JOC The Journal of Organic Chemistry

Article

pubs.acs.org/joc

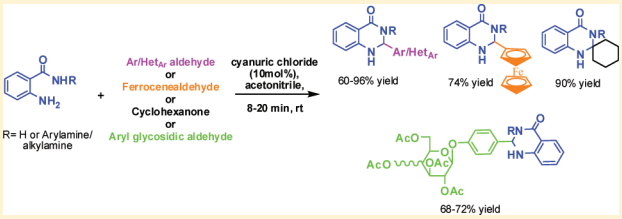
Cyanuric Chloride Catalyzed Mild Protocol for Synthesis of Biologically Active Dihydro/Spiro Quinazolinones and Quinazolinone-glycoconjugates

Moni Sharma,[†] Shashi Pandey,[†] Kuldeep Chauhan,[†] Deepty Sharma,[‡] Brijesh Kumar,[‡] and Prem M. S. Chauhan*[,†]

[†]Division of Medicinal and Process Chemistry and [‡]Sophisticated Analytical Instrumentation Facility, CSIR-Central Drug Research Institute, Lucknow 226001, India

Supporting Information

ABSTRACT: We have developed an efficient cyanuric chloride (2,4,6-trichloro-1,3,5-triazine, TCT) catalyzed approach for the synthesis of 2,3-dihydroquinazolin-4(1*H*)-one (**3a**−**3x**), 2-spiroquinazolinone (**5**, **7**), and glycoconjugates of 2,3-dihydroquinazolin-4(1*H*)-one (**10a**, **10b**) derivatives. The reaction allows rapid cyclization (8−20 min) with 10 mol % cyanuric chloride to give skeletal complexity in good to excellent yield. We believe that this novel procedure may open the door for the easy generation of new and bioactive quinazolinones.



INTRODUCTION

In the community of fused heterocycles, 2,3-dihydroquinazolin-4(1*H*)-one and 2-spiroquinazolinone are omnipresent and have been referred to as "core structures" in drug discovery. These quinazolinones displayed wide range of biological activities as antitumor,[1,2] antidefibrillatory,[3] antidepressant,[4] analgesic,[5] diuretic,[6] antihistamine,[7] vasodilating agent,[8] antihypertensive,[9] CNS stimulant,[10] tranquilizer[11] and antianxietic (Figure 1).[12] Moreover

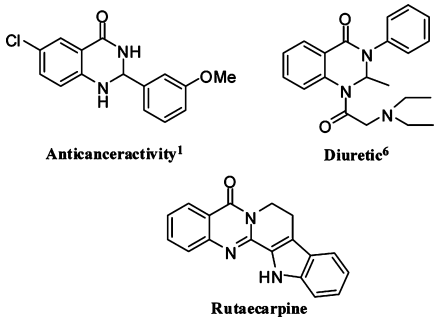


Figure 1. Biologically active quinazolinone and quinazolinone based natural product.

these quinazolinones also have plant growth regulator[13] abilities. On the other hand corresponding quinazolin-4(3*H*)-one are also important building blocks in natural products (Rutaecarpine, Figure 1) and compounds of pharmacological interest.[14−20]

Among the major classes of biomolecules carbohydrates exhibit unlimited structural variability and thus offer potential as a major probe in drug discovery.[21] Carbohydrates are involve in various physiological processes including cell-biomolecule interactions, masking of receptors by cell surface glycans, markers in certain cancer, and as ligands for proteins.[22−24] Furthermore, cancer cells display an array of tumor-associated antigens, many of which are based on a carbohydrate skeleton.[25] In recent years a composite picture of the biological role of *O*-aryl glycosides has emerged, with antitumor, anti-HIV, antibiotic, and antidiabetic activities.[26,27] Moreover, carbohydrate linked heterocyclic moieties are often proved to be an expedient entry for biological activity and can thus greatly influence the pharmacokinetics, drug targeting, and mechanism of action. In this context, several carbohydrate coupled heterocycles are also reported with excellent biological properties.[28−30] Thus, aiming to modulate the glycoside residue diversity preserving the potency of parent molecule, synthesis of the glycoconjugate of quinazolinone is obvious.

Most of the synthetic protocols for quinazolinone[31−39] and spiroquinazolinone[40−42] reported so far suffer from harsh reaction conditions,[33] prolonged time period,[34] use of hazardous acid catalysts,[40] high catalyst loading,[36] and expensive methods,[38] and therefore yields are oftentimes low due to poor selectivity in such conditions. Several nonacidic transition metal catalyzed,[36,39] nanoparticle catalyzed,[43] and ionic liquid mediated[44] syntheses of these molecules have also been reported. Despite the advances in synthetic methodologies, the synthesis of quinazolinone-glycoconjugate still has not been achieved. Therefore development of a new catalytic route toward this direction is an active area of research.

Inexpensive and readily available catalysts that bring about organic transformations in operationally simple ways are always an attractive approach for an organic as well as for a medicinal chemist, and such methodology for the selective and mild

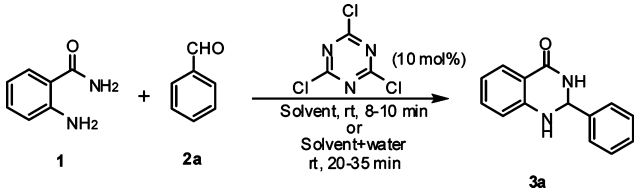
Received: October 12, 2011
Published: December 19, 2011

synthesis of 2,3-dihydroquinazolin-4(1*H*)-one, spiroquinazolinone, and corresponding quinazolinone glycoconjugates is still not explored. Careful tuning of catalysts in a synchronized manner can lead to new synthetic transformations possessing significant chemoselectivity in functionally complex systems. To exemplify this concept, we first dwell on the use of cyanuric chloride as a catalyst in organic transformations following our interest of its use in medicinal chemistry.[45−50] Moreover, the significance of cyanuric chloride as catalyst revealed that its treatment with alcohols and acids furnishes the corresponding alkyl halides[51] and activated cyanurate esters. These cyanurate esters undergo nucleophilic substitution and produce acyl chlorides,[52] amide,[53] peptide,[54] acyl azide,[55] sulphonyl chloride,[56] thiiranes,[57] diazoketones,[58] homoallylic alcohols,[59] and alcohols.[60] Cyanuric chloride and DMF adduct is used in the Beckman rearrangement[61] and formyl protection of the primary hydroxyl group,[62] and the cyanuric chloride/DMSO adduct is used in classical Swern oxidation.[63] Syntheses of some important heterocycles as xanthen derivatives[64] and polysubstituted quinolines[65] are also reported to be catalyzed by cyanuric chloride. Very recently, a mild and general method for preparation of glycosyl chloride using cyanuric chloride was also reported.[66] Here, we describe an innovative one-pot highly selective synthesis of quinazolinones catalyzed by cyanuric chloride. The reaction takes place through a cascade comprising (a) a novel and mild cyanuric chloride mediated activation of the carbonyl group of an aldehyde or ketone, which is further attacked by the amine functionality of anthralinamide to generate the imine and,(b) intramolecular cyclocondensation of imine to furnish the final quinazolinones. The assertion of the activation of carbonyl group is based on the electron deficiency of the cyanuric chloride, as in the case of cyanuric chloride/DMSO and cyanuric chloride/DMF adduct where a reactive intermediate formed, to furnish the final product.[61−63]

RESULTS AND DISCUSSION

Initially, we examined the model cyclocondensation reaction between anthranilamide (**1**) and benzaldehyde (**2a**) (Scheme 1)

Scheme 1. Model Cyclocondensation Reaction



at room temperature with altered catalyst loading, and the results are summarized in Table 1. It was found that 10 mol % of

Table 1. Catalyst Loading

entry	catalyst (mol %)	time (min)	yield (%)
1	2	45	90
2	5	20	92
3	10	10	96
4	20	10	85
5	30	10	75

cyanuric chloride efficiently catalyzed the reaction, which was complete in 10 min. On decreasing the catalyst loading the reaction time was increased (Table 1, entries 1 and 2), and increasing the catalyst loading did not significantly alter the course of reaction and time (Table 1, entry 5). Also high catalyst loading leads to the formation of side products (observed on TLC), which eventually reduces the yield of the desired product. Further to validate our assumption, we catalyzed the same reaction with 10 mol % of cyanuric acid instead of cyanuric chloride, and it was observed that the reaction proceeded quite slowly (5 h) compared to the reaction using cyanuric chloride (10 min).

To determine the effect of solvents, next we examined our reaction in different solvent systems as depicted in Table 2.

Table 2. Screening of Solvent and Mixture of Solvent

entry	solvent	time (min)	yield (%)
1	dry DCM	10	91
2	dry THF	10	80
3	dry methanol	15	87
4	dry toluene	40	72
5	dry acetonitrile	10	96
6	DCM	10	90
7	acetonitrile	10	96
8	methanol	15	80
9	THF	10	85
10	toluene	40	70
11	DMSO	20	87
12	water	45	70
13	THF/water	35	85
14	acetonitrile/water	20	90

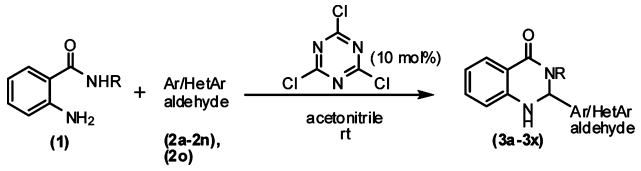
Among all the solvents screened, it was found that acetonitrile was the most suitable solvent for this reaction (Table 2, entry 7). Interestingly, in water the reaction proceeds very smoothly but requires a long reaction time, which might be attributed to the poor solubility of the starting substrates in water.

