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PAPER

Introduction of a clean and promising protocol for the synthesis of β-amino-acrylates and 1,4-benzoheterocycles: an emerging innovation†

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A highly efficient, elegant and simple procedure with exceptionally mild conditions has been proposed for the synthesis of β-amino-acrylate derivatives and an array of biologically and pharmaceutically active benzoheterocycles. The protocol offers a valuable alternative to known methods and will find applications in the field of green synthesis. The regio- and stereo-chemistry of the products were established by IR, NMR and single crystal X-ray analysis.

Introduction

Over the last two decades, globalization has been driving the chemistry community to adopt green and environmentally benign syntheses that circumvent the problems of human or ecological toxicity and safety.[1] Various applications of green chemistry have shown that materials can be made friendly to the environment by designing chemical processes in a way that can diminish or obviate the use and production of hazardous substances.[2] Due to the toxic, flammable and expensive nature of organic solvents,[3] special emphasis has been placed towards solvent-free reactions. As a result of the novelty, effectiveness and selectivity of the concept, researchers have been very attentive in rendering their reactions free of solvents to achieve the ultimate goal of waste-free, hazard-free and energy-efficient synthesis.[4]

Heterocycles are of immense chemical and biological interest. Benzoheterocycles, as synthesized in this study, belong to an important class of compounds amid *N*-heterocycles. Due to their wide range of biological,[5] pharmacological[6] and agricultural activity,[7] benzoheterocycles have captured the attention of synthetic organic chemists. For instance, the benzoxazine nucleus, found in rubradirin and rubradirin B antibiotics, represents a unique class of ansamycin-related products.[8] Benzoxazine also shows resistance factors against insects and microbial diseases. Similarly, the quinoxaline framework is present in a variety of biologically active compounds that show anticancer[9] and antiviral activities.[10] Like benzoxazine and quinoxaline derivatives, benzothiazine derivatives exhibit antitumor, antihypertensive, antifungal and immune stimulating activities.[11] These heterocycles are also active on Parkinson's and Alzheimer's diseases.[12] Michael adducts or vinylic amines bearing ester functionalities formed by the 1,4-addition of amines to DMAD or DEAD are valuable intermediates for various important chemical transformations. For example, they can be converted into indoles, bioactive heterocycles under $Pd(OAc)_2$ catalysis[13] and can also be used in the synthesis of quinolone ethers, which enhance monoclonal antibody production in mammalian cell cultures.[14] These are also biologically and pharmaceutically acceptable agents.[15]

Several procedures have been reported in the literature for the synthesis of benzoxazinones that involve the use of triphenylphosphine in toluene,[16] palladium catalysis,[17] CuO nanoparticles as a catalyst[18] and microwave assistance.[19] Recently, benzoheterocycles were also synthesized in water with heating[20] and in PEG as a reaction medium.[21] Traditional syntheses repeatedly involve the use of organic solvents such as methanol or petroleum-based solvents such as toluene. Most syntheses required recrystallization, extraction or chromatographic purification to further isolate or purify the desired product. Some methods also required heating and nearly all required stirring of the reaction components. Encouraged by the excellent performance of our catalyst-free and solvent-free green approach for the synthesis of nitroamines and nitrosulfides,[22] we have carried out the conjugate addition of aliphatic and aromatic amines and thiophenols to acetylenecarboxylates and acetylenedicarboxylates. Herein, we report a facile and clean procedure for the synthesis of β-amino-acrylates, and benzoxazinone, benzothiazinone and quinoxalinone derivatives under catalyst-free and solvent-free conditions.

Results and discussion

Reaction between aliphatic/aromatic amines and acetylenedicarboxylates (DMAD/DEAD)/ acetylenecarboxylates

Initially we focused on the direct synthesis of β-amino-acrylates from aliphatic amines and dialkyl acetylenedicarboxylates or

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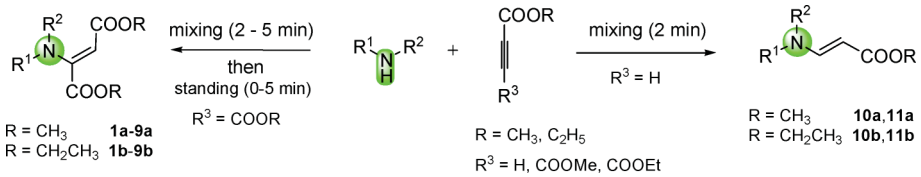
† Electronic supplementary information (ESI) available: Spectral data, table of selected IR and NMR data, copies of ^{1}H NMR (500 MHz), ^{13}C NMR (125 MHz) spectra of all the products, and 2D NMR spectra of **23a** and **23b**. CCDC reference number 827294. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c1gc15701a

Table 1 Reaction between aromatic/aliphatic amines and DMAD/DEAD/methyl propiolate/ethyl propiolate[a,b]



