Rearrangement and cyclo-α-elimination of *N*-substituted amidines using (diacetoxyiodo)benzene

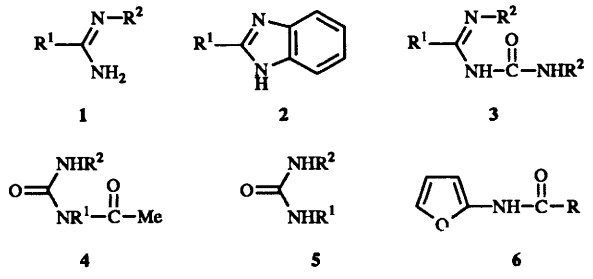
Christopher A. Ramsden * and Helen L. Rose
Department of Chemistry, Keele University, Keele, Staffordshire ST5 5BG, UK

The products of reaction of *N*-substituted amidines with (diacetoxyiodo)benzene are determined by the nature of the amidine substituents and the reaction temperature: rearrangement of N^2-phenylfuran-2-carboximidamide provides a convenient route to *N*-(2-furyl)acetamide, whereas *N*-phenyl *C*-alkyl formimidamides cyclise to give benzimidazoles in good yield.

A facet of hypervalent iodine(III) reagents,[1] such as (diacetoxyiodo)benzene (DAIB), is their ability to function as two-electron oxidising agents by a mechanism in which iodine appears to behave first as an electrophile (*e.g.* PhI^+OAc) and then as a leaving group ($PhI + AcO^-$). This ability of iodine(III) to achieve an *umpolung*, namely the direct transformation of an electron-rich centre into one which behaves as an electron-deficient function, provides the opportunity of devising new transformations of electron-rich molecules. In this context recent applications of synthetic value include reactions with phenols,[2] benzenethiols[3] and hydrazones.[4] We have investigated reactions of *N*-substituted amidines **1** with DAIB and now report novel transformations, including a rearrangement analogous to the Hofmann reaction[5] of primary carboxamides. Although the Tiemann rearrangement[6] of *N*-hydroxy amidines, which is analogous to the Lossen rearrangement[5] of hydroxamic acids, is well known and a few examples of rearrangements of simple *N*-chloro amidines and *N*-chloro guanidines have been described,[7] as far as we are aware, direct C to N rearrangements of primary amidines[8] have not been reported.

Reaction of the N^2-phenyl *C*-alkyl formimidamides **1a–c** with DAIB in toluene solution at reflux temperature gave benzimidazoles **2a–c** (see Table 1) in good yields. Similar cyclisations have been achieved previously using lead tetraacetate (LTA).[9] However, when N^2-phenylbenzimidamide **1e** was treated with DAIB under the same conditions the products were acetanilide and N^1-(*N*-phenylcarbamoyl)-N^2-phenylbenzimidamide **3e**. This behaviour is in sharp contrast to the reaction of N^2-phenylbenzimidamide **1e** with LTA,[9] which we found gives exclusively 2-phenylbenzimidazole **2** (R^1 = Ph) under identical conditions. When the reaction of the benzimidamide **1e** with DAIB was carried out at 80 °C the major product was *N*-acetyl-*N*,*N*′-diphenylurea **4e**. At a higher temperature (110 °C) this product **4e** clearly undergoes thermal cleavage forming acetanilide and phenylisocyanate which reacts with starting material **1e** to form the observed product **3e** (see Table 1).

Similar results were obtained using the *C*-aryl formimidamides **1d, f** (Table 1). We have demonstrated the potential utility of this novel rearrangement of amidines using N^2-phenylfuran-2-carboximidamide **1f**. Although 2-furoic acid and related compounds are readily available, simple 2-aminofuran derivatives are difficult to obtain due to the instability of 2-aminofuran.[10] When the *N*-acetylurea **4f**, obtained from the amidine **1f** (Table 1), was heated at 110 °C in toluene solution in the presence of 1 equiv. of aniline, *N*-(2-furyl)acetamide **6** (R = Me) was obtained (88%) together with *N*,*N*′-diphenylurea, which was easily separated. This provides a simple and safe route to the 2-aminofuran derivative **6** (R = Me) and



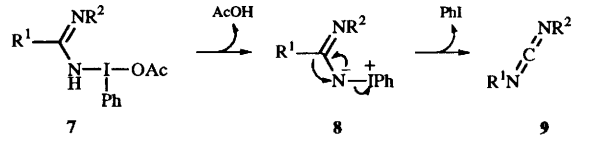
1 **2** **3**

4 **5** **6**

1–5
a R^1 = $PhCH_2$, R^2 = Ph
b R^1 = Cyclohexyl, R^2 = Ph
c R^1 = Et, R^2 = Ph
d R^1 = Ph, R^2 = Cyclohexyl
e R^1 = Ph, R^2 = Ph
f R^1 = 2-Furyl, R^2 = Ph
g R^1 = $PhCH_2$, R^2 = Cyclohexyl
h R^1 = Cyclohexyl, R^2 = $PhCH_2$
i R^1 = Cyclohexyl, R^2 = Cyclohexyl

further examples of this route as well as chemical modifications of the amide **6** to give other 2-aminofuran derivatives are under investigation. Previously the amides **6** (R = Ph, Et)[11] have been prepared from 2-furoic acid *via* a Curtius rearrangement but this procedure is potentially dangerous and not suitable for large scale preparations.

