Decomposition of 2-dialkylaminobenzoyl azides to yield isocyanates and 1,1-dialkylindazol-1-ium-3-olates

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Substituted benzoyl azides normally yield the correspondingly substituted isocyanates but when a dialkylated amino group is in the 2-position, in addition to the isocyanate, the 1,1-dialkylated indazol-1-ium-3-olate is produced. The ratio of the two products is very variable depending upon the substitution in the benzene ring. Largest yields of the zwitterionic products were found when there was a substituent in the 3-position regardless of whether the substituent was electron-donating or -withdrawing.

By 1917, Curtius had produced a long series of papers on the decomposition of acyl azides into isocyanates. In almost the last of these papers[1] he reported the anomalous decomposition of 2-dimethylaminobenzoyl azide to yield a dark, uncrystallisable material which he could not identify. Since the isocyanates were reactive and difficult to isolate in a pure state, a common procedure was to decompose the azide in ethanolic solution so that the urethane, in this case 2-dimethylaminophenylurethane, could be easily isolated. It was not found. We have investigated this decomposition and several others where identifiable products have been separated and we have briefly reported on one of them **4b**.[2]

Results and discussion

2-Dimethylaminobenzoyl azide **4a**, its 3-methyl homologue **4b** and its 2-diethylamino analogue **4c** were prepared as outlined in Scheme 1 from the appropriate methyl anthranilate **1** in a
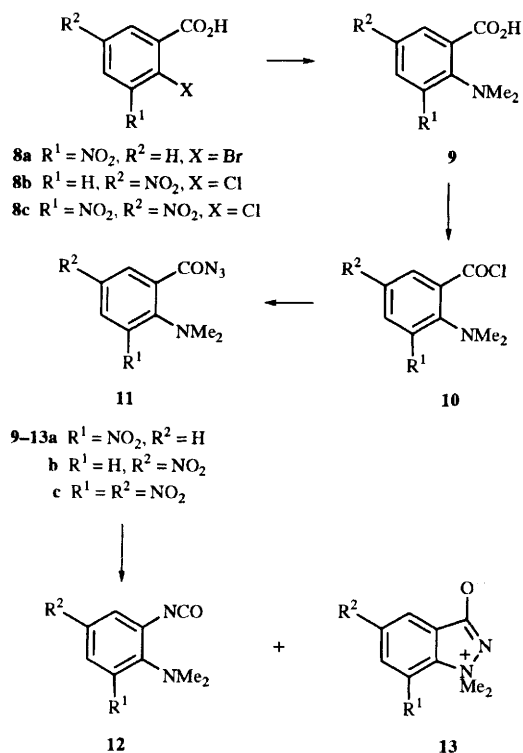

1–7a $R^1 = H, R^2 = Me$
b $R^1 = R^2 = Me$
c $R^1 = H, R^2 = Et$

Scheme 1
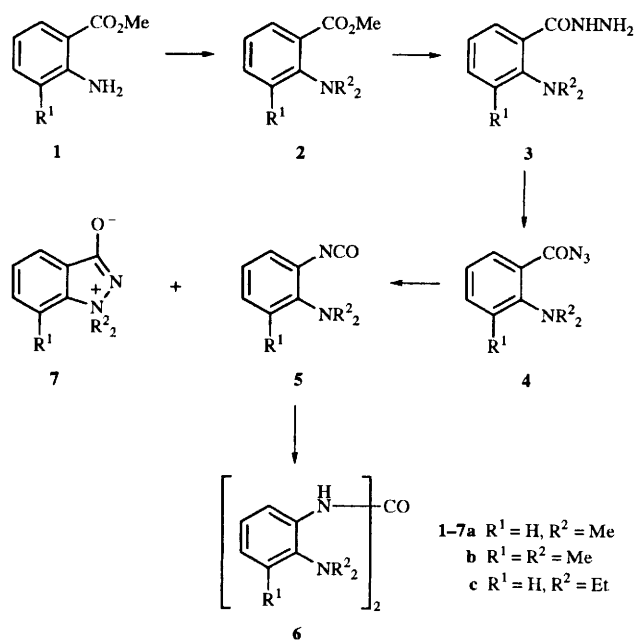
similar manner to that used by Curtius.[1] First of all, a two-step alkylation of the nitrogen atom was employed with methyl iodide in the cases of **2a** and **2b** but with ethyl bromide to yield **2c**. In each case, treatment of the alkylated ester with hydrazine

hydrate produced the hydrazide which was converted into its more stable dihydrochloride.

