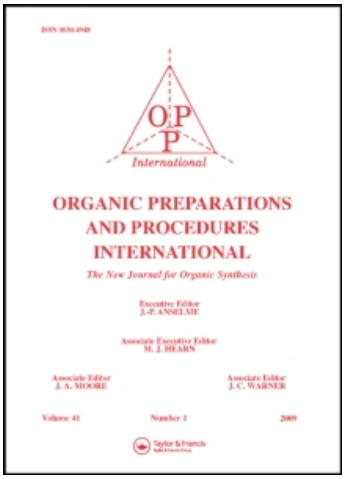

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Krzysztof Bujnowski[a]; Agnieszka Adamczyk[a]; Ludwik Synoradzki[a]
[a] Laboratory of Technological Processes, Faculty of Chemistry Warsaw University of Technology, Warsaw, POLAND

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Krzysztof Bujnowski, Agnieszka Adamczyk and Ludwik Synoradzki*

Laboratory of Technological Processes, Faculty of Chemistry
Warsaw University of Technology
Noakowskiego 3 Street, 00-664 Warsaw, POLAND
e-mail: Ludwik.Synoradzki@ch.pw.edu.pl

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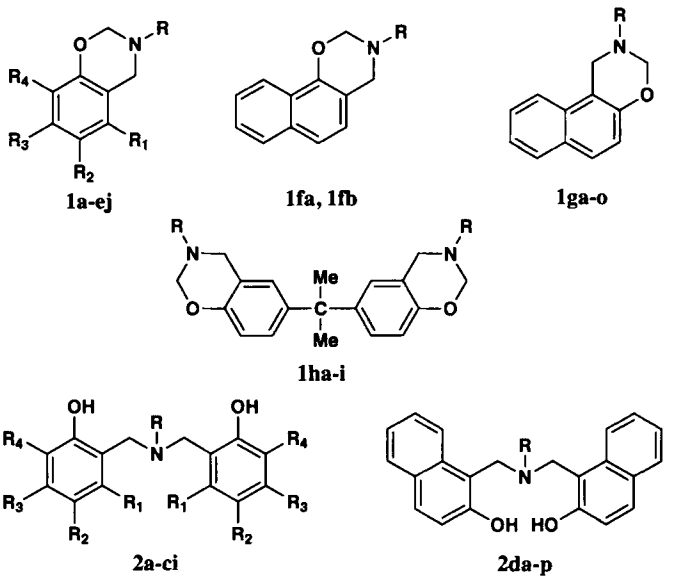
Laboratory of Technological Processes, Faculty of Chemistry
Warsaw University of Technology
Noakowskiego 3 Street, 00-664 Warsaw, POLAND
e-mail: Ludwik.Synoradzki@ch.pw.edu.pl

INTRODUCTION

Part 2 of the review of *o*-aminomethyl derivatives of phenols will deal with compounds bearing a benzoxazine (**1**) and dibenzylamine (**2**) structures (*Fig. 1*); benzylamines were examined in *Part 1*.[1] All three types of the compounds contain an amine nitrogen and an oxygen atom in their structure. Benzoxazines and dibenzylamines, as well as the previously described benzylamines are compounds of many interesting properties and applications. The



R-R_4 according to Tables 1-4

Fig. 1

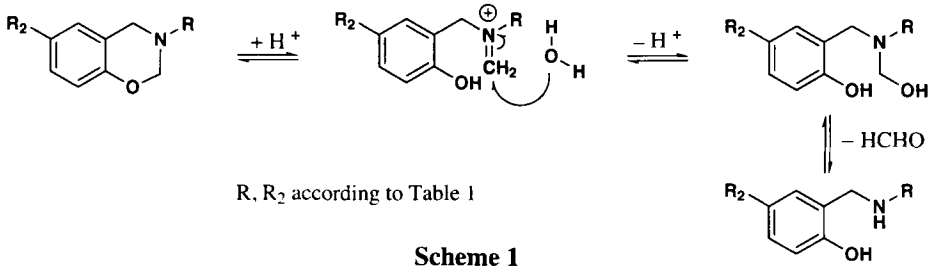
present review collects and critically evaluates all the available information on the properties and application, structure, stability and preparation of benzoxazines (**1**) and dibenzylamines (**2**) up to the year 2005.

I. BENZOXAZINES: PROPERTIES AND APPLICATIONS

The most important field of application of benzoxazines **1** is polymer chemistry and technology. They are used as monomers of polybenzoxazine resins of unusual but attractive and useful properties:[2-4] excellent dimensional stability, low water absorption and flammability,[5] high UV and chemical retardance.[6] The polymers possess a near-zero shrinkage or volumetric expansion upon curing, likely resulting from favorable hydrogen bonding interactions.[7,8] Compared with the ordinary phenolic resins, benzoxazine resins have a great deal of molecular design flexibility.[9] Benzoxazines **1** also exhibit a wide range of biological activity.[10] Some are bacteriocides, fungicides or antitumor agents.[11-13] Others have been used as herbicides, microbiocides or anti-inflammatory agents[14,15] and tyrosine mimetics.[16] Benzoxazines **1** are valuable intermediates in the synthesis of dibenzylamine ligands,[17,18] or in boron chemistry.[19] Chirachanchai *et al.* applied benzoxazine **1ha** as an effective ionophore in the liquid-liquid extraction of Li, Ni, Mg, Ca and K ions from aqueous solutions.[20]

II. BENZOXAZINES: STRUCTURE AND STABILITY

In the benzoxazine structure, the nitrogen and oxygen atoms are incorporated in a heterocyclic ring system. Ring-opening polymerization leads to the above mentioned new class of phenolic resins. Benzoxazines are susceptible to hydrolytic cleavage. Moloney *et al.* investigated their hydrolysis in a DMSO/water system by ^{1}H NMR technique and proposed a mechanism of that transformation (*Scheme 1*).[14] The stability of benzoxazines **1** is strongly dependent on their

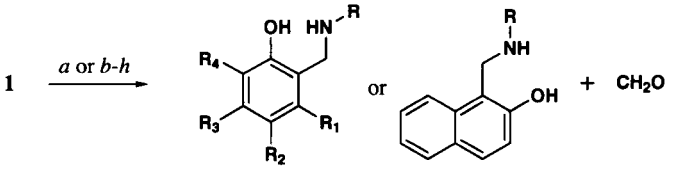


Scheme 1

structure. Electron-donating substituents *para* to the benzoxazine oxygen atom stabilize the heterocyclic ring. Electron-withdrawing groups at the substituent connected to the nitrogen atom destabilize the ring and make it more liable toward hydrolysis.[14]

The differences in stability are probably the reason for contradictory reports in the literature. Some authors describe the isolation of benzoxazines **1** as their hydrochlorides, obtained by treatment of the reaction mixture with concentrated HCl.[21] Others claim that, under such conditions, phenolic polymeric materials are formed.[22] Burke *et al.* obtained crystalline benzoxazine hydrochlorides **1ga**, **1gb**, **1gg** and **1gm** by treatment of the corresponding benzoxazines with

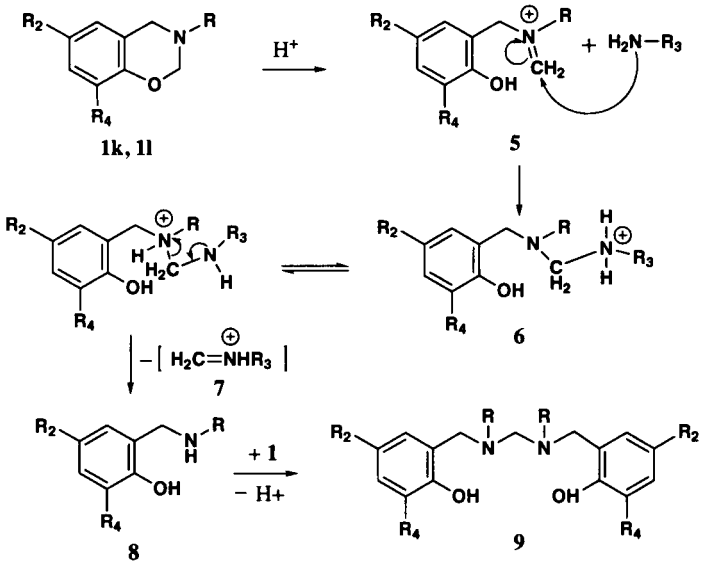
concentrated HCl in cold acetone. Heating of the salts in a water-alcohol solution resulted in the formation of benzylamines and liberation of formaldehyde.[23] In most cases, the hydrolysis proceeded smoothly under the action of hydrochloric acid[24] in solvents such as CH_2Cl_2,[12] Et_2O,[25] PrOH,[23] EtOH.[11,21,26,27] The hydrolysis of benzoxazines was also carried out in a water-ethanol solution of sulfuric acid.[22] For some benzoxazines, cleavage of the heterocyclic ring proceeds in refluxing ethanol[13] or methanol[23] without addition of mineral acid (*Scheme 2*). Tzschoppe *et al.*[28]



a) 1. HCl, CH_2Cl_2; 2. H_2O, rt, N_2, 4 days; 3. H_2O, $NaHCO_3$.[12] *b*) 1. HCl, Et_2O, -15°C; 2. EtOH; 3. NH_4OH, H_2O (26-82%).[25] *c*) 1. HCl, EtOH, reflux (99%) 2. K_2CO_3, H_2O, rt (83%).[26] *d*) HCl, H_2O (40-74%).[24] *e*) HCl, H_2O, EtOH, reflux, distillation (40-95%).[11,21,27] *f*) HCl, H_2O, PrOH, distillation (93%).[23] *g*) H_2SO_4, H_2O, $(NO_2)_2PhN{=}NH$, EtOH, rt, 45 min. (34%).[22] *h*) EtOH, reflux (89%).[13] R, R_1-R_4 according to *Tables 1* and *2*.

Scheme 2

investigated transformations of benzoxazines **1k** and **1l** in the presence of different amines in chloroform at 55°C for 24 h. The chain of successive reactions is initiated by proton attack resulting in opening of the heterocyclic ring of benzoxazine **1**. The cation **5** reacts with the nucleophilic amine to give the intermediary **6**, followed by loss of the imine cation **7** to afford benzylamine **8**. Its condensation with **1** results in the formation of the diamine product **9** (*Scheme 3*).



