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The surprising nucleophilic addition of aminochlorocarbenes to diethyl acetylenedicarboxylate and to oxalyl chloride: quinolines and benzo[1,4]diazepines from *N*-alkylformanilides and oxalyl chloride in the presence of Hünig's base

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Received 27th June 2003, Accepted 1st September 2003
First published as an Advance Article on the web 17th September 2003

Vilsmeier reagents derived from *N*-methylformanilides undergo ready deprotonation with Hünig's base. In xylene, the derived nucleophilic arylaminochlorocarbenes bearing 4-methyl- and 4-methoxy-substituents react with acetylenedicarboxylates to give 2-(2-chloro-1,2-bis(ethoxycarbonyl)vinyl)-3,4-bis(ethoxycarbonyl)-1-methyl-1,2-dihydroquinolines while most derivatives react with oxalyl chloride to give substituted 1-methyl-4-phenylbenzo[*f*][1,4]diazepine-2,3-dicarboxylic anhydrides.

Introduction

Carbenes have been extensively studied for more than half a century. They can be divided into electrophilic, nucleophilic and ambiphilic types on the basis of their chemical reactivity. The most important synthetic application of electrophilic carbenes, such as dichlorocarbene, is undoubtedly the cyclopropanation of olefins, which has been widely used in synthesis. By contrast, nucleophilic carbenes (*i.e.* those in which the divalent carbon is attached to at least one group 5 or 6 element) only add to certain electrophilic alkenes. For example, fluorophenoxycarbene is more reactive towards electron-deficient alkenes than to dimethylethenes,[1] and cyclopropanes are derived in good yield from dimethoxycarbene addition to acrylonitrile and to methyl acrylate.[2] Carbonyl groups such as in cycloheptanone,[3] certain anhydrides[4] and benzoyl chloride,[5] also behave as interceptors for dialkoxycarbenes.

An intriguing feature of nucleophilic carbenes is the unpredictable outcome of their annulation reactions with electrophiles. This is seen in their reactions with acetylenedicarboxylates,[6,7] disubstituted maleic anhydrides,[4,8] dibenzoylethylene[9] and isocyanates[10,11] making nucleophilic carbenes useful intermediates for the construction of polyfunctionalised heterocycles.

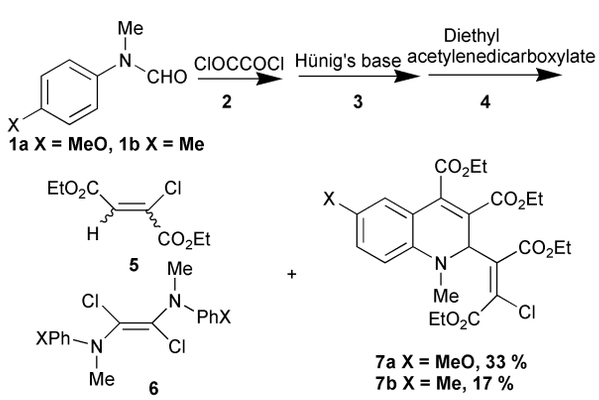
In our earlier work, we found Vilsmeier reagents are surprisingly acidic, undergoing ready deprotonation with Hünig's base. This process yields arylaminochlorocarbenes (weakly nucleophilic carbenes). However, in all cases, these carbenes reacted rapidly with the parent Vilsmeier reagent to give a dimer, which was capable of isolation or of further conversion into a series of heterocyclic compounds.[12,13,14]

We have now discovered how to inhibit this dimerisation. This has allowed us to study the reactivity of arylaminochlorocarbenes, in particular their intermolecular reactions with electrophiles. The results proved most unexpected and surprising and we herein describe the formation of quinolines and benzodiazepines by interaction of these carbenes with acetylenedicarboxylates or oxalyl chloride.

Results and discussion

The interaction of arylaminochlorocarbenes with diethyl acetylenedicarboxylate was first studied. Initially, the Vilsmeier reagent, derived from 4-methoxy- or 4-methyl-*N*-methylformanilide **1** and oxalyl chloride **2**, was deprotonated with Hünig's base **3** in dry chloroform or THF at −10 to 0 °C under a nitrogen atmosphere, followed by addition of diethyl acetylenedicarboxylate **4**. After stirring at room temperature for a period of time, work-up gave solely the known hydrogen chloride adduct of diethyl acetylenedicarboxylate **5**, together with the usual carbene dimers **6**. Isolation of these products indicated that the 'dimerisation' of the carbenes was much faster than its possible reaction with **4**.

In order to inhibit the dimerisation, firstly a non-polar solvent was used, which would minimise the solubility of the Vilsmeier reagent, and secondly, a much lower initial reaction temperature was employed. Thus, the Vilsmeier reagent prepared by reaction of 4-methoxy- or 4-methyl-*N*-methylformanilide **1a**,**b** and oxalyl chloride at 0 °C, was cooled to −78 °C. To the suspension of the Vilsmeier reagent in dry xylene, Hünig's base **3** was added followed by diethyl acetylenedicarboxylate **4**. The mixture was then allowed to reach room temperature over a 3–4 h period. A red crystalline product was isolated in both cases, the structures of which were finally put beyond doubt as quinoline derivatives **7** by X-ray crystallographic studies (Scheme 1 and Fig. 1).[15]



Scheme 1

The products derived from the interaction of one arylaminochlorocarbene and two acetylenedicarboxylate moieties are formed in 33% and 17% yield respectively.[16] A mechanism