In order to study the scope of reaction, we condensed anthralinamide (**1**) with commercially available aromatic aldehydes (**2a−2m**) having electron-donating and electron-withdrawing substituents to form a series of dihydroquinazolinones (**3a−3m**) (Table 3). The electronic effects have no significant impact on reaction rate; nevertheless in *ortho*-substituted aldehydes the reaction time was long, which directly reflects its steric property. Heteroaromatic aldehyde (**2n**) was also readily introduced into the quinazolinone skeleton at the 2-position, and desired product (**3n**) was formed in good yield. Moreover to access the feasibility of the process, 2,3-disubstituted quinazolinones (**3o−3r**) were also synthesized with aliphatic and aromatic amines, and no any significant alteration was observed in reaction rate in either case. The reaction of deactivated anilines[67] with isatoic anhydride led to the synthesis of highly deactivated *N*-substituted benzamides, which have poor nucleophilicity toward the cyclocondensation reaction in the synthesis of 3-substituted quinazolinones. To countermand this lack of reactivity, we screened cyanuric chloride as catalyst in such cyclocondensation reactions, and the results obtained are good (**3s−3u,** Table 3). These 3-substituted quinazolinones are also important molecules in pharmacological aspects. As only few methods are available for the synthesis of these 3-substituted quinazolinones,[36] our methodology can serve as a useful tool in synthesis of these pharmacologically active scaffolds.

The structure of **3a−3x** was confirmed by IR, NMR, Mass, and HRMS and also with the literature where both were in good agreement. The HRMS analysis of **3a** shows a $(M + H)^+$ peak at m/z = 225.1017 as $C_{14}H_{12}N_2O$, which matches the

dx.doi.org/10.1021/jo2020856 | J. Org. Chem. 2012, 77, 929−937

Table 3. Scope of the Reaction with Different Aromatic and Heteroaromatic Aldehydes



entry	Ar/HetAr aldehyde	R	time (min)	yield (%)
3a	benzaldehyde (**2a**)	H	10	96
3b	4-methyl benzaldehyde (**2b**)	H	10	93
3c	4-ethyl benzaldehyde (**2c**)	H	10	85
3d	4-isopropyl benzaldehyde (**2d**)	H	10	90
3e	4-chloro benzaldehyde (**2e**)	H	10	90
3f	4-methoxy benzaldehyde (**2f**)	H	8	95
3g	4-thiomethyl benzaldehyde (**2g**)	H	8	87
3h	3-bromo benzaldehyde (**2h**)	H	10	86
3i	2-fluoro benzaldehyde (**2i**)	H	15	79
3j	4-*tert*-butyl benzaldehyde (**2j**)	H	10	92
3k	3-nitro benzaldehyde (**2k**)	H	15	84
3l	4-formylbenzonitrile (**2l**)	H	10	81
3m	2-naphthaldehyde (**2m**)	H	10	76
3n	pyridine 3-aldehyde (**2n**)	H	15	84
3o	benzaldehyde (**2a**)	aniline	10	77
3p	benzaldehyde (**2a**)	benzyl amine	10	73
3q	benzaldehyde (**2a**)	2-phenylethyl amine	8	87
3r	benzaldehyde (**2a**)	tetrahydrofurfuryl amine	8	65
3s	benzaldehyde (**2a**)	2,4-difluoroaniline	10	75
3t	benzaldehyde (**2a**)	2-chloro, 4-fluoro aniline	10	67
3u	benzaldehyde (**2a**)	3-trifluoromethylaniline	10	70
3v	benzaldehyde (**2a**)	*p*-phenylenediamine	120	84
3w	terephthalaldehyde (**2o**)	H	15	60
3x	ferrocenecarboxaldehyde (**2p**)	H	10	74

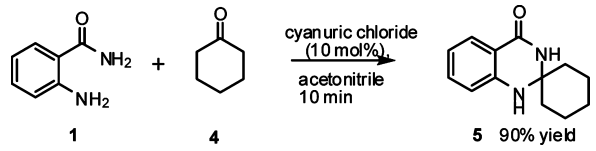
expected 2-phenyl-2,3-dihydro-1*H*-quinazolinone. In the ^{1}H and ^{13}C NMR spectrum of the molecule all of the signals are in good accord with the structure.

After the successful exploitation of our methodology with several aromatic and heteroaromatic aldehydes and several anilines (deactivated), next we explored our methodology in functional molecules where chemoselectivity is an important issue. When we applied our methodology to such functional molecules as in case of 2-amino-*N*-(4-aminophenyl)benzamide, reaction was sluggish and furnished a mixture of products with the formation of **3v** in 35% isolated yield. To further achieve chemoselectivity in such a system, the reaction was again catalyzed with cyanuric chloride at low temperature (0 °C). Exceptionally significant chemoselectivity was observed at low temperature in the process, and product (**3v**) was formed in 84% yield with longer reaction time (2 h). In a bifunctional system where both functional groups are same and have the same reactivity pattern, it is very difficult to create diversity at only one functional group. For example several groups have reported the synthesis of the bisquinazolinone system starting with terepthalaldehyde, but the monomer derivative is not reported.[68,69] However, when we applied our cyclocondensation methodology to such a bifunctional system, monomer (**3w**) was obtained as major product with 60% yield, and this monomer can be used to generate library of biologically active compounds.

Because of the increasing demand for ferrocene-containing heterocycles in organic and organometallic synthesis[70] and in medicinal chemistry,[71−73] we have attempted to expand the scope of our cyanuric chloride mediated cyclocondensation methodology in such electron-rich systems.

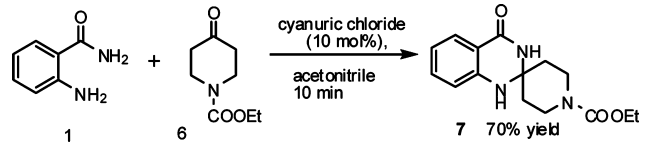
To explore the utility of cyanuric chloride-catalyzed imine formation and subsequent cyclization reaction, the methodology was extended toward alicyclic ketone, heteroalicyclic ketone, and aryl *O*-glycosidic aldehydes. The alicyclic ketone (cyclohexanone) (Scheme 2) and heteroalicyclic ketone

Scheme 2. Synthesis of Spirocyclized Product



(*N*-carbethoxy protected piperidone) (Scheme 3) were successfully entered in spirocyclized products. As relatively fewer methods

Scheme 3. Synthesis of Spirocyclized Product



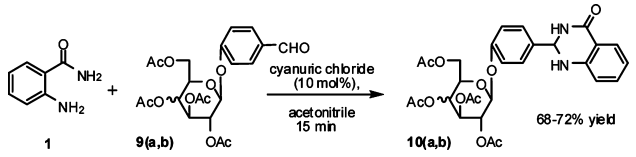
are available for such spirocyclization, our method can serve as a feasible approach for this transformation. This spirocyclization between anthranilamide and cycloalkanones was confirmed

dx.doi.org/10.1021/jo2020856 | *J. Org. Chem.* 2012, 77, 929−937

by the disappearance of the signal of quaternary carbonyl carbon of cycloalkanones, which is shifted from δ 207.1 to 70.57 ppm in the ^{13}C spectrum.

Preparation of *O*-aryl glycosides is a challenging task in synthetic organic chemistry as these *O*-glycosidic linkages are chemically sensitive.[74] Therefore more importantly, to further explore the potential of this protocol for synthesis of *O*-aryl glycosides in carbohydrate chemistry, we applied our cyanuric chloride catalyzed cyclocondensation methodology in carbohydrates (Scheme 4), and the results obtained are promising.

Scheme 4. Synthesis of Glycoconjugates



The synthesized glycoconjugate and intermediate sugar aldehyde were well characterized by the spectroscopic techniques. The molecular formula of **10a** was suggested to be $C_{28}H_{30}N_2O_{11}$ by the HRMS peak $(M + H)^+$ at 571.1926. The different cross correlations as shown in Figure 2 were very

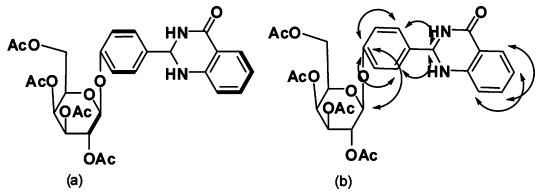
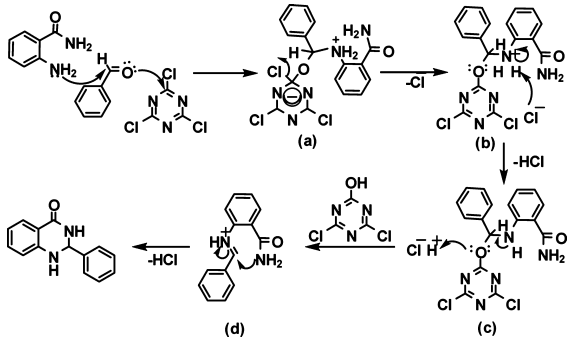


Figure 2. Important (a) COSY (dark lines) and (b) HMBC cross correlation (curved arrows) in synthesized glycoconjugates.

well characterized with the help of 2D COSY, HSQC, and HMBC experiments. The attachment of the bridged phenyl ring between sugar moiety and quinazolinone was assigned by the key HMBC cross correlations between the anomeric proton 1″H at δ 5.46 and the carbon of the phenyl ring 4′C at δ 161.7 ppm. Furthermore these assignments were confirmed by HMBC cross correlations between 2H-1′C and 2H-2′C. Beside these, other important cross correlations between 4′C-2′H/6′H and 1′C-3′H/5′H were also observed in the HMBC spectrum. The position of 6″Ha and Hb was confirmed by HSQC and HMBC spectrum as both protons having chemical shift value between δ 4.08−4.13 and 4.44−4.40 were attached at the same carbon at δ 66.2 ppm. The anomeric proton 1″H was identified at δ 5.46 ppm as a doublet with a *J* value of 7.5 Hz, and further its position was confirmed by the 2D $^1H-^1H$ correlation and HSQC cross correlation between 1″H 5.46 and 1″C 102.9. Other sugar protons appear as a multiplet between 5.17 and 5.37. A singlet for 2H appeared at δ 5.72 ppm. The 2D $^1H-^1H$ correlations between 2H δ 5.72 and 3H (NH) at δ 8.21 confirmed the formation of quinazolinone. On the basis of all of these assignments the name of the molecule is suggested as 2-[4′(6″,4″,3″,2″-tetra-*O*-acetyl-β-D-galactopyranosyloxy)-1′-phenyl]-2,3-dihydroquinazoline-4(1*H*)-one.

