Solvent-free microwave-assisted synthesis of new 2,4-dimethoxybenzylaminotriazines

Antonio de la Hoz,* Ana Sánchez-Migallón, Beatriz T. Pelado, and José R. Ramírez

Facultad de Ciencias y Tecnologías Químicas. Universidad de Castilla-La Mancha. E-13071 Ciudad Real. Spain
E-mail: Antonio.Hoz@uclm.es

Dedicated to Prof. Rosa Claramunt on the occasion of her 65th aniversary.

DOI: http://dx.doi.org/10.3998/ark.5550190.p008.245

Abstract
An efficient and green synthesis of 2,4-dimethoxybenzyaminotriazines is described, by reaction of disubstituted triazines with 2,4-dimethoxybenzylamine under microwave irradiation and in solvent-free conditions. NMR spectroscopy has been used to determine the free energy of activation of the restricted rotation of the ArylN-triazine bond that is a slow process at room temperature. Contrarily, the benzylN-triazine bond shows a rapid rotation at room temperature.

Keywords: Microwaves, solvent-free, *s*-triazine, pyrazole

Introduction

1,3,5-Triazines have found application in medicinal chemistry,[1] catalysis,[2] as herbicides[3] and by the synthesis of polymers.[4] In supramolecular chemistry the nature of the interaction depends strongly on the substituents of the heterocyclic system and 1,3,5-triazines can act as a partner in cation-π, anion-π, π–π stacking, hydrogen bond and coordination complexes.[5] In materials chemistry, triazine derivatives have been used as acceptors in D-A and D-A-A complexes with application in photovoltaic systems[6] or for the construction of star-shaped donor-acceptor complexes.[7] The melamine : cyanuric acid is probably the most studied system[8] and several supramolecular structures have been described using substituted aminotriazines.[9]

In chemistry of materials, triazine derivatives have been used as acceptor systems in D-A and D-A-A derivatives with application in photovoltaic systems[8] or for the construction of star-shaped systems with Donor and Acceptor systems as sustituents.[9]

In this paper we describe the preparation of new derivatives of aminotriazines using the green methodologies described in our group, microwave irradiation and solvent-free conditions.

Results and Discussion

A great variety of derivatives of *s*-triazine can be prepared from cyanuric chloride by sequential substitution of the chlorine atoms by nucleophiles[10] controlling the selective substitution of the three chlorine atoms by choice of reaction temperature. The first substitution is exothermic and can be performed at 0 ºC. The second substitution occurs at room temperature while the third substitution requires elevated temperatures obtained by reflux in a solvent with a boiling point above 65°C. This protocol has been used for the introduction of several nucleophiles, amines, thiols, Grignard reagents, and to obtain asymmetrical substituted triazines.

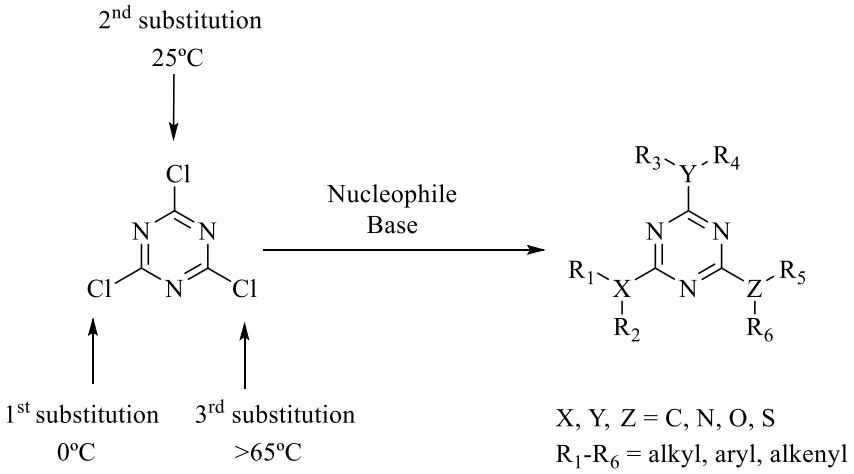


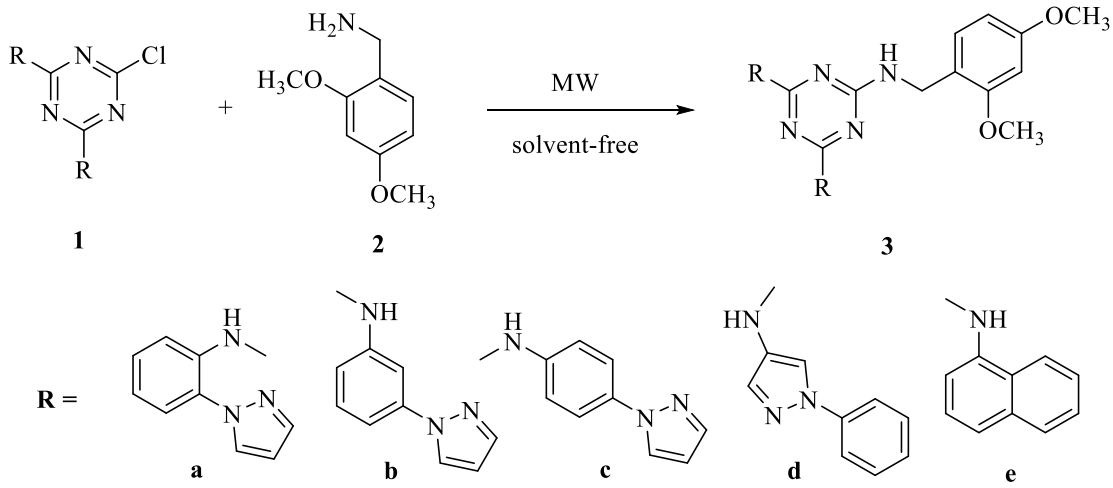
Figure 1. Preparation of trisubstituted-triazines by selective substitution of chlorine atoms by nucleophiles.