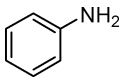
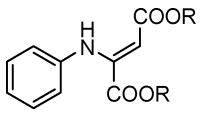
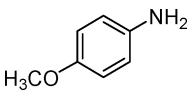
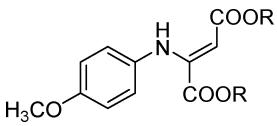
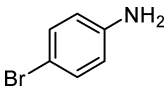
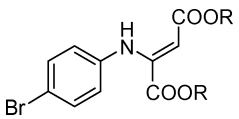
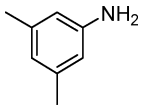
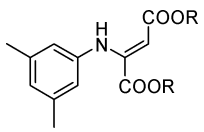
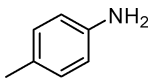
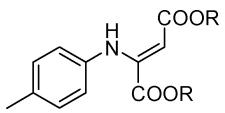
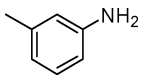
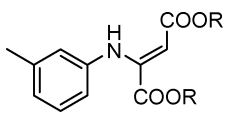
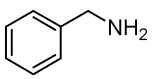
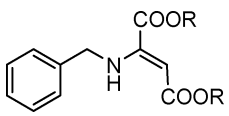
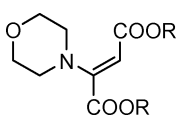
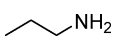
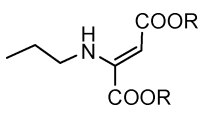
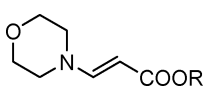
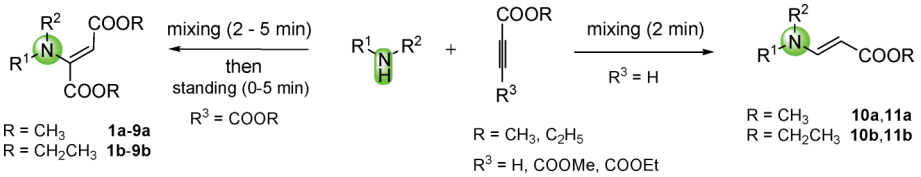
Entry	Amine derivative	R	Reaction time/min	Product		Yield[c] (%)
1		Me	3 + 5		**1a**	98
2		Et	4 + 5		**1b**	97
3		Me	2 + 5		**2a**	99
4		Et	3 + 5		**2b**	99
5		Me	4 + 5		**3a**	98
6		Et	5 + 5		**3b**	97
7		Me	3 + 5		**4a**	100
8		Et	4 + 5		**4b**	100
9		Me	3 + 5		**5a**	100
10		Et	4 + 5		**5b**	100
11		Me	3 + 5		**6a**	100
12		Et	3 + 5		**6b**	100
13		Me	3 + 5		**7a**	98
14		Et	4 + 5		**7b**	97
15		Me	3 + 0		**8a**	100
16		Et	3 + 0		**8b**	100
17		Me	3 + 0		**9a**	100
18		Et	3 + 0		**9b**	100
19		Me	2 + 0		**10a**	100
20		Et	2 + 0		**10b**	100

Table 1 (*Contd.*)



Entry	Amine derivative	R	Reaction time/min	Product	Yield[c] (%)
21		Me	2 + 0	**11a**	100
22		Et	2 + 0	**11b**	100

[a] All reactions were carried out with an equimolar (2 mM) ratio of donor and acceptor. 2.4 mM (1.2 equiv.) of methyl/ethyl propiolate was used in entries 19–22. [b] Mixing of reactants with a spatula in a Petri dish for 2–5 min followed by allowing the mixture to stand for up to 5 min if necessary. [c] Of pure Michael product.

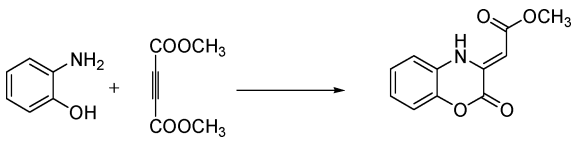
alkyl propiolates. Most of the earlier proposed procedures for the generation of these enamines were carried out in various organic solvents, such as methanol, benzene, dry THF and ether, under reflux conditions.[23] The synthesis of these compounds was reported recently by performing the reaction in water as a solvent[24] However, all of these chemical processes required a long reaction time (hours) along with purification steps. When we mixed equimolar quantities of aniline and DMAD together in a Petri dish for 3 min at room temperature with the help of a spatula, surprisingly, the reaction started immediately after mixing with gentle heat production. The progress of the reaction was monitored by thin layer chromatography and the reaction mixture was allowed to stand for 5 min to obtain product **1a** in quantitative yield. Excited by the above result, a range of β-amino-acrylate derivatives were synthesized by the simple mixing of aromatic and aliphatic amines with DMAD/DEAD or methyl/ethyl propiolate at room temperature; the results are summarized in Table 1. All of the products were obtained in quantitative yield in analytically pure form without any further purification. Of the possible two diastereomeric forms, *E* and *Z*, only *Z*-isomers were obtained in the reactions between aromatic/aliphatic amines and DMAD/DEAD (Table 1, entries 1–18). The reactions of alkyl propiolates with aliphatic amines provided *E*-isomers (Table 1, entries 19–22). While, the reactions of aniline derivatives required a standing time of 5 min after mixing, the reactions of aliphatic amines such as morpholine, piperidine and n-propylamine were very quick and reached completion within 2 to 3 min of mixing and required no standing time. When we extended this solvent-free and catalyst-free protocol to the reaction between 4-chloroaniline and DEAD, a mixture of *E*- and *Z*-diastereomers were formed in a ratio of 19 : 81, respectively (not shown in the table), in quantitative yield.

