



Cite this: *RSC Adv.*, 2021, 11, 24466

Catalyst-free synthesis of novel 1,5-benzodiazepines and 3,4-dihydroquinoxalines using isocyanide-based one-pot, three- and four-component reactions†

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Reaction of benzimidazolone derivatives, or their thio- or aza-counterparts, with an isocyanide in the presence of acetone unexpectedly gave rise to novel tricyclic benzodiazepine derivatives in good yield by means of a four-component reaction incorporating two moles of acetone. Benzimidazole starting substrates bearing an electron-withdrawing group gave rise instead to dihydroquinoxaline derivatives by means of a three-component reaction. Use of deuterated acetone instead of acetone in the reactions significantly affected yield and reactivity in the four-component reaction but not in the three-component reaction.

Received 8th June 2021

Accepted 7th July 2021

DOI: 10.1039/d1ra04444c

rsc.li/rsc-advances

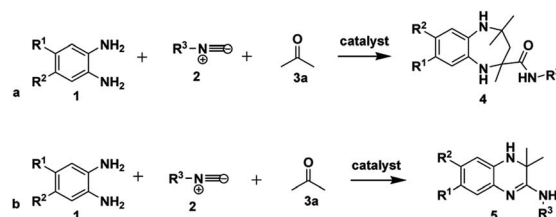
Introduction

One of the vital goals in modern synthetic chemistry approaches is adhering to the practice of green and sustainable chemistry by championing environmentally safe and atom-efficient, economical chemical processes.¹ Recently, there has been increased interest from academia and industry in the use of multicomponent reactions (MCRs) as a result of their potential contribution to sustainable chemistry.² MCRs also continue to attract attention in synthetic chemistry due to their ability to generate diversity and structural complexity in a single step.³ MCRs possess multiple advantages compared to conventional linear-step syntheses, for example: by reducing reaction times, using commercially accessible and cheaper reagents, their high atom economy and their easy-to-use, green experimental methods where the use of hazardous solvents and catalysts can be avoided. This results in both economic and environmental benefits.^{4–8}

One of the benefits of the isocyanide functional group in MCRs is its unique reactivity; thus isocyanide-based MCRs (IMCRs) are considered amongst the most versatile MCRs to generate diversity and structural complexity.^{9–11} The use of isocyanides for the synthesis of nitrogen-containing heterocyclic compounds such as benzodiazepines^{12–14} and quinoxalines^{15–18}

is well exploited. For example, the reaction of *o*-phenylenediamine **1** and isocyanide **2** in the presence of two equivalents of acetone **3a** using ammonium chloride as a catalyst was reported to give benzodiazepine-2-carboxamides **4** as shown in Scheme 1a.¹⁹ It was also reported that the reaction of *o*-phenylenediamine **1** and isocyanide **2** in the presence of one equivalent of acetone **3a**, using *p*-TsOH as a catalyst and ethanol as a solvent at room temperature gave rise to 3,4-dihydroquinoxalin-2-amines **5** (Scheme 1b).¹⁸

Benzodiazepines and quinoxaline are accessible, easy to functionalise and have a wide range of potential pharmacological applications. For example, benzodiazepines have been found to have antimicrobial and anthelmintic²⁰ activity. They also have antitumour²¹ activity and can act as calcium channel blockers,²² anti-HIV²³ agents and also have cytotoxic²⁴ properties. On the other hand quinoxalines show pharmacological properties such as antibiotic,²⁵ antimicrobial,²⁶ and antidiabetic²⁷ activity. They have also been shown to be pesticidal²⁸ and to inhibit aldose reductase^{29,30} There are several procedures



Scheme 1 Reported methods for the synthesis of (a) 1,5-benzodiazepine-2-carboxamides **4** and (b) 3,4-dihydroquinoxalin-2-amines **5**.

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† Electronic supplementary information (ESI) available. CCDC 2087921–2087924. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/d1ra04444c