A plausible mechanism for the formation of these quinazolinones is proposed in Scheme 5. Being an electron-deficient system, cyanuric chloride might activate the carbonyl group of aldehyde or ketone, which is simultaneously attacked by anthranilamide to form the intermediate with an equivalent

Scheme 5. Plausible Reaction Mechanism for the Formation of Dihydroquinazolinone



amount of HCl. The so produced HCl might further catalyze the reaction to form the Schiff base after the elimination of the bulky cynauryloxy group, and finally intramolecular cyclization affords the desired product in quantitative yield. The isolation of the intermediates in the given course of reaction is not possible as the cyanuric chloride-aldehyde/ketone adduct may be unstable or short-lived, and in next step the elimination of cyanuryloxy group might be very fast.

CONCLUSION

In summary, herein we have demonstrated a most concise, efficient, mild, and facile protocol for the synthesis of dihydroquinazolinones, spiroquinazolinone, and the hybrid of quinazolinone with sugar molecules in a selective manner. This new chemistry would provide a simple, compatible, and potentially powerful method for the modular construction of quinazolinones with flexible control over the sensitive functionalities. Furthermore the moderate reaction conditions, absence of any cocatalyst, and production of nonvolatile and essentially nontoxic cyanuric acid make this an environment-friendly methodology amenable for scale-up.

EXPERIMENTAL SECTION

General Procedure 1: Synthesis of 2,3-Dihydroquinazolin-4(1*H*)-ones (3a−3x). Cyanuric chloride (0.135 mmol, 10 mol %) was added to a solution of anthranilamide (**1**) (0.73 mmol) and desired aldehydes (1 equiv) in acetonitrile (2 mL). The mixture was stirred at room temperature for the specified period of time as indicated in Table 3. The progress of the reaction was monitored by TLC. After completion, solvent was evaporated at reduced pressure, and solid was washed with water. The corresponding solid products were obtained in quantitative yield (Table 3) through column chromatography by using 100−200 mesh silica gels or by crystallization from ethanol.

2-Phenyl-2,3-dihydroquinazolin-4(1*H*)-one (3a). The title compound was prepared according to general procedure 1 using anthranilamide (**1**) (0.1 g, 0.73 mmol), benzaldehyde (**2a**) (0.074 mL, 0.73 mmol) and cyanuric chloride (0.135 mmol, 10 mol %) in acetonitrile (2 mL). Purification by crystallization in ethanol afforded **3a** as a white solid. Yield: 158 mg (96%). Mp: 218−220 °C (lit.[39] 218−219 °C). ^1H NMR ($CDCl_3$, 200 MHz): δ 7.96 (d, *J* = 8.1 Hz, 1H) 7.58−7.26 (m, 6H), 6.94 (t, *J* = 7.2 Hz, 1H), 6.69 (d, *J* = 8.0 Hz, 1H), 5.90 (s, 1H), 5.82 (s, 1H, NH), 4.41 (s, 1H, NH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 169.5, 152.9, 145.8, 138.4, 133.8, 133.3, 132.6, 132.0, 122.6, 119.8, 119.5, 72.5. IR (KBr): 3296, 3190, 3070, 1656, 1606 cm^{-1}. Mass: 224.00. HRMS (ESI): calcd for $[C_{14}H_{12}N_2O + H^+]$ 225.1022, found 225.1017.

2-*p*-Tolyl-2,3-dihydroquinazolin-4(1*H*)-one (3b). The title compound was prepared according to general procedure 1 using anthranilamide (**1**) (0.1 g, 0.73 mmol), 4-methylbenzaldehyde (**2b**) (0.086 mL, 0.73 mmol) and cyanuric chloride (0.135 mmol, 10 mol %)

dx.doi.org/10.1021/jo2020856 | J. Org. Chem. 2012, 77, 929−937

in acetonitrile (2 mL). Purification by crystallization in ethanol afforded **3b** as a white solid. Yield: 163 mg (93%). Mp: 232−234 °C (lit.[39] 233−234 °C). ^{1}H NMR (DMSO-d_6, 300 MHz): δ 8.18 (s, 1H, NH), 7.62 (d, J = 7.5 Hz, 1H), 7.38 (d, J = 7.9 Hz, 2H), 7.26−7.17 (m, 3H), 7.02 (bs, 1H, NH), 6.75 (d, J = 8.0 Hz, 1H), 6.69 (t, J = 7.4 Hz, 1H), 5.71 (s, 1H), 2.29 (s, 3H). ^{13}C NMR (DMSO-d_6, 50 MHz): δ 164.4, 148.2, 138.9, 138.2, 133.8, 129.2, 127.7, 127.0, 117.6, 115.2, 114.8, 66.7, 21.0. IR (KBr): 3313, 3196, 3061, 1662, 1610 cm^{-1}. Mass: 238.00. HRMS (ESI): calcd for [$C_{15}H_{14}N_2O$ + H$^+$] 239.1179, found 239.1177.

2-(4′-Ethylphenyl)-2,3-dihydroquinazolin-4(1*H*)-one (3c). The title compound was prepared according to general procedure 1 using anthranilamide (**1**) (0.1 g, 0.73 mmol), 4-ethylbenzaldehyde (**2c**) (0.10 mL, 0.73 mmol) and cyanuric chloride (0.135 mmol, 10 mol %) in acetonitrile (2 mL). Purification by crystallization in ethanol afforded **3c** as a white solid. Yield: 157 (85%). Mp: 178−180 °C. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.99 (d, J = 7.8 Hz, 1H), 7.54 (d, J = 7.8 Hz, 2H), 7.39−7.29 (m, 3H), 6.95 (t, J = 7.5 Hz, 1H), 6.70 (d, J = 8.1 Hz, 1H), 5.90 (s, 1H), 5.81 (s, 1H, NH), 4.40 (s, 1H, NH), 2.76 (q, J = 7.5 Hz, 2H), 1.31 (t, J = 7.5 Hz, 3H). ^{13}C NMR ($CDCl_3$ + DMSO-d_6, 75 MHz): δ 170.0, 153.3, 150.5, 142.8, 138.7, 133.2, 133.0, 132.5, 123.2, 120.3, 119.9, 73.3, 33.7, 20.9. IR (KBr): 3343, 3198, 3056, 1657, 1612 cm^{-1}. Mass: 252.00. HRMS (ESI): calcd for [$C_{16}H_{16}N_2O$ + H$^+$] 253.1335, found 253.1330.

2-(4′-Isopropylphenyl)-2,3-dihydroquinazolin-4(1*H*)-one (3d). The title compound was prepared according to general procedure 1 using anthranilamide (**1**) (0.1 g, 0.73 mmol), isopropylbenzaldehyde (**2d**) (0.11 mL, 0.73 mmol) and cyanuric chloride (0.135 mmol, 10 mol %) in acetonitrile (2 mL). Purification by crystallization in ethanol afforded **3d** as a white solid. Yield: 176 mg (90%). Mp: 162−164 °C. ^{1}H NMR (DMSO-d_6, 300 MHz): δ 8.21 (s, 1H), 7.64 (dd, J_1 = 7.6 Hz, J_2 = 1.2 Hz, 1H), 7.44 (d, J = 8.1 Hz, 2H), 7.29−7.25 (m, 3H), 7.05 (s, 1H), 6.76−6.68 (m, 2H), 5.73 (s, 1H), 2.95 (m, 1H), 1.22 (d, J = 6.9 Hz, 6H). ^{13}C NMR (DMSO-d_6, 50 MHz): δ 164.1, 149.3, 148.4, 139.5, 133.7, 127.8, 127.4, 126.7, 117.5, 115.4, 114.8, 67.0, 33.7, 24.3. IR (KBr): 3292, 3191, 3021, 1658, 1610 cm^{-1}. Mass: 266.00. HRMS (ESI): calcd for [$C_{17}H_{18}N_2O$ + H$^+$] 267.1492, found 267.1489.

2-(4′-Chlorophenyl)-2,3-dihydroquinazolin-4(1*H*)-one (3e). The title compound was prepared according to general procedure 1 using anthranilamide (**1**) (0.1 g, 0.73 mmol), 4-chlorobenzaldehyde (**2e**) (0.10 g, 0.73 mmol) and cyanuric chloride (0.135 mmol, 10 mol %) in acetonitrile (2 mL). Purification by crystallization in ethanol afforded **3e** as a white solid. Yield: 170 mg (90%). Mp: 204−206 °C (lit.[75] 205−206 °C). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.97 (d, J = 7.8 Hz, 1H), 7.57 (d, J = 8.4 Hz, 2H), 7.45 (d, J = 8.4 Hz, 2H),7.39 (t, J = 7.2 Hz, 1H), 6.96 (t, J = 7.8 Hz, 1H), 6.70 (d, J = 8.1 Hz, 1H), 5.91 (s, 1H), 5.81 (s, 1H, NH), 4.38 (s, 1H, NH). ^{13}C NMR ($CDCl_3$ + DMSO-d_6, 50 MHz): δ 169.4, 152.5, 144.1, 139.3, 138.4, 133.6, 133.4, 132.6, 123.0, 119.9, 119.5, 72.1. IR (KBr): 3318, 3190, 3075, 1659, 1609 cm^{-1}. Mass: 258.00. HRMS (ESI): calcd for [$C_{14}H_{11}ClN_2O$ + H$^+$] 259.0633, found 259.0625

2-(4′-Methoxyphenyl)-2,3-dihydroquinazolin-4(1*H*)-one (3f). The title compound was prepared according to general procedure 1 using anthranilamide (**1**) (0.1 g, 0.73 mmol), 4-methoxybenzaldehyde (**2f**) (0.089 mL, 0.73 mmol) and cyanuric chloride (0.135 mmol, 10 mol %) in acetonitrile (2 mL). Purification by crystallization in ethanol afforded **3f** as a white solid. Yield: 177 mg (95%). Mp: 187−190 °C (lit.[76] 192−193 °C). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.86 (d, J = 7.8 Hz, 1H), 7.43 (d, J = 8.7 Hz, 2H), 7.26 (t, J = 7.8 Hz, 1H), 6.87−6.77 (m, 3H), 6.57 (d, J = 8.1 Hz, 1H), 5.75 (s, 1H), 5.63 (bs, 1H, NH), 4.24 (bs, 1H, NH), 3.74 (s, 3H). ^{13}C NMR ($CDCl_3$ + CD_3OD, 50 MHz): δ 170.4, 152.4, 138.5, 135.5, 132.9, 132.4, 123.1, 119.1, 118.9, 118.4, 72.7, 59.5. IR (KBr): 3299, 3109, 3021, 1659, 1610 cm^{-1}. Mass: 254.00. HRMS (ESI): calcd for [$C_{15}H_{14}N_2O_2$ + H$^+$] 255.1128, found 255.1125.