Reaction between 2-aminophenols/2-aminophenylamines and DMAD or DEAD

After successfully performing the Michael addition of different amines with DMAD/DEAD under solvent-free and catalyst-free conditions, we extended this protocol to *o*-aminophenols. The mixing of equimolar quantities of fine powdered 2-aminophenol and DMAD was carried out in a similar way in a Petri dish with the help of a spatula. The reaction proceeded with melting of the 2-aminophenol followed by immediate solidification. Within 4 min, a perfectly yellow colour solid, **12a**, of melting point 166–168 °C was obtained. In this case, no standing was required. In order to further examine the effect of the solvent and the regiochemistry of the product, we carried out the reaction in different solvents such as methanol, acetonitrile, THF, toluene, dichloromethane and even in water (Table 2). It was found that the product was obtained with the same regiochemistry; however, some variation of the chemical yield was observed. Later, we investigated the scope of the reaction with a variety of *o*-aminophenols and related systems by simply mixing them with DMAD/DEAD under the same reaction conditions to furnish the corresponding benzoheterocycles. In all the cases, the products were obtained in quantitative yield with spectroscopic purity without any purification steps such as column chromatography or recrystallization (Table 3).

The data reported in Table 3 show that the procedure worked well with *o*-aminophenols bearing a variety of substituents. The effect of substitution on the 2-aminophenol was examined, and it was found that the nature of the substituent gave only minor variations in the rate of the reaction. For instance, on going from chloro to alkyl substituents (**13/14/17/18** to **15/16**), the reaction time increases from 2 to 5 min at room temperature. The aza-benzoxazinone derivatives **19a** and **19b** were also synthesized based on this protocol. At this juncture, the reaction of *o*-phenylenediamine was performed with DMAD. Once again, the reaction took place spontaneously, and within 1 min of mixing it generated a yellow-colored solid product, **20a**, which decomposed at 227 °C. Similarly, clean product **20b** was formed in a quantitative yield from the reaction between *o*-phenylenediamine and DEAD. The 4-bromo derivative of *o*-phenylenediamine provided quinoxalinone derivatives **21a** and **21b** as a mixture of regioisomers in each case. *dl*-Cyclohexane-1,2-diamine reacted under these conditions to provide the corresponding heterocycles **22a** and **22b**.

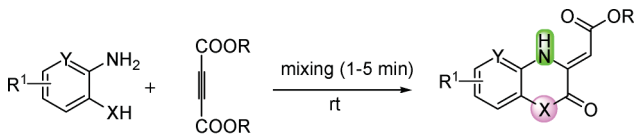
Table 2 Effect of solvents on the reaction of *o*-aminophenol with dimethyl acetylenedicarboxylate[a]



Entry	Solvent	Time/min	Yield (%)[b]	Entry	Solvent	Time/min	Yield (%)[b]
1	MeOH	5	63	6	Acetone	5	54
2	MeCN	5	60	7	Toluene	5	31
3	THF	5	45	8	CH_2Cl_2	5	47
4	Dioxane	5	37	9	Water	5	62
5	Diethyl ether	5	41	10	—	5	99[c]

[a] All reactions were performed for 5 min at room temperature. The solid obtained from the reactions in MeOH and water was purified either by washing with cold MeOH (entry 1) or by recrystallization (entry 9). In all other cases (except entry 10), the reaction mixture was concentrated and subjected to silica gel column chromatography (90 : 10 hexanes/EtOAc). [b] Of pure and isolated product. [c] The reaction was performed under solvent-free conditions and no purification methods were applied.

Table 3 Reaction between *o*-aminophenols/*o*-phenylenediamines and DMAD/DEAD[a]



X = O, NH
Y = CH, N

R = CH_3, C_2H_5

12a,b–21a,b

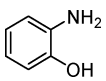
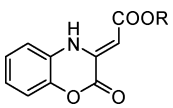
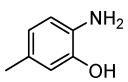
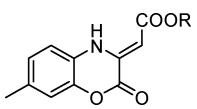
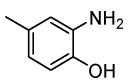
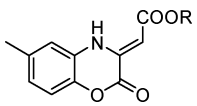
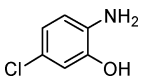
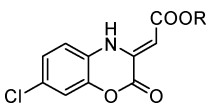
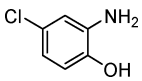
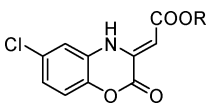
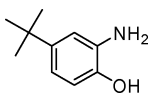
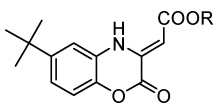
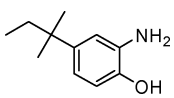
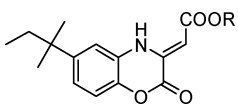
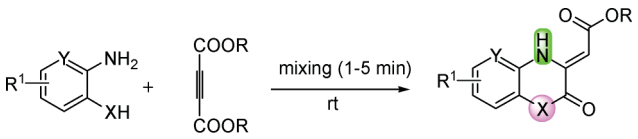
Entry	Amine derivative	R	Reaction time/min	Product		Yield[b] (%)
1		Me	4		**12a**	100
2		Et	5		**12b**	100
3		Me	2		**13a**	100
4		Et	3		**13b**	100
5		Me	2		**14a**	100
6		Et	3		**14b**	100
7		Me	4		**15a**	98
8		Et	5		**15b**	99
9		Me	4		**16a**	100
10		Et	5		**16b**	99
11		Me	2		**17a**	100
12		Et	3		**17b**	100
13		Me	2		**18a**	100
14		Et	3		**18b**	100