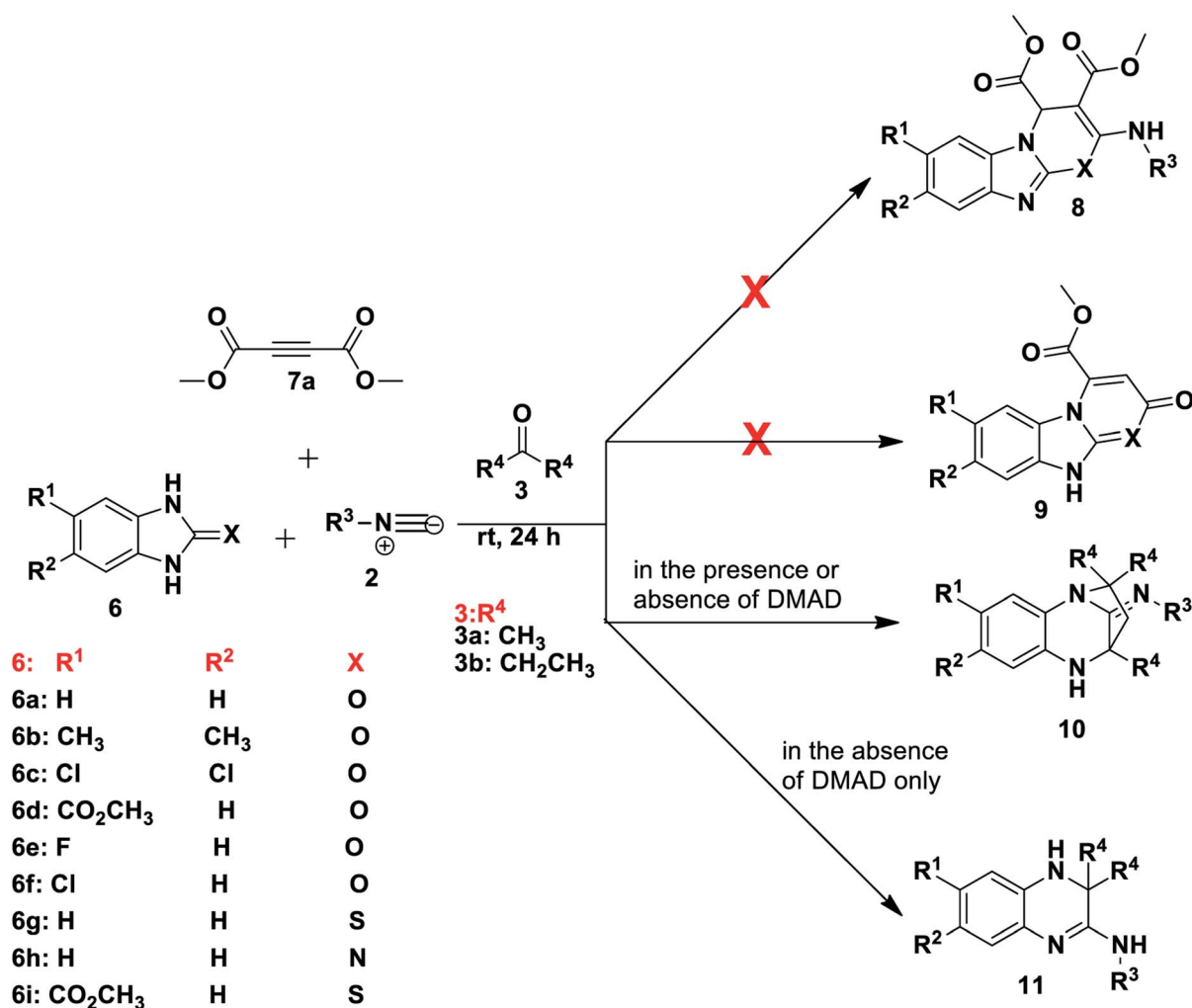
reported for the synthesis of benzodiazepines which mainly include the use of catalysts. The catalysts or stoichiometric reagents employed include zeolites,³¹ $\text{BF}_3 \cdot \text{OEt}_2$,³² $\text{Sc}(\text{OTf})_3$,³³ MgO/POCl_3 ,³⁴ H-MCM-22,³⁵ FeAlP-550,³⁶ $\text{H}_3\text{PMo}_{12}\text{O}_{40}$ and $\text{H}_3\text{PW}_{12}\text{O}_{40}$,³⁷ CH_3COOH ³⁸ and ZrOCl_2 ,³⁹ amongst others. These methods pose drawbacks such as high temperatures, generation of heavy metal waste, hazardous solvents, long reaction times and relatively expensive reagents.

In our ongoing studies on the use of multicomponent reactions for the synthesis of diverse heterocycles⁴⁴ we initiated an investigation of the reaction of benzimidazole derivatives with dimethyl acetylenedicarboxylate (DMAD) and isocyanides and unexpectedly prepared a range of diazepine and quinoxaline derivatives.

Results and discussion

Our investigation began with the reaction of *tert*-butyl isocyanide **2a** ($\text{R}^3 = t\text{-butyl}$), 1*H*-benzo[*d*]imidazol-2(3*H*)-one **6a** and dimethyl acetylenedicarboxylate (DMAD) **7a** in acetone **3a**, as the solvent. We expected to obtain one or both of two likely