R, R_2 = Me; R_3 = alkyl; R_4 = Me, *t*-Bu

Scheme 3

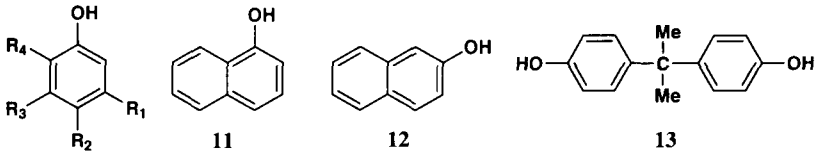
Such transformations do not occur with aromatic and tertiary aliphatic amines. The diamine **9** is also not formed with sterically hindered benzoxazines **1**. Proponet *et al.* investigated spectral properties of benzoxazines **1** (R = Me). ^{1}H NMR and ^{13}C NMR spectra were described. IR signals and their intensity in a characteristic range of 1700-2000 cm^{-1} were also given.[29] The ^{1}H NMR spectra of some *o*-alkylphenyl substituted benzoxazines exhibit the non-equivalence of the benzylic hydrogens, caused by the restricted free rotation around the aromatic carbon-nitrogen bond.[30,31]

III. BENZOXAZINES: METHODS OF SYNTHESIS

Six methods for the synthesis of benzoxazines **1** are reviewed (*Tables 1* and *2*).

a) Mannich Reaction (Method A)

In the classical Mannich-type reaction[32,33] leading to benzoxazines **1**, phenols with at least one hydrogen atom at the *ortho*-position (**10-13**), (*Fig. 2*), formaldehyde and a primary amine in molar ratio 1:2:1 have been used (*Scheme 4, Tables 1* and *2*).



10 **11** **12** **13**

R_1-R_4 according to *Table 1*

Fig. 2

In most of the cases, the reactants were mixed together; however, sometimes good results were also achieved by the preparation of the formaldehyde-amine mixure followed by the addition of the phenolic compound.[34,35] The reactions were usually carried out in water-miscible solvents such as dioxane,[18,21,26,29,36] methanol,[11,17,19,21,23,34] ethanol[37] or a dioxane/methanol[26] or dioxane/ethanol mixture[13] using saturated aqueous solution of formaldehyde (formalin).[11,17-19,21,23,25,26,29,31,34,36,37] Examples of the reactions performed in water have also been described.[25,31]

10 - 13 + RNH_2 $\xrightarrow{a \text{ or } b\text{-}l}$ **1** + H_2O

a) CH_2O, H_2O, dioxane, reflux, 2-6 h[36] (14-81%) (**1a**, **1b**, **1d**, **1e**, **1j**, **1q-w**,[29] **1g**, **1as**, **1at**, **1ci**, **1cj**, **1co**, **1cq**,[21] **1i**, **1ak**, **1as**, **1ay**,[19] **1b**, **1e**[18]). *b*) CH_2O, H_2O, dioxane/MeOH, reflux, 2 h (34-74%) (**1a**, **1an**, **1ar**, **1cg**).[26] *c*) CH_2O, H_2O, MeOH, 0°C-reflux, 1.5-24 h (12-99%) (**1c**, **1f**, **1m**, **1p**, **1ga**, **1gc**, **1gd**, **1gf**,[17] **1bb**, **1ds**,[34] **1ga**, **1gb**, **1gg**, **1gm**,[23] **1az**, **1bv**, **1bz**, **1cf**, **1cm**, **1cn**, **1cx**, **1cy**,[11] **1bf**[23]). *d*) CH_2O, H_2O, EtOH, reflux, 2 h (91%) (**1ay**).[37] *e*) CH_2O, H_2O, $Ba(OH)_2 \cdot 8H_2O$, rt-96°C, 3-6 h (**1eg**,[25] **1ea**, **1eb**, **1ef**, **1eg**[31]). *f*) CH_2O, dioxane, reflux, 2-7 h (21-74%)(**1y**, **1ac**, **1at**, **1au**, **1cl**, **1df**, **1dk**, **1dl**, **1dp-r**,**1du-w**, **1ed**, **1eh-j**,[34] **1k**, **1aa**[16]). *g*) CH_2O, dioxane/EtOH, KOH, 65°C, 1 h, then 85°C, 4 h (36-78%) (**1n-p**, **1bc-e**, **1cr**, **1cs**).[13] *h*) CH_2O, MeOH, reflux, 2-6.6 h (61-81%) (**1ah**, **1bg**, **1ck**, **1ee**).[35] *i*) CH_2O, EtOH, reflux, 1 h (92%) (**1fa**).[38] *j*) CH_2O, MeOH, KOH, 5°C-reflux, 15 min.-12 days (35-92%) (**1ci**,[21] **1x**, **1ci**, **1cq**,[27] **1dh**, **1di**, **1go**[22]). *k*) $(CH_2O)_3$, MeOH, KOH, reflux, 20 min., N_2 (30-70%) (**1i**, **1ai-m**, **1as**, **1at**, **1av**, **1aw**, **1ay**, **1ba**, **1bh-t**, **1cd**, **1ce**, **1ch**, **1cl**, **1ga**, **1ge**, **1gh-l**, **1gn**).[12] *l*) CH_2O, no solvent, 85-90°C, 2 h (69-74%) (**1ap**, **1da**, **1he**,[6] **1co**, **1hg**, **1hh**[39]).

Scheme 4

When paraformaldehyde or a formaldehyde trimer[12] were applied, the solvents used were methanol,[12,35] ethanol[12,22,27,38] or dioxane.[13,16] A solventless system was also applied.[6,39] The reactions were often performed in the presence of a basic catalyst such as KOH,[12,13,21,22,27] or $Ba(OH)_2 \cdot 8H_2O$.[25,31] Reflux temperatures for 0.25-12 h[12,17-19,21,23,25-27,29,34,35,37,38] or room temperature for 6-24 h[11,31] were generally used. The synthesis of benzoxazines **1** in the Mannich reaction is a "one-pot" process. The desired products often crystallized from the reaction mixtures, and were purified by recrystallization.[11-13,18,21-23,25,31,34,37] Alternatively, distillation of the oily products was utilized[16,21] in some cases preceeded by the removal of unreacted substrates by extraction.[6,26,27,29] Flash chromatography[17] or passing the mixture through a column of alumina[12] were also applied to purify the products. Some benzoxazines **1** were isolated in the form of their crystalline hydrochlorides after acidification of the post-reaction mixture with concentrated hydrochloric acid[21] or gaseous HCl.[38] Due to the broad spectrum of easily accessible raw materials for Mannich reaction, this process is the most important synthetic method for benzoxazines (*Table 1* and *2*).

Table 1. Structure, Preparation and Properties of Benzoxazines **1a-1ej**

Cmpd	R	R_1	R_2	R_3	R_4	Yield (%)	Method[a]	mp.(°C)	Ref.
1a	Me	H	H	H	H	34[26] 14[29]	**A**	oil	26 29[b-d]
1b	Me	H	H	H	Me	50[29] 41[18]	**A**	38-39[29] 37.5-8.5[18]	18 29[b-d]
1c	Me	H	H	H	Ph	81	**A**	87-88	17
1d	Me	H	H	Me	H	18	**A**	70	29[b-d]
1e	Me	H	Me	H	H	65 80[18]	**A**	50 49-49.5[18]	18 29[b-d]
1f	Me	H	*t*-oct	H	H	23	**A**	oil	17
1g	Me	H	NHAc	H	H	63	**A**	145	21
1h	Me	H	OH	H	H	66	**B**	158-159	24[b]
1i	Me	H	OMe	H	H	44[19]	**A**	118-119 41-43[19]	12 19
1j	Me	H	H	Me	Me	44	**A**	oil	29[b-d]
1k	Me	H	Me	H	Me	---- ----	**A** ----	---- ----	16[c] 28[b]
1l	Me	H	Me	H	*t*-Bu	45 ----	**C** ----	43-44 ----	41 28
1m	Me	H	*t*-Bu	H	*t*-Bu	69 93[69]	**A**	oil	17 69[b-e]
1n	Me	H	Cl	H	Me	69	**A**	55-56	13
1o	Me	H	Cl	H	Cl	69	**A**	56-57	13
1p	Me	H	Br	H	Br	68 51[17]	**A**	78-79 76-77[17]	13 17
1q	Me	H	Me	Me	H	60	**A**	84	29[b-d]

Table 1. Continued...

Cmpd	R	R_1	R_2	R_3	R_4	Yield (%)	Method[a]	mp.(°C)	Ref.
1r	Me	Me	H	H	H	30	**D**	oil	29[b-d]
1s	Me	Me	H	H	Me	25	**A**	45	29[b-d]
1t	Me	Me	H	H	Cl	65	**A**	70	29[b-d]
1u	Me	Me	H	Me	H	61	**A**	59-60	29[b-d]
1v	Me	Me	Me	H	H	35	**D**	35	29[b-d]
1w	Me	Me	Me	H	Cl	35	**A**	39	29[b-d]
1x	Me	Me	Cl	H	*i*-Pr	71	**A**	oil	27
1y	Et	H	NHAc	H	H	48	**A**	130-132	34
1z	Et	H	OH	H	H	87	**B**	174-175	24[b]
1aa	Et	H	Me	H	Me	----	**A**	----	16[c]
1ab	Et	H	OH	Me	H	67	**B**	182-183[f]	24[b]
1ac	*n*-Pr	H	NHAc	H	H	41	**A**	112-112.5	34
1ad	*n*-Pr	H	OH	H	H	70	**B**	152-153	24[b]
1ae	*n*-Pr	H	OH	Me	H	53	**B**	181-183[f]	24[b]
1af	*n*-Bu	H	OH	H	H	77	**B**	137-138	24[b]
1ag	*n*-Bu	H	OH	Me	H	66	**B**	166-167[f]	24[b]
1ah	$-C_6H_{13}$	OH	R_5	H	H	61	**A**	----	35
1ai	$-C_2H_4Ph$	H	NHAc	H	H	----	**A**	131-132	12
1aj	$-C_2H_4Ph$	H	NO_2	H	H	----	**A**	84-85	12
1ak	$-C_2H_4Ph$	H	OMe	H	H	63[19]	**A**	73-74 72-74[19]	12 19
1al	R_6	H	NO_2	H	H	----	**A**	77-78	12
1am	R_6	H	OMe	H	H	----	**A**	66-67	12
1an	$-C_2H_4OH$	H	H	H	H	30	**A**	52-53	26
1ao	R_7	H	OH	Me	H	85	**B**	192-193[f]	24[b]
1ap	R_8	H	H	H	H	72	**A**	oil	6
1aq	R_8	H	OH	Me	H	82	**B**	172-173[f]	24[b]
1ar	Bn	H	H	H	H	74 80	**A** **D**	66 64-65	26 26,14
1as	Bn	H	Me	H	H	54[19] 79[21]	**A**	71-72[12] 70-71[19] 71[21]	12 19 21
1at	Bn	H	NHAc	H	H	60[34] 61[21]	**A**	167-168[12] 168-169[34] 168[21]	12 34 21
1au	Bn	H	NHR_9	H	H	55	**A**	152-154	34
1av	Bn	H	NHAc	H	H	----	**A**	83-84	12
1aw	Bn	H	NO_2	H	H	----	**A**	88-89	12
1ax	Bn	H	OH	H	H	73	**B**	172-173	24[b]
1ay	Bn	H	OMe	H	H	91[37] 41[19]	**A**	74-75[12] 72-73[37] 73-74[19]	12 37 19

Table 1. Continued...