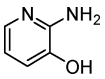
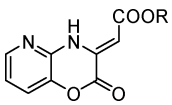
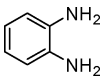
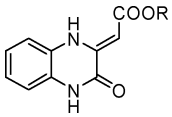
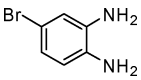
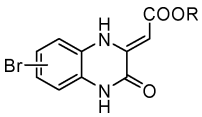
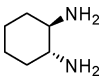
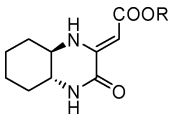
Table 3 (*Contd.*)



X = O, NH
Y = CH, N

R = CH_3, C_2H_5

12a,b–21a,b

Entry	Amine derivative	R	Reaction time/min	Product		Yield[b] (%)
15		Me	4		**19a**	98
16		Et	5		**19b**	97
17		Me	1		**20a**	100
18		Et	2		**20b**	100
19		Me	3		**21a**	100[c]
20		Et	4		**21b**	100[c]
21		Me	1		**22a**	98[d]
22		Et	2		**22b**	97[d]

[a] All reactions were carried out with an equimolar (2 mM) ratio of donor and acceptor by mixing the reactants with a spatula in a Petri dish for 1–5 min. [b] Of pure product. [c] Combined yield of regioisomers. [d] Pure product was obtained after washing with a few drops of methanol.

Reaction between 2-aminothiophenols and DMAD or DEAD

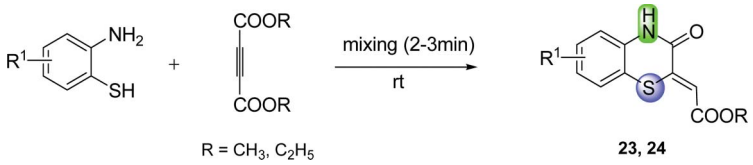
Encouraged by the results obtained from the reaction of dialkyl acetylenedicarboxylates with 2-aminophenol and *o*-phenylenediamine, we then investigated the reaction of 2-aminothiophenol with DMAD/DEAD. When 2-aminothiophenol (liquid) was mixed with DMAD (liquid) at room temperature, within minutes yellow coloured solids, **23a/23b**, were obtained in 97% yield. The chloro derivative of 2-aminothiophenol also reacted smoothly with the acetylene derivatives to afford benzothiazinone derivatives **24a** and **24b** (Table 4).

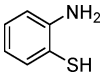
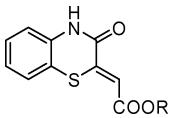
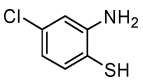
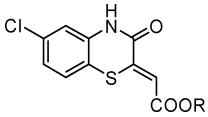
Structure elucidation

The assigned structures of the products are based on spectroscopic evidence, such as IR, ^{1}H NMR (500 MHz), ^{13}C NMR (125 MHz) and MS data. The presence of signals for two methyl/ethyl groups in the ^{1}H NMR spectra of compounds **1a,b–9a,b** indicates the two ester functionalities in each product derived from DMAD/DEAD. The olefinic C=C bond of products **1a,b–7a,b**, derived from anilines, absorbs in the range 1591–1617 cm^{-1}, whereas the ester carbonyls absorb at 1662–1681 and 1734–1742 cm^{-1}. The absorption of the β-carbonyl at a low frequency is due to hydrogen bonding between the carbonyl oxygen and the hydrogen atom connected to the nitrogen atom, confirming the *Z*-stereochemistry of the double bond. A similar trend is also present for products **7a,b** and **9a,b**, derived from benzylamine and propylamine, respectively. The absence of hydrogen bonding is clearly visible in products **8a,b**, **10a,b** and **11a,b**, derived from morpholine and piperidine, where the β-carbonyl absorbs in the range 1692–1699 cm^{-1}. The vinylic proton of compounds **1a,b** and **3a,b**, derived from aniline and 4-bromoaniline, resonates in the range δ 5.39–5.45 in ^{1}H NMR spectra. The major *Z*-isomer and the minor *E*-isomer of the Michael adduct derived from 4-chloroaniline resonate at δ 5.44 and 5.31, respectively. Substitutions, such as methoxy or alkyl groups on the arene residue, shifted the vinylic protons of the *Z*-isomers (**2** and **4–6**) upfield into the range δ 5.29–5.36. The vinylic protons on the α-carbon of enamines **10a,b** and **11a,b** resonate in the range δ 7.35–7.39. Selected spectroscopic data of some of the products are shown in Fig. 1 (for a table of selected data of coupling constants of the vinylic protons, and absorption frequencies of the vinylic C=C and carbonyl bonds, see the ESI†).