products: compound **8**, resulting from a three-component reaction or compound **9**, from a two-component reaction (Scheme 2). This expectation was based on literature precedent as Zeng and co-workers⁴⁰ reacted 1*H*-benzo[*d*]imidazole-2(3*H*)-thione **6g** ($\text{X} = \text{S}$) and DMAD using methanol as solvent to obtain compounds **9**. Adib and co-workers,⁴¹ on the other hand, treated imidazole derivative 4,5-diphenyl-1,3-dihydro-2*H*-imidazol-2-one, with an isocyanide and DMAD **7a** to produce the expected 5*H*-imidazo-[2,1-*b*][1,3]oxazine derivatives using acetone as solvent. Much to our surprise, reaction of benzimidazolone **6a**, isocyanide **2a** and DMAD **7a** in acetone as solvent yielded only compound **10** in racemic form (Scheme 2). The reaction had unexpectedly included the solvent acetone **3a** to form a diazepine-based scaffold, while DMAD **7** did not participate in the reaction. Interestingly, when the reaction was repeated using benzimidazoles **6g** and **6h** containing either nitrogen or sulfur at position *X* these reactions were also able to produce compounds **10** (Scheme 2). Reaction of unsubstituted benzimidazole derivatives ($\text{R}^1, \text{R}^2 = \text{H}$) or those bearing the electron-releasing methyl group ($\text{R}^1, \text{R}^2 = \text{CH}_3$) gave compounds **10** in generally good yields (67–84%) with a range of



Scheme 2 Synthesis of benzodiazepines and dihydroquinoxalines.

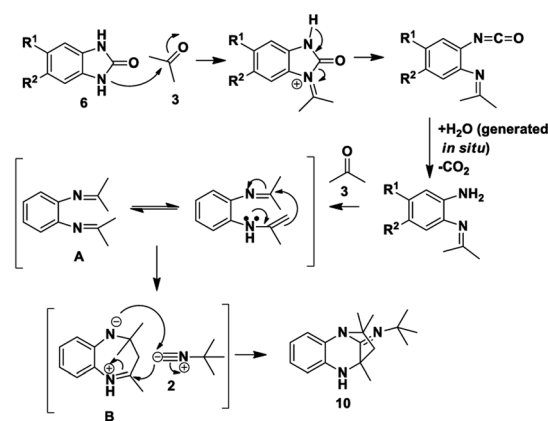


isocyanides, including *t*-Bu **2a**, tetramethylbutyl **2b**, cyclohexyl **2c** and tosylmethyl **2d** isocyanides. Reaction of benzimidazole derivatives bearing weakly deactivating groups such as carboxylate ester, fluoro or chloro under the same conditions gave no product. Replacing acetone **3a** with 3-pentanone **3b** in reaction with benzimidazoles **6b–f** and isocyanides **2a–c** also resulted in no conversion. Thus it appears that deactivating groups on **6c–d** on the aromatic ring strongly disfavoured formation of product **10**. In addition, the terminal methyl or the methylene group of 3-pentanone **3b** possibly sterically hindered the cyclisation reaction to form diazepine **10**.

To examine the role of DMAD, the reactions were repeated without addition of this reagent and the same products **10a–f** were isolated (Table 1), with no impact on yield when compared to the initial method. Interestingly, the omission of DMAD from the reactions of benzimidazoles **6** bearing electron-withdrawing substituents resulted in formation of dihydroquinoxaline products **11a–g** (Table 1). Synthesis of these dihydroquinoxalines **11** was achieved without the use of a catalyst, whereas previous reports on the preparation of similar quinoxaline compounds required the presence of various catalysts.^{15–18} Several reactions were tested using 3-pentanone **3b** in place of acetone **3a** and only product **11h** was obtained in 76% yield. Attempts to obtain these dihydroquinoxalines **11** directly from 1,2-phenylenediamine derivatives **1** instead of benzimidazoles **6** without the use of a catalyst were not successful and thus starting with benzimidazole **6** is key to the success of the reaction, although the important role played by the C=O, C=N or C=S moiety is not yet understood. The best dihydroquinoxaline **11** yields were obtained for di-substituted substrates. For example, reaction of 5,6-dichloro-1*H*-benzo[*d*]imidazol-2(3*H*)-one **6c** resulted in good yields of product **11f** (74%) and **11g**

(76%) from *tert*-butyl and tetramethylbutyl isocyanides, respectively, using acetone **3a** (Table 1). Mono-substituted deactivating groups at either position 6 or 7 such as chlorine, carboxylate ester or fluorine resulted in low to average yields (22–52%). It is worth mentioning that unsymmetrical starting materials **6** may give rise to the possibility of regioisomers. We obtained only one of the two possible regioisomers of products **11a**, **11b** and **11e** which contain one H and either an ester or Cl group at positions R¹ and R². However, when using **6e** containing an F and H at positions R¹ and R², we were able to isolate two regioisomers after the reaction, but we were unable to distinguish them (**11c** and **11d**).