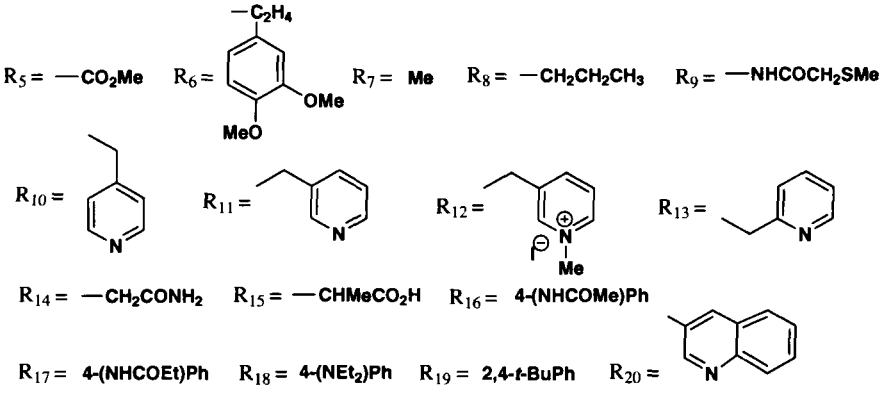
Cmpd	R	R_1	R_2	R_3	R_4	Yield (%)	Method[a]	mp.(°C)	Ref.
1az	Bn	H	OBn	H	H	61	**A**	86-87	11
1ba	Bn	H	Br	H	H	----	**A**	80-81	12
1bb	Bn	H	NHAc	H	OMe	55	**A**	166-168	34
1bc	Bn	H	Cl	H	Me	73	**A**	77-78	13
1bd	Bn	H	Cl	H	Cl	39	**A**	62-63	13
						83	**D**		
1be	Bn	H	Br	H	Br	78	**A**	77-78	13
1bf	Bn	H	OH	Me	H	98	**B**	188-190[f]	24[b]
1bg	Bn	OH	R_5	H	H	63	**A**	----	35
1bh	R_{10}	H	Br	H	H	----	**A**	111-112	12
1bi	R_{10}	H	OMe	H	H	----	**A**	99-100	12
1bj	R_{10}	H	NHAc	H	H	----	**A**	176-177	12
1bk	R_{11}	H	Br	H	H	----	**A**	99-100	12
1bl	R_{11}	H	OMe	H	H	----	**A**	89-90	12
1bm	R_{11}	H	NHAc	H	H	----	**A**	151-152	12
1bn	R_{12}	H	NHAc	H	H	----	**A**	----	12
1bo	R_{13}	H	NHAc	H	H	----	**A**	138-139	12
1bp	R_{14}	H	Me	H	H	----	**A**	182-183	12
1bq	R_{14}	H	NHAc	H	H	----	**A**	196-197	12
1br	R_{14}	H	OMe	H	H	----	**A**	184-185	12
1bs	R_{14}	H	Br	H	H	----	**A**	187-188	12
1bt	$-CH_2R_5$	H	OMe	H	H	----	**A**	oil	12
1bu	*i*-Pr	H	H	H	H	----	**D**	----	14
						70	**F**	----	15
						----	----	----	10[c]
1bv	*i*-Pr	H	OH	H	H	34	**A**	145-146	11
1bw	*i*-Pr	H	OH	Me	H	75	**B**	177-178[f]	24[b]
1bx	*i*-Pr	Me	H	H	Me	----	**D**	----	14
1by	*i*-Pr	Me	H	Me	H	----	----	----	10[c]
1bz	–CHMeEt	H	OH	H	H	12	**A**	64-65	11
1ca	–CHMeEt	H	Me	H	*t*-Bu	50	**C**	oil	41
1cb	–CHPhMe	H	H	H	H	95	**D**	oil	43[b-d,g]
1cc	–CHPhMe	H	H	H	H	71	**F**	----	15
1cd	–CHPhMe	H	Me	H	H	----	**A**	42-43	12
1ce	–CHPhMe	H	NHAc	H	H	----	**A**	145-146	12
1cf	–CHPhMe	H	OH	H	H	53	**A**	143-144	11
1cg	$-C_6H_{11}$	H	H	H	H	60	**A**	oil	26
						86	**D**	----	26
						66	**F**	----	15
1ch	$-C_6H_{11}$	H	Me	H	H	----	**A**	38-39	12

Table 1. Continued...

Cmpd	R	R_1	R_2	R_3	R_4	Yield (%)	Method[a]	mp.(°C)	Ref.
1ci	$-C_6H_{11}$	H	*t*-Bu	H	H	90[27]	**A**	93-94	27,21
						78[21]			
						95	**D**		21
1cj	$-C_6H_{11}$	H	Ph	H	H	68	**A**	72	21
1ck	$-C_6H_{11}$	OH	R_5	H	H	66	**A**	----	35
1cl	$-C_6H_{11}$	H	NHAc	H	H	----	**A**	138-139	12
						74	**A**	139-140	34
1cm	$-C_6H_{11}$	H	OBn	H	H	82	**A**	69-70	11
1cn	$-C_6H_{11}$	H	OH	H	H	90	**A**	133-134	11
1co	$-C_6H_{11}$	H	Me	H	Me	81	**A**	192-195[f]	21
						78, 69	**D**		39
1cp	$-C_6H_{11}$	H	Me	H	*t*-Bu	46	**C**	98-99	41
1cq	$-C_6H_{11}$	H	Br	H	H	35	**A**	93-92	27
						54[21]		92[21]	21
1cr	$-C_6H_{11}$	H	Cl	H	Me	44	**A**	48-49	13
1cs	$-C_6H_{11}$	H	Cl	H	Cl	36	**A**	56-57	13
						60	**D**	56-57	13
1ct	R_{15}	H	H	H	H	----	**D**	----	14
						----	----	----	10[e]
1cu	R_{15}	Me	H	H	Me	----	**D**	----	14
1cv	R_{15}	Me	H	Me	H	----	----	----	10[e]
1cw	*t*-Bu	H	H	H	H	50	**F**	----	15
1cx	*t*-Bu	H	OH	H	H	51	**A**	127-128	11
1cy	*t*-Bu	H	OBn	H	H	59	**A**	59-60	11
1cz	Ph	H	H	H	H	57	**D**	55.9	42
						----	----	----	10[e]
1da	Ph	H	H	H	R_9	74	**A**	oil	6
1db	Ph	H	H	OMe	H	----	**D**	----	14
						----	----	----	10[e]
1dc	Ph	H	H	NO_2	H	----	**D**	----	14
						----	----	----	10[e]
1de	Ph	H	Me	H	*t*-Bu	38	**C**	67-68	41
1df	Ph	H	NHAc	H	H	40	**A**	173-175	34
1dg	4-MePh	H	H	H	H	32[42]	**D**	83.9[42]	14,42
						----	----	----	10[e]
1dh	4-MePh	H	Br	H	H	69	**A**	79-80	22
1di	4-MePh	H	*t*-Bu	H	H	69	**A**	87-88	22
1dj	4-CNPh	H	H	H	H	----	**D**	----	14
1dk	R_{16}	H	NHAc	H	H	21	**A**	215-219	34
1dl	R_{17}	H	NHAc	H	OMe	61	**A**	153-156	34
1dm	R_{18}	H	H	H	H	----	**D**	----	14
						----	----	----	10[e]
1dn	4-NO_2Ph	H	H	H	H	----	**D**	----	14

Table 1. Continued...

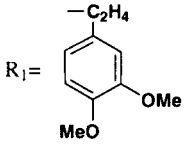
Cmpd	R	R_1	R_2	R_3	R_4	Yield (%)	Method[a]	mp.(°C)	Ref.
1do	4-MeOPh	H	H	H	H	48[42]	**D**	67.6[42]	14,42
						----	----	----	10[c]
1dp	4-MeOPh	H	NHAc	H	H	46	**A**	120-122	34
1dq	4-MeOPh	H	NHR_8	H	H	31	**A**	112-113	34
1dr	4-MeOPh	H	NHAc	H	OMe	48	**A**	160-163	34
1ds	4-EtOPh	H	NHAc	H	H	50	**A**	142-144	34
1dt	4-ClPh	H	H	H	H	32	**D**	51.3	42
1du	4-ClPh	H	NHAc	H	H	60	**A**	183-185	34
1dv	4-ClPh	H	NHR_8	H	H	43	**A**	127-128	34
1dw	4-ClPh	H	NHAc	H	OMe	36	**A**	178-180	34
1dx	4-BrPh	H	H	H	H	74	**D**	80.5	42
1dy	4-BrPh	H	H	Br	H	----	**D**	----	14
						----	----	----	10[c]
1dz	2-MePh	H	H	H	H	----	**D**[14]	----	14
						----	----	----	10[c]
1ea	2-MePh	H	*t*-Bu	H	H	64	**A**[h]	90.9-92.0	31
1eb	2-*i*-PrPh	H	*t*-Bu	H	Me	----	**A**[h]	97.5-99.0	31
1ec	$2\text{-}H_2OCPh$	H	H	H	H	----	----	----	10[c]
1ed	2-ClPh	H	NHAc	H	H	44	**A**	158-161	34
1ee	2-ClPh	OH	R_5	H	H	81	**A**	----	35
1ef	2,4-MePh	H	*t*-Bu	H	H	67	**A**[h]	oil	31
1eg	R_{19}	H	*t*-Bu	H	*t*-Bu	93[31]	**A**	174-176	25,31
1eh	2-MeOPh	H	NHAc	H	H	34	**A**	139-142	34
1ei	2-EtOPh	H	NHAc	H	H	27	**A**	130-132	34
1ej	R_{20}	H	NHAc	H	H	31	**A**	174-176	34

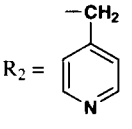


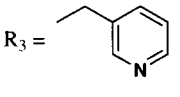
a) In text; b) ^1H NMR data; c) ^{13}C NMR data; d) IR data; e) MS data; f) hydrochloride; g) α;h) $Ba(OH)_2$ as catalyst.