DOI: 10.1039/b307278a

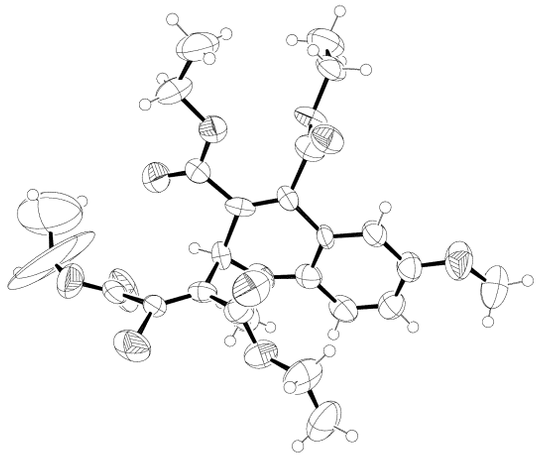
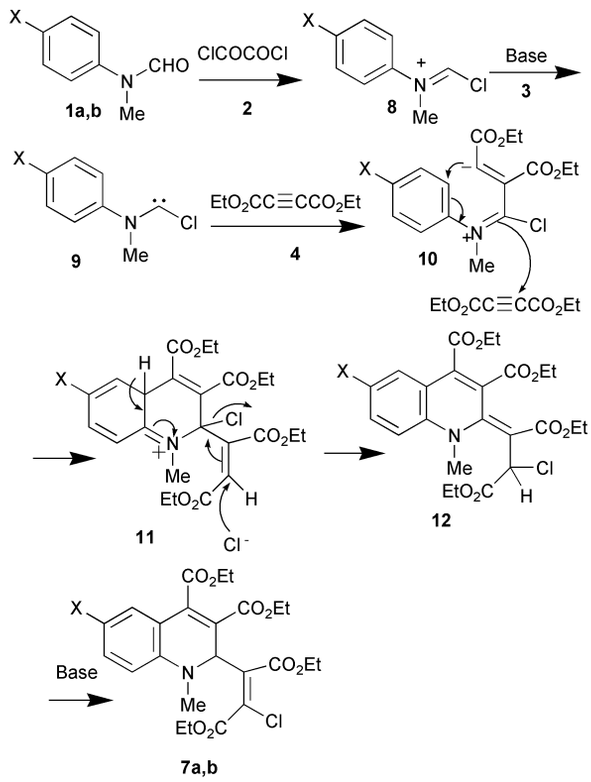


Fig. 1 ORTEP drawing of compound **7a**.

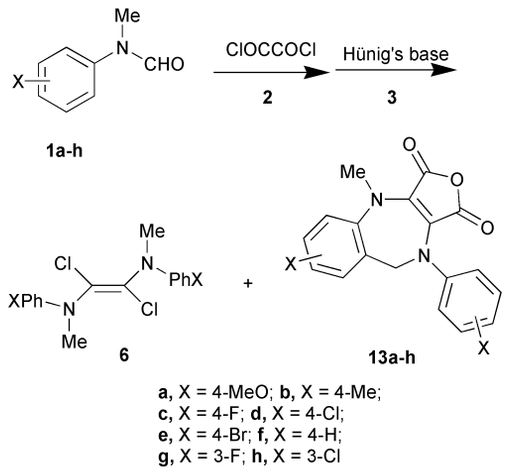


Scheme 2

for their formation is depicted in Scheme 2, and involves the bis-addition of the carbene to the acetylene.

In order to study the effect of the substituents on the nucleophilicity of the carbenes, we examined the reactions between arylaminochlorocarbenes derived from 4-fluoro- and 4-chloro-*N*-methylformanilides **1c**,**d**, and diethyl acetylenedicarboxylate under the same conditions. Although red crystalline products were again isolated, they proved to be totally different to the above quinolines. These products, **13**, showed two weak infrared absorptions at around 1800 cm^{-1} and one strong peak at about 1750 cm^{-1}, indicative of an anhydride. The NMR and MS spectra showed that the products were derived from two formanilide moieties, but incorporated *no* acetylenedicarboxylate unit. Finally, the structure of one of the products was shown to be a derivative of 1-methyl-4-phenylbenzo[1,4]-diazepine **13c** (X = F) by X-ray crystallography (Scheme 3 and Fig. 2).[17]

It would seem that the compounds **13c**,**d** were derived from the intermolecular reaction of arylaminochlorocarbenes and oxalyl chloride, the two carbonyl groups of the anhydride being derived from the oxalyl chloride. The non-involvement of the



a, X = 4-MeO; **b,** X = 4-Me;
c, X = 4-F; **d,** X = 4-Cl;
e, X = 4-Br; **f,** X = 4-H;
g, X = 3-F; **h,** X = 3-Cl