2-(4′-(Methylthio)phenyl)-2,3-dihydroquinazolin-4(1*H*)-one (3g). The title compound was prepared according to general procedure 1 using anthranilamide (**1**) (0.1 g, 0.73 mmol), 4-thiomethylbenzaldehyde (**2g**) (0.097 mL, 0.73 mmol) and cyanuric chloride (0.135 mmol, 10 mol %) in acetonitrile (2 mL). Purification by crystallization in ethanol afforded **3g** as a white solid. Yield: 173 mg (87%). Mp: 178−180 °C. ^{1}H NMR ($CDCl_3$+DMSOd_6, 300 MHz): δ 7.84 (d, J = 7.7 Hz, 1H), 7.57−7.50 (m, 2H), 7.29−7.27 (m, 3H), 7.01 (s, 1H, NH), 6.82−6.75 (m, 2H), 6.01 (s, 1H, NH), 5.83 (s, 1H), 2.51 (s, 3H). ^{13}C NMR ($CDCl_3$+ DMSOd_6, 50 MHz): δ 163.7, 147.5, 138.5, 137.4, 132.8, 127.7, 127.0, 125.3, 116.9, 114.5, 114.1, 66.3, 14.6. IR (KBr): 3298, 3189, 3063, 1657, 1610 cm^{-1}. Mass: 270.00. HRMS (ESI): calcd for [$C_{15}H_{14}N_2OS$ + H$^+$] 271.0900, found 271.0893.

2-(3′-Bromophenyl)-2,3-dihydroquinazolin-4(1*H*)-one (3h). The title compound was prepared according to general procedure 1 using anthranilamide (**1**) (0.1 g, 0.73 mmol), 3-bromobenzaldehyde (**2h**) (0.086 mL, 0.73 mmol) and cyanuric chloride (0.135 mmol, 10 mol %) in acetonitrile (2 mL). Purification by crystallization in ethanol afforded **3h** as a white solid. Yield: 191 mg (86%). Mp: 229−231 °C (lit.[75] 231−233 °C). ^{1}H NMR ($CDCl_3$, 200 MHz): δ 7.94 (d, J = 7.8 Hz, 1H), 7.77 (dd, J_1 = 7.8, J_2= 1.2 Hz, 1H),7.62 (dd, J_1 = 7.8 Hz, J_2 = 1.2 Hz, 1H), 7.41−7.20 (m, 3H), 6.91−6.83 (m, 1H), 6.69 (d, J = 8.0 Hz, 1H), 6.30 (s, 1H), 6.09 (s, 1H, NH), 4.67 (s, 1H, NH). ^{13}C NMR ($CDCl_3$, CD_3OD, 50 MHz): δ 170.0, 152.0, 146.4, 138.6, 136.7, 134.6, 132.2, 130.1, 123.0, 119.0, 71.8. IR (KBr): 3276, 3181, 3057, 1655, 1628 cm^{-1}. Mass: 302.00. HRMS (ESI): calcd for [$C_{14}H_{11}BrN_2O$ + H$^+$] 303.0128, found 303.0121.

2-(2′-Fluorophenyl)-2,3-dihydroquinazolin-4(1*H*)-one (3i). The title compound was prepared acording to general procedure 1 using anthranilamide (**1**) (0.1 g, 0.73 mmol), 2-fluorobenzaldehyde (**2i**) (0.077 mL, 0.73 mmol) and cyanuric chloride (0.135 mmol, 10 mol %) in acetonitrile (2 mL). Purification by crystallization in ethanol afforded **3i** as a white solid. Yield: 140 mg (79%). Mp: 185−187 °C (lit.[77] 189−193 °C). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.73 (dd, J_1 = 7.8 Hz, J_2 = 1.2 Hz, 1H), 7.57 (dt, J_1 = 7.5 Hz, J_2 = 1.4 Hz, 1H), 7.30−7.18 (m, 2H), 7.10−6.97 (m, 2H), 6.75 (t, J = 7.5 Hz, 1H), 6.63 (d, J = 8.1 Hz, 1H), 6.13 (s, 1H). ^{13}C NMR ($CDCl_3$ + DMSO-d_6, 50 MHz): δ 172.9, 155.2, 141.7, 138.4, 138.2, 135.9, 135.6, 134.9, 132.0, 126.1, 123.4, 123.0, 122.4, 69.0. IR (KBr): 3371, 3184, 3067, 1656, 1613 cm^{-1}. Mass: 242.00. HRMS (ESI): calcd for [$C_{14}H_{11}FN_2O$ + H$^+$] 243.0928, found 243.0922.

2-(4′-*tert*-Butylphenyl)-2,3-dihydroquinazolin-4(1*H*)-one (3j). The title compound was prepared according to general procedure 1 using anthranilamide (**1**) (0.1 g, 0.73 mmol), 4-*t*-butylbenzaldehyde (**2j**) (0.122 mL, 0.73 mmol) and cyanuric chloride (0.135 mmol, 10 mol %) in acetonitrile (2 mL). Purification by crystallization in ethanol afforded **3j** as a white solid. Yield: 189 mg (92%). Mp: 219−221 °C (lit.[75] 219−220 °C).^{1}H NMR ($CDCl_3$, 200 MHz): δ 7.88 (dd, J = 7.8 Hz, 1H), 7.47−7.18 (m, 5H), 6.85 (t, J = 7.6 Hz, 1H), 6.60 (d, J = 8.1 Hz, 1H), 5.80 (s, 1H), 5.74 (bs, 1H), 4.33 (bs, 1H, NH), 1.26 (s, 9H). ^{13}C NMR ($CDCl_3$ + DMSO-d_6, 50 MHz): δ 175.7, 169.3, 156.6, 153.1, 142.9, 138.2, 133.8, 132.5, 131.9, 130.1, 122.3, 119.9, 119.4, 72.4, 39.4, 36.2. IR (KBr): 3278, 3184, 3055, 1653, 1623 cm^{-1}. Mass: 280.00. HRMS (ESI): calcd for [$C_{18}H_{20}N_2O$ + H$^+$] 281.1648, found 281.1643.

2-(3′-Nitrophenyl)-2,3-dihydroquinazolin-4(1*H*)-one (3k). The title compound was prepared according to general procedure 1 using anthranilamide (**1**) (0.1 g, 0.73 mmol), 3-nitrobenzaldehyde (**2k**) (0.110 g, 0.73 mmol) and cyanuric chloride (0.135 mmol, 10 mol %) in acetonitrile (2 mL). Purification by crystallization in ethanol afforded **3k** as a yellow solid. Yield: 166 mg (84%). Mp: 210−212 °C (lit.[39] 216−217 °C). ^{1}H NMR ($CDCl_3$ + DMSO-d_6, 300 MHz): δ 8.42 (s, 1H), 8.24 (s, 1H, NH), 8.17 (d, J = 8.1 Hz, 1H), 7.93 (d, J = 7.5, 1H), 7.73 (d, J = 7.5 Hz, 1H), 7.61 (t, J = 7.8 Hz, 1H), 7.27 (d, J = 7.2 Hz, 1H), 6.90 (s, 1H, NH), 6.79−6.69 (m, 2H), 5.91 (s, 1H). ^{13}C NMR ($CDCl_3$+DMSO-d_6, 50 MHz): δ 169.1, 152.9, 152.0, 148.6, 138.5, 138.0, 134.4, 132.6, 128.2, 126.9, 122.9, 120.0, 119.6, 71.1. IR (KBr): 3280, 3188, 3068, 1658, 1617 cm^{-1}. Mass: 269.00. HRMS (ESI): calcd for [$C_{14}H_{11}N_3O_3$ + H$^+$] 270.0873, found 270.0875.

4-(4′-Oxo-1′,2′,3′,4′-tetrahydroquinazolin-2′-yl)benzonitrile (3l). The title compound was prepared acording to general procedure 1 using anthranilamide (1) (0.1 g, 0.73 mmol), 4-formylbenzonitrile (**2 L**) (0.096 g, 0.73 mmol) and cyanuric chloride (0.135 mmol, 10 mol %) in acetonitrile (2 mL). Purification by crystallization in ethanol

dx.doi.org/10.1021/jo2020856 | *J. Org. Chem.* 2012, 77, 929−937

afforded **3l** as a light yellow solid. Yield: 148 mg (81%). Mp: >250 °C (lit.[78] 350−351 °C). ^{1}H NMR (DMSO-d_6, 300 MHz): δ 8.43 (s, 1H, NH), 7.87 (d, J = 8.1 Hz, 2H), 7.67−7.59 (m, 3H), 7.28 (t, J = 7.4 Hz, 1H), 6.77 (d, J = 8.0 Hz, 2H), 6.71 (t, J = 7.4 Hz, 1H), 5.84 (s, 1H). ^{13}C NMR (DMSO-d_6, 75 MHz): δ 168.9, 152.2, 151.9, 138.4, 137.1, 137.0, 133.6, 132.7, 132.5, 123.3, 122.6, 119.9, 119.6, 116.6, 71.1. IR (KBr): 3286, 3178, 3056, 1651, 1613 cm^{-1}. Mass: 249.00. HRMS (ESI): calcd for [$C_{15}H_{11}N_3O$ + H$^+$] 250.0975, found 250.0973.

2-(Naphthalen-2′-yl)-2,3-dihydroquinazolin-4(1*H*)-one (3m). The title compound was prepared according to general procedure 1 using anthranilamide (**1**) (0.1 g, 0.73 mmol), 2-naphthylbenzaldehyde (**2 m**) (0.11 g, 0.73 mmol) and cyanuric chloride (0.135 mmol, 10 mol %) in acetonitrile (2 mL). Purification by crystallization in ethanol afforded **3m** as a white solid. Yield: 153 mg (76%). Mp: 172−174 °C. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.58 (s, 1H), 8.05−7.76 (m, 5H), 7.55−7.51 (m, 3H), 7.29 (t, J = 6.9 Hz 1H), 6.81−6.68 (m, 3H), 6.51 (s, 1H). ^{13}C NMR ($CDCl_3$ + CD_3OD, 75 MHz): δ 169.9, 153.4, 139.4, 139.3, 138.8, 135.6, 134.6, 133.6, 132.8, 132.1, 131.4, 130.0, 129.2, 122.8, 120.0, 71.6. IR (KBr): 3381, 3126, 3017, 1653, 1616 cm^{-1}. Mass: 274.00. HRMS (ESI): calcd for [$C_{18}H_{14}N_2O$ + H$^+$] 275.1179, found 275.1183.