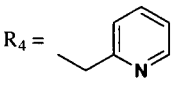
Table 2. Structure, Preparation and Properties of Benzoxazines **1fa**, **1fb**, **1ga-o**, **1ha-i**

Cmpd	R	Yield (%)	Method[a]	mp.(°C)	Ref
1fa	Bn	92	**A**	160[c]	38[b,d,e]
1fb	$-C_6H_{11}$	67	**A**	86-88	23
1ga	Me	100[17]	**A**	67-68[12,17,23]	12,17
		98	**E**	185-187[c,23]	23
1gb	*n*-Bu	87	**A**	138-140[c]	23
1gc	$-C_8H_{17}$ (n)	21	**A**	oil	17
1gd	$-C_3H_6OH$	79	**A**	oil	17
1ge	R_1	----	**A**	87-88	12
1gf	$-C_2H_4OH$	94	**A**	oil	17
1gg	Bn	99.5	**A**	126-127 169-170[c]	23
		97	**E**	----	23
1gh	R_2	----	**A**	92-93	12
1gi	R_3	----	**A**	79-80	12
1gj	R_4	----	**A**	84-85	12
1gk	$-CH_2CONH_2$	----	**A**	202-203	12
1gl	$-CH_2CO_2Me$	----	**A**	93-94	12
1gm	$-C_6H_{11}$	67	**A**	83-87	23
		100[f]		178-179[c]	
1gn	-CH(Me)Ph	----	**A**	75-77	12
1go	4-MePh	91	**A**	86-88	22
		83	**D**		
1ha	Me	----	**A**	----	20, 46
1hb	Et	----	**A**	----	46
1hc	*n*-Pr	----	**A**	----	46
1hd	Bn	----	**A**	----	46
1he	$-CH_2CH=CH_2$	71	**A**	55-58	6
1hf	$-C_6H_{11}$	----	**A**	----	46
1hg	Ph	71	**A**	----	39,46
1hh	4-MePh	70	**A**	----	39
1hi	2-FPh	----	**A**	----	46







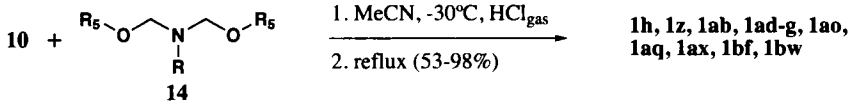


In text; b) ^{1}H NMR data; c) Hydrochloride; d) IR data; e) MS data; f) As hydrochloride

3,4-Dihydro-3-cyclohexyl-6-t-butyl-1,3,2H-benzoxazine (1ci). Typical Procedure.[21] *Cyclohexylamine (39.6 g, 0.4 mole) was added portionwise with cooling to 200 mL of dioxane containing 60 mL of aqueous 37% formaldehyde (0.8 mole). After addition of 60 g of p-(t-butyl)phenol (0.4 mole), the mixture was heated at reflux for two hours. Upon cooling to room temperature, a crystalline solid (85 g) separated. The product was recrystallized from 95% ethanol, mp. 94°C, yield 78%.*

b) Reaction of bis(Alkoxymethyl)amines with Phenols (Method B)

In the method patented by Reynolds and Cossar in 1974,[24] phenols **10** react with *bis*(alkoxymethyl)amines **14**, prepared by the condensation of primary amine, formaldehyde and an alcohol.[40] The reaction mixtures were kept at room temperature for 30 min. and then warmed rapidly to reflux in anhydrous acetonitrile solution of HCl. Crystallization of the benzoxazine hydrochlorides took place on cooling (53-98%) (*Scheme 5*).



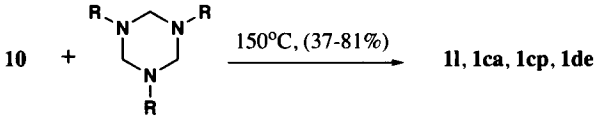
R - according to *Table 1*; R_5 = Me, *n*-Pr, *i*-Bu, C_8H_{17}, C_9H_{19}, $C_{12}H_{25}$, Bn

Scheme 5

General Procedure (1ao).[24] *To anhydrous acetonitrile (300 mL), 24.8 g (0.2 mole) of methyl hydroquinone is added and the mixture is cooled to -30°C in a Dry Ice/acetone bath. The temperature of the mixture is maintained at -30°C while 8.0 g of dry hydrogen chloride gas is introduced. Bis-(isobutoxymethyl)methylamine 40.6 g (0.2 mole) is added all at once to the above mixture. The solution is set aside for 30 minutes at room temperature and then warmed rapidly to reflux on a hot plate. The solution containing precipitated 3,4-dihydro-3,7-dimethyl-6-hydroxy-2H-1,3-benzoxazine hydrochloride is cooled, the precipitate was collected by filtration and the product dried. The yield of the crude product is 36 g (85%). An analytical sample is recrystallized from a methanol-acetonitrile mixture, mp. 192-193°C.*

c) Fusion of Hexahydrotriazines with Phenols (Method C)

Kostyuchenko *et al.*[41] obtained benzoxazines by fusion of phenols **10** with hexahydrotriazines **15** in equimolar quantities (37-81%). According to the authors, acids catalyze the reaction, whereas bases even in quantities as low as 0.001-0.1% of the phenol result in lowering of the reaction rate. The reactions were run at 150°C. No other reaction conditions or isolation procedure were given (*Scheme 6*).

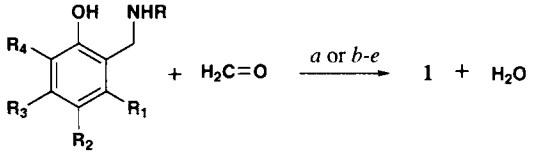


Scheme 6

General Procedure.[41] *3,4-Dihydro-3-alkyl(phenyl)-6-methyl-8-tert-butyl-1,3(2H)-benzoxazines were obtained in the reaction of 4-methyl-2-tert-butylphenol with cyclic trimethylenetriamines in equimolar ratio at 150°C.*

d) Reaction of Benzylamines with Formaldehyde (Method D)

The condensation of benzylamines **16** with formaldehyde proceeds smoothly in refluxing methanol for 2 h, especially in the presence of the basic catalyst such as KOH, which additionally improves the solubility of the paraformaldehyde used (78-95%).[14,21,26] The reactions performed at room temperature and without the basic catalyst required much longer reaction times (12 days).[22] Similar reactions were also carried out in dioxane resulting in low yields of benzoxazines (30-35%).[29] In some cases, formalin in methanol[42] or a THF[43] solution was used (*Scheme 7*).



16

a) MeOH, KOH, reflux, 1.5-2 h (78-95%) (**1ar**, **1bu**, **1bx**, **1ct**, **1cu**, **1db**, **1dc**, **1dg**, **1dj**, **1dm-o**, **1dy**, **1dz**,[14] **1ci**, **1co**,[21] **1ar**, **1cb**, **1cg**[26]). *b*) MeOH, rt, 12 days (69%) (**1go**).[22] *c*) dioxane, 3 h (30-35%) (**1r**, **1v**).[29] *d*) H_2O, MeOH, reflux, 2 h, rt, 3 days (32-74%) (**1cz**, **1dg**, **1do**, **1dt**, **1dx**).[42] *e*) H_2O, THF, rt, 12 h (95%) (**1cb**).[43] R-R_4 according to *Table 1*.

Scheme 7

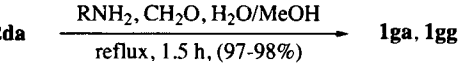
The benzoxazines crystallized after addition of water and cooling of the reaction mixture[21] or after removal of the volatile solvent.[22,29] Some benzoxazines **1** were purified by distillation[26,29] or were transformed into their crystalline hydrochlorides by treatment of the reaction mixture with concentrated hydrochloric acid.[21] The isolation of benzoxazine hydrochloride is possible only for substituted phenol derivatives. If R_1-R_4 are H, the benzoxazines are highly sensitive to mineral acids and decompose with liberation of formaldehyde (*Scheme 2*).

3,4-Dihydro-3-cyclohexyl-1,3,2H-benzoxazine (1cg). Typical Procedure.[26] *To 1.5 g of paraformaldehyde (0.05 mole) dissolved in 50 mL of methanol containing 0.05 g of potassium hydroxide was added 10.29 g of 2-cyclohexylaminomethylphenol (0.05 mole) and 50 mL of methanol. After the reaction mixture was heated under gentle reflux for 1.5 h the methanol was removed under reduced pressure. The residue was treated with 30 mL of 10% aqueous potassium hydroxide and extracted with ether. The ether extract was dried over sodium sulphate. The product obtained by removal of ether distilled at 133-135°C (0.7 mm) to give 9.4 g (86% yield) of a nearly colorless oil.*

e) From Dibenzylamine (Method E)

Burke *et al.* also described the preparation of benzoxazines **1ga** and **1gg** in the reaction of dibenzylamine **2da** with primary amine and formaldehyde in a water-methanol solution at

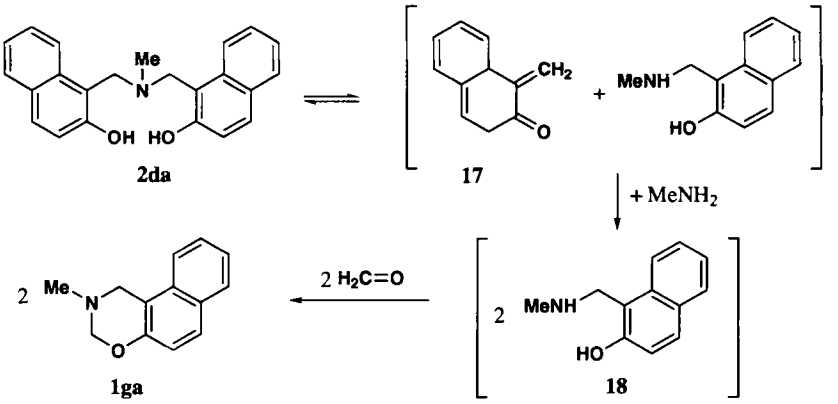
reflux for 1.5 h (*Scheme 8*).[23] Benzoxazines crystallized from the cooled reaction mixtures after addition of water (97-98%). They were purified by crystallization from ethyl acetate.



Scheme 8

2,3-Dihydro-2-methyl-1H-naphth[1,2-e]-m-oxazine (1ga). Typical Procedure.[23] *A mixture of 3 g of the dibenzylamine (0.0088 mole), 12.4 g of aqeous 25% methylamine (0.01 mole) and 15 mL of 37% aqueous formaldehyde (0.20 mole) in 100 mL of methanol was heated under gentle reflux for 1.5 hours. The white crystalline product (3.4 g, 98% yield) which formed upon cooling and addition of 100 mL of water melted at 67-69°C, after recrystallization from methanol.*

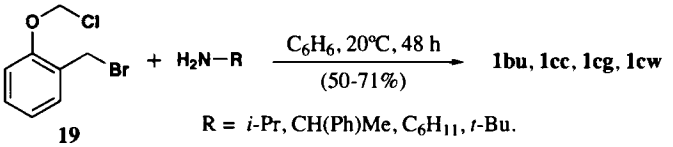
The mechanism of that transformation was proposed by Fields *et al. (Scheme 9)*.[40] Benzylamine **2da** decomposes under reaction conditions giving the methide intermediate **17**, which further reacts with methylamine resulting in formation of benzylamine **18**. Benzoxazine **1ga** is the product of **18** condensation with formaldehyde.



Scheme 9

f) Reaction of Dihalogenated Aromatic Compound with Primary Amines (Method F)

The reactions of **19** with excess of primary amines (4 equiv.) were carried out in benzene at room temperature for 48 h. The products were purified by column chromatography (50-70%) (*Scheme 10*).[15]

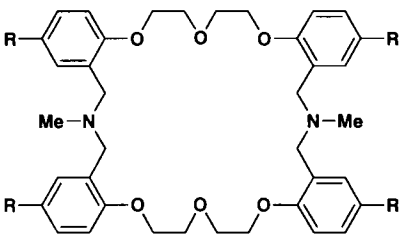


Scheme 10

The method seems to be highly selective, since very reactive formaldehyde is not present in the system. It is a method of choice for unsubstituted phenols, which are the most sensitive for side-reactions possible in all the previously described methods. However, the necessity to synthesize **19** first makes the process laborious and expensive.

