Diazines. 13. Metalation without Ortho-Directing Group Functionalization of Diazines via Direct Metalation

Nelly Plé, Alain Turck, Karine Couture, and Guy Quéguiner*

Laboratoire de Chimie Organique Hétérocyclique de l'Institut de Recherche en Chimie Organique Fine, URA CNRS 1429, Institut National des Sciences Appliquées de Rouen, BP 08, 76131 Mont-Saint-Aignan Cedex, France

Received December 8, 1994[⊗]

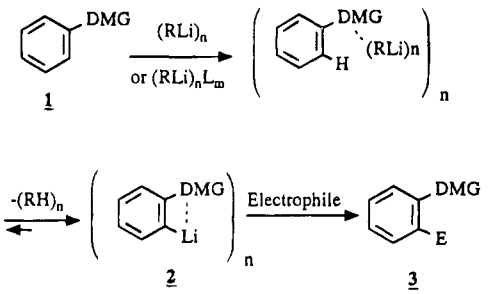
The successful metalation of diazines without an ortho-directing group is described. In some cases, dimers were obtained. The metalation was optimal with LTMP if a 4-fold excess of metalating agent was used, with a very short metalation reaction time at −75 °C. This procedure was applied to pyrimidine, 2-substituted pyrimidines, pyridazine, and pyrazine, allowing for the synthesis of various monosubstituted diazines.

Introduction

The regiospecific introduction of lithium onto aromatic rings generally requires the presence of substituents with heteroatoms. This transformation (known as "ortho-directed lithiation") has great synthetic potential. Since the time of the pioneering work of Gilman[1] and Wittig[2] and the systematic studies by Hauser and his students,[3] such reactions have been reviewed extensively.[4–16] Studies to date indicate that a variety of directing metalation groups (DMG) can be used to achieve metalation of π-deficient heteroaromatic systems, especially pyridines, quinolines, and, more recently, diazines (pyrazines, pyrimidines, and pyridazines),[17,18] and provide a basis for new and useful synthetic methodologies.

Few attempts to metalate π-deficient aromatics without DMG have been described in the literature. Brandsma[19] investigated the metalation of pyridine with the LICKOR base (*n*-BuLi/*t*-BuOK) at very low temperatures (−105 °C). Attempts with alkylamide bases (LDA/Et_2O, −78 °C) have been made with pyridine, quinoline, and isoquinoline.[20] Under these conditions, only dimeric products were observed and all attempts to trap the lithiated species with various electrophiles were unsuccessful. In contrast, it was shown that 5-methylpyrimidine gives the 6-lithiated species.[20] The lithiation of 4-*tert*-butylpyridine has also been achieved at room temperature with the in situ-generated base–electrophile combination of LTMP and TMSCl, leading to 2-silylated pyridines.[21]

Scheme 1



Moreover, in the literature, some surprising examples of metalation at positions other than those ortho to the DMG have been reported. Recently, the metalation of 4-chloropyrimidines with LTMP was found to not occur regioselectively at the position ortho to the chlorine atom (DMG), a high ratio of metalation being observed at C-6, ortho to the ring nitrogen.[17,22] Pyrazinecarboxamide underwent a para metalation with respect to the DMG,[23] and in the pyridine series, metalation meta to the DMG was described.[24]

These results prompted us to investigate metalation without DMG in the diazine series. We first assessed the different roles played by the DMG (Scheme 1), so as to anticipate the consequences of its absence.

During the metalation reaction, the assistance of the DMG can be described as follows: (1) The inductive electron-withdrawing effect of the DMG activates the

[⊗] Abstract published in *Advance ACS Abstracts*, June 1, 1995.

(1) Gilman, H.; Bebb, R. L. *J. Am. Chem. Soc.* **1939**, *61*, 109.
(2) Wittig, G.; Fuhrman, G. *Chem. Ber.* **1940**, *73*, 1197.
(3) (a) Puterbaugh, W. H.; Hauser, C. R. *J. Org. Chem.* **1964**, *29*, 853. (b) Slocum, D. W.; Sugarman, D. I. *Adv. Chem. Ser.* **1974**, *130*, 227.
(4) Gilman, H.; Morton, J. W. *Org. React.* **1954**, *8*, 258.
(5) Wakefield, B. J. *The Chemistry of Organolithium Compounds*; Pergamon: Oxford, 1974.
(6) Gschwend, H. W.; Rodriguez, H. R. *Org. React.* **1979**, *26*, 1.
(7) Snieckus, V. *Heterocycles* **1980**, *14*, 1649.
(8) Beak, P.; Snieckus, V. *Acc. Chem. Res.* **1982**, *15*, 306.
(9) Narasimhan, N. S.; Mali, R. S. *Synthesis* **1983**, 957.
(10) Marsais, F.; Queguiner, G. *Tetrahedron* **1983**, *39*, 2009.
(11) Brandsma, L.; Verkruijsse, H. *Preparative Polar Organometallic Chemistry 1*; Springer-Verlag: Berlin, 1986.
(12) Narasimhan, N. S.; Mali, R. S. *Top. Curr. Chem.* **1987**, *138*, 63.
(13) Tamao, K.; Kumada, M. In *The Chemistry of the Metal-Carbon bond. The use of Organometallic Compounds in Organic Synthesis*; Hartly, F. R., Ed.; Wiley: London, 1987.
(14) Snieckus, V. *Bull. Soc. Chim. Fr.* **1988**, 67.
(15) Snieckus, V. *Chem. Rev.* **1990**, *90*, 879.
(16) Quéguiner, G.; Marsais, F.; Snieckus, V.; Epsztajn, J. *Adv. Heterocycl. Chem.* **1991**, *52*, 187.
(17) Plé, N.; Turck, A.; Martin, P.; Barbey, S.; Quéguiner, G. *Tetrahedron Lett.* **1993**, *34*, 1605.
(18) (a) Turck, A.; Plé, N.; Quéguiner, G. *Heterocycles* **1994**, *37*, 2149 and references cited therein. (b) Turck, A.; Plé, N.; Mojovic, L.; Quéguiner, G. *Bull Soc. Chim. Fr.* **1993**, *130*, 488. (c) Turck, A.; Plé, N.; Tallon, V.; Quéguiner, G. *J. Heterocycl. Chem.* **1993**, *30*, 1491.
(19) (a) Verbeek, J.; George, A. V. E.; de Jong, R. L. P.; Brandsma, L. J. *J. Chem. Soc., Chem. Commun.* **1984**, 257. (b) Verbeek, J.; Brandsma, L. J. *J. Org. Chem.* **1984**, *49*, 3857.
(20) Clarke, A. J.; McNamara, S.; Meth-Cohn, O. *Tetrahedron Lett.* **1974**, 2373.
(21) (a) Krizan, T. D.; Martin, J. C. *J. Am. Chem. Soc.* **1983**, *105*, 6155. (b) Taylor, S. L.; Lee, D. Y.; Martin, J. C. *J. Org. Chem.* **1983**, *48*, 4158.
(22) Plé, N.; Turck, A.; Couture, K.; Quéguiner, G. *Tetrahedron* **1994**, *50*, 10299.
(23) Turck, A.; Plé, N.; Trohay, D.; Ndzi, B.; Quéguiner, G. *J. Heterocycl. Chem.* **1992**, *29*, 699.
(24) Radinov, R.; Chanev, C.; Haimova, H. *J. Org. Chem.* **1991**, *56*, 4793.