Scheme 3

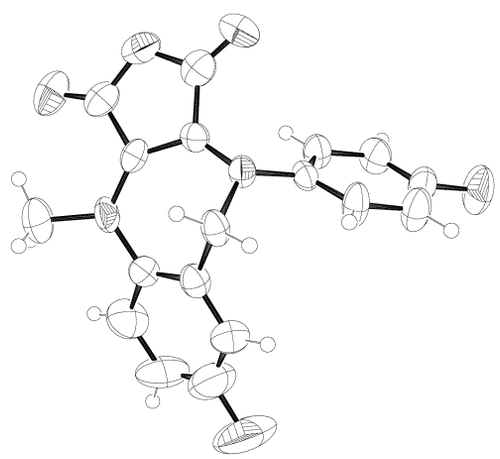


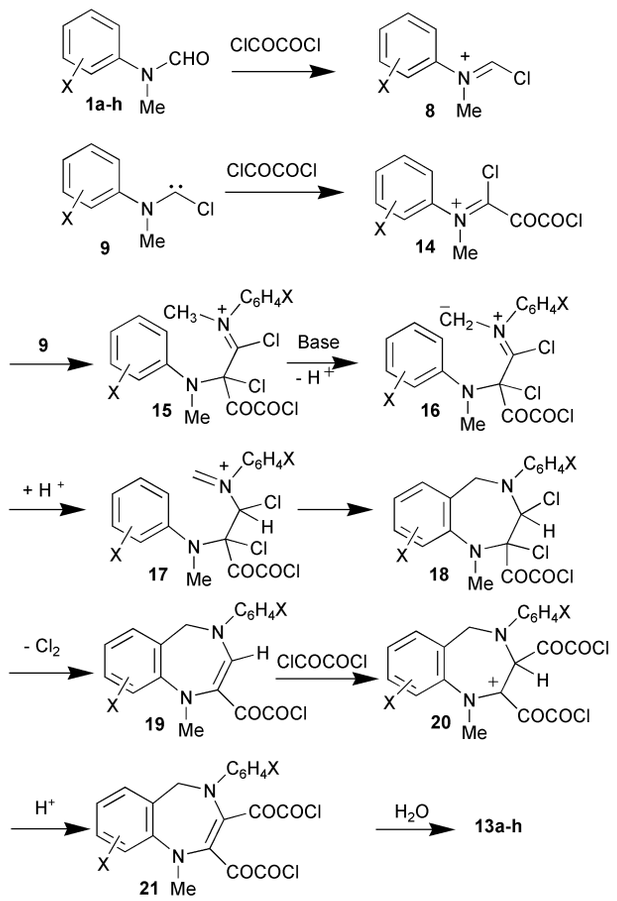
Fig. 2 ORTEP drawing of compound **13c**.

acetylenedicarboxylate was proved by repeating the reaction in its absence, the same products **13c**,**d** being formed in similar yield (41 and 26% respectively).

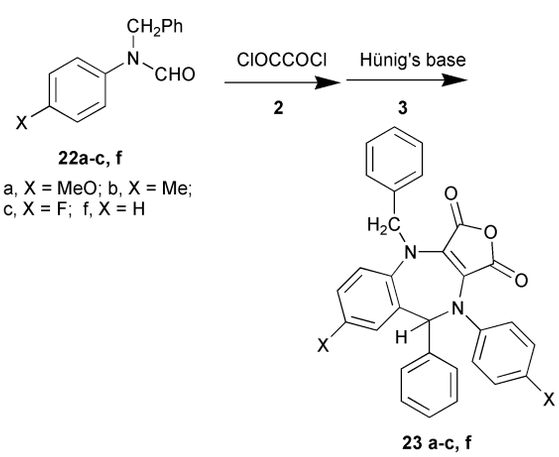
Other substituted formanilides, **1e**–**h**, reacted similarly to give the products **13e**–**h** (Scheme 3) in 22–60% yield.

The mechanism for the formation of the benzo[1,4]-diazepinedicarboxylic anhydrides **13** is not trivial to explain being formed solely from the formanilide **1** and oxalyl chloride. The formation of **13** appears to involve addition of the carbene **9** to oxalyl chloride to form an iminium salt **14** and thence **15**. The proton of the methyl group adjacent to the iminium function appears to be sufficiently acidic to be deprotonated by the base[18] allowing the new iminium ion **17** to cyclise to a diazepine **18**. The resulting enamine **19** can then undergo electrophilic addition of oxalyl chloride at the less hindered carbon atom of the double bond. The bis-acid chloride **21** might undergo decarbonylation in the warm-up process or during the removal of xylene to form the anhydrides **13** with traces of water or upon work-up (Scheme 4).

In order to prove that the key cyclisation step (**17** ⟶ **18**) does indeed utilise the *N*-methyl group of the *N*-methylformanilide we treated several examples of the corresponding *N*-benzylformanilide **22** with oxalyl chloride in the presence of Hünig's base. Gratifyingly, benzo[1,4]diazepines **23** bearing an aryl group at the 5-carbon atom were isolated in 18–32% yield (Scheme 5). In the proton NMR of **23**, a one proton singlet appeared at about 5.5 ppm, and the equivalent methylene protons of the azepines **13** had disappeared. Meanwhile, two doublet peaks with a large coupling constant (~15 Hz) appeared at ~4.7 ppm, indicative of the two non-equivalent protons of the *N*-benzyl methylene. This data was further supported by X-ray crystallography (Fig. 3).[19]



Scheme 4



Scheme 5

Xylene proved to be the optimally effective solvent, poor or no yields being obtained using chloroform, dichloromethane, THF or toluene. Varying the molar ratio of formanilide to oxalyl chloride showed that the best yields were derived from the ratio of 1 : 1.5. Larger excesses of oxalyl chloride did not improve the yield of azepine, but led to dark reaction mixtures. It seemed that the reactions were very sensitive to acidic conditions, moisture, temperature, and particularly the physical status of the Vilsmeier reagent in xylene. Finely suspended Vilsmeier reagent (as generally obtained with xylene as solvent) resulted in smooth deprotonation and normally good yields of products. On the other hand, if the Vilsmeier reagent dissolved or aggregated to form a large mass of solid in the solvent, the yields of azepine were generally poor.