There is ambiguity in previous literature reports regarding the regiochemistry of the products derived from 2-aminophenols and 2-aminothiophenols in reactions with DMAD/DEAD (Fig. 2). Some reports present structures **A** as the products from 2-aminophenol and DMAD/DEAD, where an initial attack of nitrogen takes place on the sp carbon of the electrophile, followed by ring closure through the attack of the phenolic oxygen on the α-carbonyl carbon; others report its regioisomer,

Table 4 Reaction between *o*-aminothiophenols and DMAD/DEAD[a]



Entry	*o*-Aminothiophenol	R	Reaction time/min	Product		Yield[b] (%)
1		Me	2		**23a**	97
2		Et	2		**23b**	97
3		Me	3		**24a**	97
4		Et	3		**24b**	96

[a] All reactions were carried out with an equimolar (2 mM) ratio of donor and acceptor by mixing the reactants with a spatula in a Petri dish for 2–3 min. [b] Of pure product obtained after washing with a few drops of methanol.

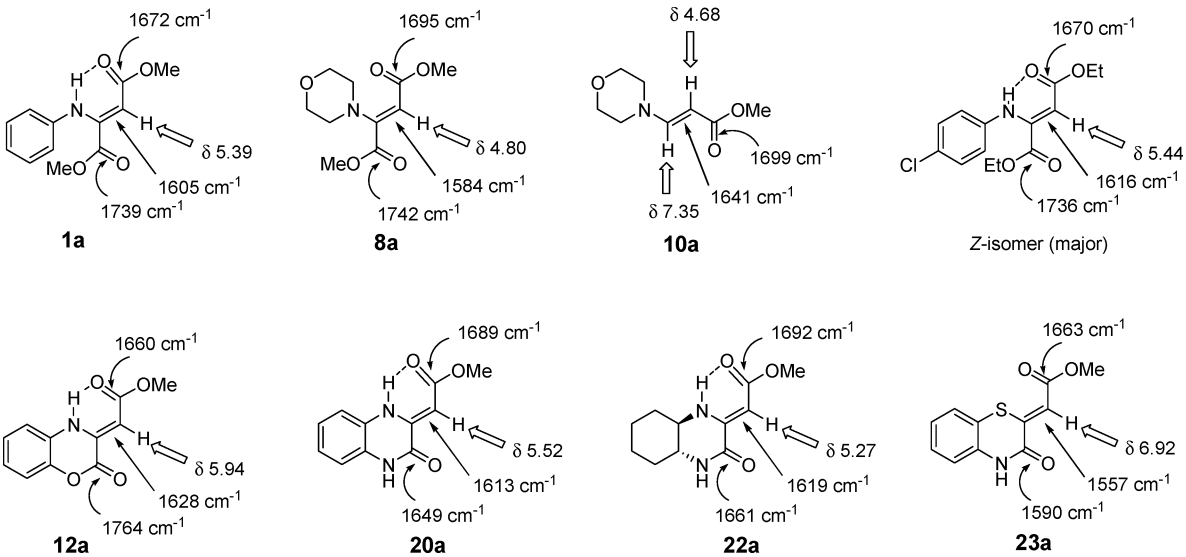


Fig. 1 Absorption frequencies (ν in cm^{-1}) of the vinylic C=C and carbonyl bonds, and chemical shifts (δ in ppm) of the vinylic protons of selected products.

C. Structure **B** was reported for the products from the reaction between 2-aminothiophenols and DMAD/DEAD, where the initial attack of sulfur takes place on the *sp* carbon of the acetylene derivative, followed by ring closure through the attack of the nitrogen of the amino functionality on the α-carbonyl carbon; other reports present regioisomeric structure **D**.

Benzoxazinone can exist in two tautomeric forms, **A** and **E** (Fig. 3). It has been reported that in acidic media, both the enamine and imine forms are equilibrated.[25] The tautomeric equilibrium is strongly affected by the solvent; it shifts from structure **A** towards structure **E** from $CDCl_3$ to trifluoroacetic acid (TFA). Such a shift can be easily followed by NMR (Fig. 4). For instance, the ^{1}H NMR spectrum of compound **12a**, when measured in TFA, shows evidence of both methylene at δ 4.23 and methine at δ 6.00 proton signals. Broadening of the CH signal is observed in TFA due to rapid exchange of the methine and methylene protons, and the methine signal disappeared in CF_3COOD due to deuteration of the methine proton (see the ESI†). Whereas, in the NMR spectra of **12a** and other benzoxazinone derivatives recorded in $CDCl_3$, there is no evidence of methylene protons; a lower field proton signal, δ 5.94, shows the existence of **A** as the only tautomer of **12a** in $CDCl_3$ with an *exo* double bond and intramolecular hydrogen bonding between the NH and the oxygen atom of the ester carbonyl. This was further confirmed by a marked lower frequency shift, 1660 cm^{-1}, in the carbonyl band when compared to normal α,β-unsaturated ester carbonyls at ~1700 cm^{-1} and a broad maximum at 3464 cm^{-1} corresponding to the N–H bond stretching frequency in the IR spectrum of compound **12a**.