Based on the proposed reaction mechanisms, rationalisation of the formation of the two different products is possible. For benzimidazole substrates **6** that are unsubstituted or with



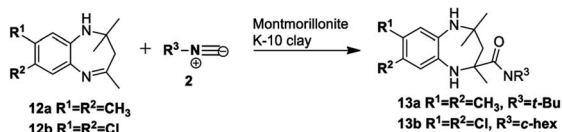
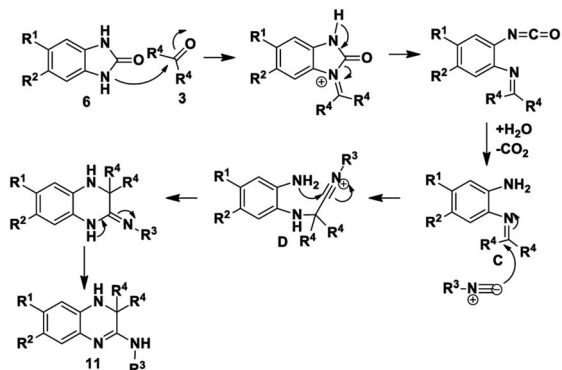
Scheme 3 Proposed reaction mechanism for the formation of **10**.

Table 1 Catalyst-free synthesis of 1,5-benzodiazepines and 3,4-dihydroquinoxalines excluding DMAD^b

Starting material	X	Product	R ¹	R ²	R ³	R ⁴	Yield%
6a	O	10a	H	H	<i>t</i> -Bu	CH ₃	81
6g	S	10a	H	H	<i>t</i> -Bu	CH ₃	83
6h	N	10a	H	H	<i>t</i> -Bu	CH ₃	84
6a	O	10b	H	H	Tetramethylbutyl	CH ₃	77
6g	S	10b	H	H	Tetramethylbutyl	CH ₃	79
6h	N	10b	H	H	Tetramethylbutyl	CH ₃	80
6a	O	10c	H	H	Cyclohexyl	CH ₃	80
6g	S	10c	H	H	Cyclohexyl	CH ₃	82
6h	N	10c	H	H	Cyclohexyl	CH ₃	84
6h	N	10d	H	H	TosMe	CH ₃	71
6b	O	10e	CH ₃	CH ₃	<i>t</i> -Bu	CH ₃	74
6b	O	10f	CH ₃	CH ₃	Tetramethylbutyl	CH ₃	67
6d	O	11a	CO ₂ CH ₃	H	<i>t</i> -Bu	CH ₃	46
6d	O	11b	CO ₂ CH ₃	H	Tetramethylbutyl	CH ₃	52
6e	O	11c ^a	F	H	Tetramethylbutyl	CH ₃	30
6e	O	11d ^a	H	F	Tetramethylbutyl	CH ₃	22
6f	O	11e	Cl	H	Tetramethylbutyl	CH ₃	46
6c	O	11f	Cl	Cl	<i>t</i> -Bu	CH ₃	74
6c	O	11g	Cl	Cl	Tetramethylbutyl	CH ₃	76
6h	N	11h	H	H	<i>t</i> -Bu	CH ₃ CH ₂	76

^a Compounds **11c** and **11d** were isolated from the same reaction. ^b Reaction conditions: isocyanide **2** (1 eq.), ketone **3** (2 eq.) and benzimidazole derivative **6** (1 eq.) were stirred at room temperature for 24 h.



Scheme 4 Benzodiazepine **13** obtained from imine **12**.

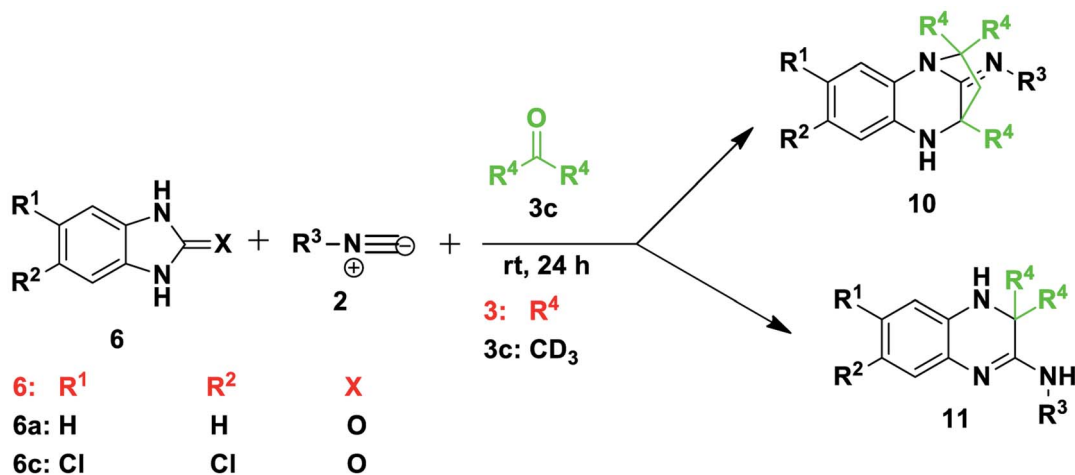
Scheme 5 Possible mechanism for the formation of dihydroquinoline **11**.