The reactions between 4-methoxy- or 4-methyl-*N*-methylformanilide, oxalyl chloride and Hünig's base gave the diazepine **13a** and **13b** respectively under the optimised conditions described above. However, the more weakly nucleophilic carbenes derived from halogen substituted formanilides needed to be warmed to 40–50 °C to ensure complete reaction. Because of the sensitivity of the reactions to the conditions employed we found that while products were always formed, yields proved somewhat erratic. The best results are listed in Table 1.

Table 1 Reaction conditions for and chemical yields of compounds **13** and **23**

Reactants				Yield (%)	
1	**22**	Reaction temp./°C	Reaction time/h	**13**	**23**
1a		−78 to rt	7	26	
1b		−78 to rt	4	30	
1c		−78 to 50	9	46	
1d		−78 to 50	7	28	
1e		−78 to 50	7	22	
1f		−78 to rt	9	60	
1g		−78 to 50	7	35	
1h		−78 to 50	7	26	
	22a	−78 to rt	18		32
	22b	−78 to rt	18		18
	22c	−78 to 50	7		29
	22f	−78 to rt	18		23

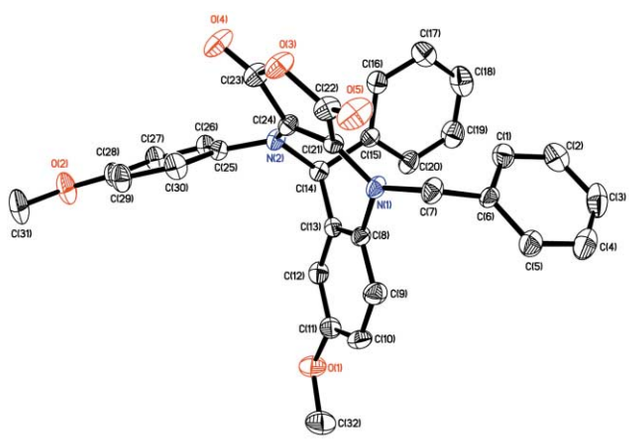


Fig. 3 ORTEP drawing of compound **23a**.

It would appear that only the more nucleophilic carbenes derived from the 4-methyl- and the 4-methoxy-substituted formanilides, are sufficiently nucleophilic to react with acetylenedicarboxylate, while all react with the more electrophilic oxalyl chloride.

As well as diethyl acetylenedicarboxylate and oxalyl chloride, other electrophiles were examined. These included *N*-phenylmaleimide, diethyl maleate, phenyl isocyanate and phenyl isothiocyanate. All of these reagents proved ineffective. The *N*-phenylmaleimide, diethyl maleate, and phenyl isothiocyanate were recovered and the phenyl isocyanate was converted to diphenylurea during work-up.

In summary, we have discovered the unique nucleophilicity of arylaminochlorocarbenes which afford a simple method to novel benzo[1,4]diazepine derivatives by the interaction of substituted formanilides and oxalyl chloride with base and to quinolines with the same reagents plus diethyl acetylenedicarboxylate.

Experimental

General

Melting points are uncorrected. ^{1}H NMR and ^{13}C NMR were obtained on a Bruker Avance 500; chemical shifts are given in ppm and coupling constants in Hz. IR spectra were recorded using an AVATAR 360 FT-IR spectrometer. Mass spectra were recorded on a Trace MS instrument (EI-MS) or Bruker

APEX-2 (HRMS) and elemental analyses were performed on a GMBH Vario EL instrument.

All glassware was oven dried (120 °C) over a 10 h period. Xylene was distilled from sodium benzophenone ketyl. Light petroleum refers to the fraction bp 60–90 °C.

General procedure for the preparation of quinolines 7a,b

Under a nitrogen atmosphere, 4-substituted *N*-methylformanilides **1a**,**b** (10 mmol) and oxalyl chloride (11 mmol) were mixed at 0 °C to form a sticky solid, which was then cooled to −78 °C. To this solid Vilsmeier reagent, xylene (5 ml) followed by a solution of Hünig's base (12 mmol) in xylene (10 ml) was added with stirring to form a suspension. After a ½ h, diethyl acetylenedicarboxylate **4** in xylene (5 ml) was added and the temperature increased from −78 °C to room temperature during 3 h. The reaction mixture was stirred at room temperature for 2 h and then at 50 °C for another 2 h. The reaction mixture was chromatographed directly. The xylene was removed by washing the column with light petroleum. Compound **5** and dimers **6** were eluted with a mixture of light petroleum and ethyl acetate (10 : 1). Finally, the red products **7a**,**b** were isolated by eluting with light petroleum : ethyl acetate (4 : 1).