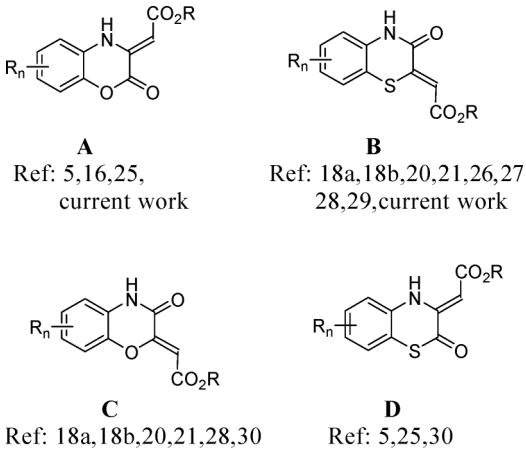


Fig. 2 Regioisomeric structures of 1,4-benzoxazinones and 1,4-benzothiazinones.

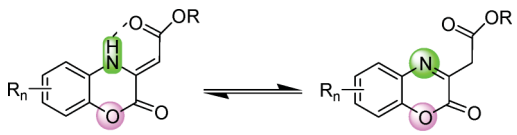


Fig. 3 Structures **A** and **E** of 1,4-benzoxazinones, representing enamine–imine tautomerism.

Furthermore, the assigned structure of benzoxazinone **17b** in the solid state was also confirmed by single crystal X-ray analysis (Fig. 5).† Thus, the spectroscopic data, including NMR experiments and crystallographic analysis, of compound **17b** unambiguously confirm the assigned structures of these benzoxazinone derivatives.

In benzothiazinone derivatives **23** and **24**, the absorption frequencies of the ester carbonyl bond are in the range 1663–1670 cm^{-1}, whereas those of the ring carbonyl are in the range 1583–1590 cm^{-1} and the C=C bond absorbs in the range 1557–1563 cm^{-1}. Due to its greater size, the sulfur shows a lower tendency for lone pair conjugation in heteroatom-substituted vinylic compounds in comparison with oxygen or nitrogen atoms which are smaller in size. The simultaneous presence of

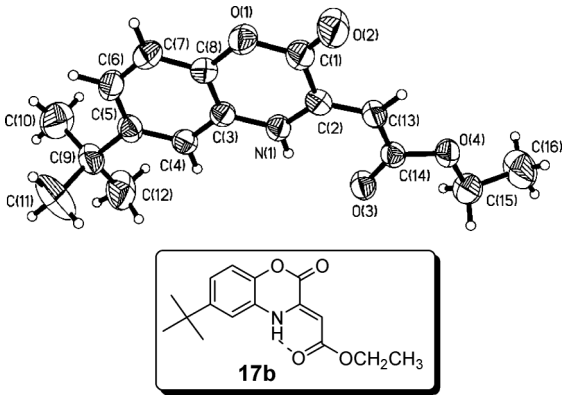


Fig. 5 The X-ray crystal structure of compound **17b**.

donor (p,π-conjugation) and acceptor (on account of vacant orbitals) properties in the sulfur atom partially cancel each other out. This effect of sulfur is clearly visible in the NMR spectra of these compounds. The vinylic CH of these heterocyclic compounds resonates in the region δ 6.89–6.92 in ^{1}H NMR spectra and at around δ 114 ppm in ^{13}C NMR spectra. A singlet of the methine hydrogen appearing at δ 6.93 in the ^{1}H NMR spectrum of product **23a** (Fig. 6) indicates that the cyclic compound could have either structure **B** or **D** (Fig. 7). A careful analysis of the crude material by ^{1}H NMR and ^{13}C NMR spectroscopy revealed that mixing 2-aminothiophenol with DMAD generates **B** as the only product, which was further supported by the NMR spectra acquired in TFA and high-field two-dimensional NMR spectroscopy HMBC (proton-detected multiple bond coherence) experiments discussed below. No sign of enamine–imine tautomerization was seen when a ^{1}H NMR spectrum was recorded in TFA. Both spectra obtained in TFA and DMSO-d_6 look similar, except for a slight shift of the chemical shifts due to the solvent effect. This points out the absence of a C=C bond adjacent to the NH group, which is required to switch the hydrogen between the imine and enamine tautomers. This clearly indicates the correct structure as being regioisomer **B**.

With the help of HSQC two-dimensional NMR experiments, peak assignments for benzothiazinone compound **23a** were carried out (ESI†). The HMBC analysis, a two-dimensional