0022-3263/95/1960-3781$09.00/0

ortho hydrogens toward strong bases.[25,26] Coordination of heteroatom-containing DMG to the lithium atom leads to various effects: disaggregation of the metalating agent, which becomes more reactive;[25] coordination between the DMG and the lithium atom, which increases the electron-withdrawing effect of the DMG; and the proximity effect of the complexed base, which favors ortho deprotonation. (3) The ortho-lithiated **2** species is more or less coordinated and stabilized by the DMG. Complexation has been supported by various kinds of data (thermochemical,[27,28] steric,[29-31] and ab initio calculations[32-34]).

In the diazine series, where the electron deficiency of the nucleus increases the acidity of the hydrogens, this effect could balance the lack of a DMG. However, the electron-withdrawing effect of the sp^2 nitrogen atoms decreases the energy level of the LUMO of these compounds and makes them more sensitive to nucleophilic additions than other π-deficient heteroaromatics (pyridines and quinolines[35]). So the use of strong bases, such as alkyllithium, that are also good nucleophiles must be avoided, and less powerful bases, such as alkylamides (LDA or LTMP), must be used. These alkylamides, used as metalating agents, are in equilibrium between monomer and dimer in solution in THF,[36-40] so the role of the DMG in inducing the disaggregation of the metalating agent becomes much less important than it is with alkyllithium.

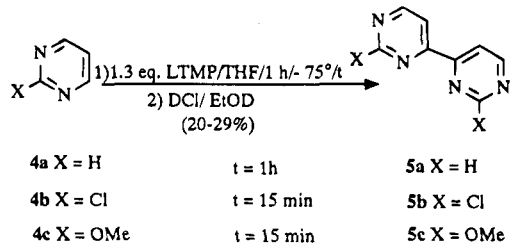
Nevertheless, it can be suspected during a metalation without a DMG that, since there is no possible coordination of the lithio derivative and the DMG, the lithio species might be less stable and more subject to side reactions.

The functionalization of diazines without a DMG presents a challenge and a potential method for accessing new diazines that are difficult to synthesize by classical routes, such as: (1) diazine ring construction by condensation reactions, (2) nucleophilic displacement of leaving groups, especially in the position ortho to the ring nitrogens, (3) halogen–metal exchange, and (4) metalation of diazines bearing a DMG.

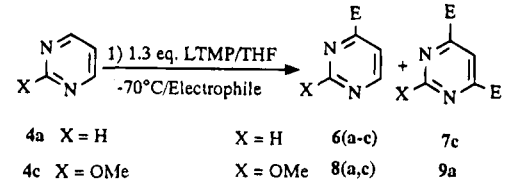
Halogen–metal exchange has been used to functionalize pyrimidine[41] and recently has been applied to syntheses of these heterocycles.[42] However, this method requires the prior introduction of a halogen atom.

Thus, the metalation sans DMG approach may lead to diazines such as those with carbon atoms ortho to the ring nitrogen which are difficult to obtain otherwise.

Scheme 2



Scheme 3



We report here on our systematic search for suitable conditions for the metalation of diazines without a DMG. Preliminary studies have been performed with the pyrimidine nucleus and extended to pyrazine and pyridazine.

Results

1. Metalation of Pyrimidine and 2-Substituted Pyrimidines. In order to metalate without a DMG, superbases were first tried. Attempts to metalate pyrimidine **4a** with the LICKOR superbase in THF at low temperatures (−75 to −100 °C) were unsuccessful. In all cases, tarry products were obtained without recovery of the starting material, and no aromatic compounds could be identified.

Attempts to metalate pyrimidine **4a** with LDA in THF for 1 h at room temperature followed by treatment with electrophiles were unsuccessful, only small amounts of starting material and dimer **5a** being identified. Reaction of pyrimidine **4a** with LTMP was performed in THF and ether for 1 h at −75 °C, trapping the lithiated species with DCl to afford the 6,6′-bipyrimidine **5a** as the sole product in about 20% yield, without recovery of the starting material (Scheme 2). The dimeric compound **5a** was also the sole product observed when **4a** was treated with LTMP for a shorter reaction time (5 min) with a large excess of metalating agent (4 equiv) and at various temperatures (−100 to −10 °C).

The reaction was also investigated with 2-substituted pyrimidines. With these compounds, the substituent at C-2 could not act as a DMG but could increase the acidity of the hydrogens and stabilize the lithio species by its electron-withdrawing effect. Treatment of 2-chloropyrimidine **4b** and 2-methoxypyrimidine **4c** with LTMP at −75 °C for 15 min, followed by reaction with DCl, led to dimeric compounds in 21–27% yield.

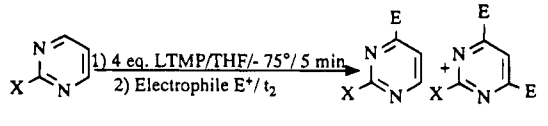
The compatibility of LTMP and some electrophiles allowed for the in situ quenching of lithiated species.[43,44] Compounds **4a,c** (Scheme 3, Table 1) resulting from a metalation were isolated. With 2-chloropyrimidine **4b** under these conditions, only traces of dimer, besides small amounts of 4- and 6-substituted compounds, were obtained, without recovery of the starting material. Treatment of **4c** and **4d** with an excess of LTMP at −75