Diethyl 2-(2-chloro-1,2-bis(ethoxycarbonyl)vinyl)-6-methoxy–1-methyl-1,2-dihydroquinoline-3,4-dicarboxylate 7a. 0.86 g, 33%, as red crystals, mp 108–109 °C; IR (KBr) (ν_{max}/cm^{-1}): 1742 (C=O), 1733 (C=O), 1722 (C=O), 1698 (C=O); δ_H (500 MHz, $CDCl_3$) 6.85 (1H, dd, *J* 8.9, 2.7), 6.52 (1H, d, *J*, 2.7), 6.50 (1H, d, *J* 9.0), 6.33 (1H, s), 4.37–4.42 (4H, m), 4.20 (2H, q, *J* 7.1), 3.75 (2H, q, *J* 6.8), 3.70 (3H, s), 3.04 (3H, s), 1.36–1.42 (6H, m), 1.25 (3H, t, *J* 7.1), 1.10 (3H, t, *J* 7.2); δ_C (125 MHz, $CDCl_3$) 167.4, 165.5, 163.8, 162.4, 152.2, 141.6, 140.6, 139.7, 122.3, 119.8, 118.2, 117.6, 113.4, 112.1, 63.2, 62.7, 62.0, 61.7, 57.4, 56.2; HRMS (FAB): 524.1694, $C_{25}H_{30}ClNO_9$ requires 524.1682.

Diethyl 2-(2-chloro-1,2-bis(ethoxycarbonyl)vinyl)-1,6-dimethyl-1,2-dihydroquinoline-3,4-dicarboxylate 7b. 0.43 g, 17%, as red crystals, mp 105–106 °C (Found: C 58.9, H 5.4, N 2.65. $C_{25}H_{30}ClNO_8$ requires C 59.1, H 5.95, N 2.8%); IR (KBr) (ν_{max}/cm^{-1}): 1744 (C=O), 1722 (C=O), 1696 (C=O); δ_H (500 MHz, $CDCl_3$) 6.96 (1H, d, *J* 8.2), 6.65 (1H, s), 6.39 (1H, d, *J* 8.3), 6.28 (1H, s), 4.27–4.36 (4H, m), 4.13 (2H, q, *J* 7.1), 3.66 (2H, q, *J* 7.1), 2.98 (3H, s), 2.10 (3H, s), 1.27–1.36 (6H, m), 1.17 (3H, t, *J* 7.1), 1.01 (3H, t, *J* 7.1); HRMS (EI): 507.1665, $C_{25}H_{30}ClNO_8$ requires 507.1660

General procedure for the preparation of benzo[1,4]diazepines 13 and 23

Under a nitrogen atmosphere, substituted *N*-methylformanilide **1a**–**h** or *N*-benzylformanilide **22a**–**c**,**f** (10 mmol) and oxalyl chloride (15 mmol) were mixed at 0 °C to form a sticky solid. To this solid Vilsmeier reagent, xylene (5 ml) was added with stirring to form a suspension, which was then cooled to −78 °C. A solution of Hünig's base (15 mmol) in xylene (10 ml) was added dropwise to the Vilsmeier reagent over 30 min. The temperature was then increased from −78 °C to room temperature during 3 h. The reaction mixture was stirred at room temperature or at 50 °C for a period of time (see Table 1). After removal of the xylene under vacuum, the reaction mixture was chromatographed on silica gel. The red products **13** and **23** were isolated by eluting with light petroleum : ethyl acetate (4 : 1) and further purified by crystallisation from ethyl acetate and light petroleum.

7-Methoxy-4-(4-methoxyphenyl)-1-methylbenzo[*f*][1,4]-diazepine-2,3-dicarboxylic anhydride 13a. 0.48 g, 26%, as red crystals, mp 160–161 °C (Found: C 65.7, H 4.5, N 7.5. $C_{20}H_{18}N_2O_5$ requires C 65.6, H 4.95, N 7.65%); IR (KBr) (ν_{max}/cm^{-1}): 1832, 1803 and 1740 (O=COC=O), 1629 (C=C); δ_H (500 MHz, $CDCl_3$) 7.08 (1H, d, *J* 8.9), 6.90 (2H, d, *J* 8.9), 6.85 (1H, dd, *J* 8.9, 2.9), 6.82 (2H, d, *J* 8.9), 6.41 (1H, d, *J* 2.9), 4.66 (2H, s), 3.79 (3H, s), 3.71 (3H, s), 3.65 (3H, s); δ_C (125 MHz, $CDCl_3$) 161.9, 160.5, 156.8, 155.1, 142.6, 138.3, 131.6, 129.2, 123.7, 123.4, 122.5, 115.6, 114.7, 113.9, 57.6, 55.5, 55.4, 40.9; HRMS (EI): 366.1207, $C_{20}H_{18}N_2O_5$ requires 366.1216.

1,7-Dimethyl-4-(4-methylphenyl)benzo[*f*][1,4]diazepine-2,3-dicarboxylic anhydride 13b. 0.50 g, 30%, as red crystals, mp 155–156 °C (Found: C 71.5, H 5.3, N 8.5. $C_{20}H_{18}N_2O_3$ requires C 71.8, H 5.4, N 8.4%); IR (KBr) (ν_{max}/cm^{-1}): 1833, 1815 and 1749 (O=COC=O), 1635 (C=C); δ_H (500 MHz, $CDCl_3$) 7.09–7.13 (3H, m), 7.02 (1H, d, *J* 8.1), 6.86 (2H, d, *J* 7.5), 6.70 (1H, s), 4.71 (2H, s), 3.67 (3H, s), 2.32 (3H, s), 2.71 (3H, s); δ_C (125 MHz, $CDCl_3$) 162.3, 160.7, 147.6, 142.9, 134.4, 133.7, 130.8, 130.6, 130.4, 129.5, 123.6, 122.2, 121.4, 57.4, 41.2, 21.2, 20.9; *m*/*z* (EI) 334 (90, M^+).