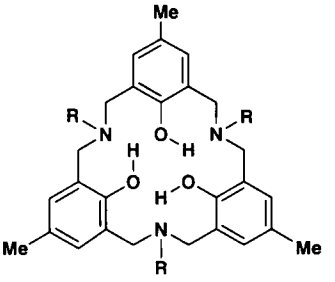
IV. DIBENZYLAMINES: PROPERTIES AND APPLICATIONS

Dibenzylamines **2**, called also benzoxazine dimers, have been used as model compounds in phenol-benzoxazine resins research. The properties of those polymeric materials probably result from the unique net of hydrogen bonds in their structure.[3,5,7,44-47] Dibenzylamines **2** have three active sites, one amine and two phenol hydroxyl. These sites are able to form complexes with different metal ions *e.g.* Mo,[48] Ti, Zr and Hf.[49-54] Some of the complexes were used as catalysts for α-olefin polymerization,[49-54] ring-opening polymerization of norbornene (bicyclo[2.2.1]hept-2-ene) as well as oxidation reactions.[48] Dibenzylamines **2** exhibit inclusion phenomena with transition metal ions (Cu, Zn and Cd)[55] which was confirmed by UV-Vis, ^{1}H NMR and ^{1}H-^{1}H NOESY techniques.[2] The host-guest ratio was verified to be of 2:1 for copper ions. The extraction of metal ions from their aqueous solutions with dibenzylamines **2** in chloroform was also investigated. The copper extraction percentage ranged from 24 to 80% depending on the bulkiness of the substituent adjacent to the nitrogen atom. Cd(II) ions exhibited much lower interactions than Zn(II), probably due to their bigger size. Dibenzylamines **2** are valuable intermediates in the synthesis of the new class of macrocyclic compounds of structure **20-22** (*Fig. 3*);[2,55-58] some of them (**20**, **22**) are able to bind alkali metal ions such as Na, K or Cs.[57]

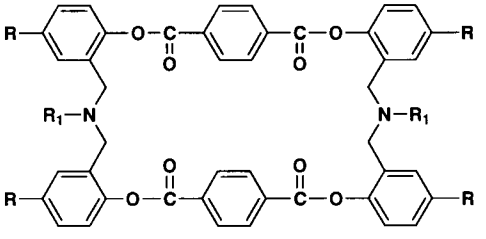


R = Me, Et

20


Me
R
N
O
H
Me
R = Bn, CHMePh, *i*-Bu, allyl

21



R = Me, Et; $R_1 = C_3H_7, C_6H_{11}$

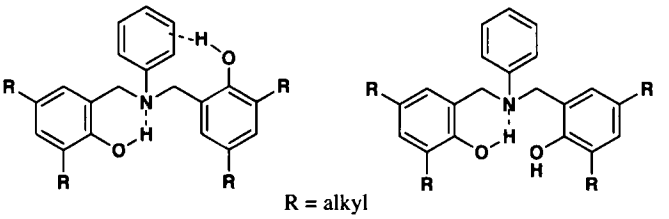
22

Fig. 3

Some dibenzylamines have been patented as rubber antioxidants[59] and components of diazo type materials.[60-62] They were also tested as potentialy biologically active species[63] and used in the synthesis of nitrogen containing phosphorus compounds.[64]

V. DIBENZYLAMINES: STRUCTURE AND STABILITY

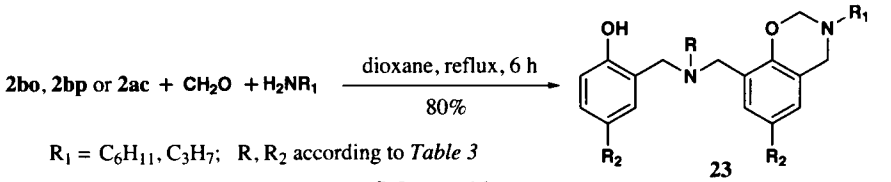
The structure of dibenzylamines **2** is stabilized by intramolecular hydrogen bonds not only in the solid-state[65] but also in solution (*Fig. 4*).[44] The hydrogen bonds result in the chemical non-equivalence of the phenolic rings in dibenzylamine **2** structure.



R = alkyl

Fig. 4

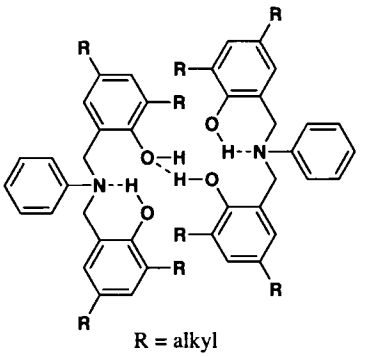
In reactions of dibenzylamines **2bo**, **2bp** and **2ac** with formaldehyde and primary amines, unsymmetrical benzoxazine products (*Scheme 11*) have also been obtained. The reactions were carried out in non-polar solvents, such as dioxane and cyclohexane, or in a solventless system (yields 75-80%). The use of methanol as a solvent led to much lower yields (20-30%) of **23**.[65]



$R_1 = C_6H_{11}, C_3H_7$; R, R_2 according to *Table 3*

Scheme 11

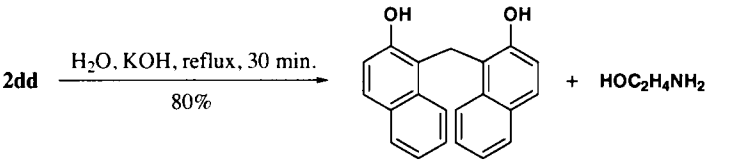
A solid-state ^1H NMR[7,66] and FT-IR[47] analysis showed that some dibenzylamines **2** have a dimeric (*Fig. 5*) or ladder structure as a result of intermolecular hydrogen bonds.



R = alkyl

Fig. 5

Dibenzylamine **2dd** is not resistant toward strong alkali and was converted to the di-(2-hydroxynaphthyl-1)methane **24** in 80% yield by refluxing in aqueous KOH solution for 30 min. (*Scheme 12*).[23,17]



24

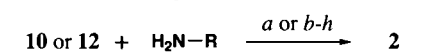
Scheme 12

VI. DIBENZYLAMINES: METHODS OF SYNTHESIS

Six methods for the synthesis of dibenzylamines **2** have been reviewed (*Tables 3* and *4*).

a) Mannich Reaction (Method A)

In the Mannich reaction leading to dibenzylamines **2** (*Fig. 1, Table 2*), phenols **10** or **12**, formaldehyde and primary amines in a molar ratio of 2:2:1 were used. In the majority of cases, formalin[13,23,27,49,51,59-62,64,67] and sometimes paraformaldehyde[16,63] or trioxane[12] were used. Usually the solvents were methanol,[12,23,27,49,51,59-62,64,67] dioxane,[13,16] or ethanol.[63] In some cases KOH was utilized as a catalyst (*Scheme 13*).[12,27] In the Mannich reaction system, the formation of several different products, *e. g.* resinous materials, benzylamines[1] and benzoxazines **1** is possible; however, application of the appropriate reaction conditions often resulted in high yields of dibenzylamines (up to 99%).[33] Burke *et al.* claimed that generation of dibenzylamines **2** is favored for phenols with steric hindrance at the position *ortho* to the phenolic hydroxy group, making the formation of the benzoxazine ring difficult.[27]

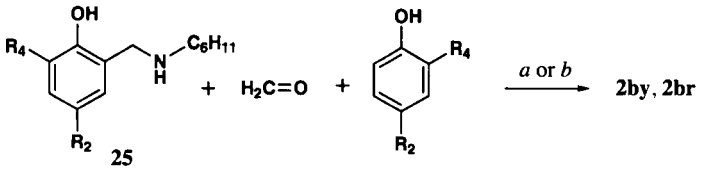


a) CH_2O, H_2O, MeOH, rt, 3-several h (64-91%) (**2g**, **2q**, **2r**, **2t**, **2aa**, **2ab**, **2ah**, **2bd**, **2bh**, **2bi**, **2bn**, **2bz**,[61] **2l**, **2q**, **2s**, **2t**, **2aa**, **2ab**, **2ah**, **2al**, **2bd**, **2bi**, **2bz**,[62] **2l**, **2r**, **2t**, **2u**, **2aa**, **2ab**, **2ag**, **2ah**, **2aj**, **2bd**, **2bh**, **2bi**, **2bn**, **2bz**,[60] **2da**, **2db**, **2dg**[23]). *b*) CH_2O, H_2O, MeOH, reflux, 1-48 h (50-61%) (**2ax**, **2ay**, **2be**, **2bf**, **2bj-l**,[51] **2az**, **2ba**,[67] **2af**, **2ay**[49]). *c*) CH_2O, H_2O, MeOH, rt,16-20 h then reflux, 3-4 h (26-99%) (**2l**, **2o**, **2p**, **2an**,[64] **2p**, **2bs**[59]). *d*) CH_2O, H_2O, MeOH, KOH, reflux, 2 h (43-80%) (**2l**, **2m**, **2w**, **2bb**, **2bn**).[27] *e*) CH_2O, H_2O, dioxane, rt, 16 days (13-88%) (**2h-k**, **2bt**, **2bw**, **2bx**).[13] *f*) CH_2O, EtOH, reflux, 12 h (23-31%) (**2bc**, **2bm**).[63] *g*) CH_2O, dioxane, reflux, 2 h (**2l**, **2z**, **2ad**).[16] *h*) $(CH_2O)_3$, MeOH, KOH, reflux, 20 min. (**2f**, **2aq**, **2ar-u**, **2df**).[12]

Scheme 13

Dibenzylamines **2** have also been obtained in the Mannich reaction of the benzylamines **25** with formaldehyde (formalin) and the appropriate phenol in equimolar ratio (*Scheme 14*).

