 2927, 2849, 1352 (CH_2); 1733 (C=O); 1610, 1508, 1475, 764, 755 (Ar); 1205, 1046, 986, 878 (oxazacycle)
13	$C_{12}H_{20}N_4O_4$	50.13 50.69	7.19 7.09	19.82 19.71	157—159	($CDCl_3$) 3.06 (t, 4 H, $N\underline{CH_2}CH_2$, J = 6.8); 3.75 (t, 4 H, $CH_2\underline{CH_2}O$, J = 6.8); 4.17 (s, 4 H, $NCH_2C(O)$); 4.26; 4.37 (both s, each 4 H, NCH_2N, OCH_2N)	2946, 2884, 1451, 1396, 1336 (CH_2); 1657 (C=O); 1171, 1011, 981, 869 (oxazacycle)
14	$C_{10}H_{13}N_4O$	58.54 58.81	6.10 5.92	27.23 27.43	96—98	—	3070, 3030, 2985, 1615, 1495, 1455, 750, 720 (Ar); 2945, 2885, 1405, 1390, 1365 (CH_2); 1185, 1155, 1005, 985, 875 (oxazacycle)

* An intermediate product.
** A solution in CH_2Cl_2, C = 1.7 wt %.

20 mmol), and formalin (1.94 mL, 22 mmol of CH_2O). Yield 5.3 g, (93%), m.p. 87—89 °C. Recrystallization from a CCl_4—heptane mixture gave the product with m.p. 88—89 °C.

2,2-Dinitro-1,3-bis(tetrahydro-1,3-oxazino)propane (3). A solution of 2,2-dinitropropane-1,3-diol (3.32 g, 20 mmol) in 6 mL of water was added with stirring at 2—4 °C to a solution of 3-aminopropanol (3 g, 40 mmol) in 5 mL of water. The reaction mixture was kept for 1 h and, after addition of formalin (3.9 mL, 44 mmol of CH_2O), for additional 2 h. The precipitate was filtered off, washed with water, dried, and recrystallized from CCl_4. Yield 4.4 g (72%), m.p. 87—88 °C (decomp.).

6,6-Dinitro-4,8-diazaundecane-1,11-diol (4) and its reaction with formaldehyde. A solution of 2,2-dinitropropane-1,3-diol (3.32 g, 20 mmol) in 6 mL of water was added with stirring at 0—2 °C to a solution of 3-aminopropanol (2.8 g, 37 mmol) in 5 mL of water. The reaction mixture was kept for 1.5 h. The product was extracted with CH_2Cl_2, and the extract was washed with water and dried over $MgSO_4$. The solvent was removed *in vacuo*, and the residue was twice recrystallized from a $CHCl_3$—CCl_4 mixture. The yield of compound **4** was 0.42 g (8%), m.p. 65—66 °C.

Formalin (0.48 mL, 5.5 mmol of CH_2O) was added dropwise with stirring to a solution of compound **4** (0.7 g, 2.5 mmol) in 3 mL of water. The reaction mixture was kept for 2 h. The precipitate was filtered off, washed with water, and dried. The yield of compound **3** was 0.62 g (82%), m.p. 87—88 °C (decomp.). Its spectral parameters are identical with those of compound **3** described above.

***N,N′*-Bis(tetrahydro-1,3-oxazinomethyl)oxamide (5).** A mixture of oxamide (8.8 g, 0.1 mol), Pr^iOH (60 mL), water (30 mL), 3-aminopropanol (15 g, 0.2 mol), and formalin (35.3 mL, 0.4 mol of CH_2O) was stirred at 70 °C for 2.5 h and then concentrated *in vacuo*. Organic material was extracted from the residue with 100 mL of $CHCl_3$. The organic layer was separated, washed with water, and dried over $MgSO_4$. The chloroform was removed to give compound **5** (19.8 g, 69%), m.p. 136—140 °C. Recrystallization from $CHCl_3$—CCl_4 gave the product with m.p. 142—144 °C.

***N,N′*-Bis(tetrahydro-1,3-oxazinomethyl)succindiamide (6).** A mixture of succindiamide (5.8 g, 50 mmol), water (70 mL), 3-aminopropanol (7.5 g, 0.1 mol), and formalin (17.7 mL, 0.2 mol of CH_2O) was stirred at 70 °C for 0.5 h. The water was

removed *in vacuo*, and the products were extracted from the residue with 80 mL of $CHCl_3$. The lower layer was separated, washed with water, and dried over $MgSO_4$. After removal of the chloroform *in vacuo*, the residue was recrystallized from $CHCl_3$—CCl_4 to give compound **6** (3.8 g, 24%), m.p. 122—124 °C.

1,4-Bis(tetrahydro-1,3-oxazinomethyl)piperazine-2,5-dione (7). A mixture of piperazine-2,5-dione (5.7 g, 50 mmol), Pr^iOH (16 mL), 3-aminopropanol (7.5 g, 0.1 mol), and formalin (17.65 mL, 0.2 mol of CH_2O) was stirred at 70 °C for 1 h. The resulting solution was cooled to −10 °C and kept for 18 h. The precipitate that formed was filtered off. The yield of **7** was 6.6 g (42%), m.p. 168—170 °C. Recrystallization from Pr^iOH gave the product with m.p. 168—170 °C.