The dialkyl amidines **1g–i** also undergo rearrangement (Table 1). At reflux temperature a mixture of the *N*-acyl urea **4** and the urea **5** is formed, but reaction at 80 °C results in exclusive formation of the urea **5**. The nature of the products formed from *N*-substituted amidines is clearly determined by the substituent type and the temperature. A well defined pattern can be recognised in the results shown in Table 1. We have rationalised the formation of the rearrangement products **3–5** by the general mechanism shown in Scheme 1. Electrophilic



7 **8** **9**

Scheme 1

attack (PhI^+OAc) with formation of acetic acid gives the hypervalent iodine species **7** which upon elimination of a second molecule of acetic acid forms the ylide **8**. A concerted rearrangement and loss of iodobenzene generates the carbodiimide **9** which then reacts with acetic acid in a well established manner[12,13] to give the observed products **4** and **5**. Evidence

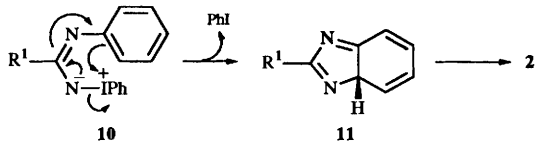
Table 1 Reaction of *N*-substituted amidines **1** with (diacetoxyiodo)benzene

Amidine	R^1	R^2	Temp. (°C)	Product yield (%) and mp (°C)[a] 2	3	4	5
1a	$PhCH_2$	Ph	110	82 (187–189)	—	—	—
1b	Cyclohexyl	Ph	110	95 (258–260)	—	—	—
1c	Et	Ph	110	72 (173–175)	—	—	—
1d	Ph	Cyclohexyl	110	—	96 (137–140)	—	—
1e	Ph	Ph	110	—	99 (175–177)	—	—
			80	9 (288–291)	—	67 (105–106)	—
			50	16	—	65	—
			25[b]	—	—	—	26 (242–243)
1f	2-Furyl	Ph	110	—	99 (168–169)	—	—
			80	—	—	67 (107–109)	—
1g	$PhCH_2$	Cyclohexyl	110	—	—	17 (95)	77 (150–153)
			80	—	—	—	83
1h	Cyclohexyl	$PhCH_2$	110	—	—	27 (107–109)	56 (153–156)
1i	Cyclohexyl	Cyclohexyl	110	—	—	21 (125–126)	28 (231–233)
			80	—	—	—	68

[a] For known compounds mps are in agreement with literature values and full details will be reported in a full paper. Satisfactory spectroscopic and microanalytical data were obtained for all compounds. [b] Diphenylcarbodiimide trimer (30%) (mp 163–166 °C) was also formed under these conditions.

for formation of a carbodiimide was provided when the amidine **1e** was treated with DAIB at 25 °C. Under these conditions the products were the urea **5e** and diphenylcarbodiimide, isolated as its trimer (30%).

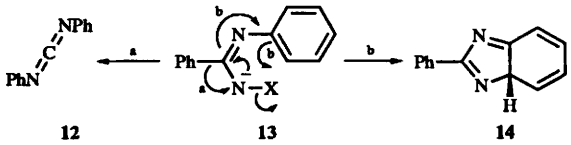
We presume that the *C*-alkyl *N*-phenyl formimidamides **1a–c** form a similar ylide intermediate **10** which then reacts by an alternative concerted cyclo-α-elimination pathway giving benzimidazoles **2** *via* the intermediates **11** (Scheme 2). In this context



10 **11**

Scheme 2

it is interesting to consider how the nature of the leaving group X influences the preferred reaction pathway (rearrangement, path a, or cyclo-α-elimination, path b) in the series of *N*-phenylbenzamidamide derivatives **13** (Scheme 3). When X is an



12 **13** **14**

Scheme 3

exceptionally good leaving group rearrangement appears to be preferred. This is the case for the results described in this paper (**13**; $X = I^+Ph$) and also for the systems **13** [$X = N_2^+$,[14] $X = Cl^+Ag$[15] and $X = OSO_2Ph$ (in aqueous media)].[16] In contrast, when the leaving group X is less nucleofugic in the derivatives **13** [X = Cl,[17] $X = S^+Me_2$,[18] $X = N^+Me_3$[19] and $X = OSO_2Ph$ (in non-aqueous media)][16,20] cyclo-α-elimination is preferred and *N*-phenylbenzimidazole formation occurs *via* the intermediate **14**. The triphenylphosphonium derivative **13** ($X = P^+Ph_3$) reacts by neither pathway: at high temperature and under vacuum a different fragmentation occurs giving benzonitrile and tetraphenylphosphimide ($PhN^- - P^+Ph_3$).[21] The mode of reaction of LTA with benzimidamides[9] is not clear but may involve cyclo-α-elimination of an intermediate of the type **13** [$X = Pb(OAc)_3$]. Nitrene intermediates have invariably been proposed for formation of the products **2** (R^1 = Ph) and **12** from the derivatives **13** but there is no evidence that nitrenes are involved in any of these reactions. In the case of the *C*-alkyl *N*-phenyl derivatives **1a–c** the electronic structure of the alkyl groups presumably promotes cyclisation and at the same time they are less favourable migrating groups.