(25) Bauer, W.; Schleyer, P. v. R. *J. Am. Chem. Soc.* **1989**, *111*, 7191.
(26) Krizan, T. D.; Martin, J. C. *J. Org. Chem.* **1982**, *47*, 2681.
(27) Roberts, J. D.; Curtin, D. Y. *J. Am. Chem. Soc.* **1946**, *68*, 1658.
(28) Klumpp, G. W.; Sinnige, M. J. *Tetrahedron Lett.* **1986**, *27*, 2247.
(29) Shirley, D. A.; Hendrix, J. P. *J. Organomet. Chem.* **1968**, *11*, 217.
(30) Shirley, D. A.; Harmon, T. E.; Cheng, C. F. *J. Organomet. Chem.* **1974**, *69*, 327.
(31) Slocum, D. W.; Koonsvitsky, B. P. *J. Org. Chem.* **1973**, *38*, 1675.
(32) Pross, A.; Radom, L. *Prog. Phys. Org. Chem.* **1981**, *13*, 1.
(33) Ellison, R. A.; Kotsonis, F. N. *J. Org. Chem.* **1973**, *38*, 4192.
(34) Graybill, B. M.; Shirley, D. A. *J. Org. Chem.* **1966**, *31*, 1221.
(35) Plé, N.; Turck, A.; Quéguiner, G.; Glassl, B.; Neunhoeffer, H. *Liebigs Ann. Chem.* **1993**, 583.
(36) Bauer, W.; Seebach, D. *Helv. Chim. Acta* **1984**, *67*, 1972.
(37) Renaud, P.; Fox, M. A. *J. Am. Chem. Soc.* **1988**, *110*, 5702.
(38) Kim, Y. J.; Bernstein, M. P.; Galiano-Roth, A. S.; Romesberg, F. E.; Williard, P. G.; Fullere, D. J.; Harrison, A. T.; Collum, D. B. *J. Org. Chem.* **1991**, *56*, 4435.
(39) Galiano-Roth, A. S.; Collum, D. B. *J. Am. Chem. Soc.* **1989**, *111*, 6772.
(40) Hall, P. L.; Gilchrist, J. H.; Harrison, A. T.; Fuller, D. J.; Collum, D. B. *J. Am. Chem. Soc.* **1991**, *113*, 9575.
(41) (a) Rajkumar, T. V.; Binkley, S. B. *J. Med. Chem.* **1963**, *6*, 555. (b) Gronowitz, S.; Röe, J. *Acta Chem. Scand.* **1965**, *19*, 1741.
(42) Sandoshman, J.; Undheim, K. *Tetrahedron* **1994**, *50*, 275.
(43) Taguchi, T.; Nishi, M.; Watanabe, K.; Mukaiyama, T. *Chem. Lett.* **1973**, 1307.
(44) Trécourt, F.; Mallet, M.; Marsais, F.; Quéguiner, G. *J. Org. Chem.* **1988**, *53*, 1367.

Table 1

X	electrophile	E	yield (%)
H	TMSCl	TMS	54 (**6a**)
	PhCHO	PhCH(OH)	16 (**6b**)
	Ph_2CO	$Ph_2C(OH)$	26 (**6c**), 11 (**7c**)
OMe	TMSCl	TMS	16 (**8a**), 49 (**9a**)
	Ph_2CO	$Ph_2C(OH)$	48 (**8c**)

Scheme 4



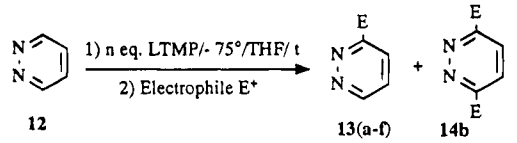
4c X = OMe X = OMe **8(b-g)** **9(a,h,j)**
4d X = p(OMe)Ph X = p(OMe)Ph **10(a-e)** **11e**

Table 2

X	electrophile	E	t_2 (min)	yield (%)
OMe	TMSCl	TMS	90	41 (**9a**)
	PhCHO	PHCH(OH)	60	29 (**8b**)
	CH_3CHO	$CH_3CH(OH)$	60	26 (**8d**)
	ArCH(OH)[a]	ArCH(OH)	120	28 (**8e**)
	DCl	D	10	56 (**8f**)
	HCOOEt	CHO	90	16 (**8g**)
	PhSSPh	SPh	70	25 (**9h**)
	I_2[b]	I	30	6 (**9i**)
	BrCN[c]	Br	10	–
p-(OMe)Ph	TMSCl	TMS	30	39 (**10a**)
	PhCHO	PhCH(OH)	70	13 (**10b**)
	CH_3CHO	$CH_3CH(OH)$	30	16 (**10c**)
	DCl	D	10	66 (**10d**)
	BrCN	Br	10	35 (**10e**), 27 (**11e**)

[a] Ar = 2,3,4-$(OMe)_3$Ph. [b] With I_2 as an electrophile, only the diiodo derivative and the triiodo derivative were obtained in low yields of 6 and 7%, respectively. [c] Only a tribromo derivative **9j** was obtained in 21% yield.

Scheme 5



12 **13(a-f)** **14b**

°C for a shorter reaction time of 5 min, followed by reaction with various electrophiles for a time t_2, led to 2,4- or 2,4,6-substituted pyrimidines due to a metalation (Scheme 4, Table 2). The same conditions applied to **4c**, followed by quenching with DCl as the electrophile, led in low yield (30%) to a mixture of mono- and dideuterated compounds, besides dimeric deuterated compounds, all identified by their NMR spectra.

The best experimental conditions found in the pyrimidine series were applied to metalate two other diazines: pyrazine and pyridazine.

2. Metalation of Pyridazine. The lithiation of pyridazine **12** was performed under the experimental conditions of the in situ trapping method (t = 0 min) and by treatment with an excess of LTMP for a short reaction time (t = 6 min), followed by reaction with electrophiles (Scheme 5, Table 3). In these cases, mono- and disubstituted pyridazines were obtained and identified by their ^{1}H NMR spectra.

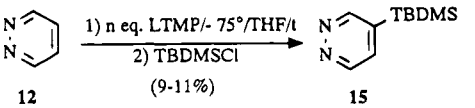
Surprisingly, when the *tert*-butyldimethylsilyl chloride was used as an electrophile with either t = 0 or 6 min, the 4-substituted pyridazine **15** was obtained as the sole product in low yield (Scheme 6). We cannot explain this unexpected regioselectivity.

3. Metalation of Pyrazine. With the previous conditions, 2-substituted pyrazines were obtained; however, with benzaldehyde as the electrophile, a small amount of 2,5-disubstituted pyrazine **18a** was obtained besides the major monosubstituted compound **17a** (Scheme 7, Table 4).

Table 3

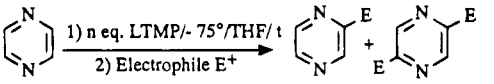
t (min)	n	electrophile	E	yield (%)
0	1.3	PhCHO	PhCH(OH)	33 (**13a**)
		Ph_2CO	$Ph_2C(OH)$	47 (**13b**), 6 (**14b**)
		PhSSPh	PhS	7 (**13c**)
6	4.0	PhCHO	PhCH(OH)	31 (**13a**)
		DCl	D	32 (**13d**)
		CH_3CHO	$CH_3CH(OH)$	26 (**13e**)
		I_2	I	16 (**13f**)

Scheme 6



12 **15**

Scheme 7



16 **17(a-d)** **18a**

Table 4

t (min)	n	electrophile	E	yield (%)
0	1.3	PhCHO	PhCH(OH)	10 (**17a**), 2 (**18a**)
		Ph_2CO	$Ph_2C(OH)$	30 (**17b**)
6	4.0	PhCHO (1 equiv)	PhCH(OH)	39 (**17a**)
		PhCHO (3 equiv)	PhCH(OH)	64 (**17a**), 16 (**18a**)
		CH_3CHO (10 equiv)	$CH_3CH(OH)$	65 (**17c**)
		I_2 (1 equiv)	I	44 (**17d**)

Discussion

When pyrimidines were submitted to lithiation with LTMP in THF at −75 °C for a reaction time longer than 15 min before reaction with various electrophiles, only dimeric products were observed in low yields and no starting material was recovered. Such dimeric compounds have been observed during reaction of LDA with pyridine, quinoline, or isoquinoline[20] or during reaction of 1-lithiodithiane with 1,8-naphthyridine.[45] Dimer formation was first rationalized as resulting from the occurrence of the lithiated intermediate's addition to the starting material. Besides the carbanionic mechanism, some authors proposed that the heteroaromatic coupling reaction could result from a radical−anion intermediate leaving the solvent cage, initiated by one-electron transfer from LDA.[10,46]

To check these hypotheses, the metalation of 2-chloropyrimidine **4b** was performed in the presence of $CuCl_2$,[49] which is known to prevent radical reactions.[50] Under these experimental conditions, dimer **5b** was obtained in yield similar to that shown in Scheme 2.