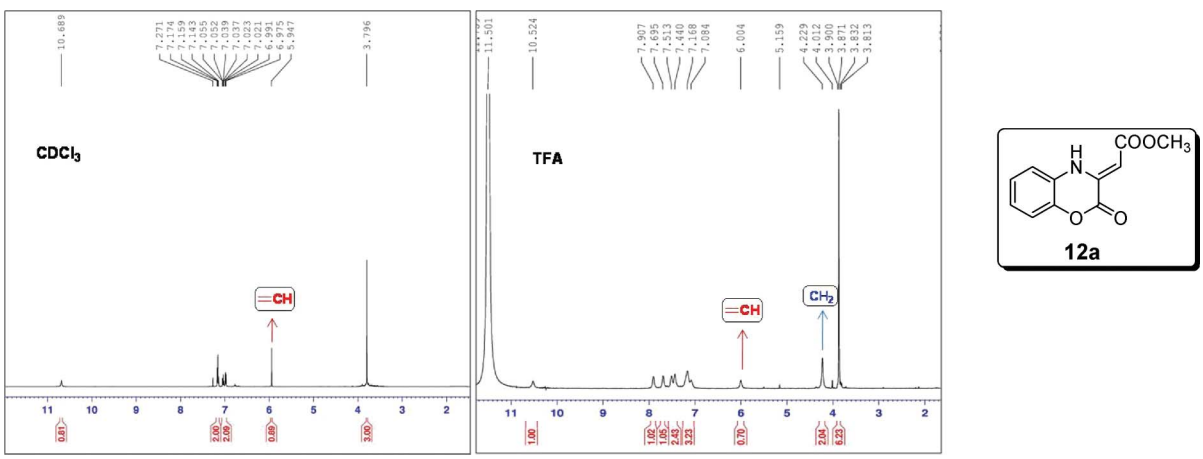


Fig. 4 ^{1}H NMR spectra of compound **12a** in $CDCl_3$ and CF_3COOH (TFA).

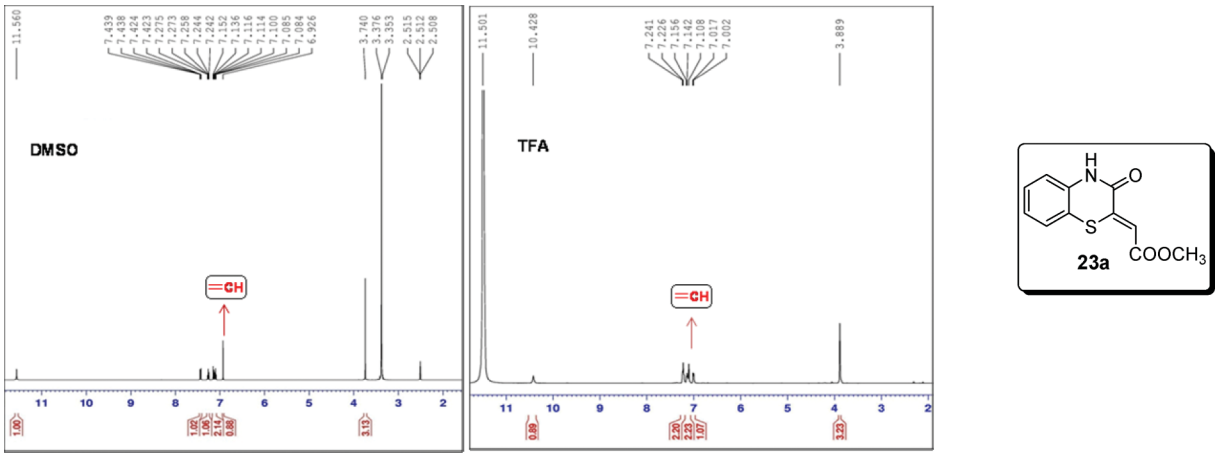


Fig. 6 ^{1}H NMR spectra of compound **23a** recorded in DMSO-d_6 and TFA.

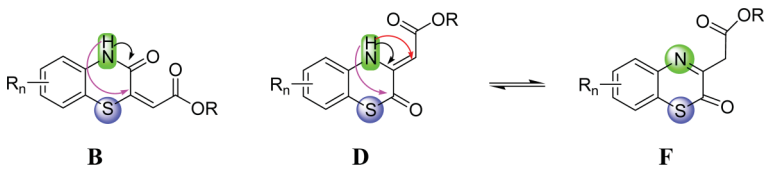
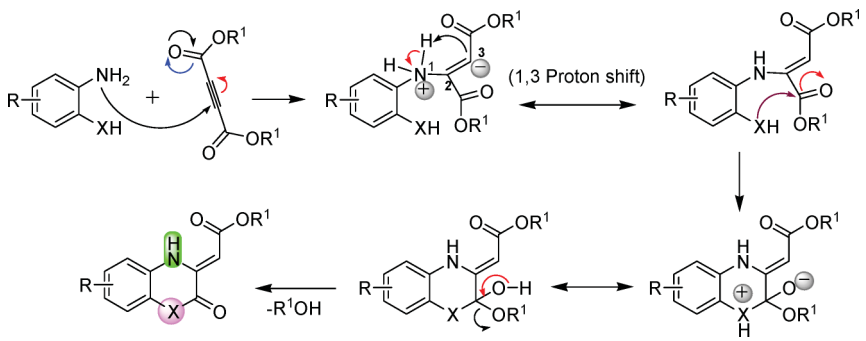


Fig. 7 Structures of 1,4-benzothiazines **B**, and enamine–imine tautomers **D** and **F**.



Scheme 1 Proposed mechanistic approach for the synthesis of benzoxazinones (X = O) and quinoxalinones (X = NH).