2-(Pyridin-3′-yl)-2,3-dihydroquinazolin-4(1*H*)-one (3n). The title compound was prepared according to general procedure 1 using anthranilamide (**1**) (0.1 g, 0.73 mmol), pyridine-3-carboxaldehyde (**2n**) (0.069 mL, 0.73 mmol) and cyanuric chloride (0.135 mmol, 10 mol %) in acetonitrile (2 mL). Purification by column chromatography (chloroform/methanol, 9.9:0.1) afforded **3n** as a white solid. Yield: 140 mg (84%). Mp: 190−192 °C (lit.[39] 187−188 °C). ^{1}H NMR ($CDCl_3$, 200 MHz): δ 8.62 (s, 1H), 8.54−8.51 (m, 1H), 7.99−7.93 (m, 1H), 7.80 (dd, J_1 = 7.8 Hz, J_2 = 1.4 Hz, 1H), 7.38−7.22 (m, 2H), 6.84 (t, J = 7.8 Hz, 1H), 6.67 (d, J = 8.0 Hz, 1H), 5.87 (s, 1H). ^{13}C NMR ($CDCl_3$ + CD_3OD, 75 MHz): δ 169.6, 153.6, 151.9, 151.5, 143.0, 140.3, 139.6, 138.2, 131.8, 128.0, 122.8, 118.5, 117.7, 69.7. IR (KBr): 3326, 3264, 3068, 1659, 1613 cm^{-1}. Mass: 225.00. HRMS (ESI): calcd for [$C_{13}H_{11}N_3O$ + H$^+$] 226.0975, found 226.0972.

2,3-Diphenyl-2,3-dihydroquinazolin-4(1*H*)-one (3o). The title compound was prepared according to general procedure 1 using 2-amino-*N*-phenylbenzamide (0.1 g, 0.47 mmol), benzaldehyde (**2a**) (0.045 mL, 0.44 mmol) and cyanuric chloride (0.048 mmol, 10 mol %) in acetonitrile (2 mL). Purification by column chromatography (chloroform/methanol, 9.9:0.1) afforded **3o** as a white solid. Yield: 109 mg (77%). Mp: 212−214 °C (lit.[39] 214−215 °C). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.04 (d, J = 7.8 Hz, 1H), 7.38−7.19 (m, 11H), 6.92 (t, J = 7.5 Hz, 1H), 6.65 (d, J = 7.8 Hz, 1H), 6.11 (s, 1H), 4.88 (bs, 1H, NH). ^{13}C NMR ($CDCl_3$ + CD_3OD, 75 MHz): δ 165.6, 147.8, 142.1, 141.6, 135.8, 130.6, 130.5, 130.2, 128.7, 128.4, 120.5, 117.5, 116.5, 76.2. IR (KBr): 3327, 3261, 3063, 1649, 1610 cm^{-1}. Mass: 300.00. HRMS (ESI): calcd for [$C_{20}H_{16}N_2O$ + H$^+$] 301.1335, found 301.1333.

3-Benzyl-2-phenyl-2,3-dihydroquinazolin-4(1*H*)-one (3p). The title compound was prepared according to general procedure 1 using 2-amino-*N*-benzylbenzamide (0.1 g, 0.44 mmol), benzaldehyde (**2a**) (0.045 mL, 0.44 mmol) and cyanuric chloride (0.044 mmol, 10 mol %) in acetonitrile (2 mL). Purification by crystallization in ethanol afforded **3p** as a white solid. Yield: 101 mg (73%). Mp: 125−127 °C. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.96 (dd, J_1 = 7.8 Hz, J_2 = 1.2 Hz, 1H), 7.25−7.13 (m, 11H), 6.80 (t, J = 7.2 Hz, 1H), 6.44 (d, J = 8.1 Hz, 1H), 5.54−5.49 (m, 2H), 4.41 (bs, 1H, NH), 3.62 (d, J = 15.3 Hz, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 163.3, 145.2, 139.4, 136.7, 133.6, 129.2, 128.9, 128.7, 128.6, 127.9, 127.4, 126.5, 119.0, 115.5, 114.3, 71.0, 46.9. IR (KBr): 3322, 3263, 3067, 1658, 1613 cm^{-1}. Mass: 314.00. HRMS (ESI): calcd for [$C_{21}H_{18}N_2O$ + H$^+$] 315.1492, found 315.1481.

3-Phenethyl-2-phenyl-2,3-dihydroquinazolin-4(1*H*)-one (3q). The title compound was prepared according to general procedure 1 using 2-amino-*N*-phenethylbenzamide (0.1 g, 0.41 mmol), benzaldehyde (**2a**) (0.045 mL, 0.44 mmol) and cyanuric chloride (0.041 mmol, 10 mol %) in acetonitrile (2 mL). Purification by column chromatography (chloroform/methanol, 9.9:0.1) afforded **3q** as a white solid. Yield: 119 mg (87%). Mp: 145−147 °C. ^{1}H NMR ($CDCl_3$, 200 MHz): δ 8.04 (d, J_1 = 7.8 Hz, J_2 = 1.2 Hz, 1H), 7.39−7.12 (m, 11H), 6.94 (t, J = 6.7 Hz, 1H), 6.59 (d, J = 8.0 Hz, 1H), 5.59 (s, 1H), 4.44 (bs, 1H, NH), 4.16−4.06 (m, 1H), 3.13−2.75 (m, 3H). ^{13}C NMR ($CDCl_3$, 50 MHz): δ 163.3, 145.3, 139.6, 139.2, 133.5, 129.5, 129.3, 129.0, 128.9, 128.5, 126.9, 126.4, 119.3, 114.4, 73.0, 47.0, 34.2. IR (KBr): 3473, 3299, 3019, 1628, cm^{-1}. Mass: 328.00. HRMS (ESI): calcd for [$C_{22}H_{20}N_2O$ + H$^+$] 329.1648, found 329.1652.

2-Phenyl-3-((tetrahydrofuran-2-yl)methyl)-2,3-dihydroquinazolin-4(1*H*)-one (3r). The title compound was prepared according to general procedure 1 using of 2-amino-*N*-(tetrahydrofuran-2-ylmethyl)benzamide (0.1 g, 0.46 mmol), benzaldehyde (**2a**) (0.045 mL, 0.44 mmol) and cyanuric chloride (0.046 mmol, 10 mol %) in acetonitrile (2 mL). Purification by column chromatography (chloroform/methanol, 9.9:0.1) afforded **3r** as a white solid. Yield: 91 mg (65%). Mp: >250 °C. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.97 (d, J = 6.8 Hz, 1H), 7.32−7.20 (m, 6H), 6.85 (t, J = 7.3 Hz, 1H), 6.53 (d, J = 7.8 Hz, 1H), 6.06 (s, 1H), 4.69 (bs, 1H, NH), 4.35−4.26 (m, 1H), 4.11−4.10 (m, 1H), 3.98−3.91 (m, 1H), 3.83−3.71 (m, 1H), 3.06 (dd, J_1 = 3.6 Hz, J_2 = 3.6 Hz, 1H), 2.03−1.79 (m, 4H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 163.8, 145.1, 140.0, 133.4, 128.9, 128.8, 128.5, 126.5, 126.3, 119.1, 116.2, 114.5, 72.3, 68.3, 46.3, 28.3, 26.1. IR (KBr): 3475, 3297, 3019, 1628, 1037 cm^{-1}. Mass: 308.00. HRMS (ESI): calcd for [$C_{19}H_{20}N_2O_2$ + H$^+$] 309.1598, found 309.1584.

3-(2,4-Difluorophenyl)-2-phenyl-2,3-dihydroquinazolin-4(1*H*)-one (3s). The title compound was prepared according to general procedure 1 using of 2-amino-*N*-(3,4-difluorophenyl)-benzamide (0.1 g, 0.40 mmol), benzaldehyde (**2a**) (0.045 mL, 0.44 mmol) and cyanuric chloride (0.040 mmol, 10 mol %) in acetonitrile (2 mL). Purification by column chromatography (chloroform/methanol, 9.9:0.1) afforded **3s** as a white solid. Yield: 100 mg (75%). Mp: 210−212 °C. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.04 (d, J = 7.5 Hz, 1H), 7.44−7.28 (m, 6H), 7.04−6.92 (m, 2H), 6.79−6.69 (m, 3H), 6.18 (s, 1H), 4.65 (bs, 1H, NH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 163.6, 146.5, 137.8, 134.1, 129.7, 129.3, 128.6, 127.7, 119.7, 115.8, 114.5, 111.4, 104.5, 104.1, 74.78. IR (KBr): 3414, 3311, 3074, 1635, 1098 cm^{-1}. Mass: 336.00. HRMS (ESI): calcd for [$C_{20}H_{14}F_2N_2O$ + H$^+$] 337.1147, found 337.1146.

3-(2-Chloro-4-fluorophenyl)-2-phenyl-2,3-dihydroquinazolin-4(1*H*)-one (3t). The title compound was prepared according to general procedure 1 using 2-amino-*N*-(2-chloro-4-fluorophenyl)-benzamide (0.1 g, 0.37 mmol), benzaldehyde (**2a**) (0.045 mL, 0.44 mmol) and cyanuric chloride (0.037 mmol, 10 mol %) in acetonitrile (2 mL). Purification by column chromatography (chloroform/methanol, 9.9:0.1) afforded **3t** as a white solid. Yield: 89 mg (67%). Mp: 220−222 °C. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.02 (d, J = 7.8 Hz, 1H), 7.37−7.24 (m, 7H), 7.02−7.00 (m, 2H), 6.94 (t, J = 7.5 Hz, 1H), 6.67 (d, J = 7.8, 1H), 6.07 (s, 1H), 4.78 (bs, 1H, NH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 163.5, 158.2, 145.6, 138.8, 136.7, 134.3, 129.8, 129.5, 129.0, 128.9, 127.4, 127.2, 126.9, 119.6, 116.7, 116.4, 116.0, 114.8, 74.9. IR (KBr): 3410, 3309, 3064, 1629, 1087 cm^{-1}. Mass: 352.00. HRMS (ESI): calcd for [$C_{20}H_{14}ClFN_2O$ + H$^+$] 353.0851, found 353.0850.