7-Fluoro-4-(4-fluorophenyl)-1-methylbenzo[*f*][1,4]diazepine-2,3-dicarboxylic anhydride 13c. 0.79 g, 46%, as red crystals, mp 208–209 °C; IR (KBr) (ν_{max}/cm^{-1}): 1838, 1812 and 1748 (O=COC=O), 1637 (C=C); δ_H (500 MHz, $CDCl_3$) 7.12–7.13 (1H, m), 6.99–7.06 (3H, m), 6.94 (2H, t, *J* 4.2), 6.60 (1H, d, *J* 7.5), 4.69 (2H, s), 3.68 (3H, s); δ_C (125 MHz, $CDCl_3$) 161.9, 161.3, 160.5, 159.3 (d), 157.4, 146.0, 141.4, 132.5 (d), 130.0, 124.2 (d), 123.4 (d), 117.1, 116.9 (d), 116.7, 116.6, 57.4, 41.4; HRMS (EI): 342.0813, $C_{18}H_{12}O_3F_2N_2$ requires 342.0810.

7-Chloro-4-(4-chlorophenyl)-1-methylbenzo[*f*][1,4]diazepine-2,3-dicarboxylic anhydride 13d. 0.53 g, 28%, as red crystals, mp 179–180 °C (Found: C 57.1, H 2.8, N 6.9. $C_{18}H_{12}Cl_2N_2O_3$ requires C 57.6, H 3.2, N 7.5%); IR (KBr) (ν_{max}/cm^{-1}): 1840, 1818 and 1763 (O=COC=O), 1637 (C=C); δ_H (500 MHz, $CDCl_3$) 7.32 (1H, dd, *J* 8.7, 2.4), 7.27 (2H, d, *J* 9.6), 7.08 (1H, d, *J* 8.7), 6.90 (2H, d, *J* 8.7), 6.88 (1H, d, *J* 2.4), 4.71 (2H, s), 3.69 (3H, s); δ_C (125 MHz, $CDCl_3$) 161.7, 160.2, 148.4, 143.6, 132.2, 130.7, 130.4, 130.1, 130.0, 129.3, 123.2, 123.1, 122.7, 56.8, 41.5; HRMS (EI): 374.0229, $C_{18}H_{12}Cl_2N_2O_3$ requires 374.0225.

7-Bromo-4-(4-bromophenyl)-1-methylbenzo[*f*][1,4]diazepine-2,3-dicarboxylic anhydride 13e. 0.51 g, 22%, as red crystals, mp 143–146 °C (Found: C 47.0, H 2.4, N 5.7. $C_{18}H_{12}Br_2N_2O_3$ requires C 46.6, H 2.6, N 6.0%); IR (KBr) (ν_{max}/cm^{-1}): 1838, 1817 and 1752 (O=COC=O), 1637 (C=C); δ_H (500 MHz, $CDCl_3$) 7.46 (1H, d, *J* 8.5), 7.41 (2H, d, *J* 8.4), 7.03 (1H, s), 7.02 (1H, d, *J* 8.8), 6.84 (2H, d, *J* 8.4), 4.71 (2H, s), 3.69 (3H, s); δ_C (125 MHz, $CDCl_3$) 161.6, 160.1, 148.9, 144.1, 133.0, 132.8, 132.5, 130.0, 123.5 (two carbons), 122.7, 118.0, 116.9, 56.6, 41.4; *m*/*z* (EI) 462 (30, M^+)/464 (32)/466 (25)/468 (10), 155 (100, BrC_6H_4).

1-Methyl-4-phenylbenzo[*f*][1,4]diazepine-2,3-dicarboxylic anhydride 13f. 0.92 g, 60%, as red crystals, mp 162–163 °C (Found: C 70.4, H 4.2, N 9.0. $C_{18}H_{14}N_2O_3$ requires C 70.6, H 4.6, N 9.1%); IR (KBr) (ν_{max}/cm^{-1}): 1838, 1805 and 1753 (O=COC=O), 1637 (C=C); δ_H (500 MHz, $CDCl_3$) 7.32–7.34 (1H, m), 7.29 (2H, t, *J* 8.5), 7.15 (1H, d, *J* 8.2), 7.10 (1H, t, *J* 7.4), 6.97 (2H, d, *J* 7.7), 6.90 (2H, m), 4.79 (2H, s), 3.72 (3H, s); δ_C (125 MHz, $CDCl_3$) 161.7, 160.2, 149.7, 144.9, 130.6, 129.9, 129.7, 129.6, 129.4, 124.3, 123.8, 122.8, 121.6, 121.2, 56.8, 40.9; *m*/*z* (EI) 306 (100, M^+).

8-Fluoro-4-(3-fluorophenyl)-1-methylbenzo[*f*][1,4]diazepine-2,3-dicarboxylic anhydride 13g. 0.60 g, 35%, as red crystals, mp 186–188 °C (Found: C 63.2, H 3.1, N 8.0. $C_{18}H_{12}F_2N_2O_3$ requires C 63.2, H 3.5, N 8.2%); IR (KBr) (ν_{max}/cm^{-1}): 1834, 1817 and 1754 (O=COC=O), 1635(C=C); δ_H (500 MHz, $CDCl_3$) 7.23–7.25 (1H, m), 6.87–6.91 (2H, m), 6.78–6.82 (1H, m), 6.68–6.73 (2H, m), 6.64–6.65 (1H, m), 4.74 (2H, s), 3.71 (3H, s); δ_C (125 MHz, $CDCl_3$) 164.3/164.2 (d), 162.4/162.3 (d), 161.2, 159.8, 150.7, 146.3, 131.3/131.2 (d), 130.6/130.6 (d), 129.9,

129.5, 122.1/122.0 (d), 116.9, 111.3/111.1(d), 110.9/110.7 (d), 109.1/108.9 (d), 108.5/108.2 (d), 56.0, 40.8; *m/z* (EI) 342 (35, M^+)/343 (12), 95 (100, FC_6H_4).