Curtius did not make clear the precise amount of sodium nitrite required for conversion of the hydrazide into the azide. We found that when only 1 molar equiv. was used, large amounts of hydrazide were recovered unchanged, so it was essential to use 2 molar equiv. of sodium nitrite at $-15\,°C$ followed by neutralisation of the excess of nitrous acid with sodium hydroxide at the end of the reaction period. The addition of one equivalent of the weak base sodium nitrite probably only deprotonates the dialkylamino group and a second equivalent is needed to deprotonate the hydrazide before reaction to yield the azide can take place. In consequence, one equivalent of the nitrous acid generated was not used and, if not neutralised, it disproportionated or was oxidised into other oxidised nitrogen compounds which caused oxidation and nitration of the azides and their decomposition products. The uncrystallisable material obtained by Curtius was the result of attack by this mixture. The isolation of the nitrate salt of zwitterion **7b**[2] confirms that the mixture contained nitric acid. In our cases therefore, excess of acid was neutralised with sodium hydroxide before extraction of the azide products with ether. Usually no attempt was made to isolate the azides because of their rapid decomposition and for the same reason the ether solution could not be dried sufficiently quickly to decompose them under anhydrous conditions. Benzene was added to the ether solution and the ether removed by rotary evaporation at $5\,°C$ to leave the decomposing azide in benzene solution. When small amounts of ether solution of the azide were rotary evaporated in a bath at $-20\,°C$ it was possible to observe the oily azide briefly, but almost at once a spontaneous explosion occurred even with amounts of 1 g or less. Attempted isolation of these azides is consequently extremely hazardous. Due to the presence of water, when the azides decomposed by warming the benzene solution, the symmetrical ureas **6** were produced *via* the isocyanates **5** in solution and the zwitterions **7** filtered off as crystalline precipitates. The isocyanates **6** did have a brief existence in the benzene solution, indicated by a sharp isocyanate odour and the IR spectra of evaporated benzene solutions which always showed a peak near $2200\ cm^{-1}$ (**6a**, 2210 cm^{-1}; **6b**, 2115 cm^{-1}; **6c**, 2097 and 2125 cm^{-1}). The zwitterion **7a** crystallised with three molecules of water of crystallisation; zwitterion **7b** had one molecule of water and zwitterion **7c** crystallised without any defined amount of water though it was slightly hygroscopic.

The nitro substituted azides **11** were prepared as indicated in Scheme 2 by reaction of sodium azide with the substituted 2-dimethylaminobenzoyl chlorides **10** in excellent yield. This

8a $R^1 = NO_2$, $R^2 = H$, $X = Br$
8b $R^1 = H$, $R^2 = NO_2$, $X = Cl$
8c $R^1 = NO_2$, $R^2 = NO_2$, $X = Cl$

9–13a $R^1 = NO_2$, $R^2 = H$
b $R^1 = H$, $R^2 = NO_2$
c $R^1 = R^2 = NO_2$

Scheme 2

Table 1 ^1H and ^{13}C NMR chemical shifts of alkyl substituents of zwitterions **7** and **13**

Zwitterion	δ_H	δ_C
7a	3.42 (CH$_3$)	56.70
7b	3.40 (CH$_3$)	54.86
7c	3.87 (CH$_2$)	—
13a	3.79 (CH$_3$)	55.77
13b	3.53 (CH$_3$)	—
13c	3.73 (CH$_3$)	56.03

Table 2 Yield of products (%) from decompositions of 2-dialkyl-aminobenzoyl azides

Azide	Isocyanate **12** or urea **6**	Zwitterion **7** or **13**
4a	56	31
4b	11	81
4c	9	79
11a	7	77
11b	86	0.7
11c	65	31

compound **13c** was also isolated and its structure suggested, though not confirmed, thus constituting the first isolation of this type of compound.

The structure of the zwitterion **7b** has been demonstrated by X-ray diffraction in a preliminary publication.[2] All the zwitterions prepared in this work have similar structures since the ^1H NMR and ^{13}C NMR spectra shown in Table 1 are similar and confirm the quaternary nature of the alkylated nitrogen atom.

The azide decompositions produced the two types of compound in very different proportions as shown in Table 2. This wide variation in yield of the two products suggests that the decomposition of the azide may proceed *via* either a concerted mechanism or the nitrene intermediate **14** which could yield the isocyanate **15** or the ylide **16** at rates which are dependent on the other ring substituents (Scheme 3).