In this way three different substituents can be introduced giving access to a wide variety of substrates that may act as ligands, molecular tectons, molecular materials and supramolecular systems based on s-triazine.

The conditions for the third substitution depend on the strength of the nucleophile, of steric factors and of the nature of the solvent.

By replacement of the third chlorine microwave irradiation has proved to be advantageous providing improved yields and shorter reaction times. Thus, trisubstituted 1,3,5-triazines were obtained in one step from cyanuric chloride or from 2-chloro-4,6-disubstituted triazines in high yield using this methodology.[11] Under traditional reaction conditions replacement of the third chlorine atom with an amino group requires heating with ammonia to 100-105ºC for 8 h in a close vessel or heating with an amine to high temperatures.[12] In these reactions use of microwave irradiation leads to improved yields, reduced reaction times and reduced decomposition of reagents and products.[13]

In this paper we propose the introduction of a 2,4-dimethoxybenzylamino group because the benzyl group can be removed in a wide variety of conditions (acid, basic and oxidative conditions) to deprotect the free amino group.[14] Reactions of 2-chloro-4,6-diaminotriazines (**1**) with 2,4-dimethoxybenzylamine (**2**) were performed under microwave irradiation and in solvent-free conditions (Scheme 1).The starting disubstituted triazines have been previously prepared by our group.[15]



Scheme 1

2,4-Dimethoxybenzyl amine (**2**) amine was used in a 2 mol excess to serve both as a nucleophile, as a base to neutralize acid formed by the substitution process and to assist homogenization of the reaction mixture.

Reactions were optimized using reaction times of 5-10 min. and temperatures from 120 to 150 ºC using a monomode microwave reactor. Finally, the best conditions were obtained in 5 min. at 150 ºC and with 50W of irradiation power (Table 1). It should be noted that some benzylaminotriazines have been previously described using classical conditions (heating at 90 ºC in toluene for 12h).[16]

Table 1

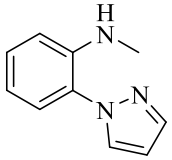
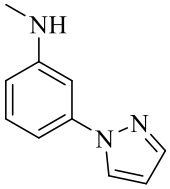
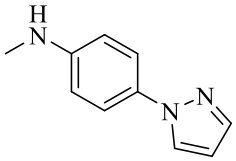
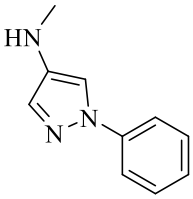
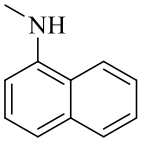
Entry[a]	R	Starting material	Yield (%)[b]
1	 **3a**	**1a**	57

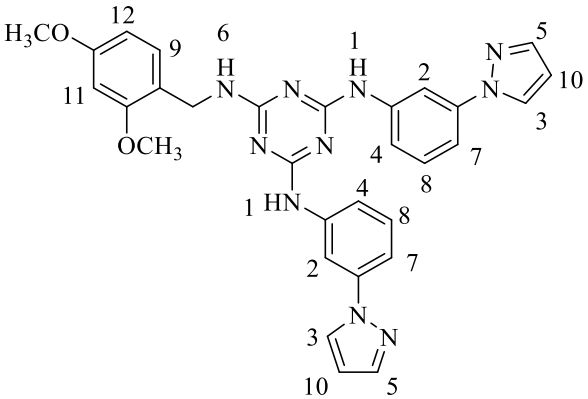
Table 1 (continued)

Entry[a]	R	Starting material	Yield (%)[b]
2	 **3b**	**1b**	43
3	 **3c**	**1c**	55
4	 **3d**	**1d**	33
5	 **3e**	**1e**	58

a) 5 min., 150ºC, 50W. b) isolated yields.

NMR spectra

The NMR spectra of compounds **3** show that several signals appear duplicated. This effect is especially important in the N-H group and the proton close to the N-H groups (Figure 2).