To prevent this competitive coupling, and in order to increase the rate of metalation, we used an excess of

(45) Wiessenfels, M.; Ulrici, B. *Z. Chem.* **1978**, *18*, 382.
(46) Newkome, G. R.; Hager, D. C. J. *J. Org. Chem.* **1982**, *47*, 601.
(47) Delaby, R.; Reynaud, P. *Bull. Soc. Chim. Fr.* **1957**, 714.
(48) Kocevar, M.; Mlacar, B.; Perdih, M.; Petric, A.; Slovenko, P.; Vercek, B. *Tetrahedron Lett.* **1992**, *33*, 2195.
(49) Metalation of **4b** with 1.3 equiv of LTMP at −75 °C for 15 min in the presence of 12% $CuCl_2$ gave as products 20% of **5b** and 9% of starting material.
(50) (a) Hoz, S.; Bunnett, J. F. *J. Am. Chem. Soc.* **1977**, *99*, 4690. (b) Zhao, W.; Liu, Y.; Huang, Z. *Synth. Commun.* **1993**, *23*, 591.

metalating agent. Unfortunately, when pyrimidine was reacted with 4 equiv of LTMP at −75 °C for 1 h, followed by reaction with DCl, only tarry products and dimers were obtained without starting material. Besides the conditions with excess metalating agent, a severe shortening of the metalation reaction time was employed in order to limit the fast degradation of the lithiated species.

In summary, the problems of competitive addition and instability of lithiated species were overcome by the in situ trapping technique when LTMP and electrophiles were compatible and were overcome even better by the use of an excess of metalating agent and shorter reaction times.

Conclusion

Due to the greater instability of the lithio intermediates obtained with pyrimidine, the metalation can be accomplished with the in situ trapping technique. The functionalization of the parent pyridazine and pyrazine or (*p*-methoxyphenyl)pyrimidine can be achieved with an excess of LTMP and very short reaction times, and this allowed for the synthesis of various monosubstituted diazines.

Experimental Section

General. Melting points are uncorrected. The ^{1}H NMR spectra were recorded in $CDCl_3$ with TMSCl as internal standard or in deuterated DMSO with hexamethyldisiloxane as internal standard. The IR spectra were obtained as potassium bromide pellets and are given in cm^{-1}.

Solvent. THF was distilled from benzophenone sodium and used immediately. Water content of the solvent was estimated by the modified Karl−Fischer method (THF less than 50 ppm of water).

Starting Materials. Commercial pyrimidine, 2-chloropyrimidine, pyridazine, pyrazine, 2,2,6,6-tetramethylpiperidine, and diisopropylamine were distilled from CaH_2 and stored over a dry argon atmosphere. 2-Methoxypyrimidine was prepared by methoxylation of the commercial 2-chloropyrimidine (MeONa/MeOH, 60 °C, 20 h, 78%).

A 1.6 M commercial solution of *n*-butyllithium in hexane was stored under a desoxygenated argon atmosphere. LDA was prepared by reaction of diisopropylamine (0.49 mL, 3.5 mmol) in THF (20 mL) and *n*-butyllithium (2.2 mL, 1.6 M, 3.5 mmol) at −75 °C for 15 min. LTMP was prepared by reaction of 2,2,6,6-tetramethylpiperidine (0.55 mL, 3.24 mmol) in THF (20 mL) and *n*-butyllithium (2.02 mL, 1.6 M, 3.24 mmol) at −30 °C and then at 0 °C for 30 min.

General Procedure A: Synthesis of Dimers. Pyrimidine (**4a**), 2-chloropyrimidine (**4b**), or 2-methoxypyrimidine (**4c**) (2.7 mmol) in THF solution (5 mL) was slowly added to a cold (−75 °C) solution of LTMP in dry THF (30 mL) as given in the product description. The resulting mixture was stirred for 1 h at −75 °C, then hydrolyzed at the same temperature by an excess of HCl/EtOH/THF, warmed to rt, treated with 10 mL of a saturated aqueous solution of $NaHCO_3$, and extrated with CH_2Cl_2.

General Procedure B: Synthesis of Substituted Diazines by the in Situ Trapping Technique. A solution of diazine derivative (2.7 mmol) in THF (5 mL) and a solution of the required electrophile (3.5 mmol) in THF (5 mL) were added simultaneously to a cold (−75 °C) solution of LTMP (3.2 mmol) in dry THF (30 mL). The mixture was stirred for 2 h at −75 °C before hydrolysis by an excess of HCl/EtOH/THF. The solution was warmed to rt, treated with 10 mL of a saturated aqueous solution of $NaHCO_3$, and extracted with CH_2Cl_2.

General Procedure C: Synthesis of Substituted Diazines by Metalation. A solution of diazine derivative (1.56 mmol) in THF (5 mL) was slowly added to a cold (−75 °C) solution of LTMP in dry THF (30 mL) as given in the product description. The mixture was stirred for 6 min at −75 °C before addition of the required electrophile. Stirring was continued for a time *t* as mentioned in the product description at −75 °C before hydrolysis (−75 °C) by an excess of HCl/EtOH/THF. The solution was gently warmed to rt, treated with 5 mL of a saturated solution of $NaHCO_3$, and extracted with CH_2Cl_2.

2-(4-Methoxyphenyl)pyrimidine (4d). Compound **4d** was prepared from 2-(4-methoxyphenyl)pyrimidine 1-oxide obtained according to ref 48 with (4-methoxyphenyl)amidoxime[47] as starting material. A mixture of 0.314 g (1.55 mmol) of 2-(4-methoxyphenyl)pyrimidine 1-oxide, 6 mL of AcOEt, and 0.81 mL (9.5 mmol) of PCl_3 was warmed under reflux for 1 h. The solution was cooled and treated with an aqueous solution of $NaHCO_3$ and extracted with AcOEt to quantitatively give **4d**: mp 76 °C; ^{1}H NMR ($CDCl_3$) δ 3.80 (s, 3H), 6.88 (d, J' = 9 Hz, 2 H), 6.93 (t, J = 4.6 Hz, 1H), 8.35 (d, J' = 9 Hz, 2H), 8.60 (d, J = 4.6 Hz, 2H); IR (KBr) 2985, 2843, 1605, 1579, 1505. Anal. Calcd for $C_{11}H_{10}N_2O$ (186): C, 70.97; H, 5.38; N, 15.05. Found: C, 70.82; H, 5.41; N, 15.26.