electron-releasing substituents *para* to the reacting nitrogen atoms, both nitrogen atoms are sufficiently nucleophilic to participate in imine formation with acetone and give rise to compound **10** (Scheme 3). Initially, reaction of one of the nitrogen atoms takes place to give the imine, which is followed by ring-opening of the five-membered ring. The resulting isocyanate reacts with water generated *in situ* during imine formation, leading to decomposition of the isocyanate to give an amine and CO₂.⁴² Reaction of the this amine with acetone leads to intermediate **A** that then cyclises internally to give intermediate **B**. We are suggesting that some kind of concerted process takes place where the iminium ion moiety of **B** is attacked by the isocyanide **2** while an internal nitrogen nucleophile attacks the developing nitrilium ion to give the final

product **10**. The reason for suggesting a concerted mechanism is that when we prepared and isolated imines **12** (Scheme 4) as possible intermediates in the mechanism, and subjected them to reaction with an isocyanide **2**, no reaction occurred. When we added an acid catalyst such as Montmorillonite K-10 clay to the reaction to first generate the iminium ion of **12**, we were only able to isolate products **13**, with no product **10** being observed at all.

In contrast, for benzimidazole derivatives bearing an electron-withdrawing group only one of the nitrogen atoms reacts with acetone and results in the formation of compound **11** (Scheme 5). Kolla and Lee¹⁵ describe a similar mechanism for formation of **11** starting from *o*-phenylenediamines, using EDTA as a catalyst. The reaction of compound **6** proceeds as described above for Scheme 3 until formation of imine **C** that is then directly attacked by the isocyanide to give a nitrilium ion **D** (Scheme 5). This is then intercepted by an internal nitrogen nucleophile to give the final dihydroquinoxaline **11**. Based on this mechanism, it is probable that the initial nucleophilic attack is made by the nitrogen that is *meta* to the electron-withdrawing group. This makes it likely that the single regioisomer isolated for products, **11a**, **11b** and **11e**, had $R^1 = H$ and $R^2 = \text{ester or Cl}$. This is supported by results obtained by Shaabani *et al.* for 1,2-phenylenediamines.¹⁹ When these workers reacted 1,2-phenylenediamines with an isocyanide and one equivalent of acetone, using NH_4Cl as a catalyst, they isolated dihydroquinoxalines such as **11**. Interestingly, when they reacted 1,2-phenylenediamines with an isocyanide and two equivalents of acetone in the presence of NH_4Cl , they isolated benzodiazepine derivatives such as **13**, with no tricyclic benzodiazepines **10** being reported from their reaction. This clearly indicates a unique mechanism when starting with benzimidazole derivatives (**6**) as we have done: no catalyst is required for these reactions and use of certain derivatives gives unique products **10**. It is interesting to note that none of our reactions starting from **6** gave alternative benzodiazepine product **13**.

The role and involvement of acetone in these reactions was further elucidated by replacing normal acetone **3a** with



Scheme 6 Catalyst-free synthesis of benzodiazepines **10** and dihydroquinoxalines **11** using deuterated acetone.

Table 2 Yields obtained in the synthesis of 1,5-benzodiazepines and 3,4-dihydroquinoxalines using deuterated acetone^a

Starting material	X	Product	R ¹	R ²	R ³	R ⁴	Acetone- <i>d</i> ₆ yield% (time)
6a	O	10g	H	H	Tetramethylbutyl	CD ₃	57 (24 h)
6a	O	10h	H	H	Cyclohexyl	CD ₃	61 (24 h)
6a	O	11i	H	H	<i>t</i> -Bu	CD ₃	70 (24 h)
6c	O	11j	Cl	Cl	<i>t</i> -Bu	CD ₃	72 (24 h)
6c	O	11k	Cl	Cl	Tetramethylbutyl	CD ₃	80 (24 h)

^a Reaction conditions: isocyanide **2** (1 eq.), deuterated acetone **3c** (2 eq.) and benzimidazole derivative **6** (1 eq.) were stirred at room temperature for 24 h.

Table 3 Yields from catalyst-free synthesis of benzo-1,5-diazepines^a

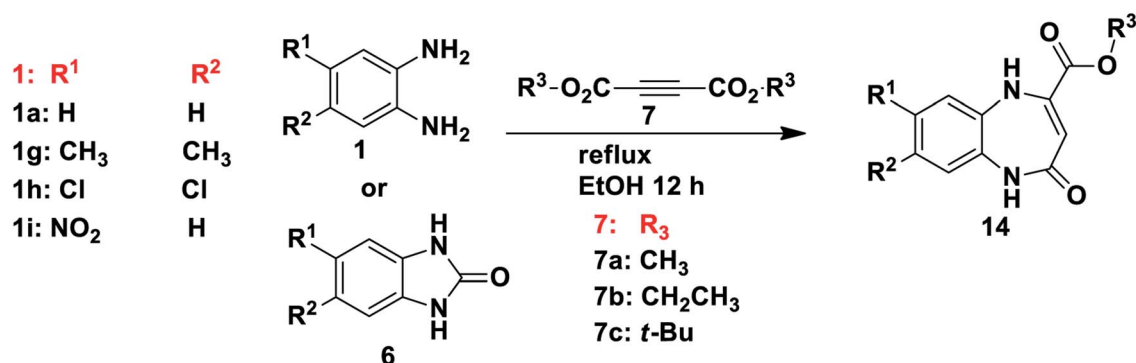
Product	R ¹	R ²	R ³	Yield% A	Yield% B
14a	H	H	CH ₃	83	72
14b	H	H	CH ₂ CH ₃	79	68
14c	H	H	<i>t</i> -Bu	75	62
14d	NO ₂	H	CH ₃	92	—
14e	NO ₂	H	CH ₂ CH ₃	85	—
14f	NO ₂	H	<i>t</i> -Bu	80	—
14g	Cl	Cl	CH ₃	83	71
14h	Cl	Cl	CH ₂ CH ₃	76	64
14i	Cl	Cl	<i>t</i> -Bu	75	66
14j	CH ₃	CH ₃	CH ₃	62	60