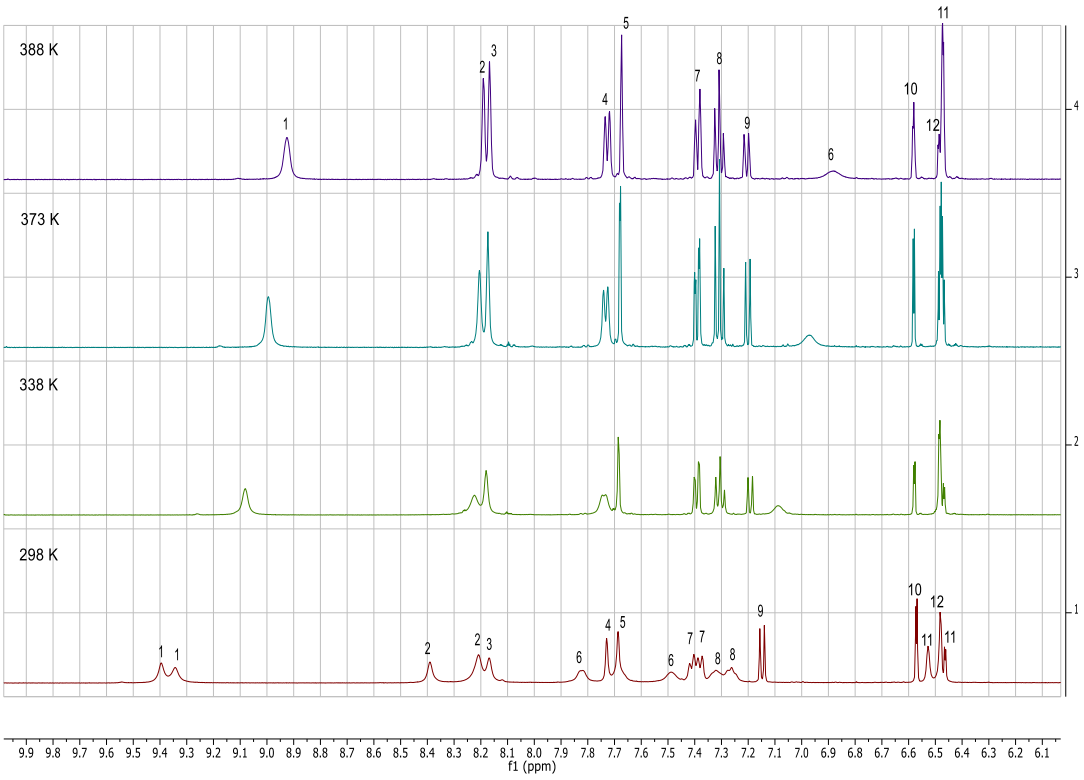


Figure 2. NMR spectra of compound **3b** at different temperatures.

In previous studies we have shown that conformers A and B are observed at low temperature while conformers B and C are not observed.

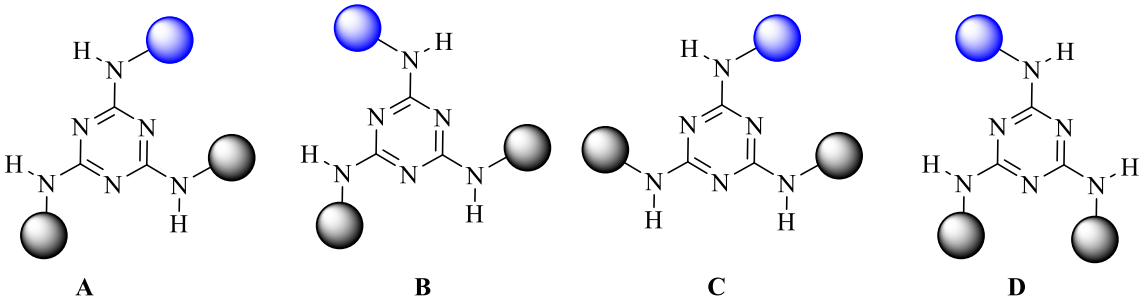


Figure 3.Possible conformers of compounds **3**, by restricted rotation of the N-triazine bond.

In compounds **3** signals corresponding to the N-H groups and other duplicated signals appears with the same integral. This indicates that conformers A and B are interchanged rapidly at 298 K due to the lower conjugation of the benzylic amine nitrogen. Increasing the temperature produces the coalescence of all signals and at temperatures higher than 353 K only one conformer was observed. It is remarkable that the N-H protons are displaced to high field (0.5

ppm for the NH-Aryl and up to 1 ppm for the NH-benzyl) probably due to a lower aggregation of the conformers through hydrogen bonds.