***N*-(Tetrahydro-1,3-oxazinomethyl)succinimide (8).** A mixture of succinimide (14.85 g, 0.15 mol), Pr^iOH (45 mL), 3-aminopropanol (11.25 g, 0.15 mol), and formalin (26.5 mL, 0.3 mol of CH_2O) was stirred at 50 °C for 1 h. The solvent was removed *in vacuo*. Pr^iOH (30 mL) and heptane (30 mL) were added to the residue, and the resulting mixture was stirred and cooled to 0 °C. The precipitate that formed was filtered off. Yield 22.5 g (76%), m.p. 58—60 °C. Recrystallization from Pr^iOH—heptane gave the product with m.p. 64—66 °C.

***N*-(Tetrahydro-1,3-oxazinomethyl)phthalimide (9).** A mixture of phthalimide (7.35 g, 50 mmol), Pr^iOH (22 mL), 3-aminopropanol (3.75 g, 50 mmol), and formalin (9 mL, 0.1 mol of CH_2O) was stirred at 50 °C for 1 h. The solvent was removed *in vacuo*. Pr^iOH (30 mL) was added to the residue, and the resulting mixture was stirred and cooled to 0 °C. The precipitate that formed was filtered off. Yield 6.8 g (55%), m.p. 84—86 °C. Recrystallization from Pr^iOH—heptane gave the product with m.p. 85—87 °C.

1-(Tetrahydro-1,3-oxazinomethyl)benzimidazole (10). A mixture of benzimidazole (1.18 g, 10 mmol), Pr^iOH (14 mL), 3-aminopropanol (0.75 g, 10 mmol), and formalin (1.77 mL, 20 mmol of CH_2O) was stirred at 70 °C for 2.5 h. The solvent was removed *in vacuo*. The residue was allowed to solidify at 0 °C. Recrystallization from CCl_4—heptane and then from heptane—Pr^iOH gave compound **10** (0.69 g (32%), m.p. 58—60 °C.

1-(Tetrahydro-1,3-oxazinomethyl)benzotriazole (11). A mixture of benzotriazole (11.9 g, 0.1 mol), Pr^iOH (40 mL), 3-aminopropanol (7.5 g, 0.1 mol), and formalin (17.65 mL, 0.2 mol of CH_2O) was stirred at 50 °C for 0.5 h, cooled to 0 °C, and kept for 1 h. The precipitate that formed was filtered off. The yield of **11** was 18.5 g (85%), m.p. 105—107 °C. Recrystallization from water gave the product with m.p. 105—107 °C.

1-(Tetrahydro-1,3-oxazinomethyl)isatin (12). A mixture of isatin (2.94 g, 20 mmol), Pr^iOH (29 mL), 3-aminopropanol (1.5 g, 20 mmol), and formalin (3.53 g, 40 mmol of CH_2O) was stirred at 50 °C for 1 h and cooled to 15 °C. The precipitate that formed was filtered off. Yield 3.9 g (79%), m.p. 128—130 °C. Recrystallization from CCl_4 gave the product with m.p. 130—131 °C.

1,4-Bis(oxazolidinomethyl)piperazine-2,5-dione (13). A mixture of 2-aminoethanol (12.2 g, 0.2 mol), Pr^iOH (24 mL), formalin (35.5 mL, 0.4 mol of CH_2O), and piperazine-2,5-dione (11.4 g, 0.1 mol) was stirred at 70 °C for 3 h. After removal of the solvent *in vacuo*, $CHCl_3$ (60 mL) and CH_2Cl_2 (90 mL) were added, and the resulting mixture was stirred. The lower layer was separated and dried over $MgSO_4$. The solvents were removed *in vacuo*. Ethyl acetate (10 mL), CCl_4 (10 mL), and Pr^iOH (5 mL) were added with stirring, and the mixture was kept at −15 °C for 18 h. The precipitate that formed was filtered off and washed with a mixture of Pr^iOH with MeOH. Yield 1.7 g (6%), m.p. 147—151 °C. Recrystallization from Pr^iOH gave the product with m.p. 157—159 °C.

1-(Oxazolidinomethyl)benzotriazole (14). A mixture of 2-aminoethanol (3.1 g, 50 mmol), Pr^iOH (15 mL), formalin (8.82 mL, 0.1 mol of CH_2O), and benzotriazole (5.95 g, 50 mmol) was stirred at 70 °C for 1 h. The solvents were removed *in vacuo*. $CHCl_3$ (20 mL), CH_2Cl_2 (20 mL), CCl_4 (10 mL), and heptane (30 mL) were added with stirring. The lower layer was separated and dried over $MgSO_4$. The solvents were removed *in vacuo*. Pr^iOH (26 mL) and heptane (6.5 mL) were added with stirring, and the mixture was kept at −15 °C for 24 h. The precipitate that formed was filtered off. Yield 5.6 g (55%), m.p. 94—98 °C. Recrystallization from Pr^iOH—MeCN gave the product with m.p. 96—98 °C.

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