2-Phenyl-3-(3-(trifluoromethyl)phenyl)-2,3-dihydroquinazolin-4(1*H*)-one (3u). The title compound was prepared according to general procedure 1 using 2-amino-*N*-(3-(trifluoromethyl)phenyl)-benzamide (0.1 g, 0.35 mmol), benzaldehyde (**2a**) (0.045 mL, 0.44 mmol) and cyanuric chloride (0.035 mmol, 10 mol %) in acetonitrile (2 mL). Purification by column chromatography (chloroform/methanol, 9.9:0.1) afforded **3u** as a white solid. Yield: 92 mg (70%). Mp: 140−142 °C. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.85 (d, J = 7.3 Hz, 1H), 7.64 (s, 1H), 7.35−7.33 (m, 2H), 7.24−7.20 (m, 3H), 6.90 (d, J = 8.5 Hz, 2H), 6.75−6.68 (m, 2H), 6.55 (d, J = 8.5 Hz, 2H), 6.00 (s, 1H), 4.20 (bs, 1H, NH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 163.2, 145.5, 140.8, 138.9, 134.2, 130.5, 129.3, 129.1, 128.8, 126.9, 124.1, 123.4, 119.8, 114.9, 74.7. IR (KBr): 3300, 3029, 3019, 1616, 1127 cm^{-1}. Mass: 368.00. HRMS (ESI): calcd for [$C_{21}H_{15}F_3N_2O$ + H$^+$] 369.1209, found 369.1196.

3-(4-Aminophenyl)-2-phenyl-2,3-dihydroquinazolin-4(1*H*)-one (3v). The title compound was prepared according to general procedure 1 using 2-amino-*N*-(4-aminophenyl)benzamide (0.1 g, 0.44 mmol), benzaldehyde (**2a**) (0.045 mL, 0.44 mmol) and cyanuric

dx.doi.org/10.1021/jo2020856 | J. Org. Chem. 2012, 77, 929−937

chloride (0.044 mmol, 10 mol %) in acetonitrile (2 mL). Purification by column chromatography (hexane/ethyl acetate, 7.5:2.5) afforded **3v** as a white solid. Yield: 116 mg (84%). Mp: >250 °C. ^{1}H NMR (DMSO-d_6, 300 MHz): δ 7.70 (d, J = 7.3 Hz, 1H), 7.43 (bs, 1H, NH), 7.35−7.21 (m, 6H), 6.86 (d, J = 8.5 Hz, 1H), 6.72 (m, 2H), 6.47 (d, J = 8.5 Hz, 2H), 6.06 (s, 1H), 5.05 (bs, 2H, NH). ^{13}C NMR (DMSO-d_6, 75 MHz): δ 162.6, 147.5, 147.0, 141.5, 133.8, 129.7, 128.7, 128.6, 128.3, 127.0, 117.7, 115.9, 114.9, 114.0, 73.8. IR (KBr): 3384, 3286, 3047, 1620, 1159. Mass: 315.00. HRMS (ESI): calcd for [$C_{20}H_{17}N_3O$ + H^+] 316.1444, found 316.1455.

4-(4-Oxo-1,2,3,4-tetrahydroquinazolin-2-yl)benzaldehyde (3w). The title compound was prepared according to general procedure 1 using anthranilamide (**1**) (0.1 g, 0.73 mmol), terephthalaldehyde (**2o**) (0.098 g, 0.73 mmol) and cyanuric chloride (0.135 mmol, 10 mol %) in acetonitrile (2 mL). Purification by column chromatography (chloroform/methanol, 9.85: 0.15) afforded **3w** as a white solid. Yield: 115 mg (60%). Mp: 185−187 °C. ^{1}H NMR ($CDCl_3$ + DMSO-d_6 300 MHz): δ 9.95 (s, 1H), 7.85−7.67 (m, 5H), 7.38 (s, 1H), 7.24−7.19 (m, 2H), 6.75−6.67 (m, 2H), 5.87 (s, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 193.2, 163.8, 148.7, 147.9, 136.6, 133.9, 130.0, 127.9, 117.8, 115.3, 114.9, 66.3. IR (KBr): 3296, 3190, 3070, 1656, 1606 cm^{-1}. Mass: 252.08. HRMS (ESI): calcd for [$C_{15}H_{12}N_2O_2$ + H^+] 253.0972, found 253.0965.

2-Ferrocenyl-2,3-dihydroquinazolin-4(1*H*)-one (3x). The title compound was prepared according to general procedure 1 using anthranilamide (**1**) (0.1 g, 0.73 mmol), ferrocenecarboxaldehyde (**2p**) (0.16 g, 0.74 mmol) and cyanuric chloride (0.135 mmol, 10 mol %) in acetonitrile (2 mL). Purification by crystallization in ethanol afforded **3x** as a white solid. Yield: 180 mg (74%). Mp: 240−242 °C. ^{1}H NMR ($CDCl_3$, 200 MHz): δ 7.89 (d, J = 7.7 Hz, 1H), 7.29−7.18 (m, 2H), 6.85 (t, J = 7.7 Hz, 1H), 6.61 (d, J = 8.0 Hz, 1H), 6.01 (bs, 1H, NH), 5.53 (s, 1H),, 4.38−4.20 (m, 10H). ^{13}C NMR (DMSO-d_6, 75 MHz): δ 163.7, 147.8, 133.6, 127.6, 117.3, 115.6, 114.8, 90.9, 69.1, 67.9, 66.6, 66.4, 63.4. IR (KBr): 3489, 3399, 3251, 1640, 1024 cm^{-1}. Mass: 332.00. HRMS (ESI): calcd for [$C_{18}H_{16}FeN_2O$ + H^+] 333.0685, found 333.0705.

General Procedure 2: General Method for the Synthesis of Spiroquinazolinones (5, 7). Cyanuric chloride (0.135 mmol, 10 mol %) was added to a solution of anthranilamide (**1**) (0.73 mmol) and appropriate cyclic ketone (1 equiv) in acetonitrile (2 mL). The mixture was stirred at room temperature for the specified period of time as indicated in Schemes 2 and 3. The progress of the reaction was monitored by TLC. After completion, solvent was evaporated at reduced pressure and solid was washed with water. The corresponding solid products were obtained through column chromatography by using 100−200 mesh silica gels.

1′*H*-Spiro [cyclohexane-1,2′-quinazolin]-4′(3′*H*)-one (5). The title compound was prepared according to general procedure 2 using anthranilamide (**1**) (0.1 g, 0.73 mmol), cyclohexanone (**4**) (0.076 mL, 0.73 mmol) and cyanuric chloride (0.135 mmol, 10 mol %) in acetonitrile (2 mL). Purification by column chromatography (chloroform/methanol, 9.5:0.05) afforded **5** as a white solid. Yield: 143 mg (90%). Mp: 217−219 °C (lit.[79] 217−219 °C). ^{1}H NMR ($CDCl_3$, 200 MHz): δ 7.89 (dd, J_1 = 7.8 Hz, J_2 = 1.2 Hz, 1H), 7.33−7.28 (m, 1H), 6.84 (t, J = 7.5 Hz, 1H), 6.67 (d, J = 7.8 Hz, 1H), 6.43 (s, 1H, NH), 4.40 (s, 1H, NH), 1.84 (bs, 4H), 1.68−1.47 (m, 6H). ^{13}C NMR ($CDCl_3$+CD_3OD, 75 MHz): δ 167.0, 148.0, 136.2, 130.3, 120.7, 117.0, 70.5, 39.7, 26.8, 24.0. IR (KBr): 3362, 3179, 3016, 1647, 1618 cm^{-1}. Mass: 216.00. HRMS (ESI): calcd for [$C_{13}H_{16}N_2O$ + H^+] 217.1335, found 217.1326.

Ethyl 4′-Oxo-3′,4′-dihydro-1′*H*-spiro[piperidine-4,2′-quinazoline]-1-carboxylate (7). The title compound was prepared according to general procedure 2 using anthranilamide (**1**) (0.1 g, 0.73 mmol), ethyl 4-oxopiperidine-1-carboxylate (**6**) and cyanuric chloride (0.135 mmol, 10 mol %) in acetonitrile (2 mL). Purification by column chromatography (chloroform/methanol, 9.85:0.15) afforded **7** as a white solid. Yield: 150 mg (70%). Mp: 188−190 °C (lit.[80] 224−225 °C). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.88 (d, J = 7.5 Hz, 1H), 7.34−7.26 (m, 2H), 6.88 (t, J = 7.2 Hz 1H), 6.69 (d, J = 8.1 Hz, 1H), 4.33 (s, 1H, NH), 4.20 (q, J = 6.6 Hz, 1H), 3.62 (bs, 4H), 2.03−1.82 (m, 4H), 1.28 (t, J = 6.9 Hz, 3H). ^{13}C NMR ($CDCl_3$ + CD_3OD, 50 MHz): δ 155.5, 145.5, 134.2, 128.1, 119.0, 115.2, 66.7, 61.7, 39.5, 36.8, 29.6, 14.5. IR (KBr): 3359, 3202, 3064, 1657, 1618 cm^{-1}. Mass: 289.00. HRMS (ESI): calcd for [$C_{15}H_{19}N_3O_3$ + H^+] 290.1499, found 290.1482.

2′,3′,4′,6′-Tetra *O*-acetyl 4-formylphenyl-*O*-β-D-galactopyranoside (9b). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 9.93 (s, 1H), 7.87 (d, J = 8.5 Hz, 2H), 7.13 (d, J = 8.5 Hz, 2H), 5.52−5.47 (m, 2H), 5.18−5.16 (m, 2H), 4.23−4.12 (m, 3H), 2.19 (s, 3H), 2.15 (s, 6H), 2.02 (s, 3H). ^{13}C NMR ($CDCl_3$, 50 MHz): δ 190.6, 170.2, 170.1, 170.0, 169.2, 161.2, 131.8, 116.7, 98.5, 71.3, 70.6, 68.4, 66.7, 61.3, 20.6, 20.5, 20. Mass: 452.00.