We have determined the free energy of activation in compound **3e** by variable temperature experiments (Figure 3). Experiments were performed increasing the temperature slowly and giving 10 min. for stabilization of the temperature, in order to determine the coalescence temperature with a precision of 1 K. For compound **3e** the coalescence temperature was 329 K and the free energy of activation was determined as described by Sandström.[17]

$$\Delta G^{\#} = a\ T\ [9{,}972 + \log (T/\Delta\nu)]$$

$a = 1{,}914 * 10^{-2}$ KJ mol^{-1}
$a = 4{,}575 * 10^{-3}$ Kcal mol^{-1}

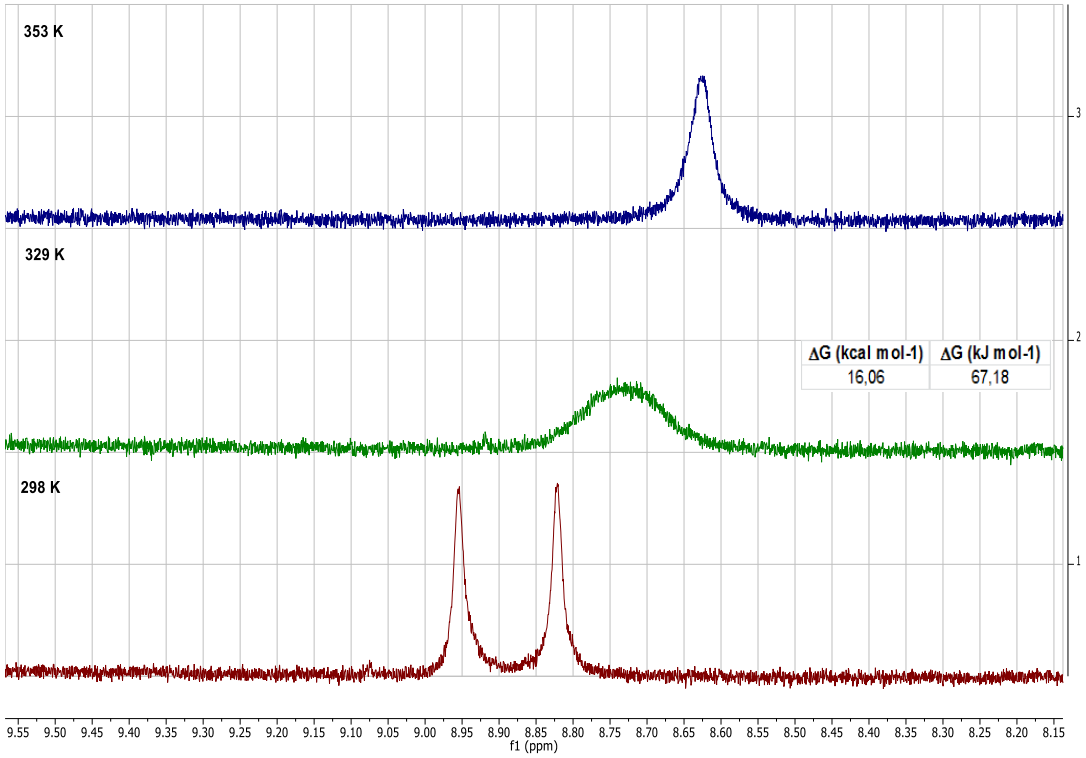


Figure 3. Coalescence of the NH groups of compound **3e**.

This free energy of activation is some lower than the determined for related compounds[5] and should be ascribed the lower conjugation of compounds **3** due to the presence of the benzyl group.

Conclusions

We have described a new series of 1,3,5-triazine-2,4,6-triamines with a 2,4-dimethoxylbenzylamino group that can be deprotected by great variety of standard method to give the free amino group. Reactions have been performed in green conditions, under microwave irradiation and solvent-free conditions in short reaction time. These compounds show a restricted rotation of the ArylNH-triazine bond. The free energy of activation was determined and was some lower that described values for related triazines.

Experimental Section

General. All reagents were purchased from commercial sources and used without further purification. Reactions were performed in a focused microwave reactor (CEM Discover) provided with an infrared pyrometer. Thin layer chromatography was performed in silica gel plates Merck F254. Flash Chromatography was performed on silicagel Merck type 60 (230-400 mesh). Melting points were determined in a SMP-3 apparatus. IR spectra were recorded on a Shimadzu IRPRESTIGE-21 spectrophotometer. ^{1}H- and ^{13}C-NMR spectra were recorded in a Varian Innova-500 spectrometer working a 499.772 MHz for ^{1}H and 125.423 MHz for ^{13}C-NMR, internal standard was the signal of the deuterated solvent; δ in ppm; coupling constants (J) in Hz. MALDI-TOF/TOF mass spectra were measured with a Bruker Autoflex II TOF/TOF spectrometer by using 2,5-dihydroxybenzoic acid (Ditranol) as the matrix. Samples co-crystallized with the matrix on the probe were ionized with a nitrogen laser pulse (337 nm) and accelerated under 20 kV with time-delayed extraction before entering the time-of-flight mass spectrometer. Matrix (10 mg/mL) and sample (1 mg/mL) were separately dissolved in methanol/DMSO and mixed in a matrix/sample ratio ranging from 100:1 to 50:1. Typically, a 5 μL mixture of matrix and sample was applied to a MALDI-TOF MS probe and air-dried. MALDI-TOF MS in positive reflector mode was used for all the compounds. Elemental analysis were made at the SIDI (Autonoma University of Madrid) on a LECO CHNS-932 Elemental Analyzer.