^a Reaction conditions: *o*-phenylenediamine **1** (1 eq.) or benzimidazole derivative **6** (1 eq.) and acetylenedicarboxylate **7** (1 eq.) were refluxed in ethanol (30 ml) for 12 h.

deuterated acetone (acetone-*d*₆) **3c** to probe reactivity and trace atom involvement in the formation of benzodiazepine **10** and dihydroquinoxaline **11** products (Scheme 6). The expense of acetone-*d*₆ restricted us to fewer reactions and a total of 5 reactions were tested. The reactions were set up in the same way as described for acetone **3a** (Table 1). When 1*H*-benzo[*d*]imidazol-2(3*H*)-one **6a** was reacted with acetone-*d*₆ **3c** and either *t*-Bu-, tetramethylbutyl- or cyclohexyl isocyanides, two deuterated benzodiazepines **10g–h** and one dihydroquinoxaline **11i** were isolated (Table 2). Interestingly, reaction of 1*H*-benzo[*d*]

imidazol-2(3*H*)-one **6a** and *tert*-butyl isocyanide **2a** with acetone-*d*₆ **3c** did not give rise to the benzodiazepine product, instead giving only the deuterated dihydroquinoxaline *N*-(3,3-dimethyl-3,4-dihydroquinoxalin-2(1*H*)-ylidene)-2-methylpropan-2-amine **11i**, in contrast to the result seen for acetone **3a**. When 5,6-dichloro-1*H*-benzo[*d*]imidazol-2(3*H*)-one **6c** was reacted with *tert*-butyl isocyanide **2a** or tetramethylbutyl isocyanide **2b** in acetone-*d*₆ **3c** two dihydroquinoxalines **11j–k** were obtained. For the synthesis of partially deuterated benzodiazepines **10g–h** the yield obtained was average, hence it appears that the acetone-*d*₆ was relatively less reactive compared to normal acetone for synthesis of benzodiazepines. However, for the synthesis of the deuterated dihydroquinoxaline derivatives **11i–k** acetone-*d*₆ was relatively reactive and resulted in comparable yields to those obtained using normal acetone. The highest yield was of **10k** from reaction of deactivating di-substituted 5,6-dichloro-1*H*-benzo[*d*]imidazol-2(3*H*)-one **6c**.

We then moved on to investigate the reactions of benzimidazole derivatives **6** with dialkyl acetylenedicarboxylates **7** as Michael acceptors under reflux conditions and comparing this to the reactions of 1,2-phenylenediamines **1** under the same conditions. In this case, unlike the reactions described earlier, the same results were observed for reaction of the benzimidazole **6** and 1,2-phenylenediamine **1**. In both cases the reactions in refluxing ethanol gave rise to 4-oxo-4,5-dihydro-1*H*-benzo-1,5-diazepine-2-carboxylate derivatives **14** (Table 3 and Scheme 7). Solomko and co-workers⁴³ reported the synthesis of a similar product, ethyl 2,3-dihydro-2-oxo-1*H*-1,5-benzodiazepine-4-

Scheme 7 Catalyst-free synthesis of benzodiazepines **14** under ethanol reflux.

carboxylate, from *o*-phenylenediamine and oxaloacetic ester in *o*-xylene under reflux. This kind of reaction involves Michael addition/intramolecular cyclization leading to the formation of interesting fused [6–7] diazepine scaffolds. The benzodiazepine-2-carboxylate derivatives **14** were successfully synthesised in various yields according to the different nature of their functional groups from 1,2-phenylenediamines **1** (yield A) and benzimidazoles **6** (yield B) (Table 3). When comparing the reactivity of benzimidazole **6** and 1,2-phenylenediamines **1** towards product formation it was observed that 1,2-phenylenediamines **1** containing free primary amines gave higher yields compared to the benzimidazoles **6**. When using 1,2-phenylenediamines **1** the highest yield obtained was that of product **14d** with a strongly deactivating and electron-withdrawing nitro group at position 8. This might be attributable to the fact that the nitro-products **14d–f** readily precipitated out of the reaction mixture as yellow solids, making isolation highly efficient. The lowest yield was obtained for product **14j**, di-substituted with the activating and electron-donating methyl group at positions 7 and 8. Substrates di-substituted with the weakly deactivating chlorine atoms at position 7 and 8 gave good yields when using 1,2-phenylenediamine starting