8-Chloro-4-(3-chlorophenyl)-1-methylbenzo[*f*][1,4]diazepine-2,3-dicarboxylic anhydride 13h. 0.49 g, 26%, as red crystals, mp 192–193 °C (Found: C 58.0, H 2.7, N 7.3. $C_{18}H_{12}Cl_2N_2O_3$ requires C 57.6, H 3.2, N 7.5%); IR (KBr) (ν_{max}/cm^{-1}): 1841, 1821 and 1750 (O=COC=O), 1643 (C=C); δ_H (500 MHz, $CDCl_3$) 7.27 (1H, t, *J* 8.0), 7.22 (1H, t, *J* 8.0), 7.03–7.10 (1H, s), 7.02 (4H, m), 6.92 (1H, d, *J* 7.9), 5.08 (2H, s), 3.70 (3H, s); δ_C (125 MHz, $CDCl_3$) 161.2, 159.6, 151.5, 145.5, 134.8, 134.2, 130.1, 129.9, 129.4, 128.6, 125.3, 124.8, 123.2, 122.3, 120.3, 120.2, 51.6, 41.3; HRMS (EI): 374.0232, $C_{18}H_{12}Cl_2N_2O_3$ requires 374.0225.

1-Benzyl-7-methoxy-4-(4-methoxyphenyl)-5-phenylbenzo[*f*]-[1,4]diazepine-2,3-dicarboxylic anhydride 23a. 0.57 g, 32%, as red crystals, mp 169–170 °C (Found: C 73.9, H 4.95, N 5.3. $C_{32}H_{26}N_2O_5$ requires C 74.1, H 5.05, N 5.4%); IR (KBr) (ν_{max}/cm^{-1}): 1824 and 1752 (O=COC=O), 1642 (C=C); δ_H (500 MHz, $CDCl_3$) 7.45–7.46 (3H, m), 7.33–7.34 (2H, m), 7.13–7.19 (3H, m), 7.05 (2H, d, *J* 8.9), 6.94 (1H, d, *J* 8.9), 6.87 (2H, d, *J* 8.9), 6.80 (1H, dd, *J* 8.9, 2.9), 6.70 (2H, d, *J* 7.2), 6.61 (1H, d, *J* 2.9), 5.52 (1H, s), 4.67 (1H, d, *J* 15.1), 4.61 (1H, d, *J* 15.1), 3.82 (3H, s), 3.76 (3H, s); δ_C (125 MHz, $CDCl_3$) 161.2, 161.0, 157.3, 155.5, 140.3, 129.5, 139.4, 137.3, 133.9, 129.2, 128.3, 128.0, 127.8, 127.6, 127.1, 126.0, 124.9, 124.4, 123.4, 117.7, 114.8, 113.5, 74.0, 56.5, 55.5 (two carbon); *m/z* (EI) 518 (67, M^+)/519 (24), 250 (100, 7-methoxy-5-phenylbenzodiazepine).

1-Benzyl-7-methyl-4-(4-methylphenyl)-5-phenylbenzo[*f*]-[1,4]diazepine-2,3-dicarboxylic anhydride 23b. 0.44 g, 18%, as red crystals, mp 210–212 °C (Found: C 79.0, H 5.2, N 5.6. $C_{32}H_{26}N_2O_3$ requires C 79.0, H 5.4, N 5.8%); IR (KBr) (ν_{max}/cm^{-1}): 1827, 1751 (O=COC=O), 1639 (C=C); δ_H (500 MHz, $CDCl_3$) 7.43–7.45 (3H, m), 7.29–7.31 (2H, m), 7.10–7.18 (6H, m), 7.01 (2H, d, *J* 8.3), 6.96 (1H, d, *J* 8.3), 6.80 (1H, s), 6.63 (2H, d, *J* 7.3), 5.65 (1H, s), 4.85 (1H, d, *J* 15.3), 4.70 (1H, d, *J* 15.3), 2.36 (3H, s), 2.27 (3H, s); δ_C (125 MHz, $CDCl_3$) 161.0, 160.8, 145.2, 143.8, 140.0, 137.3, 134.8, 133.7, 132.5, 132.2, 130.2, 130.1, 129.2, 128.3, 128.0, 127.5, 127.2, 127.0 126.0, 123.0, 122.3, 73.7, 56.3, 20.9, 20.6; *m/z* (EI) 486 (100, M^+)/487 (25), 234 (85, 7-methyl-5-phenylbenzodiazepine), 91 (100, $PhCH_2$).