General Procedure 3: Synthesis of Glycoconjugates of Quinazolinone (10a, 10b). Cyanuric chloride (0.004 g, 0.022 mmol, 10 mol %) was added to a solution of desired aryl *O*-glycosidic aldehydes[81] (0.1 g, 0.22 mmol) and anthranilamide (**1**) (0.03 g, 0.22 mmol) in acetonitrile (2 mL). The mixture was stirred at room temperature for the specified period of time as indicated in Scheme 4. The progress of the reaction was monitored by TLC. After completion, solvent was evaporated at reduced pressure, and solid products were purified through column chromatography by using 100−200 mesh silica gel and recrystallized from ethanol. Synthesized glycoconjugates were well characterized using 2D NMR experiments as HMBC, COSY, and HSQC.

2-[4′(2″,3″,4″,6″-Tetra-*O*-acetyl-β-D-glucopyranosyloxy)-1′-phenyl]-2,3 dihydroquinazoline-4(1*H*)-one (10a). The title compound was prepared according to general procedure 3 using 2′,3′,4′,6′-tetra-*O*-acetyl-4-formylphenyl-*O*-β-D-glucopyranoside (0.1 g, 0.22 mmol), anthralinamide (**1**) (0.03 g, 0.22 mmol) and cyanuric chloride (0.004 g, 0.022 mmol, 10 mol %) in acetonitrile. Purification by column chromatography (chloroform/methanol, 9.9: 0.1) afforded **10a** as a white solid. Yield: 85 mg (68%). Mp: 118−120 °C. ^{1}H NMR (DMSO-d_6, 300 MHz): δ 8.23 (s, 1H, NH), 7.61 (d, J = 7.0 Hz, 1H), 7.45 (d, J = 8.2 Hz, 2H), 7.26 (t, J = 7.2 Hz, 1H), 7.04−6.98 (m, 2H, 1NH), 6.74−6.64 (m, 2H), 5.71 (s, 1H), 5.54 (d, J = 7.9 Hz, 1H), 5.42 (t, J = 9.6 Hz, 1H), 5.07−4.96 (m, 2H), 4.24−4.17 (m, 2H), 4.07−4.04 (m, 1H), 2.00−1.96 (m, 12H). ^{13}C NMR (DMSO-d_6, 75 MHz): δ 170.4, 170.0, 169.7, 169.5, 164.1, 159.6, 148.3, 136.5, 133.7, 128.7, 127.8, 117.6, 116.6, 115.4, 114.8, 97.5, 72.4, 71.2, 71.1, 68.5, 66.4, 62.0, 20.9, 20.8, 20.7. IR (KBr): 3374, 2928, 1756, 1654, 1227, 1047 cm$^{-1;}$ Mass: 570.00. HRMS (ESI): calcd for [$C_{28}H_{30}N_2O_{11}$ + H^+] 571.1923, found 571.1926.

2-[4′(6″,4″,3″,2″-Tetra-*O*-acetyl-β-D-galactopyranosyloxy)-1′ phenyl]-2,3 dihydroquinazoline-4(1*H*)-one (10b). The title compound was prepared according to general procedure 3 using 2′,3′,4′,6′-tetra-*O*-acetyl 4-formylphenyl-*O*-β-D-galactopyranoside (0.1 g, 0.22 mmol), anthralinamide (**1**) (0.03 g, 0.22 mmol) and cyanuric chloride (0.004 g, 0.022 mmol, 10 mol %) in acetonitrile. Purification by column chromatography (chloroform/methanol, 9.9:0.1) afforded **10b** as white solid. Yield: 90 mg (72%). Mp: 158−160 °C. ^{1}H NMR (DMSO-d_6, 300 MHz): δ 8.19 (bs, 1H, NH), 7.62 (dd, J_1 = 7.6 Hz, J_2 = 1.2 Hz,1H), 7.46 (d, J = 8.6 Hz, 2H), 7.26 (t, J = 8.2 Hz, 1H), 7.01 (d, J = 8.6 Hz, 2H), 6.74−6.65 (m, 2H), 5.72 (s, 1H), 5.46 (d, J = 7.5 Hz, 1H), 5.37−5.17 (m, 3H,1NH), 4.44 (t, J = 6.0 Hz, 1H), 4.13−4.08 (m, 2H), 2.16−1.94 (m, 12H). ^{13}C NMR (DMSO-d_6,75 MHz): δ 175.1, 175.0, 174.7, 174.4, 168.8, 161.7, 153.1, 141.1,138.4, 134.8, 133.5, 132.5, 122.3, 121.3, 120.2, 119.6, 102.9, 75.5, 75.3, 73.5, 72.4, 71.2, 66.2, 25.7, 25.6, 25.6, 25.5. IR (KBr): 3372, 2926, 1753, 1659, 1231, 1043 cm^{-1}. Mass: 570.00. HRMS (ESI): calcd for [$C_{28}H_{30}N_2O_{11}$ + H^+] 571.1923, found 571.1928.

■ ASSOCIATED CONTENT

Supporting Information

Copies of ^{1}H and ^{13}C NMR spectra of selected compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

dx.doi.org/10.1021/jo2020856 | J. Org. Chem. 2012, 77, 929−937

AUTHOR INFORMATION

Corresponding Author

*Tel: +91 522 2612411. Fax: +91 522 2623405. E-mail: prem_chauhan_2000@yahoo.com; premsc58@hotmail.com.

ACKNOWLEDGMENTS

M.S. and S.P. thank ICMR and UGC for providing financial support for the work. We also thank SAIF division of the CDRI for providing all analytical data. CDRI communication no. is 8179.

REFERENCES

(1) Hour, M. J.; Huang, L. J.; Kuo, S. C.; Xia, Y.; Bastow, K.; Nakanishi, Y.; Hamel, E.; Lee, K. H. *J. Med. Chem.* **2000**, *43*, 4479−4487.

(2) Birch, H. L.; Buckley, G. M.; Davies, N.; Dyke, H. J.; Frost, E. J.; Gilbert, P. J.; Hannah, D. R.; Haughan, A. F.; Madigan, M. J.; Morgan, T.; Pitt, W. R.; Ratcliffe, A. J.; Ray, N. C.; Richard, M. D.; Sharpe, A.; Taylor, A. J.; Whitworth, J. M.; Williams, S. C. *Bioorg. Med. Chem. Lett.* **2005**, *15*, 5335−5339.

(3) Bonola, G.; Da, R. P.; Magistretti, M. J.; Massarani, E.; Setnikar, I. *J. Med. Chem.* **1968**, *11*, 1136−1139.

(4) Rexall Drug Co., U.S. Patent 3257397, 1966 .

(5) Okumura, K.; Oine, T.; Yamada, Y.; Hayashi, G.; Nakama, M. *J. Med. Chem.* **1968**, *11*, 348−351.

(6) Cohen, E.; Klarberg, B.; Vaughan, J. R. *J. Am. Chem. Soc.* **1959**, *81*, 5508−5509.

(7) Alagarsamy, V.; Solomon, V. R.; Murugan, M. *Bioorg. Med. Chem.* **2007**, *15*, 4009−4015.

(8) Levin, J. I.; Chan, P. I.; Bailey, T.; Katocs, A. S.; Venkatesan, A. M. *Bioorg. Med. Chem. Lett.* **1994**, *4*, 1141−1146.

(9) Instituto De Angeli S.p.A. French Patent M 1893, 1963.

(10) Shulton Inc. U.S. Patent 3265697, 1966.

(11) Hirose, N.; Kuriyama, S.; Sohda, S.; Sakaguchi, K.; Yamamoto, H. *Chem. Pharm. Bull.* **1973**, *21*, 1005−1013.

(12) Mustazza, C.; Borioni, A.; Sestili, I.; Sbraccia, M.; Rodomonte, A.; Ferretti, R.; Giudice, M. R. D. *Chem. Pharm. Bull.* **2006**, *54*, 611−622.

(13) Schramm, S.; Schmitz, E.; Grundemann, E. *J. Prakt. Chem.* **1984**, *326*, 279.

(14) Michael, J. P. *Nat. Prod. Rep.* **2008**, *25*, 166−187.

(15) Alagarsamy, V.; Solomon, V. R.; Dhanabal, K. *Bioorg. Med. Chem.* **2007**, *15*, 235−241.

(16) Imagawa, J.; Sakai, K. *Eur. J. Pharmacol.* **1986**, *131*, 257−264.

(17) Dempcy, R. Q.; Skibo, E. B. *Biochemistry* **1991**, *30*, 8480−8487.

(18) Gackenheimer, S. L.; J. Schaus, J. M.; Gehlert, D. R. *J. Pharmacol. Exp. Ther.* **1995**, *274*, 1558−1565.

(19) Mannschreck, A.; Koller, H.; Stuhler, G.; Davies, M. A.; Traber, J. *Eur. J. Med. Chem.* **1984**, *19*, 381.

(20) Molamas, M. S.; Miller, J. *J. Med. Chem.* **1991**, *34*, 1492−1503.

(21) Gruner, S. A. W.; Locardi, E.; Lohof, E.; Kessler, H. *Chem. Rev.* **2002**, *102*, 491−514.

(22) Varki, A. *Glycobiology* **1993**, *3*, 97−130.

(23) Dwek, R. A. *Chem. Rev.* **1996**, *96*, 683−720.

(24) Sears, P.; Wong, C. H. *Cell. Mol. Life Sci.* **1998**, *54*, 223−252.

(25) Petersen, L.; Jensen, K. J. *J. Org. Chem.* **2001**, *66*, 6268−6275.

(26) McKay, M. J.; Naab, B. D.; Mercer, G. J.; Nguyen, H. M. *J. Org. Chem.* **2009**, *74*, 4705−4711.

(27) Meng, W.; Ellsworth, B. A.; Nirschl, A. A.; Mccann, P. J.; Patel, M.; Girotra, R. N.; Wu, G.; Sher, P. M.; et al. *J. Med. Chem.* **2008**, *51*, 1145−1149.