4,4′-Bipyrimidine (5a). The general procedure A applied to **4a** with LTMP (3.2 mmol) gave **5a** in 29% yield (eluent, $AcOEt/CH_2Cl_2$ (6/4)): mp 196 °C dec; ^{1}H NMR ($CDCl_3$) δ 8.42 (dd, J = 1.2, 5.2 Hz, 2H), 8.96 (d, J = 5.2 Hz, 2H), 9.35 (d, J = 1.2 Hz, 2H); IR (KBr) 3066, 1569, 1540, 1461. Anal. Calcd for $C_8H_6N_4$ (158.2): C, 60.76; H, 3.80; N, 35.44. Found: C, 60.80; H, 3.99; N, 35.29.

2-Chloro-4-(2-chloro-4-pyrimidyl)pyrimidine (5b). The general process A applied to **4b** with LTMP (3.2 mmol) gave **5b** in 27% yield (eluent, CH_2Cl_2/AcOEt (9/1)): mp 176 °C dec; ^{1}H NMR ($CDCl_3$) δ 8.37 (d, J = 5 Hz, 2H), 8.88 (d, J = 5 Hz, 2H); IR (KBr) 3060, 1554, 1514, 1403. Anal. Calcd for $C_8H_4Cl_2N_4$ (227): C, 42.29; H, 1.76; N, 24.67. Found: C, 42.24; H, 1.48; N, 24.69.

2-Methoxy-4-(2-methoxy-4-pyrimidyl)pyrimidine (5c). The general process A applied to **4c** with LTMP (5.9 mmol) gave **5c** in 21% yield (eluent, CH_2Cl_2/AcOEt (9/1)): mp 138 °C; ^{1}H NMR ($CDCl_3$) δ 3.9 (s, 6H), 7.89 (d, J = 5 Hz, 2H), 8.89 (d, J = 5 Hz, 2H); IR (KBr) 2996, 2952, 1576, 1468. Anal. Calcd for $C_{10}H_{10}N_4O_2$ (218.2): C, 55.05; H, 4.59; N, 25.69. Found: C, 55.21; H, 4.84; N, 25.86.

4-(Trimethylsilyl)pyrimidine (6a). The general procedure B applied to **4a** using TMSCl gave **6a** in 54% yield (eluent, CH_2Cl_2/EtOAc (5/5)): oil; ^{1}H NMR ($CDCl_3$) δ 0.28 (s, 9H), 7.43 (dd, J = 4.4, 1.8 Hz, 1H), 8.56 (d, J = 4.4 Hz, 1H), 9.24 (sd, J = 1.8 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ −2.6, 126.14, 154.62, 157.99, 177.89; IR (KBr) 2980, 1610, 1576, 1513, 1423. Calcd for $C_7H_{12}N_2Si$ (152): C, 55.23; H, 7.89; N, 18.41. Found: C, 55.12; H, 8.02; N, 18.47.

4-Pyrimidylphenylmethanol (6b). The general procedure B applied to **4a** using benzaldehyde gave **6b** in 16% yield (eluent, EtOAc/hexane (6/4)): mp 94 °C; ^{1}H NMR ($CDCl_3$) δ 5.20 (m, 1H), 5.69 (s, 1H), 7.24−7.36 (m, 6H), 8.54 (d, J = 5.3 Hz, 1H), 9.02 (s, 1H); IR (KBr) 3315, 3060, 1668, 1581, 1550, 1452. Anal. Calcd for $C_{11}H_{10}N_2O$ (186.2): C, 70.93; H, 5.37; N, 15.05. Found: C, 71.10; H, 5.17; N, 15.07.

4-Pyrimidyldiphenylmethanol (6c). The general procedure B applied to **4a** using benzophenone gave **6c** in 26% yield (eluent, EtOAc/cyclohexane (5/5)): mp 192 °C; ^{1}H NMR ($CDCl_3$) δ 5.56 (m, 1H), 7.20 (dd, J = 5.3, 1.3 Hz, 1H), 7.26−7.39 (m, 10H), 8.69 (d, J = 5.3 Hz, 1H), 9.23 (sd, J = 1.3 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 116.11, 127.84, 128.17, 144.51, 156.96, 157.79, 171.9; IR (KBr) 3186, 1583, 1542, 1490, 1466, 1444. Anal. Calcd for $C_{17}H_{14}N_2O$ (262.3): C, 77.83; H, 5.34; N, 10.68. Found: C, 77.53; H, 5.41; N, 10.90.

α,α,α′,α′-Tetraphenyl-4,6-pyrimidinedimethanol (7c). The general procedure B applied to **4a** using benzophenone gave **7c** in 11% yield (eluent, EtOAc/cyclohexane (5/5)): ^{1}H NMR ($CDCl_3$) δ 5.48 (s, 2H), 7.10 (d, J = 1.3 Hz, 1H), 7.20−7.30 (m, 20H), 9.18 (d, J = 1.3 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 116.62, 127.7, 128.1, 144.17, 156.39, 172.17; IR (KBr) 3552, 3059, 1578, 1535, 1490. Anal. Calcd for $C_{30}H_{24}N_2O_2$ (444.5): C, 81.06; H, 5.40; N, 6.30. Found: C, 80.92; H, 5.48; N, 6.52.

2-Methoxy-4-(trimethylsilyl)pyrimidine (8a). The general procedure B applied to **4c** using TMSCl (5.94 mmol) gave **8a** in 16% yield (eluent, CH_2Cl_2/EtOAc (88/12)): oil; ^{1}H NMR ($CDCl_3$) δ 0.29 (s, 9H), 4.00 (s, 3H), 7.08 (d, J = 5 Hz, 1H),

8.40 (d, J = 5 Hz, 1H); IR (KBr) 2955, 1572, 1551, 1464, 1374. Anal. Calcd for $C_8H_{14}N_2OSi$ (182.1): C, 52.72; H, 7.69; N, 15.38. Found: C, 52.99; H, 7.80; N, 15.00.

(2-Methoxy-4-pyrimidinyl)phenylmethanol (8b). The general procedure C applied to **4c** using LTMP (6.25 mmol) and benzaldehyde (6.25 mmol) during t = 1 h gave **8b** in 29% yield (eluent, CH_2Cl_2/EtOAc, (8/2)): oil; ^1H NMR ($CDCl_3$) δ 4.00 (s, 3H), 4.70 (s, 1H), 5.62 (s, 1H), 6.87 (d, J = 5 Hz, 1H), 7.35 (m, 5H), 8.30 (d, J = 5 Hz, 1H); IR (KBr) 3322, 3062, 2956, 2871, 1671, 1565, 1468. Anal. Calcd for $C_{12}H_{12}N_2O_2$ (216.2): C, 66.66; H, 5.55; N, 12.96. Found: C, 66.82; H, 5.72; N, 13.02.