The reactions were carried out in dioxane at room temperature for 13 days (60%)[13] or the mixture was refluxed for 1 h and then kept at room temperature for additional 16 h (43%).[27] The products were crystallized from methanol after removal of the solvent under reduced pressure.[13,27] The Mannich reaction seems to be the most useful method for the synthesis of dibenzylamines, mainly due to the large variety of easily accessible starting materials, and it has been the most often used preparation (*Tables 3 and 4*).



a) R_2, R_4 = Cl, H_2O, dioxane, rt, 13 days (60%) (**2by**).[13] b) R_2, R_4 = Me, H_2O, dioxane, reflux, 1 h and then rt, 16 h (43%) (**2br**).[27]

Scheme 14

Table 3. Structure, Preparation and Properties of Dibenzylamines **2a-cj**

Cmpd	R	R_1	R_2	R_3	R_4	Yield (%)	Method[a]	mp. (°C)	Ref.
2a	Me	H	H	H	Me	60	**D**	148	18
2b	Me	H	H	H	OMe	81	**B**	88-89	68[b]
2c	Me	H	Me	H	H	90	**D**	163	2[b,c]
						----	----	----	57
2d	Me	H	Et	H	H	90	**D**	130	2[b,c]
						----	----	----	57
2e	Me	H	*t*-oct	H	H	10	**D**	oil	17[b,d-f]
2f	Me	H	OMe	H	H	----	**A**	157-158	12
2g	Me	H	H	Me	Me	----	**A**	65[g,h]	61
2h	Me	H	Cl	H	Cl	18	**A**	118-119	13
2i	Me	H	Br	H	Br	88[i] 13[j]	**A**	129-130	13
2j	Me	H	Cl	H	Me	66	**A**	104-105	13
2k	Me	H	*t*-Bu	H	Br	50	**A**	122-123	13
2l	Me	H	Me	H	Me	85[27]	**A**	124-125[27]	16,[d]
								65[g,h] 60	27,
								65[g,h] 62	46,[b,d]
									47,[b,d]
									48,60,
									62
						80	**D**	123[2]	2[b,c]
								128-130[45]	45[b,d,e]
						----	----	----	7[b]
2m	Me	H	*t*-Bu	H	Cl	52	**A**	169-171[g]	27
2n	Me	H	*t*-Bu	H	*t*-Bu	----	**A**	----	48
						11.7	**B**	126-127	69[b,d-f]
						80-85[72] 83[73]	**E**	132-133	72,73
						81	**A**	118-121	64[b]

Table 3. Continued...

Cmpd	R	R_1	R_2	R_3	R_4	Yield (%)	Method[a]	mp. (°C)	Ref.
2o	Me	H	Me	H	Me	97	**D**	127	18
2p	Me	H	Me	H	*t*-Bu	90 92[59]	**A**	100-103[64] 113-113.5	64,[b]59
2q	Me	H	Me	Me	H	----	**A**	166-167[61] 166-167[62]	61,62
2r	Me	Me	H	H	*t*-Bu	----	**A**	175-176[g,h]	60,61
2s	Me	Me	H	Me	H	----	**A**	177-178	62
2t	Me	Me	H	Et	H	----	**A**	78[g,h,60] 78[g,h,61] 78[g,62]	60,61 62
2u	Me	Me	Me	H	H	----	**A**	65[g,h]	60
2v	Me	H	Me	Me	Br	----	**F**[k]	116-117	74
2w	Me	Me	*t*-Bu	H	*t*-Bu	55	**A**	130-131	27
2x	Me	H	Cl	H	Me	29	**D**	105	18
2y	Me	Br	Br	Br	Br	----	**F**[k]	205-207	75
2z	Et	H	Me	H	Me	----	**A**	----	46,[b,d] 16[d]
						----	----	----	7[b]
2aa	Et	Me	H	H	Me	----	**A**	189-190[g]	62,60 61
2ab	Et	Me	H	Me	H	----	**A**	178-180	60,61 62
2ac	*n*-Pr	H	Me	H	H	80	**D**	149	2[b,c]
2ad	*n*-Pr	H	Me	H	Me	----	**A**	----	46,[b,d] 16[d]
						----	----	----	7[b]
2ae	*n*-Pr	H	*t*-Bu	H	*t*-Bu	----	**A**	----	50
2af	*n*-Pr	H	Me	Me	H	50	**A**	180-181	49[b]
2ag	*n*-Pr	Me	H	Me	H	----	**A**	183-184	60
2ah	*n*-Pr	Me	H	Et	H	----	**A**	169	60,61
2ai	*n*-Bu	H	Me	H	Me	----	----	----	7[b]
2aj	*n*-Bu	Me	H	Me	H	----	**A**	151-152	60
2ak	$-(CH_2)_3OH$	Me	H	Me	H	----	**A**	167-168	62
2al	R_5	Me	H	H	Me	----	**A**	60[g,h]	60,62
2am	R_6	H	Me	H	R_7	50	**F**[l]	-----	58[b,d,f]
2an	Bn	H	Me	H	*t*-Bu	26	**A**	152-155	64[b]

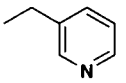
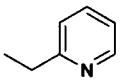
Table 3. Continued...

Cmpd	R	R_1	R_2	R_3	R_4	Yield (%)	Method[a]	mp. (°C)	Ref.
2ao	Bn	H	Me	H	R_8	55	**F**[l]	----	58[b,d,f]
2ap	Bn	H	Me	Me	Br	----	**F**[k]	147-148	74
2aq	R_9	H	NHAc	H	H	----	**A**	164-165	12
2ar	R_9	H	OMe	H	H	----	**A**	167-168	12
2as	R_{10}	H	Me	H	H	----	**A**	177-178	12
2at	R_{10}	H	OMe	H	H	----	**A**	150-151	12
2au	R_{10}	H	Br	H	H	----	**A**	223-225	12
2av	R_{11}	H	Me	H	R_{12}	59	**F**[l]	----	58[b,d,f]
2aw	R_{13}	H	Me	H	R_{14}	53	**F**[l]	----	58[b,d,f]
2ax	R_{15}	H	Me	H	Me	----	**A**	----	51
2ay	R_{15}	H	Me	Me	H	61[49]	**A**	178-179[49]	51,49[b]
2az	$-C_2H_4OH$	H	$-C_6H_{11}$	H	H	----	**A**	170-171	67
2ba	$-C_2H_4OH$	H	Ph	H	H	----	**A**	102	67
2bb	$-C_2H_4OH$	H	Me	H	Me	60	**A**	128-129 185-186[g]	27
2bc	$-C_2H_4OH$	H	R_{13}	H	OMe	31	**A**	86	63
2bd	$-C_2H_4OH$	Me	H	Me	H	----	**A**	162-163	60,61 62
2be	R_{15}	H	*t*-Bu	H	*t*-Bu	----	**A**	----	51,50 52
2bf	R_{17}	H	Cl	H	Cl	----	**A**	----	51
2bg	R_{16}	H	*t*-Bu	H	*t*-Bu	----	**A**	----	50
2bh	R_{16}	Me	H	H	Me	----	**A**	90-95[g,h]	60,61
2bi	R_{16}	Me	H	Me	H	----	**A**	90-92[g,h]	60,62 61
2bj	R_{17}	H	Me	H	Me	----	**A**	----	51
2bk	R_{17}	H	*t*-Bu	H	*t*-Bu	----	**A**	----	50,51
2bl	R_{17}	H	Cl	H	Cl	60	**A**	115-116	51[b,d,f]
2bm	$-C_2H_4OEt$	H	R_{13}	H	OMe	23	**A**	137	63
2bn	R_{18}	Me	H	Me	H	----	**A**	167-168	60,61
2bo	$-C_6H_{11}$	H	Me	H	H	80	**D**	181	2[b,c]
2bp	$-C_6H_{11}$	H	Et	H	H	----	----	----	65
2bq	$-C_6H_{11}$	H	*t*-Bu	H	H	8	**D**	165	18
2br	$-C_6H_{11}$	H	Me	H	Me	43[27]	**A**	146-147[46] 213-215[g]	27 46[b,d]
						52	**A**[m]		27

Table 3. Continued...

Cmpd	R	R_1	R_2	R_3	R_4	Yield (%)	Method[a]	mp. (°C)	Ref.
2bs	$-C_6H_{11}$	H	Me	H	*t*-Bu	99	**A**	145-146	59
2bt	$-C_6H_{11}$	H	Me	H	*t*-Oc	----	**A**	oil	59
2bu	$-C_6H_{11}$	H	Me	H	Cl	48	**A**	124-125	13
2bv	$-C_6H_{11}$	H	*t*-Bu	H	Cl	59	**A**	167-168 149-150[g]	27
2bw	$-C_6H_{11}$	H	*t*-Bu	H	Br	43	**A**	167-168	13
2bx	$-C_6H_{11}$	H	Cl	H	Me	53	**A**	140-141	13
2by	$-C_6H_{11}$	H	Cl	H	Cl	60	**A**[m]	53-54	13
2bz	$-C_6H_{11}$	Me	H	H	Me	----	**A**	142-144[g,h]	60,61 62
2ca	Ph	H	Me	H	Me	----	**A**	----	46,[b,d] 47[b,d]
2cb	Ph	H	Me	H	NO_2	47	**F**[l]	187	76[b,d,f]
2cc	Ph	Br	Br	Br	Br	----	**F**[k]	205-207	75
2cd	4-MePh	H	H	H	H	25	**C**	155.4	42
2ce	2-MePh	H	*t*-Bu	H	H	64	**A**	88-90	31
2cf	2,6-MePh	H	*t*-Bu	H	H	67	**A**	oil	31
2cg	2-*i*PrPh	H	*t*-Bu	H	Me	44	**A**	91-97	31
2ch	4-MeOPh	H	H	H	H	16	**C**	160.6	42
						0.5	**F**[n]		42
						31	**C**	168.4	42
2ci	4-ClPh	H	H	H	H	3	**F**[n]		42
2cj	4-BrPh	H	H	H	H	40	**C**	156.4	42
						5	**F**[n]		42

R_5 = —$(CH_2)_3OMe$ R_6 = —$CH_2CH(Me)_2$ R_7 = —$CH_2NHCH_2CH(Me)_2$ R_8 = —CH_2NHPh

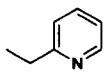
R_9 =  R_{10} =  R_{11} = —CH(Me)Ph R_{12} = —$CH_2NHCH(Me)Ph$

R_{13} = —CH_2CHCH_2 R_{14} = —$CH_2NHCH_2CHCH_2$ R_{15} = —$C_2H_4N(Me)_2$

R_{16} = —$C_2H_4N(Et)_2$ R_{17} = —C_2H_4OMe R_{18} = —$CH_2CH(Me)OH$

a) In text; b) ^1H NMR data; c) FT-IR data; d) ^{13}C NMR data; e) IR data; f) MS data; g) Hydrochloride; h) Decomposition; i) 14 days reaction time; j) 3 days reaction time; k) Benzyl bromide as substrate; l) Benzyl chloride as substrate; m) Benzylamine as substrate; n) Benzyl alcohol as substrate.