(28) Tietze, L. F.; Schuster, H. J.; Krewer, B.; Schuberth, I. *J. Med. Chem.* **2009**, *52*, 537−543.

(29) Zhao, H.; Donnelly, A. C.; Kusuma, B. R.; Brandt, G. E. L.; Brown, D.; Rajewski, R. A.; Vielhauer, G.; Holzbeierlein, J.; Cohen, M. S.; Blagg, B. S. J. *J. Med. Chem.* **2011**, *54*, 3839−3853.

(30) Wilkinson, B. L.; Bornaghi, L. F.; Houston, T. A.; Innocenti, A.; Vullo, D.; Supuran, C. T.; Poulsen, S. A. *J. Med. Chem.* **2007**, *50*, 1651−1657.

(31) Baghbanzadeh, M.; Salehi, P.; Dabiri, M.; Kozehgarya, G. *Synthesis* **2006**, *2*, 344−348.

(32) Su, W. K.; Yang, B. B. *Aust. J. Chem.* **2002**, *55*, 695.

(33) Dabiri, M.; Salehi, P.; Baghbanzadeh, M.; Zolfigol, M. A.; Agheb, M.; Heydari, S. *Catal. Commun.* **2008**, *9*, 785−788.

(34) Dabiri, M.; Salehi, P.; Otokesh, S.; Baghbanzadeh, M.; Kozehgarya, G.; Mohammadi, A. A. *Tetrahedron Lett.* **2005**, *46*, 6123−6126.

(35) Khurana, J. M.; Kukreja, G. *J. Heterocycl. Chem.* **2003**, *40*, 677−679.

(36) Yoo, C. L.; Fettinger, J. C.; Kurth, M. J. *J. Org. Chem.* **2005**, *70*, 6941−6943.

(37) Shi, D. Q.; Rong, L. C.; Wang, J. X.; Zhuang, Q. Y.; Wang, X. S.; Hu, H. W. *Tetrahedron Lett.* **2003**, *44*, 3199−3201.

(38) Chen, J.; Su, W.; Wu, H.; Liu, M.; Jin, C. *Green Chem.* **2007**, *9*, 972−975.

(39) Chen, J.; Wu, D.; He, F.; Liu, M.; Wua, H.; Ding, J.; Su, W. *Tetrahedron Lett.* **2008**, *49*, 3814−3818.

(40) Reza, S. H.; Reza, O. A. *Chin. J. Chem.* **2009**, *27*, 2418−2422.

(41) Li, F.; Feng, Y.; Meng, Q.; Li, W.; Li, Z.; Wang, Q.; Tao, F. *Arkivoc* **2007**, *i*, 40−50.

(42) Miklos, F.; Bagi, T. A.; Fulopa, F. *Arkivoc* **2009**, *iii*, 5−12.

(43) Zhang, Z. H.; Lu, H. Y.; Yang, S. H.; Gao, J. W. *J. Comb. Chem.* **2010**, *12*, 643−646.

(44) Wang, X. S.; Yang, K.; Zhou, J.; Tu, S. J. *J. Comb. Chem.* **2010**, *12*, 417−421.

(45) Agarwal, A.; Srivastava, K.; Puri, S. K.; Chauhan, P. M. S. *Bioorg. Med. Chem. Lett.* **2005**, *15*, 531−533.

(46) Kumar, A.; Srivastava, K.; Kumar, S. R.; Puri, S. K.; Chauhan, P. M. S. *Bioorg. Med. Chem. Lett.* **2009**, *19*, 6996−6999.

(47) Sunduru, N.; Sharma, M.; Srivastava, K.; Kumar, S. R.; Puri, S. K.; Saxena, J. K.; Chauhan, P. M. S. *Bioorg. Med. Chem.* **2009**, *17*, 6451−6462.

(48) Katiyar, S. B.; Srivastava, K.; Puri, S. K.; Chauhan, P. M. S. *Bioorg. Med. Chem. Lett.* **2005**, *15*, 4957−4960.

(49) Sunduru, N.; Nishi, Palne, S.; Chauhan, P. M. S.; Gupta, S. *Eur. J. Med. Chem.* **2009**, *44*, 2473−2481.

(50) Kumar, A.; Srivastava, K.; Kumar, S. R.; Puri, S. K.; Chauhan, P. M. S. *Bioorg. Med. Chem. Lett.* **2008**, *18*, 6530−6533.

(51) Luca, L. D.; Giacomelli, G.; Porcheddu, A. *Org. Lett.* **2002**, *4*, 553−555.

(52) Luo, G.; Xu, L.; Poindexter, G. S. *Tetrahedron Lett.* **2002**, *43*, 8909−8912.

(53) Rayle, H. L.; Fellmeth, L. *Org. Process Res. Dev.* **1999**, *3*, 172−176.

(54) Masala, S.; Tadei, M. *Org. Lett.* **1999**, *1*, 1355−1357.

(55) Bandgar, B. P.; Pandit, S. S. *Tetrahedron Lett.* **2002**, *43*, 3413−3414.

(56) Blotny, G. *Tetrahedron Lett.* **2003**, *44*, 1499−1501.

(57) Bandgar, B. P.; Joshi, N. S.; Kamble, V. T. *Tetrahedron Lett.* **2006**, *47*, 4775−4777.

(58) Forbes, D. C.; Barrett, E. J.; Lewis, D. L.; Smith, M. C. *Tetrahedron Lett.* **2000**, *41*, 9943−9947.

(59) Das, B.; Laxminarayana, K.; Ravikanth, B.; Ramarao, B. *Tetrahedron Lett.* **2006**, *47*, 9103−9106.

(60) Falorni, M.; Porcheddu, A.; Taddei, M. *Tetrahedron Lett.* **1999**, *40*, 4395−4396.

(61) Luca, L. D.; Giacomelli, G.; Porcheddu, A. *J. Org. Chem.* **2002**, *67*, 6272−6274.

(62) Luca, L. D.; Giacomelli, G.; Porcheddu, A. *J. Org. Chem.* **2002**, *67*, 5152−5155.

(63) Luca, L. D.; Giacomelli, G.; Porcheddu, A. *J. Org. Chem.* **2001**, *66*, 7907−7909.

(64) Bigdelia, M. A.; Heravib, M. M.; Mahdavinia, G. H. *Catal. Commun.* **2007**, *8*, 1595−1598.

(65) Bandgar, B. P.; More, P. E.; Kamble, V. T. *J. Chinese Chem. Soc.* **2008**, *55*, 947−951.
(66) Chang, C. W.; Chang, S. S.; Chao, C. S.; Mong, K. K. T. *Tetrahedron Lett.* **2009**, *50*, 4536−4540.
(67) Yale, H. L. *J. Heterocycl. Chem.* **1977**, *14*, 1357−1359.
(68) Ghosh, S.; Tochtrop, G. P. *Tetrahedron Lett.* **2009**, *50*, 1723−1726.
(69) Baghbanzadeh, M.; Salehi, P.; Dabiri, M.; Kozehgary, G. *Synthesis* **2006**, *2*, 0344−0348.
(70) Talancon, D.; Bosque, R.; Lopez, C. *J. Org. Chem.* **2010**, *75*, 3294−3300.
(71) Biot, C.; Daher, W.; Ndiaye, C. M.; Melnyk, P.; Pradines, B.; Chavain, N.; Pellet, A.; Fraisse, L.; Pelinski, L.; Jarry, C.; Brocard, X. J.; Khalife, J.; Bares, I. F.; Dive, D. *J. Med. Chem.* **2006**, *49*, 4707−4714.
(72) Dubar, F.; Anquetin, G.; Pradines, B.; Dive, D.; Khalife, J.; Biot, C. *J. Med. Chem.* **2009**, *52*, 7954−7957.
(73) Bellot, F.; Cosledan, F.; Vendier, L.; Brocard, J.; Meunier, B.; Robert, A. *J. Med. Chem.* **2010**, *53*, 4103−4109.
(74) Rodriguez, E. C.; Winans, K. A.; King, D. S.; Bertozzi, C. R. *J. Am. Chem. Soc.* **1997**, *119*, 9905−9906.
(75) Cai, G.; Xu, X.; Li, Z.; Weber, W. P.; Lu, P. *J. Heterocycl. Chem.* **2003**, *39*, 1271−1272.
(76) Hour, M.; Huang, L.; Kuo, S.; Xia, Y.; Bastow, K.; Nakanishi, Y.; Hamel, E.; Lee, K. *J. Med. Chem.* **2000**, *43*, 4479−4487.
(77) Wang, X. S.; Yang, K.; Zhang, M. M.; Yao, C. S. *Synth. Commun.* **2010**, *40*, 2633−2646.
(78) Rostamizadeh, S.; Amani, A. M.; Aryan, R.; Hamid Reza Ghaieni, H. R.; Shadjou, N. *Synth. Commun.* **2008**, *38*, 3567−3576.
(79) Shi, D. Q.; Shi, C. L.; Wang, J. X.; Rong, L. C.; Zhuang, Q. Y.; Wang, X. S. *J. Heterocycl. Chem.* **2005**, *40*, 173−183.
(80) Wang, X. S.; Yang, K.; Zhou, J.; Tu, S. J. *J. Comb. Chem.* **2010**, *12*, 417−421.
(81) Wen, H.; Lin, C. L.; Que, L.; Ge, H. *Eur. J. Med. Chem.* **2008**, *43*, 166−173. (a) Whistler, R. L.; Wolfrom, M. L. Methods in Carbohydrate Chemistry, vol. II; Academic Press Inc.: New York and London, 1963. (b) Fletcher Jr., H. G.; Hudson, C. S. *J. Am. Chem. Soc.* **1947**, *69*, 921−926. (c) Ness, R. K.; Fletcher Jr., H. G.; Hudson, C. S. *J. Am. Chem. Soc.* **1951**, *73*, 959−964. (d) Oulmi, D.; Maillard., P.; Guerquin-Kern, J. L.; Huel, C.; Momenteau, M. *J. Org. Chem.* **1995**, *60*, 1554−1564. (e) Jyothish, K.; Avirah, R.R.; Ramaiah, D. *Org. Lett.* **2006**, *8*, 111−114.