(2-Methoxy-4-pyrimidinyl)diphenylmethanol (8c). The general procedure B applied to **4c** using benzophenone (5.94 mmol) gave **8c** in 48% yield (eluent, CH_2Cl_2/EtOAc (88/12)): ^1H NMR ($CDCl_3$) δ 4.00 (s, 3H), 5.42 (s, 1H), 6.77 (d, J = 5 Hz, 1H), 7.20 (m, 10H), 8.40 (d, J = 5 Hz, 1H); IR (KBr) 3216, 1579, 1466, 1374. Anal. Calcd for $C_{18}H_{16}N_2O_2$ (292.3): C, 73.97; H, 5.48; N, 9.59. Found: C, 73.96; H, 5.81; N, 9.30.

1-(2-Methoxy-4-pyrimidinyl)ethanol (8d). The general procedure C applied to **4c** using LTMP (6.25 mmol) and acetaldehyde (16 mmol) during t = 1 h gave **8d** in 26% yield (eluent, CH_2Cl_2/EtOAc (5/5)): oil; ^1H NMR ($CDCl_3$) δ 1.52 (s, 3H), 3.78 (m, 1H), 4.02 (s, 3H), 4.83 (m, 1H), 7.00 (d, J = 5 Hz, 1H), 8.42 (d, J = 5 Hz, 1H); IR (KBr) 3390, 2973, 2933, 1713, 1586, 1566. Anal. Calcd for $C_7H_{10}N_2O_2$ (154.2): C, 54.55; H, 6.49; N, 18.18. Found: C, 54.68; H, 6.66; N, 17.84.

(2-Methoxy-4-pyrimidinyl)(3,4,5-trimethoxyphenyl)methanol (8e). The general procedure C applied to **4c** using LTMP (6.25 mmol) and 2,3,4-trimethoxybenzaldehyde (6.25 mmol) during t = 2 h gave **8e** in 28% yield (eluent, CH_2Cl_2/EtOAc, (8/2)): oil; ^1H NMR ($CDCl_3$) δ 3.70–4.00 (m, 12H), 4.78 (m, 1H), 5.83 (s, 1H), 6.62–7.08 (m, 3H), 8.38 (d, J = 5 Hz, 1H); IR (KBr) 3378, 2941, 1584, 1495, 1467. Anal. Calcd for $C_{15}H_{18}N_2O_5$ (306.3): C, 58.82; H, 5.88; N, 9.15. Found: C, 59.02; H, 6.08; N, 8.93.

4-Deuterio-2-methoxypyrimidine (8f). The general procedure C applied to **4c** using LTMP (6.25 mmol) and DCl/EtOD (1/1) (6.25 mmol) during t = 10 min gave **8f** in 56% yield (eluent, CH_2Cl_2/EtOAc (84/16)): mp 144 °C; ^1H NMR ($CDCl_3$) δ 3.89 (s, 3H), 6.84 (d, J = 4.7 Hz, 1H), 8.41 (d, J = 4.7 Hz, 1H); IR (KBr) 2980, 2851, 1576, 1550, 1496. Anal. Calcd for $C_5H_5DN_2O$ (110.1): C, 54.55; H, 4.55; N, 25.45. Found: C, 54.61; H, 4.49; N, 25.22.

4-Formyl-2-methoxypyrimidine (8g). The general procedure C applied to **4c** using LTMP (6.25 mmol) and ethyl formiate (10 mmol) during t = 90 min gave **8g** in 16% yield (eluent, CH_2Cl_2/EtOAc (9/1)): mp 116 °C; ^1H NMR ($CDCl_3$) δ 4.03 (s, 3H), 7.37 (d, J = 5 Hz, 1H), 8.68 (d, J = 5 Hz, 1H), 9.87 (s, 1H); IR (KBr) 3348, 3097, 2960, 1709, 1570, 1473. Anal. Calcd for $C_6H_6N_2O_2$ (138.1): C, 52.17; H, 4.35; N, 20.29. Found: C, 52.32; H, 4.53; N, 20.57.

2-Methoxy-4,6-bis(trimethylsilyl)pyrimidine (9a). The general procedure B applied to **4c** using TMSCl (5.94 mmol) gave **9a** in 49% yield (eluent, CH_2Cl_2/EtOAc (88/12)): oil. The general procedure C applied to **4c** using LTMP (6.25 mmol) and TMSCl (6.25 mmol) during t = 90 min gave **9a** in 41% yield (eluent, CH_2Cl_2/EtOAc (88/12)): oil; ^1H NMR ($CDCl_3$) δ 0.23 (s, 18H), 4.00 (s, 3H), 7.18 (s, 1H); IR (KBr) 2955, 2899, 1564, 1522, 1463. Anal. Calcd for $C_{11}H_{22}N_2OSi_2$ (254): C, 51.97; H, 8.66; N, 11.02. Found: C, 52.06; H, 8.84; N, 10.77.

2-Methoxy-4,6-bis(phenylthio)pyrimidine (9h). The general procedure C applied to **4c** using LTMP (6.25 mmol) and diphenyldisulphide (6.25 mmol) during t = 70 min gave **9h** in 25% yield (eluent, CH_2Cl_2/EtOAc (5/5)): mp 98 °C; ^1H NMR ($CDCl_3$) δ 3.82 (s, 3H), 7.32 (m, 11H); IR (KBr) 2976, 1520, 1458. Anal. Calcd for $C_{17}H_{14}N_2OS_2$ (326): C, 62.58; H, 4.29; N, 8.59. Found: C, 62.69; H, 4.40; N, 8.37.

4,5,6-Tribromo-2-methoxypyrimidine (9j). The general procedure C applied to **4c** using LTMP (6.25 mmol) and BrCN (6.25 mmol) during t = 10 min gave **9j** in 21% yield (eluent, CH_2Cl_2): mp 130 °C; ^1H NMR ($CDCl_3$) δ 4.05 (s, 3H); IR (KBr) 1539, 1485, 1465, 1360. Anal. Calcd for $C_5H_3Br_3N_2O$ (346.7): C, 17.31; H, 0.87; N, 8.08. Found: C, 17.77; H, 0.70; N, 7.79.

2-(4-Methoxyphenyl)-4-(trimethylsilyl)pyrimidine (10a). The general procedure C applied to **4d** using LTMP (6.25 mmol) and TMSCl (6.25 mmol) during t = 30 min gave **10a** in 39% yield (eluent, cyclohexane/CH_2Cl_2 (7/3)): oil; ^1H NMR ($CDCl_3$) δ 0.45 (s, 9H), 3.92 (s, 3H), 6.98 (d, J = 9 Hz, 2H), 7.25 (d, J = 4 Hz, 1H), 8.47 (d, J = 9 Hz, 2H), 8.63 (d, J = 4 Hz, 1H); IR (KBr) 2957, 2836, 1607, 1553, 1513, 1407. Anal. Calcd for $C_{14}H_{18}N_2OSi$ (258.1): C, 65.12; H, 6.98; N, 10.85. Found: C, 65.31; H, 7.12; N, 10.62.