Table 4. Structure, Preparation and Properties of Dibenzylamines **2da-dp**

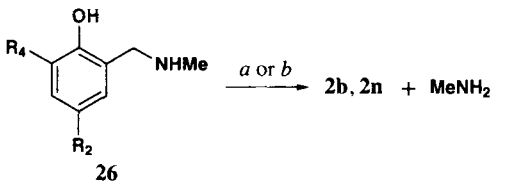
Cmpd	R	mp. (°C)	Yield (%)	Method[a]	References
2da	Me	145-146[b] 148-151[b]	98, 99 91	**D** **A**	17,[b,d-f] 18 23
2db	*n*-Bu	137-138 135-137[b]	64	**A**	23
2dc	$-C_8H_{17}$	133-134	75	**D**	17[b,d-f]
2dd	$-C_2H_4OH$	133-135	85	**D**	17[b,d-f]
2de	$-C_3H_6OH$	66-67	67	**D**	17[b,d-f]
2df		190-191	----	**A**	12
2dg	$-C_6H_{11}$	120-122 172-174[b]	86	**A**	23
2gh	Ph	46-48	78	**A**	22
2di	4-MePh	86-88	91	**A**	22
2dj	$4\text{-}HO_2CPh$	215	59	**A**	22
2dk	2-MePh	57-60	83	**A**	22
2dl	$4\text{-}NO_2Ph$	168-170	61	**A**	22
2dm	$3\text{-}NO_2Ph$	133-134	81	**A**	22
2dn	$2\text{-}NO_2Ph$	108-109	27	**A**	22
2do	4-BrPh	118-119	91	**A**	22
2dp	2,3,6-BrPh	99-100	39	**A**	22

a) In text; b) Hydrochloride

N,N-bis-(3,5-Di-t-butyl-2-hydroxy-6-methylbenzyl)methylamine (2w). Typical Procedure.[27] *Methylamine (6.2 g 25% solution, 0.05 mole) dissolved in 30 mL of dioxane was added portion-wise with agitation to a cooled solution of 7.5 mL of 37% aqueous formaldehyde (0.1 mole) in 20 mL of dioxane. After addition of 22 g (0.1 mole) of 2,4-di-t-butyl-5-methylphenol in 25 mL of dioxane, the mixture was kept at room temperature for 3 h. Removal of the solvent yielded a solid (10.3 g) which was separated by filtration and washed with cold methanol. An additional 3.5 g of product was obtained from the filtrate: yield 56%, mp. 128-130°C.*

b) Condensation of Benzylamines (Method B)

Hara *et al.* obtained dibenzylamine **2b** by heating of the corresponding benzylamines **26** at 140°C for 1 h (80%).[68] Dibenzylamine **2n** was similarly obtained by Sparfel *et al.* from benzylamine in methanol for 24 h at reflux (12%),[69] with simultaneous liberation of the primary amine (*Scheme 15*). The products were purified by column chromatography. In both cases, the authors suggest the formation of dibenzylamines through the quinone methide intermediate.[70] The same mechanism was also assumed by Burke *et al.* in the investigation of the polymerization of *o*-hydroxybenzylamines.[71,1]



26

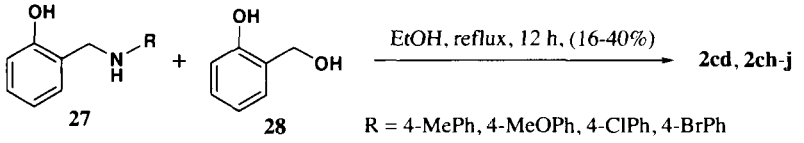
a) R_2 = *t*-Bu, R_4 = *t*-Bu, MeOH, reflux, 24 h (12%) (**2n**).[69] *b*) R_2 = H, R_4 = OMe, 140°C, 1 h (80%) (**2b**).[68]

Scheme 15

N,N-bis-(3,5-Di-t-butyl-2-hydroxy-6-methylbenzyl)methylamine (2w). Typical Procedure.[69] *The solution of the benzylamine (100 mg) in 20 mL of methanol was refluxed for 24 h under an argon atmosphere. After removal of the solvent the product was purified by column chromatography (eluent C_6H_{14} :CH_2Cl_2, 1:1, v:v). Yield 11.7%.*

c) Reaction of Benzylamines with 2-Hydroxybenzylalcohol (Method C)

Dibenzylamines were obtained by Noda in the reaction of hydroxybenzylamines **27** with saligenin **28** (*Scheme 16*) in equimolar quantities. The reactions were carried out in refluxing ethanol for 12 h. After cooling the reaction mixture in an ice bath, the crystalline products were collected and then purified by crystallization (16-40%).[42]



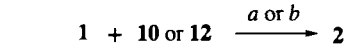
27 28

Scheme 16

N,N-bis(2-Hydroxybenzyl)-p-bromoaniline (2y). Typical Procedure.[42] *To a solution of 2.5 g of saligenin (0.02 mole) in 2.0 mL of ethanol, 2.8 g of N-(2-hydroxybenzyl)-p-bromoaniline (0.01 mole) was added. After heating on a water bath for 12 h under reflux, the reaction mixture was cooled in an ice bath and a crystalline substance was obtained. The product was recrystallized from ethanol yielding white leaflets; yield 40%, mp. 156.4°C.*

d) Reaction of Phenols with 3,4-Dihydro-3-alkyl-2H-1,3-benzoxazines (Method D)

An equimolar mixture of reagents dissolved in methanol was kept at room temperature for several days until precipitation of the products, which were purified by crystallization from acetone[17] or methanol[18] (8-99%). Woodgate *et al.* reported much lower yields of phenol **10** derivatives (10%) in comparison with phenol **12** derivatives (67-98%).[17] The results strongly depended on factors such as steric effects, the basicity of the benzoxazine nitrogen and the electron density of the active sites on both phenolic and benzoxazine substrate.[17,18] Dibenzylamines **2** were also obtained in a solventless system at 60°C[2] or at 155°C[45]. The crude products were purified by crystallization from chloroform or diethyl ether (80-90%) (*Scheme 17*).



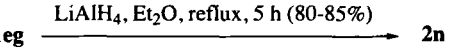
a) MeOH, rt, 9 h (8-98%) (**2da**, **2dc-e**,[17] **2a**, **2o**, **2x**, **2bq**[18]). *b*) no solvent, 60-155°C, 1 h (80-90%) (**2c**, **2d**, **2l**, **2ac**, **2bo**,[2] **2l**[45]).

Scheme 17

N,N-bis(2-Hydroxy-1-napthylmethyl)methylamine (2da). Typical Procedure.[18] *2-Naphthol (1.44 g, 0.01 mole) was added to a solution of 2,3-dihydro-2-methyl-1H-naphth[1,2-e][1,3]oxazine (2.00g, 0.01 mole) in 50 mL of methanol. After 9 h at 25°C, the solution was cooled overnight. The resulting solid (2.85 g) was pulverized, collected, and washed with methanol: mp. 145-146°C. An additional 0.55 g (mp. 145-145.5°C) was obtained from the filtrate. The total yield of product was 99%, mp. 145-146°C after recrystallization from acetone solution by the addition of 2-propanol.*

e) Reduction of 3,4-Dihydro-3-aryl-2H-1,3-benzoxazine (Method E)

Komissarova *et al.* obtained *N*-methyldibenzylamine **2n** in 81% yield by reduction of the benzoxazine **1eg** with lithium aluminium hydride in refluxing ether for 5 h (*Scheme 18*).[72,73] The method is quite effective but its application is limited to *N*-methyldibenzylamines.

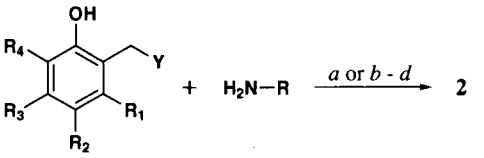


Scheme 18

Methyl-di(2-hydroxy-3,5-di-tert-butylbenzyl)amine (2n). Typical Procedure.[73] *An etheral solution of the corresponding benzoxazine (0.3 g) was added to the etheral solution of 0.11 g $LiAlH_4$. The resulting mixture was refluxed for 5 h. A 10% aqueous solution of NH_4Cl was added and the product was extracted with ether. After removal of the solvent the product was crystallized from acetone; 0.25 g, yield 83%, mp. 132-133°C.*

f) N-Alkylation of Primary Amines with Benzyl Halides or Benzyl Alcohol (Method F)

The method was first applied by Auwers *et al.* in 1906 for benzyl bromides;[74,75] however, neither reaction data nor yields were given. In subsequent years, benzyl chlorides rather than bromides were used. The reactions were carried out in the presence of hydrochloric acid in Me_2SO (47%)[76] or K_2CO_3 in DMF (50-59%).[58] Dibenzylamines **2** were isolated as by-products (0.5-5%) in the reaction of aromatic amines with 2-hydroxybenzylalcohols, giving 2-hydroxybenzylamines.[1,42] The synthesis was carried out in the presence of KOH under reflux of ethanol for 12-24 h (*Scheme 19*).[42] In this method, it is probable that mixtures of mono- and dibenzylamines are formed resulting in moderate yields. Furthermore, the number of accessible parent *o*-hydroxybenzylalcohol substrates is rather limited and they need to be synthesized.



a) Y = Cl, 1. DMF, K_2CO_3, rt, 24 h; 2. $NaBH_4$, MeOH, rt, 24 h; 3. HCl_{aq}, reflux, 4 h, (50-59%) (**2am**, **2ao**, **2av**, **2aw**).[58] *b*) Y = Cl, Me_2SO, HCl_{aq} (47%) (**2cb**).[76] *c*) Y = Br, no reaction details given (**2v**, **2ap**,[74] **2y**, **2cc**[75]). *d*) Y = OH, EtOH, KOH, reflux, 12-24 h (0.5-5%) (**2cd**, **2ch-j**).[42] R-R_4 = according to *Fig 1, Table 2*

Scheme 19

4,4'-Dimethyl-6,6'-dinitro-2,2'-(phenyliminodimethylene)diphenol (2cb). Typical Procedure.[76]
A solution of the corresponding benzyl chloride (0.244 g, 1.21 mmol) in Me_2SO (10 mL) was added to aniline (0.388 g, 3.62 mmol) in Me_2SO (10 mL). This mixture was dripped into dilute HCl (1 L), and the product was obtained as a yellow precipitate, yield 47%, mp. 187.3°C.

VII. SUMMARY

The properties and application, structure, stability and methods of preparation of benzoxazines **1** and dibenzylamines **2** have been presented. The compounds described have been tabulated according to their structures following Cahn, Ingold and Prelog system.[77] The tables contain structure, method of preparation, and some properties of substances **1** and **2** or their hydrochlorides. References will allow the reader to locate their published spectral properties. Benzoxazines **1** and dibenzylamines **2** contain a phenyl ring, tertiary amine nitrogen and oxygen atom in their structure. The specific arrangement of the functional groups implies the ability to create complexes with metal ions, which is the most important feature of dibenzylamines **2**. Benzoxazines **1** also bind metal ions but they are better known as valued monomers of polybenzoxazines resins with attractive and useful properties. Both benzoxazines **1** and dibenzylamines **2** are reactive compounds making them valuable intermediates in organic chemistry but this also causes difficulties in their preparation.