***N*-(2,4-Dimethoxybenzyl)-*N´*,*N´´*-bis-(2-pyrazol-1-ylphenyl)-1,3,5-triazine-2,4,6-triamine (3a).** In a microwave flask provided with a reflux condenser 6-chloro-2,4-bis-(2-pyrazol-1-ylphenylamine)-1,3,5-triazine (**1a**) (0.11 g, 0.25 mmol) and 2,4-dimethoxybenzylamine (**2**) (0.084 g, 0.50 mmol) were introduced. The mixture was irradiated for 5 min. at 50 W (150 ºC). The crude was cooled and washed with ethanol (3 mL) and filtered in vacuo to give pure compound **3a** (0.08 g, 57%), mp 114-117 ºC. IR (neat): υ 3422 (NH), 1506, 1408 (C=N and C=C), 1205 (C-O) cm$^{-1.}$ ^{1}H-NMR (DMSO, T = 368 K): δ 3.75 (s, 3H, OCH_3), 3.81 (s, 3H, OCH_3), 4.37 (d, *J* 5.37 Hz, 2H, NCH_2), 6.44 (d, *J* 7.32 Hz, 1H, $H_{5',\ phenyl}$), 6.53 (s, 2H, $H_{4\ pyrazole}$), 6.56 (s, 1H, $H_{3',\ phenyl}$), 7.10 (d, *J* 7.8Hz, 1H, $H_{6',\ phenyl}$), 7.17 (t, *J* 7.56 Hz, 3H, $H_{4\ phenyl}$, NH), 7.32

(bs, 2H, $H_{5\ phenyl}$), 7.48 (d, *J* 7.8Hz, $H_{3\ phenyl}$), 7.84 (s, 2H, $H_{3\ pyrazole}$), 8.13 (s, 2H, $H_{5\ pyrazole}$), 8.29 (bs, 2H, $H_{6\ phenyl}$), 9.10 (bs, 2H, NH). ^{13}C-NMR (DMSO, T = 368 K): δ 38.12 (NCH_2), 54.85 (OCH_3), 55.17 (OCH_3), 98.31 ($C_{3'phenyl}$), 104.44 ($C_{5'phenyl}$), 106.43 ($C_{4\ pyrazole}$), 119.37 ($C_{1'phenyl}$), 122.58 ($C_{6\ phenyl}$), 123.27 ($C_{4\ phenyl}$), 123.38 ($C_{3\ phenyl}$), 126.82 ($C_{5\ phenyl}$), 128.42 ($C_{6'phenyl}$), 129.84 ($C_{2\ phenyl}$), 130.66 ($C_{5\ pyrazole}$), 132.05 ($C_{1\ phenyl}$), 140.31 ($C_{3\ pyrazole}$), 157.51 ($C_{4'phenyl}$), 159.35 ($C_{2'phenyl}$), 163.74 ($C_{4,6\ triazine}$), 165.58 ($C_{2\ triazine}$). MS (MALDI-TOF): *m/z* (%) = 561.293 (100) $[M+ H]^+$. Anal. Calcd for $C_{30}H_{28}N_{10}O_2$: C, 64.27; H, 5.03; N, 24.98. Found: C, 64.28; H, 5.05; N, 24.97.

***N*-(2,4-Dimethoxybenzyl)-*N´*,*N´´*-bis-(3-pyrazol-1-ylphenyl)-1,3,5-triazine-2,4,6-triamine (3b).** In a microwave flask provided with a reflux condenser 6-chloro-2,4-bis-(3-pyrazol-1-ylphenylamine)-1,3,5-triazine (**1b**) (0.11 g, 0.25 mmol) and 2,4-dimethoxybenzylamine (**2**) (0.084 g, 0.50 mmol) were introduced. The mixture was irradiated for 5 min. at 50 W (150ºC). The crude as cooled and water (4 mL) was added and the mixture was sonicated and the solid was filtered in vacuo and dried. By column chromatography on silica gel using hexane : ethyl acetate (1 : 1) as the eluent the pure compound **3b** was obtained (0.06 g, 43%), mp 115-118 ºC. IR (neat): υ 3447 (NH), 1584, 1506 (C=N and C=C), 1022 (C-O) cm^{-1}. ^{1}H-NMR (DMSO, T = 373 K): δ3.76 (s, 3H, OCH_3), 3.82 (s, 3H, OCH_3), 4.55 (s, 2H, NCH_2), 6.46-6.48 (m, 2H, $H_{3'}$, $H_{5'phenyl}$), 6.58 (d, *J* 2.44 Hz, 2H, $H_{4\ pyrazole}$), 6.97 (bs, 1H, NH), 7.20 (d, *J* 8.29 Hz, 1H, $H_{6'\ phenyl}$), 7.31(t, *J* 8.05Hz, 2H, $H_{5\ phenyl}$), 7.38 (d, *J* 7.81Hz, 2H, $H_{4\ phenyl}$), 7.68 (d, *J* 1.46 Hz, 2H, $H_{3\ pyrazole}$), 7.73 (d, *J* 7.81 Hz, 2H, $H_{6\ phenyl}$), 8.17 (s, 2H, $H_{5\ pyrazole}$), 8.20 (s, 2H, $H_{2\ phenyl}$), 8.99 (bs, 2H, NH). ^{13}C-NMR (DMSO, T = 373 K): δ 38.33 (NCH_2), 54.88 (OCH_3), 55.14 (OCH_3), 98.39 ($C_{3'\ phenyl}$), 104.53 ($C_{5'\ phenyl}$), 106.92 ($C_{4\ pyrazole}$), 110.36 ($C_{2\ phenyl}$), 111.93 ($C_{4\ phenyl}$), 117.72 ($C_{6\ phenyl}$), 119.44 ($C_{1'\ phenyl}$), 126.96 ($C_{5\ phenyl}$), 128.26 ($C_{6'\ phenyl}$), 128.68 ($C_{5\ pyrazole}$), 139.65 ($C_{3\ phenyl}$), 140.08 ($C_{3\ pyrazole}$), 140.68 ($C_{1\ phenyl}$), 157.54 ($C_{4'\ phenyl}$), 159.45 ($C_{2'\ phenyl}$), 163.75 ($C_{4,6\ triazine}$), 165.41 ($C_{2\ triazine}$). MS (MALDI-TOF): *m/z* (%) = 561.426 (100) $[M+ H]^+$. Anal. Calcd for $C_{30}H_{28}N_{10}O_2$: C, 64.27; H, 5.03; N, 24.98. Found: C, 64.30; H, 5.05; N, 24.97.