(2-(4-Methoxyphenyl)-5-pyrimidinyl)phenylmethanol (10b). The general procedure C applied to **4d** using LTMP (6.25 mmol) and benzaldehyde (6.25 mmol) during t = 70 min gave **10b** in 13% yield (eluent, CH_2Cl_2/EtOAc (96/4)): mp 130 °C; ^1H NMR ($CDCl_3$) δ 3.85 (s, 3H), 5.05 (d, J = 4 Hz, 1H), 5.67 (d, J = 4 Hz, 1H), 6.88 (d, J = 5 Hz, 1H), 6.93 (d, J = 9 Hz, 2H), 7.30 (s, 5H), 8.38 (d, J = 9 Hz, 2H), 8.53 (d, J = 5 Hz, 1H); IR (KBr) 3188, 2960, 1607, 1585, 1552, 1420. Anal. Calcd for $C_{18}H_{16}N_2O_2$ (292.3): C, 73.97; H, 5.48; N, 9.59. Found: C, 74.22; H, 5.36; N, 9.38.

(2-(4-Methoxyphenyl)-5-pyrimidinyl)ethanol (10c). The general procedure C applied to **4d** using LTMP (6.25 mmol) and acetaldehyde (16 mmol) during t = 30 min gave **10c** in 16% yield (eluent, CH_2Cl_2/EtOAc (9/1)): oil; ^1H NMR ($CDCl_3$) δ 1.55 (d, J = 7.2 Hz, 3H), 3.87 (s, 3H), 4.90 (m, 1H), 6.15 (m, 1H), 6.92 (d, J = 9 Hz, 2H), 7.15 (d, J = 5 Hz, 1H), 8.33 (d, J = 9 Hz, 2H), 8.63 (d, J = 5 Hz, 1H); IR (KBr) 3394, 2972, 2932, 1607, 1555. Anal. Calcd for $C_{13}H_{14}N_2O_2$ (230.3): C, 67.83; H, 6.09; N, 12.17. Found: C, 67.86; H, 6.02; N, 12.48.

4-Deuterio-2-(4-methoxyphenyl)pyrimidine (10d). The general procedure C applied to **4d** using LPMT (6.25 mmol) and DCl/EtOD (1/1) (6.25 mmol) during t = 10 min gave **10d** in 66% yield (eluent, cyclohexane/EtOAc (6/4)): mp 65 °C; ^1H NMR ($CDCl_3$) δ 3.84 (s, 3H), 6.98 (d, J = 8.9 Hz, 2H), 7.06 (d, J = 4.9 Hz, 1H), 8.40 (d, J = 8.9 Hz, 2H), 8.71 (d, J = 4.9 Hz, 1H); IR (KBr) 3000, 2984, 2838, 1605, 1581, 1554, 1510. Anal. Calcd for $C_{11}H_9DN_2O$ (186.2): C, 70.97; H, 4.84; N, 15.05. Found: C, 70.89; H, 5.01; N, 15.06.

4-Bromo-2-(4-methoxyphenyl)pyrimidine (10e) and 4,6-Dibromo-2-(4-methoxyphenyl)pyrimidine (11e). The general procedure C applied to **4d** using LTMP (6.25 mmol) and BrCN (6.25 mmol) during t = 10 min gave **10e** in 35% yield and **11e** in 27% yield (eluent, cyclohexane/EtOAc (8/2)). **10e**: ^1H NMR ($CDCl_3$, 200 MHz) δ 3.86 (s, 3H), 6.98 (d, J = 4 Hz, 1H), 6.99 (d, J = 9 Hz, 2H), 8.42 (d, J = 9 Hz, 2H), 8.69 (d, J = 4 Hz, 1H). **11e**: ^1H NMR ($CDCl_3$, 200 MHz) δ 3.86 (s, 3H), 6.94 (s, 1H), 6.99 (d, J = 9 Hz, 2H), 8.42 (d, J = 9 Hz, 2H).

3-Pyridazinylphenylmethanol (13a). The general procedure B applied to **12** using benzaldehyde (3.24 mmol) gave **13a** in 33% yield (eluent, EtOAc/cyclohexane (9/1)). The general procedure C applied to **12** using LTMP (6.25 mmol) and benzaldehyde (1.56 mmol) during t = 90 min gave **13a** in 31% yield (eluent, EtOAc): mp 148 °C; ^1H NMR ($CDCl_3$) δ 4.75 (m, 1H), 6.03 (s, 1H), 7.33 (m, 7H), 9.00 (dd, J = 5.00, 2.00 Hz, 1H); IR (KBr) 3134, 2854, 1578, 1452. Anal. Calcd for $C_{11}H_{10}N_2O$ (186.2): C, 70.93; H, 5.37; N, 15.05. Found: C, 70.81; H, 5.38; N, 15.23.

Diphenyl-3-pyridazinylmethanol (13b). The general procedure B applied to **12** using benzophenone (3.24 mmol) gave **13b** in 47% yield (eluent, EtOAc/cyclohexane (6/4)): mp 156 °C; ^1H NMR ($CDCl_3$) δ 6.10 (s, 1H), 7.35 (m, 12H), 9.05 (m, 1H); IR (KBr) 3125, 2775, 1718, 1491, 1447, 1426. Anal. Calcd for $C_{17}H_{14}N_2O$ (262.3): C, 77.83; H, 5.34; N, 10.68. Found: C, 77.92; H, 5.31; N, 10.67.

3-(Phenylthio)pyridazine (13c). The general procedure B applied to **12** using diphenyl disulfide (3.24 mmol) gave **13c** in 7% yield (eluent, CH_2Cl_2/EtOAc (7/3)): oil; ^1H NMR ($CDCl_3$) δ 7.00–7.40 (m, 2H), 7.48 (m, 5H), 8.85 (dd, 1H); IR (KBr) 3016, 2889, 1564, 1487, 1456. Anal. Calcd for $C_{10}H_8N_2S$ (188): C, 63.83; H, 4.25; N, 14.89. Found: C, 63.52; H, 4.53; N, 15.02.

3-Deuteriopyridazine (13d). The general procedure C applied to **12** using LTMP (6.25 mmol) and DCl/EtOD (1/1) (6.25 mmol) during t = 10 min gave **13d** in 32% yield (eluent, EtOAc/cyclohexane (5/5)): mp 62 °C; ^1H NMR ($CDCl_3$) δ 7.60 (m, 2H), 9.25 (m, 1H); IR (KBr) 2978, 1575, 1552, 1504, 1423. Anal. Calcd for $C_4H_3DN_2$ (80.1): C, 60.00; H, 3.75; N, 35.00. Found: C, 60.15; H, 3.78; N, 34.78.