materials **1**. The reaction of substrates **1** or **6** containing mono-substituted deactivating groups (F, Cl and CO₂CH₃) were not successful, and neither was the reaction of the substrate mono-substituted with the activating CH₃ group. From the outcome it was observed that the reactions were more favoured with a strongly deactivating mono-substituent (nitro), rather than an activating group (methyl) at position 7 or 8. As expected, the unsymmetrical starting material **1i** may give rise to the possibility of two regioisomeric products **14d** and **14f**, however, in each case we obtained only one regioisomer but we were unable to establish unequivocally which one was present.

The structures of the benzodiazepines and dihydroquinoxalines obtained (**10a–h**, **11a–k** and **14a–j**) were elucidated by FTIR spectroscopy, NMR spectroscopy, HRMS and in certain instances these were confirmed using single-crystal X-ray crystallographic analysis (for compounds **10a**, **10e**, **11f** and **11g**). By way of a representative example the spectroscopic data for compound **10a** (Table 1) is given: the ¹H NMR spectrum showed multiplet peaks corresponding to four aromatic CH groups (positions 6–9) at δ = 6.69–6.52, a broad NH singlet at δ = 3.90, two doublets at δ 2.04–2.00 ppm and 1.79–1.76 ppm corresponding to the CH₂ at position 3, a singlet from CH₃ at

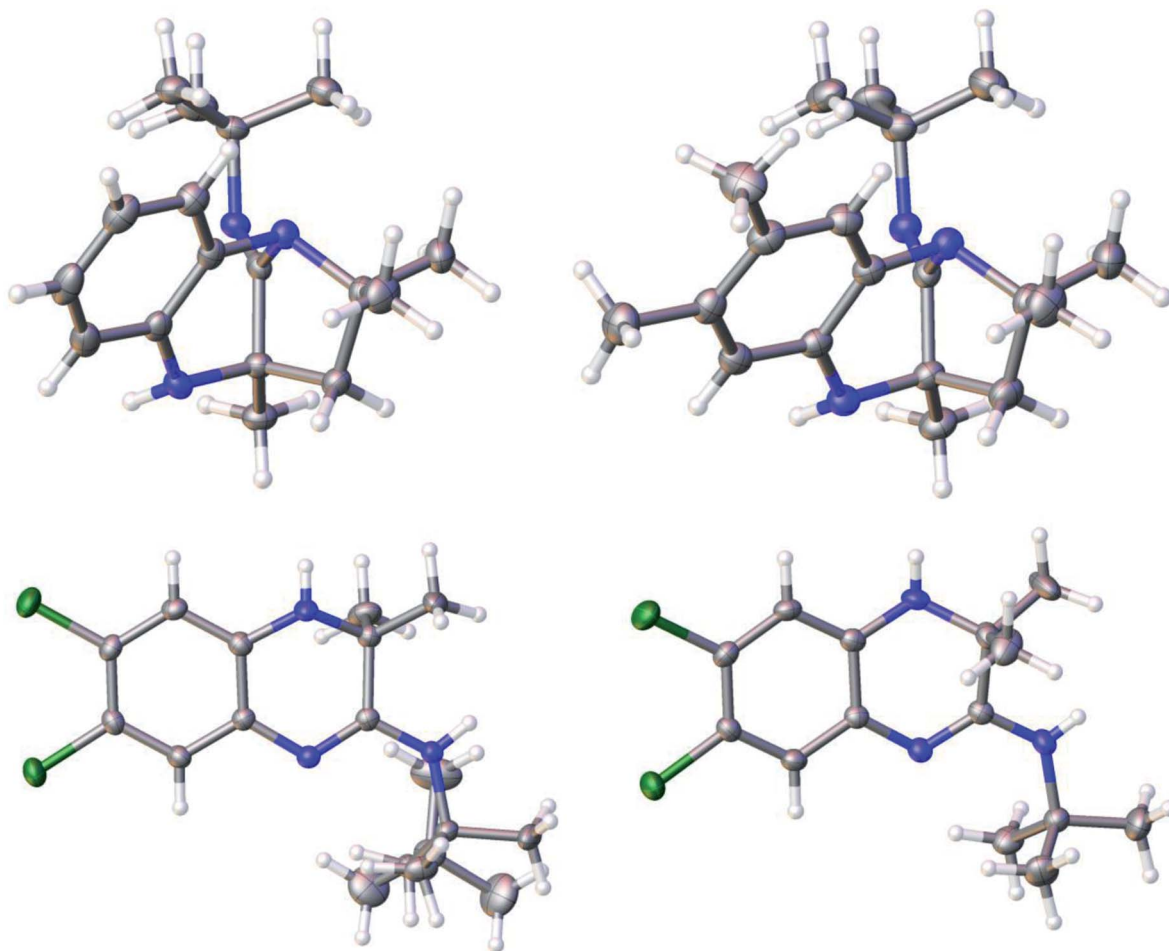


Fig. 1 Crystal structures of **10a** (top left), **10e** (top right), **11f** (bottom right) and **11g** (bottom left). Carbon atoms are represented as grey spheres, nitrogen atoms as blue spheres, hydrogen atoms as white spheres and chlorine atoms as green spheres.