***N*-(2,4-Dimethoxybenzyl)-*N´*,*N´´*-bis-(4-pyrazol-1-ylphenyl)-1,3,5-triazine-2,4,6-triamine (3c).** In a microwave flask provided with a reflux condenser 6-chloro-2,4-bis-(3-pyrazol-1-ylphenylamine)-1,3,5-triazine (**1c**) (0.08 g, 0.19 mmol) and 2,4-dimethoxybenzylamine (**2**) (0.063 g, 0.38 mmol) were introduced. The mixture was irradiated for 5 min. at 50 W (150ºC). The crude as cooled and water (4 mL) was added and the mixture was sonicated and the solid was filtered in vacuo and dried. By column chromatography on silica gel using hexane : ethyl acetate (1 : 1) as the eluent the pure compound **3c** was obtained (0.057 g, 55%), mp 90-93 ºC. IR (neat): υ 3415 (NH), 1520, 1504 (C=N and C=C), 1207 (C-O), 1032 (C-O) cm^{-1}. ^{1}H-NMR (DMSO, T = 353 K): δ 3.72 (s, 3H, OCH_3), 3.80 (s, 3H, OCH_3), 4.46 (d, *J* 5.8 Hz, 2H, NCH_2), 6.46 (dd, *J* 8.3, 2.4 Hz, 1H, $H_{5'\ phenyl}$), 6.48 (t, *J* 2.4 Hz, 2H, $H_{5\ pyrazole}$), 6.55 (d, *J* 2.5 Hz, 1H, $H_{3'\ phenyl}$), 6.93 (t, *J* 5.8 Hz, 1H, NH), 7.15 (d, *J* 8.3 Hz, 1H, $H_{6'\ phenyl}$), 7.62 (d, *J* 8.8 Hz, $H_{2,6\ phenyl}$), 7.66 (d, *J* 1.4 Hz, 2H, $H_{5\ pyrazole}$),7.80 (d, *J* 8.3 Hz, 4H, $H_{3,5\ phenyl}$), 8.23 (d, *J* 2.5 Hz, 2H, $H_{5\ pyrazole}$), 8.88 (bs, 2H, NH). ^{13}C-NMR (DMSO, T = 353 K): 38.81 (NCH_2), 55.38 (OCH_3), 55.65 (OCH_3), 98.64 ($C_{3\ phenyl}$), 104.87 ($C_{5'\ phenyl}$), 107.44 ($C_{4\ pyrazole}$), 119.04 ($C_{2,6\ phenyl}$), 119.92 ($C_{1'}$

$_{phenyl}$), 120.92 ($C_{3,5\ phenyl}$), 127.44 ($C_{5\ pyrazole}$), 128.62 ($C_{6',\ phenyl}$), 134.44 ($C_{4\ phenyl}$), 138.51 ($C_{1\ phenyl}$), 140.52 ($C_{3\ pyrazole}$), 157.96 ($C_{4',\ phenyl}$), 159.43 ($C_{2',\ phenyl}$), 164.27 ($C_{4,6\ triazine}$), 166.08 ($C_{2\ triazine}$). MS (MALDI-TOF): *m/z* (%) = 561.243 (100) $[M+ H]^+$. Anal. Calcd for $C_{30}H_{28}N_{10}O_2$: C, 64.27; H, 5.03; N, 24.98. Found: C, 64.26; H, 5.05; N, 24.99.