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REFERENCES

1. K. Bujnowski, A. Adamczyk and L. Synoradzki, *Org. Prep. Proced. Int.*, **38**, 153 (2007).

2. S. Phongtamrug, B. Pulpoka and S. Chirachanchai, *Supramol. Chem.*, **16**, 269 (2004).

3. C. P. R. Nair, *Prog. Polym. Sci.*, **29**, 401 (2004).

4. F. Kasapoglu, J. Cianga, Y. Yagci and T. Takeichi, *J. Polym. Sci. Pol. Chem.*, **41**, 3320 (2003).

5. K. Hemvichian, A. Laobuthee, S. Chirachanchai and H. Ishida, *Polym. Degrad. Stabil.*, **76**, 1 (2002).

6. T. Agag and T. Takeichi, *Macromolecules*, **36**, 6010 (2003).

7. I. Schnell, S. P. Brown, H. Y. Low, H. Ishida and H. W. Spiess, *J. Am. Chem. Soc.*, **120**, 11784 (1998).

8. P. Wei and D. A. Atwood, *Polyhedron*, **18**, 641 (1999).

9. X. Ning and H. Ishida, *J. Polym. Sci. Pol. Chem.*, **32**, 1121 (1994).

10. G. P. Moloney, *Magn. Reson. Chem.*, **28**, 824 (1990).

11. W. J. Burke, C. Weatherbee, H. Lau, G. Van Lear and G. Goken, *J. Am. Chem. Soc.*, **28**, 1098 (1963).

12. M. E. Kuehne and E. A. Konopka, *J. Med. Pharmaceut. Ch.*, **5**, 257 (1962).

13. W. J. Burke, E. L. M. Glennie and C. Weatherbee, *J. Am. Chem. Soc.*, **29**, 909 (1964).

14. G. P. Moloney, D. J. Craik and M. N. Iskander, *J. Pharm. Sci.*, **81**, 692 (1992).

15. J. L. Colin and B. Loubinoux, *Tetrahedron Lett.*, **23**, 4245 (1982).

16. M. K. Dewar, R. B. Johns, D. P. Kelly and J. F. Yates, *Australian J. Chem.*, **28**, 917 (1975).

17. P. D. Woodgate, G. M. Horner, N. P. Maynard and C. E. F. Rickard, *J. Organomet. Chem.*, **592**, 180 (1999).

18. W. J. Burke, J. L. Bishop, E. L. Mortensen Glennie and W. N. Bauer Jr., *J. Org. Chem.*, **30**, 3423 (1965).

19. R. E. Lyle and D. A. Walsh, *J. Organometal. Chem.*, **67**, 363 (1974).

20. S. Chirachanchai, A. Laobuthee, S. Phongtamburg, W. Siripatanasarakit and H. Ishida, *J. Appl. Polym. Sci.*, **77**, 2561 (2000).

21. W. J. Burke, *J. Am. Chem. Soc.*, **71**, 609 (1949).

22. W. J. Burke, K. C. Murdock and G. Ec, *J. Am. Chem. Soc.*, **20**, 1677 (1954).

23. W. J. Burke, M. J. Kobezen and C. W. Stephens, *J. Am. Chem. Soc.*, **74**, 3601 (1952).

24. D. D. Reynolds and B. C. Cossar, *DE Patent 2122767*, **1971**; *Chem. Abstr.*, **76**, 72532 (1972).

25. E. C. Horswill, D. A. Lindsay and K. U. Ingold, *Can. J. Chem.*, **48**, 579 (1970).

26. W. J. Burke and C. W. Stephens, *J. Am. Chem. Soc.*, **74**, 1518 (1952).

27. W. J. Burke, R. P. Smith and C. Weatherbee, *J. Am. Chem. Soc.*, **74**, 602 (1952).

28. D. Tzschoppe, J. Verbel, J. M. Schwob, M. Roche and G. Riess, *Bull. Soc. Chim. Belg.*, **95**, 45 (1986); *Chem. Abstr.*, **104**, 206456c (1986).

29. Ch. Proponet, B. Laude, M. Ramah and G. Riess, *Spectrochim. Acta A*, **38**, 323 (1982).

30. S. Brownstein, E. C. Horswill and K. U. Ingold, *Can. J. Chem.*, **49**, 1350 (1971).

31. S. Brownstein, E. C. Horswill and K. U. Ingold, *Can. J. Chem.*, **47**, 3243 (1969).

32. M. Tramontini, *Synthesis*, 703 (**1973**).

33. M. Tramontini and L. Angiolini, *Tetrahedron*, **46**, 1791 (1990).

34. A. Pedrazzoli and G. M. Cipelletti, *Boll. Chim. Farm.*, **105**, 503 (1966); *Chem. Abstr.*, **66**, 104967z (1967).

35. Y. Omura, Y. Taruno, Y. Irisa, M. Morimoto, H. Saimoto and Y. Shigemasa, *Tatrahedron Lett.*, **42**, 7273 (2001).

36. J. Dunkers and H. Ishida, *Spectrochim. Acta A*, **51**, 1061 (1995).

37. A. N. Grinev and S. A. Zotova, *Pharm. Chem. J.*, **8**, 588 (1974); *Chem. Abstr.* **82**, 72597r (1975).

38. H. Möhrle and K. Tröster, *Arch. Pharm.*, **315**, 619 (1982).

39. H. Ishida, Y. Rodriguez and D. A. Zimmerman, *US Patent 5543516*, **1996**; *Chem. Abstr.*, **124**, 203404m (1996).

40. D. L. Fields, J. B. Miller and D. D. Reynolds, *J. Org. Chem.*, **27**, 2749 (1962).

41. V. M. Kostyuchenko and G. A. Kiryukhina, *Zh. Org. Khim.*, **10**, 2243 (1985); *Chem. Abstr.*, **104**, 129847b (1986).

42. M. Noda, *J. Org. Chem.*, **24**, 1209 (1959).

43. C. Cimarelli, G. Palmieri and E. Volpini, *Tetrahedron*, **57**, 6089 (2001).

44. J. Dunkers, E. A. Zarate and H. Ishida, *J. Phys. Chem.*, **100**, 13514 (1996).

45. A. J. Dunkers and H. Ishida, *Spectrochim. Acta A*, **51**, 855 (1995).

46. H. Kim and H. Ishida, *Macromolecules*, **36**, 8320 (2003).

47. H. Kim and H. Ishida, *J. Phys. Chem.*, **106**, 3271 (2002).

48. A. Lehtonen and R. Sillanpää, *Polyhedron*, **24**, 257 (2005).

49. E. Y. Tshuva, M. Versano, I Goldberg, M. Kol, H. Weitman and Z. Goldschmidt, *Inorg. Chem. Commun.*, **2**, 371 (1999).

50. M. Kol, E. Y. Tshuva and Z. Goldschmidt, *Beyond Metallocenes. Next-Generation Polymerization Catalysts, ACS Symposium Series No. 187;* Chapter 5, *"Complexes of amine phenolate ligands as catalysts for polymerization of alpha-olefins"*, 1 (**2002**).

51. S. Groysman, E. Y. Tshuva, I. Goldberg, M. Kol, Z. Goldschmidt and M. Shuster, *Organometallics*, **23**, 5291 (2004).

52. E. Y. Tshuva, I. Goldberg and M. Kol, *J. Am. Chem. Soc.*, **122**, 10706 (2000).

53. E. Y. Tshuva, I. Goldberg, M. Kol and Z. Goldschmidt, *Inorg. Chem. Commun.*, **3**, 611 (2000).

54. E. Y. Tshuva, I. Goldberg, M. Kol and Z. Goldschmidt, *Inorg. Chem.*, **40**, 4263 (2001).

55. A. Laobuthee, H. Ishida and S. Chirachanchai, *J. Incl. Phenom. Macro.*, **47**, 179 (2003).

56. S. Chirachanchai and A. Laobuthee, *Chem. Lett.*, **6**, 614 (2002).

57. S. Chirachanchai, S. Phongtamrug and A. Laobuthee, *Chem. Lett.*, **32**, 432 (2003).

58. P. Chirakul, P. D. Hampton and Z. Bencze, *J. Org. Chem.*, **65**, 8297 (2000).

59. J. C. Bill, *US Patent 2802810*, **1957**; *Chem. Abstr.*, **51**, 18682a (1957).

60. H. Schelsinger and W. Mueller, *US Patent 3183093*, **1965**; *Chem. Abstr.*, **63**, 4440 (1965).

61. H. Schlesinger and W. Mueller, *DE Patent 1230669*, **1966**; *Chem. Abstr.*, **66**, 96227r (1967).

62. Kalle A.-G., *GB Patent 948965*, **1964**; *Chem. Abstr.*, **52**, *13454* (1964).

63. F. Toffler, M. M. Shatshat, S. Chiavarelli and E. Federici, *Farmaco, Ed. Sc.*, **29**, 541 (1974).

64. N. V. Timosheva, A. Chandrasekaran, R. O. Day and R. R. Holmes, *Inorg. Chem.*, **37**, 4945 (1998).

65. A. Laobuthee, S. Chirachanchai, H. Ishida and K. Tashiro, *J. Am. Chem. Soc.*, **123**, 9946 (2001).

66. G. R. Goward, D. Sebastiani, I. Schnell, H. W. Spiess, H.-D. Kim and H. Ishida, *J. Am. Chem. Soc.*, **125**, 5792 (2003).

67. H. A. Bruson, *J. Am. Chem. Soc.*, **58**, 1741 (1936).

68. H. Hara, R. Shirai, O. Hoshino and B. Umezawa, *Chem. Pharm. Bull.*, **33**, 3107 (1985).

69. D. Sparfel, J. Baranne-Lafont, N. K. Cuong, P. Capdevielle and M. Maumy, *Tetrahedron*, **46**, 803 (1990).

70. L. A. Kudryavtseva, Zh. V. Molodykh, I. S. Ryzhkina, R. A. Shagidullina, I. V. Timofeeva and V. E. Bel'skii, *Khim. Farm. Zh.*, **31**, 33 (1997); *Chem. Abstr.*, **128**, 252500f (1998).

71. W. J. Burke, B. A. Barton, P. D. Gardner and J. D. Lewis, *J. Am. Chem. Soc.*, **80**, 3438 (1958).

72. N. L. Komissarova, I. S. Belostotskaya, O. V. Shubina, V. V. Ershov and V. N. Voznesenskii, *Izv. AN SSSR Khim.*, **9**, 2186 (1988); *Chem. Abstr.*, **110**, 212723c (1989).

73. N. L. Komissarova, I. S. Belostotskaya, O. V. Shubina, E. A. Grishina and V. V. Ershov, *Zh. Org. Khim.*, **28**, 188 (1992); *Chem. Abstr.*, **117**, 170877t (1992).

74. K. Auwers and C. Kipke, *Justus Liebigs Ann. Chem.*, **344**, 194 (1906).

75. K. Auwers and O. Schröter, *Justus Liebigs Ann. Chem.*, **344**, 141 (1906).

76. G. Stein, H. Kämmerer and V. Böhmer, *J. Chem. Soc. Perkin Trans. 1*, 1285 (**1984**).

77. M. B. Smith and J. March, *"March's Advanced Organic Chemistry. Reactions, Mechanisms and Structure"*, p. 139, J. Wiley & Sons, New York, NY, 2001, 5th Edition.

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