3-Pyridazinylethanol (13e). The general procedure C (x = 6.25 mmol) applied to **12** using LTMP (6.25 mmol) and

acetaldehyde (y = 16 mmol) during t = 60 min gave **13e** in 26% yield (eluent, EtOAc/ethanol (9/1)): oil; ^{1}H NMR ($CDCl_3$) δ 1.58 (d, J = 7 Hz, 3H), 4.62 (m, 1H), 5.10 (quint, J = 7 Hz, 1H), 7.30–7.83 (m, 2H), 9.00 (dd, J = 5.00, 2.00 Hz, 1H); IR (KBr) 3145, 2913, 2860, 1467, 1112. Anal. Calcd for $C_6H_8N_2O$ (124.1): C, 58.06; H, 6.45; N, 22.58. Found: C, 57.89; H, 6.27; N, 22.93.

3-Iodopyridazine (13f). The general procedure C applied to **12** using LTMP (6.25 mmol) and iodine (1.56 mmol) during t = 40 min gave **13f** in 16% yield (eluent, AcOEt/CH_2Cl_2 (6/4)): mp 152 °C dec; ^{1}H NMR ($CDCl_3$) δ 7.17 (dd, J = 9.00, 5.00 Hz, 1H), 7.88 (dd, J = 9.00, 2.00 Hz, 1H), 9.12 (dd, J = 5.00, 2.00 Hz, 1H); IR (KBr) 3018, 1552, 1458, 1408. Anal. Calcd for $C_4H_3IN_2$ (205.9): C, 23.31; H, 1.46; N, 13.59. Found: C, 23.52; H, 1.72; N, 13.42.

α,α,α′,α′-Tetraphenyl-3,6-pyridazinedimethanol (14b). The general procedure B applied to **12** using benzophenone (3.24 mmol) gave **14b** in 6% yield (eluent, EtOAc/cyclohexane (6/4)): mp 152 °C; ^{1}H NMR ($CDCl_3$) δ 5.78 (s, 1H), 7.30–7.50 (m, 22H); IR (KBr) 3123, 2778, 1571, 1491, 1447. Anal. Calcd for $C_{30}N_{24}N_2O_2$ (444.5): C, 81.08; H, 5.41; N, 6.31. Found: C, 80.82; H, 5.37; N, 6.39.

4-(*tert*-Butyldimethylsilyl)pyridazine (15). The general procedure B applied to **12** using *tert*-butyldimethylsilyl chloride (3.24 mmol) gave **15** in 11% yield (eluent, EtOAc/CH_2Cl_2 (8/2)). The general procedure C applied to **12** using LTMP (6.25 mmol) and *tert*-butyldimethylsilyl chloride (1.56 mmol) during t = 90 min gave **15** in 9% yield (eluent, EtOAc/CH_2Cl_2 (8/2)): oil; ^{1}H NMR ($CDCl_3$) δ 0.33 (s, 6H), 0.93 (s, 9H), 7.50 (dd, J = 5.00, 2.00 Hz, 1H), 9.08 (m, 2H); IR (KBr) 3424, 2953, 2928, 2857, 1470. Anal. Calcd for $C_{10}H_{18}N_2Si$ (194.1): C, 61.82; H, 9.28; N, 14.43. Found: C, 61.53; H, 9.57; N, 14.68.

2-Pyrazinylphenylmethanol (17a). The general procedure B applied to **16** using benzaldehyde (3.24 mmol) gave **17a** in 10% yield (eluent, EtOAc/cyclohexane (7/3)): oil. The general procedure C applied to **16** using LTMP (6.25 mmol) and benzaldehyde (1.56 mmol) during t = 90 min gave **17a** in 39% yield (eluent, EtOAc/cyclohexane (7/3)): oil; ^{1}H NMR ($CDCl_3$) δ 5.02 (m, 1H), 5.78 (s, 1H), 7.28 (m, 5H), 8.27–8.53 (m, 3H); IR (KBr) 3320, 3060, 1493, 1453. Anal. Calcd for $C_{11}H_{10}N_2O$ (186.2): C, 70.93; H, 5.37; N, 15.05. Found: C, 71.12; H, 5.28; N, 15.15.

2-Pyrazinyldiphenylmethanol (17b). The general procedure B applied to **16** using benzophenone (3.24 mmol) gave **17b** in 30% yield (eluent, cyclohexane/EtOAc (9/1)): mp 123 °C; ^{1}H NMR ($CDCl_3$) δ 5.43 (s, 1H), 7.17 (m, 10H), 8.32 (m, 3H); IR (KBr) 3178, 1491, 1446, 1396. Anal. Calcd for $C_{17}H_{14}N_2O$ (262.3): C, 77.86; H, 5.34; N, 10.69. Found: C, 77.50; H, 5.17; N, 10.39.

2-Pyrazinylethanol (17c). The general procedure C applied to **16** using LTMP (6.25 mmol) and acetaldehyde (16 mmol) during t = 75 min gave **17c** in 65% yield (eluent, EtOAc): oil; ^{1}H NMR ($CDCl_3$) δ 1.55 (d, J = 7 Hz, 3H), 4.65 (m, 1H), 5.03 (quint, J = 7 Hz, 1H), 8.48–8.75 (m, 3H); IR (KBr) 3372, 2975, 2930, 1666, 1404. Anal. Calcd for $C_6H_8N_2O$ (124.1): C, 58.06; H, 6.45; N, 22.58. Found: C, 58.25; H, 6.21; N, 22.44.

2-Iodopyrazine (17d). The general procedure C applied to **16** using LTMP (6.25 mmol) and iodine (1.56 mmol) during t = 40 min gave **17d** in 44% yield (eluent, CH_2Cl_2): mp 90 °C dec; ^{1}H NMR ($CDCl_3$) δ 8.43 (apparent dd, J = 8.00, 2.00 Hz, 2H), 8.82 (d, J = 2.00 Hz, 1H); IR (KBr) 3434, 2927, 2868, 1504, 1448. Anal. Calcd for $C_4H_3IN_2$ (205.9): C, 23.31; H, 1.46; N, 13.59. Found: C, 23.50; H, 1.60; N, 13.39.

α,α′-Diphenyl-2,5-pyrazinedimethanol (18a). The general procedure B applied to **16** using benzaldehyde (3.24 mmol) gave **18a** in 2% yield (eluent, AcOEt/cyclohexane (7/3)). The general procedure C applied to **16** using LTMP (6.25 mmol) and benzaldehyde (4.68 mmol) during t = 90 min gave **18a** in 16% yield (eluent, EtOAc/cyclohexane (7/3)): mp 114 °C; ^{1}H NMR ($CDCl_3$) δ 4.65 (m, 2H), 5.72 (s, 2H), 7.23 (m, 10H), 8.38 (s, 2H); IR (KBr) 3334, 3060, 2925, 2861, 1493, 1457. Anal. Calcd for $C_{18}H_{16}N_2O_2$ (292.3): C, 73.95; H, 5.48; N, 9.59. Found: C, 73.78; H, 5.67; N, 9.60.

JO942079U