Experimental

The products described were obtained using the following typical procedures.

Reactions of (diacetoxyiodo)benzene

(a) With *N*-(phenyl)phenylacetimidamide 1a at 110 °C. A solution of (diacetoxyiodo)benzene (3.22 g, 10 mmol) in toluene (50 cm^3) was heated under reflux (110 °C) and a solution of the amidine **1a** (1.96 g, 10 mmol) in toluene (50 cm^3) was added dropwise. The solvent was removed by evaporation and the residual mixture was purified by flash chromatography (silica gel: $CHCl_3$–MeOH 9:1 as eluent). In addition to iodobenzene, two products were isolated. The first component was obtained as a solid which after recrystallisation was identified as compound **3e** (1.56 g, 99%), needles (from MeCN), mp 175–177 °C (lit.,[22] 169–170 °C) (Found: C, 76.3; H, 5.5; N, 13.4. Calc. for $C_{20}H_{17}N_3O$: C, 76.2; H, 5.4; N, 13.3%); ν_{max}/cm^{-1} 3216, 3108, 1678, 1634, 1590, 1546, 1484, 1444, 1290 and 1260; $\delta_H(CDCl_3)$ 6.73–7.52 (m, 15 H, ArH), 7.99 (br s, 1 H, NH) and 12.11 (br s, 1 H, NH). The second product was recrystallised and identified as acetanilide (0.54 g, 80%), needles (from MeCN), mp 112–114.5 °C (lit.,[23] 115–116 °C) (Found: C, 70.8; H, 6.4; N, 10.6. Calc. for C_8H_9NO: C, 71.1; H, 6.7; N, 10.4%).

(b) With *N*²-phenylfuran-2-carboximidamide 1f at 80 °C. Using a heating bath maintained at 80 °C, the above procedure was followed using (diacetoxyiodo)benzene (1.61 g, 5 mmol) and the amidine **1f** (0.93 g, 5 mmol). A single product was isolated using chromatography (silica gel: $CHCl_3$–MeOH 9:1 as eluent) and after recrystallisation was identified as *N-acetyl-N-(2-furyl)-N'-phenylurea* **4f** (0.82 g, 67%), prisms (from MeCN), mp 107–109 °C (Found: C, 64.3; H, 4.8; N, 11.7. $C_{13}H_{12}N_2O_3$ requires C, 63.9; H, 4.9; N, 11.5%); ν_{max}/cm^{-1} 3206, 3134, 1718, 1596, 1544, 1498, 1444, 1424, 1370, 1270, 1216 and 1178; $\delta_H(CDCl_3)$ 2.0 (s, 3 H, CH_3), 6.2–6.5 (m, 2 H, furyl 3-H and 5-H), 6.9–7.6 (m, 6 H, Ph and furyl 4-H) and 10.6 (br s, 1 H, NH); *m/z* 244 (M^+).

Thermolysis of *N*-acetyl-*N*-(2-furyl)-*N'*-phenylurea 4f

A mixture of compound **4f** (0.24 g, 1 mmol) and freshly distilled aniline (0.093 g, 1 mmol) in toluene (10 cm^3) was heated under reflux (20 min). After cooling the solid which had separated was filtered off, recrystallised and identified as *N*,*N'*-diphenylurea **5e** (0.2 g, 94%), needles (from EtOH), mp 242–243 °C (lit.,[24] 242–244 °C). The yellow filtrate was evaporated to give a solid which was recrystallised and identified as N-(2-*furyl*)*acetamide* **6** (R = Me) (0.11 g, 88%), buff needles (from MeCN), mp 111–113 °C. (Found: C, 57.9; H, 5.3; N, 11.0. $C_6H_7NO_2$ requires C, 57.6, H, 5.6, N, 11.2%); ν_{max}/cm^{-1} 3200, 3042, 2836, 1656, 1610, 1566, 1366, 1280, 1232, 1216, 1148 and 1068; $\delta_H(CDCl_3)$ 2.16 (s, 3 H, CH_3), 6.29–6.31 (d, 1 H, *J* 0.9, furyl 3-H), 6.34–6.35 (m, 1 H, furyl 4-H) and 7.02–7.03 (m, 1 H, furyl 5-H); *m*/*z* 125 (M^+).

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