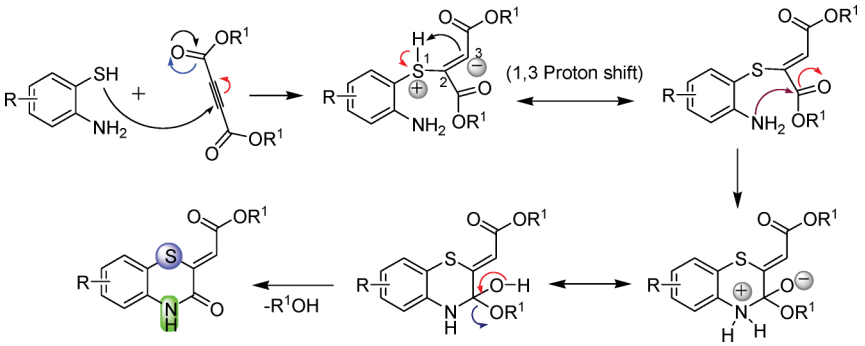
NMR experiment, provided diagnostic proton–carbon correlations over multiple bonds, which were found to be extremely helpful for confirming the structure of the product. Fig. 7 shows a two-bond H(N)–(C═O) and a three-bond H(N)–C–(C═CH) correlation in structure **B**. Meanwhile, structure **D** holds an extra three-bond H(N)–C–(C═CH) correlation, along with a two-bond H(N)–C and a three-bond H(N)–C(C═O) correlation. The HMBC spectrum of product **23b** (ESI†), obtained by the reaction of 2-aminothiophenol with DEAD, shows peaks for a two-bond H(N)–C and a three-bond H(N)–C correlation, and no peak was found for a H(N)–CH correlation, which reveals that the structure of the product is identical to that of **B**. On the basis of the above spectroscopic analysis, the structure of the product was assigned as **B**.

Herein, we propose the following mechanism for the formation of the title heterocyclic compounds. The reaction between 2-aminophenol and dialkyl acetylenedicarboxylate commences with an initial attack of nitrogen on the *sp* carbon of the electrophile, followed by the ring closure through attack of the phenolic oxygen on the α-carbonyl carbon, leading to the formation of benzoxazinone derivatives (Scheme 1).

For the formation of benzothiazinone products from the reaction between 2-aminothiophenols and DMAD/DEAD, the initial attack of sulfur takes place on the *sp* carbon of the acetylene derivative, followed by ring closure through attack of the nitrogen of the amino functionality on the α-carbonyl carbon (Scheme 2).

Conclusion

In conclusion, we have established a fast, cleaner, safer, energy efficient and environmentally sustainable approach by carrying out all our reactions at exceptionally mild reaction conditions such as, ambient temperature and pressure, open to air, solvent-free, catalyst-free and without using any external energy (heat source) which produces high purity products with excellent to quantitative yields. By means of this new methodology a number of β-amino-acrylate derivatives and benzoheterocycles were



Scheme 2 Proposed mechanistic approach for the generation of benzothiazinones.

synthesized under the tenet of "green technologies" by eliminating the use of highly volatile and hazardous conventional organic solvents, and purification steps such as column chromatography or crystallization. We have eradicated the ambiguity over the structures of the products generated by the reaction of 2-aminophenols and 2-aminothiophenols with DMAD/DEAD. The structures were unambiguously determined by the analytical tools such as IR, 1D and 2D NMR, GC-MS and X-ray crystallographic analysis.

Experimental

We were not involved in any incidents while carrying out these reactions on the scale chosen. However, as the Michael addition of the substrate combinations presented herein are exothermic, slow addition of the Michael acceptor DMAD/DEAD is recommended.

Reaction between amines and dialkyl acetylenedicarboxylates/alykl propriolates

The solid reactants were powdered to fine particles prior to their reaction. Amine (2 mmol) was taken in a pre-weighed Petri dish, and dialkyl acetylenedicarboxylate (2 mmol) was then added slowly with thorough mixing for 2–5 min with the help of a spatula to form a homogeneous paste. Then, the reaction mixture was allowed to stand (if required) at room temperature for 5 min to obtain the product in quantitative yield. In the cases of the more volatile amines, 1.2 equiv. of amine was used (Table 1, entries 15–22). The progress of the reaction was monitored by TLC.

Reaction between aminophenols/aminothiophenols/diamines and dialkyl acetylenedicarboxylates

The aminophenol/aminothiophenol/diamine (2 mmol) was taken in a pre-weighed Petri dish, dialkyl acetylenedicarboxylate (2 mmol) was then added slowly with thorough mixing for 1–5 min with the help of a spatula to form a homogeneous paste. The reaction was complete within minutes and afforded a solid product. The thus obtained products were either opened to the air or transferred to a round-bottomed flask and vacuum was applied to remove the traces of MeOH/EtOH formed during the reaction. Products **22–24** were obtained in analytically pure form after washing the reaction mixture with a few drops of methanol. All the products were solids and no standing was required. The progress of the reaction was monitored by TLC.

Acknowledgements

We are indebted to Professor V. R. Pedireddi, Indian Institute of Technology, Bhubaneswar for carrying out the X-ray crystal analysis. We thank MHRD (Scheme B) for financial assistance. G. C. thanks CSIR, New Delhi for a research fellowship.

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