1-Benzyl-7-fluoro-4-(4-fluorophenyl)-5-phenylbenzo[*f*][1,4]-diazepine-2,3-dicarboxylic anhydride 23c. 0.72 g, 29%, as orange crystals, mp 193–194 °C (Found: C 72.7, H 3.8, N 5.5. $C_{30}H_{20}F_2N_2O_3$ requires C 72.7, H 4.1, N 5.7%); IR (KBr) (ν_{max}/cm^{-1}): 1845, 1822 and 1752 (O=COC=O), 1642 (C=C); δ_H (500 MHz, $CDCl_3$) 7.47–7.48 (3H, m), 7.30–7.31 (2H, m), 7.20 (1H, t, *J* 7.2), 7.14 (2H, t, *J* 7.6), 7.06–7.08 (4H, m), 7.02 (1H, d, *J* 6.2), 6.81 (1H, d, *J* 7.8), 6.66 (2H, d, *J* 7.4), 5.56 (1H, s), 4.74 (1H, d, *J* 15.1), 4.64 (1H, d, *J* 15.1); δ_C (125 MHz, $CDCl_3$) 162.8, 162.2, 162.0, 160.0, 160.9, 160.6, 158.6, 144.8, 143.6, 140.1, 138.1, 135.8, 130.9, 129.9, 129.8, 129.2, 128.8, 127.2, 126.93/126.87 (d), 126.03/125.96 (d), 124.5, 123.1/122.9 (d), 119.9/119.1 (d), 118.1/117.9 (d), 117.8/117.6 (d), 74.8, 58.0; *m/z* (EI) 494 (55, M^+)/495 (20), 238 (52, 7-fluoro-5-phenylbenzodiazepine), 91 (100, $PhCH_2$).

1-Benzyl-4,5-diphenylbenzo[*f*][1,4]diazepine-2,3-dicarboxylic anhydride 23f. 0.53 g, 23%, as red crystals, mp 211–213 °C (Found: C 78.6, H 4.5, N 6.0. $C_{30}H_{22}N_2O_3$ requires C 78.6, H 4.8, N 6.1%); IR (KBr) (ν_{max}/cm^{-1}): 1844, 1822 and 1751 (O=COC=O), 1641 (C=C); δ_H (500 MHz, $CDCl_3$) 7.45–7.46 (3H, m), 7.35–7.37 (2H, m), 7.31–7.34 (3H, m), 7.16–7.20 (2H, m), 7.11–7.14 (5H, m), 7.07–7.08 (1H, m), 7.02–7.05 (1H, m), 6.63 (2H, d, *J* 7.4), 5.77 (1H, s), 4.94 (1H, d, *J* 15.3), 4.76 (1H, d, *J* 15.3); δ_C (125 MHz, $CDCl_3$) 160.8, 160.7, 147.9, 146.2, 139.8, 137.1, 132.5, 132.0, 129.9, 129.5, 129.3, 128.4, 128.1, 127.5, 127.4, 127.1, 126.0, 125.1 124.1, 123.1, 122.9, 122.4, 73.7, 56.3; *m/z* (EI) 458 (85, M^+)/459 (35), 220 (65, 5-phenylbenzodiazepine), 91 (100, $PhCH_2$).

Single crystals of compounds **7a**, **13c** and **23a** suitable for X-ray diffraction were selected directly from the analytical samples.

Crystal structure determination of compound 7a

$C_{25}H_{30}ClNO_9$, *M* = 523.95, triclinic, space group $P\bar{1}$, *a* = 8.312(12), *b* = 8.487(13), *c* = 19.91(3) Å, *α* = 78.19(3)°, *β* = 81.52(3)°, *γ* = 88.99(3)°, *V* = 1360(4) Å^3, *T* = 293(2) K, *Z* = 2, D_x = 1.280 Mg m^{-3}, *μ* = 0.191 mm^{-1}, 4331 reflections measured, 3760 unique (R_{int} = 0.1060) which were used in all calculations. The final *R* indices [$I > 2\sigma(I)$] R_1 = 0.0803, wR_2 = 0.1756; R indices R_1 = 0.1848, wR_2 = 0.2216 (all data).

Crystal structure determination of compound 13c

$C_{18}H_{12}F_2N_2O_3$, *M* = 342.30, monoclinic, space group *P*2(1)/*c*, *a* = 15.752(6), *b* = 11.767(4), *c* = 8.688(3) Å, *α* = 90°, *β* = 103.607(7)°, *γ* = 90°, *V* = 1565.2(9) Å^3, *T* = 293(2) K, *Z* = 4, D_x = 1.453 Mg m^{-3}, *μ* = 0.116 mm^{-1}, 6550 reflections measured, 2883 unique (R_{int} = 0.1421) which were used in all calculations. The final *R* indices [$I > 2\sigma(I)$] R_1 = 0.0569, wR_2 = 0.1063; *R* indices R_1 = 0.2534, wR_2 = 0.1883 (all data).

Crystal structure determination of compound 23a

$C_{32}H_{26}N_2O_5$, *M* = 518.55, triclinic, space group $P\bar{1}$, *a* = 12.0481(11), *b* = 14.5004 (17), *c* = 16.407(2) Å, *α* = 81.45(3), *β* = 83.18(5), *γ* = 67.320(17)°, *V* = 2609.3(5) Å^3, *T* = 293(2) K, *Z* = 4, D_x = 1.320 Mg m^{-3}, *μ* = 0.090 mm^{-1}, 17892 reflections measured, 11548 unique (R_{int} = 0.0682) which were used in all calculations. The final *R* indices [$I > 2\sigma(I)$] R_1 = 0.0481, wR_2 = 0.0726; *R* indices R_1 = 0.2119, wR_2 = 0.0918 (all data).

Acknowledgements

This work was supported by the National Natural Science Foundation of China and the Excellent Young Teachers Program of MOE, P. R. C.

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