$\delta = 1.39$, one singlet for three *tert*-butyl CH_3 groups at $\delta = 1.28$, and two CH_3 singlets at $\delta = 1.16$ and $\delta = 1.08$. The ^{13}C NMR spectrum of **10a** showed 15 distinct resonances in accordance with the proposed structure. The mass spectrum of **10a** showed the molecular ion $[\text{M} + \text{H}]^+$ peak at m/z 272.2119 which is consistent with the mass of the proposed product for which the calculated value is 272.2121. The FTIR spectrum displayed characteristic absorption bands for the imine group at 1696 cm^{-1} and for the amine group at 2922 cm^{-1} . Unambiguous evidence for the structures of **10a** and **10e** was obtained from single-crystal X-ray analysis as shown in Fig. 1.

For **11a** the ^1H NMR spectrum showed a doublet at $\delta = 7.51$ – 7.49 with a J value of 8 Hz corresponding to an aromatic CH, a doublet between $\delta = 7.28$ – 7.27 with a J value of 1.6 Hz corresponding to CH, a doublet appeared at $\delta = 7.08$ – 7.06 with a J value of 8.4 Hz corresponding to an aromatic CH, two singlets were found at $\delta = 4.46$ and $\delta = 3.60$ corresponding to two NH groups, a singlet at $\delta = 3.89$ was assigned to the methoxy group, a singlet from the *tert*-butyl group appeared at $\delta = 1.51$ and a singlet from two methyl groups was observed at $\delta = 1.31$. The ^{13}C NMR spectrum of **11a** showed 13 distinct resonances in accordance with the proposed structure. The mass spectrum of **11a** showed the molecular ion $[\text{M} + \text{H}]^+$ peak at m/z 290.1865 which is consistent with the mass of the proposed product for which the calculated value is 290.1863. The FTIR spectrum displayed characteristic absorption bands for the carbonyl group at 1693 cm^{-1} , imine group at 1616 cm^{-1} and for the amine group at 2901 cm^{-1} . The structures of **11f** and **11g** were confirmed by X-ray crystallography (Fig. 1).

For **14a** (Table 3) the ^1H NMR spectrum showed two singlets at δ 11.74 and 11.03 corresponding to two NH groups. Multiplet peaks were found around δ 7.40–7.39 and δ 7.05–7.03 corresponding to four aromatic CH protons. A singlet CH peak at δ 5.52 from position 3 and a singlet methyl peak at δ 3.68 were also observed. The ^{13}C NMR spectrum of **14a** showed 11 distinct resonances in accordance with the proposed structure. The mass spectrum of **14a** showed the molecular ion $[\text{M} + \text{H}]^+$ peak at m/z 219.0752 which is consistent with the mass of the proposed product. The FTIR spectrum displayed characteristic absorption bands for the carbonyl group at 1686 cm^{-1} and 1614 cm^{-1} and for the amine group at 3215 cm^{-1} and 2902 cm^{-1} .

Conclusions

We have developed a novel, catalyst-free, solvent-free green method for the synthesis of benzodiazepines **10** and dihydroquinoxalines **11**. Two different series of compounds, **10** and **11**, were synthesised *via* a multicomponent reaction of benzimidazole **6**, isocyanide **2** and acetone **3a**. The generated benzodiazepine scaffolds **10** were only obtained when the benzimidazole substituents were electron-donating or where the benzimidazoles were unsubstituted. The omission of DMAD from the initial method resulted in dihydroquinoxaline derivatives **11** from benzimidazoles **6** with only deactivating groups such as Cl, F and CO_2CH_3 as substituents on R^1 and R^2 . When 1,2-phenylenediamine **1** or benzimidazole **6** were reacted with

electron deficient alkynes (DMAD, DEtAD and DTAD) **7** under ethanol reflux conditions as a two component reaction they resulted in formation of benzodiazepine derivatives **14**. Reaction of benzimidazoles **6** gave lower yields of **14** when compared to reaction of 1,2-phenylenediamines **1**.

Conflicts of interest

There are no conflicts of interest to declare.

Acknowledgements

The research study was funded by the National Research Foundation of South Africa (PDP UID 100947 and 121102) and Mintek. The authors also acknowledge financial support and services from the University of the Witwatersrand, South Africa.

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