***N*-(2,4-Dimethoxybenzyl)-*N´*,*N´´*-bis-(1-phenylpyrazol-4-yl)-1,3,5-triazine-2,4,6-triamine (3d).** In a microwave flask provided with a reflux condenser 6-chloro-2,4-bis-(1-phenylpyrazol-4-ylamine)-1,3,5-triazine (**1d**) (0.11 g, 0.25 mmol) and 2,4-dimethoxibenzylamine (**2**) (0.084 g, 0.50 mmol) were introduced. The mixture was irradiated for 5 min. at 50 W (150 ºC). The crude as cooled and water (4 mL) was added and the mixture was filtered in vacuo and dried to obtain pure compound **3d** (0.058 g, 40%), mp 197-200 ºC. IR (neat): υ3 428 (NH), 1559, 1506 (C=N and C=C), 1211 (C-O), 1032 (C-O) cm^{-1}. ^{1}H-NMR (DMSO, T = 388 K): δ3.76 (s, 3H, OCH_3), 3.83 (s, 3H, OCH_3), 4.55 (d, *J* 6.34 Hz, 2H, NCH_2), 6.50 (d, *J* 8.29 Hz, 1H, $H_{5',\ phenyl}$), 6.60 (s, 1H, $H_{3',\ phenyl}$), 6.97 (bs 1H, NH), 7.21 (d, *J* 8.78 Hz, 1H, $H_{6',\ phenyl}$), 7.26 (t, *J* 7.32 Hz, 2H, $H_{4\ phenyl}$), 7.45 (t, *J* 7.32 Hz, 4H, $H_{3\ phenyl}$), 7.70 (bs, 4H, $H_{2\ phenyl}$), 7.83 (s, 2H, $H_{3\ pyrazole}$), 8.51 (bs, 2H, $H_{5\ pyrazole}$), 8.80 (bs, 2H, NH). ^{13}C-NMR (DMSO, T = 388 K): δ 38.06 (NCH_2), 54.83 (OCH_3), 55.13 (OCH_3), 98.42 ($C_{3',\ phenyl}$), 104.60 ($C_{5',\ phenyl}$), 116.79 ($C_{5\ pyrazole}$), 117.41 ($C_{2,6\ phenyl}$), 119.63 ($C_{1',\ phenyl}$), 124.72 ($C_{6',\ phenyl}$), 124.95 ($C_{4\ phenyl}$), 127.94 ($C_{3\ pyrazole}$), 128.71 ($C_{3,5\ phenyl}$), 133.33 ($C_{4\ pyrazole}$), 139.65 ($C_{1\ phenyl}$), 157.32 ($C_{4',\ phenyl}$), 159.32 ($C_{2',\ phenyl}$), 163.45 ($C_{4,6\ triazine}$), 166.12 ($C_{2\ triazine}$). MS (MALDI-TOF): *m/z* (%) = 561.284 (100) $[M+ H]^+$. Anal. Calcd for $C_{30}H_{28}N_{10}O_2$: C, 64.27; H, 5.03; N, 24.98. Found: C, 64.29; H, 5.01; N, 25.00.

2-*N*-(2,4-Dimethoxybenzyl)-*N´*,*N´´*-di(naphth-1-yl)-1,3,5-triazine-2,4,6-triamine (3e)

In a microwave flask provided with a reflux condenser 6-chloro-2,4-bis-(naphtylamino)-1,3,5-triazine (**1e**) (0.99 g, 0.25 mmol) y 2,4-dimethoxybenzylamine (**2**) (0.084 g , 0.50 mmol) were introduced. The mixture was irradiated for 10 min. at 150ºC. The crude was cooled and washed with HCl 0.1 M (2 x 3 mL). The resulting solid was filtered and purified by column chromatography on silica gel using hexane : ethyl acetate (9 : 1) as the eluent to obtain pure compound **3e** (0.077 g, 58%), mp 83-86 ºC. IR (neat): υ 3426 (NH), 1587, 1479 (C=N and C=C), 1263 (C-O), 1034 (C-O). ^{1}H-NMR (DMSO, T = 353 K): δ 3.73 (d, *J* 2.2 Hz, 3H, OCH_3), 3.75 (d, *J* 2.2 Hz, 3H, OCH_3), 4.29 (bs, 2H, NCH_2), 6.36 (s, 1H, $H_{5\ phenyl}$), 6.50 (s, 1H, $H_{3\ phenyl}$), 6.65 (s, 1H, NH), 6.94 (s, 1H, $H_{6\ phenyl}$), 7.36 (d, *J* 5.1 Hz, 2H, $H_{2\ naphtyl}$), 7.48 (d, *J* 3.6 Hz, 4H, H_6 and $H_{7\ naphtyl}$), 7.63 (s, 2H, $H_{4\ naphtyl}$) , 7.67 (d, *J* 6.5 Hz, 4H, $H_{3\ naphtyl}$), 7.89 (s, 2H, $H_{5\ naphtyl}$), 8.04 (s, 2H, $H_{8\ naphtyl}$), 8.63 (s, 2H, NH). ^{13}C-NMR (DMSO, T = 353 K): δ 38.12 (NCH_2), 54.90 (OCH_3), 55.09 (OCH_3), 98.13 ($C_{3\ phenyl}$), 104.18 ($C_{5\ phenyl}$), 119.78 ($C_{1\ phenyl}$), 122.00 ($C_{4\ naphtyl}$), 122.78 ($C_{8\ naphtyl}$), 123.95 ($C_{3\ naphtyl}$), 124.98 ($C_{6,7\ naphtyl}$), 125.22 ($C_{2\ naphtyl}$), 127.46 ($C_{5\ naphtyl}$), 128.52 ($C_{6\ phenyl}$), 157.48 ($C_{4\ phenyl}$), 159.26 ($C_{2\ phenyl}$), 165.62 ($C_{4,6\ triazine}$), 166.03 ($C_{2\ triazine}$). MS (MALDI-TOF): *m/z* (%) = 529.177 (100) $[M+ H]^+$. Anal. Calcd for $C_{32}H_{28}N_6O_2$: C, 72.71; H, 5.34; N, 15.90. Found: : C, 72.69; H, 5.37; N, 15.93.

Acknowledgements

The authors acknowledge financial support from Spanish Ministry of Economy and Competitiveness (project CTQ2011-22410).

References

1. Ronchi, S., Prosperi, D., Compostella, F., Panza. L. *Synlett* **2004**, 1007.
2. Hu, X. P., Chen, H. L., Zheng. Z. *Adv. Synth. Catal*. **2005**, *347*, 541. http://dx.doi.org/10.1002/adsc.200404240
3. Oliva, J. M., Asean, E. M. D. G., Burrows, H. D., Coimbra, R., de Melo, J. S. S., Canle, M. L., Fernández, M. I., Santaballa, J. A., Serrano-Andres, L. *ChemPhysChem* **2005**, *6*, 306. http://dx.doi.org/10.1002/cphc.200400349 PMid:15751354
4. Pedroso, L. M., Castro, M. M. C. A., Simoes, P., Portugal, A. *Polymer* **2005**, *46*, 1766. http://dx.doi.org/10.1016/j.polymer.2004.12.046
5. Mooibroek, T. J., Gamez, P. *Inorg. Chim. Acta* **2007**, 360, 381. http://dx.doi.org/10.1016/j.ica.2006.07.061
6. Wu, Y., Zhu, W. *Chem. Soc. Rev.*, 2013, **42**, 2039. http://dx.doi.org/10.1039/c2cs35346f PMid:23192709
7. Meier. H. *Angew. Chem. Int. Ed*. **2005**, *44*, 2482. Pang, J., Tao, Y., Freiberg, S., Yang, X.-P., D'Iorio, M., Wang. S. *J. Mater. Chem*. **2002**, *12*, 206.
8. Seto, C. T., Whitesides. G. M. *J. Am. Chem. Soc*. **1990**, *112*, 6409. Whitesides, G. M., Mathias, J. P., Seto. C. T. *Science* **1991**, *254*, 1312. PMid:1962191
9. Vera, F., Barberá, J., Romero, P., Serrano, J. L., Ros, M. B., Sierra, T. *Angew. Chem. Int. Ed.* **2010**, *49*, 4910. Mooiebroek, T. J., Teat, S. J., Massera, C., Gamez, P. Reedijk, J. *Cryst. Growth Des*. **2006**, *6*, 1569. López, J. L., Atienza, C., Seitz, W., Guldi, D. M., Martín, N. *Angew. Chem. Int. Ed.* **2010**, *49*, 9876.
10. Carofiglio, T., Varotto, A., Tonellato, U. *J. Org. Chem*. **2004**, *69*, 8121. http://dx.doi.org/10.1021/jo048713d PMid:15527302
11. Díaz-Ortiz, A., Elguero, J., de la Hoz, A., Jiménez, A., Moreno, A., Moreno, S., Sánchez-Migallón, A., *QSAR Comb. Sci.* **2005**, *24*, 649. http://dx.doi.org/10.1002/qsar.200420116
12. Blotny. G. *Tetrahedron* **2006**, *62*, 9507. Zerkowski, J. A., Mathias, J. P., Whitesides, G. M. *J. Am. Chem. Soc.* **1994**, *116*, 4305.

13. de la Hoz, A.; Loupy A. Eds. *Microwaves in Organic Synthesis* 3rd Edn.; Wiley: Weinheim, 2012.
14. Kociensky, P. *Protecting Groups*, 3rd Edn.; Thieme Verlag: Stuttgart, 2006.
15. Díaz-Ortiz, A., Elguero, J., Foces-Foces, C., de la Hoz, A., Moreno, A., Moreno, S., Sánchez-Migallón, A., Valiente, G., *Org. Biomol. Chem.* **2003**, *1*, 4451. http://dx.doi.org/10.1039/b310693d PMid:14727638
16. Hollink, E., Simanek, E.E., Bergbreiter, D.E. *Tetrahedron Lett.* **2005**, *46*, 2005-2008. http://dx.doi.org/10.1016/j.tetlet.2005.01.150
17. Sandström, J. *Dynamic NMR Spectroscopy* Academic Press: New York, 1982, p. 96.

8245 Graphical Abstract

Solvent-free Microwave Assisted Synthesis of New 2,4-Dimethoxybenzyl aminotriazines *Antonio de la Hoz*, Ana Sánchez-Migallón, Beatriz T. Pelado, José R. Ramírez*