Scheme 3

method could not be used to prepare the azides which did not have a nitro substituent, since all attempts to make the acid chlorides resulted in black gums. The nitro substituted azides were precipitated as crystalline materials from the acetone reaction mixture in all three cases. The crystals of mono-nitroazides **11a** and **11b** could be filtered and washed with cold acetone at temperatures below 0 °C. They did not explode below 0 °C though slow decomposition did occur. The dinitro azide **11c** appeared to be stable at temperatures up to 20 °C. It was always inadvisable to isolate sizeable quantities of these azides. Very small quantities were stable for a short time so that decomposition points of 57 (**11a**), 70 (**11b**), and 76 °C (**11c**) were found. These nitro azides, when warmed gently in benzene, produced soluble isocyanates **12** and crystalline precipitates of the zwitterions **13**.

The IR spectra of these isocyanates are unusual in that the absorption peak near 2200 cm^{-1} was absent. Instead there was a very strong broad peak near 1800 cm^{-1} (**12a**, 1854 cm^{-1}; **12b**, 1796 cm^{-1}; **12c**, 1848 cm^{-1}). This may be a large vinylogous shift, though Williams and Fleming[3] comment that the figure of 2200 cm^{-1} is based on very few observations. Isolation of the isocyanates was confirmed by their reactions with water to produce symmetrical ureas and with aniline to yield unsymmetrical diphenyl ureas. The dinitro derivative **12c** was investigated more extensively by reactions with aqueous acetone to produce the corresponding amine and with methanol giving the methyl carbamate to confirm the results of the azide decomposition, since this was the first azide decomposition investigated by one of us in 1952.[4] At this time the zwitterionic
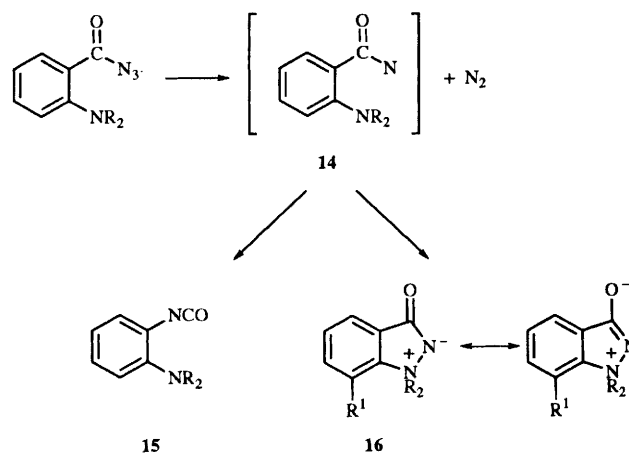
Decomposition of acid azides with an *o*-dialkylamino group present has been discussed previously[5] chiefly in the context of the decomposition of sulfonyl azides which yield ylides similar to **16**. Anchimeric assistance of the decomposition, *via* a nitrene intermediate, was suggested since the azides all decomposed at low temperatures even if the product was only the isocyanate. All the azides reported here also decomposed at low temperatures.

The most remarkable feature of Table 2 is that the azide **11b** yields almost no zwitterionic material. This is in agreement with the findings of Martin, Meth-Cohn and Suschitzky[5] where only the isocyanates or symmetrical ureas were isolated when the nitro group was in the 5-position (as in this case) but where the dialkylamino groups were pyrrolidine, piperidine and azepane. They had hoped to prepare these indazol-1-ium-3-olates since they had shown that the decomposition of sulfonyl azides did produce analogous zwitterionic structures. When the nitro group is in the 5-position, electron withdrawal of the lone pair on the nitrogen atom of the dialkylamino group into the benzene ring must take place to such an extent that it is not readily available for cyclisation before rearrangement of the azide to the isocyanate occurs.

However, when the nitro group is in the 3-position of the azide **11a** the yield of zwitterion is high and similar to that found for the 3-methyl derivative **4b**. Since nitro and methyl groups normally have opposite electronic effects in a benzene ring, the probability must be that these substituents produce the high yield *via* a steric effect which must exist to some extent with three groups of this size in adjacent positions on the benzene ring. A substituent in the 3-position may cause the lone pair of electrons on the adjacent dimethylamino group to be orientated favourably for cyclisation instead of rearrangement to the isocyanate.

The proportions of isocyanate and zwitterion produced by decomposition of the 3,5-dinitro azide **11c** are intermediate between the yields from the 3- and 5-mononitro azides reflecting both electron withdrawal into the ring and steric interaction.

The unsubstituted diethylamino azide, unlike its dimethylamino analogue, gives a high yield of zwitterionic product. Possibly in the case of the azide **4c** the two ethyl groups create greater electron availability on the alkylated nitrogen atom and greater steric hindrance to favour larger amounts of the zwitterion **7c**.

Zwitterion **13b** has been made previously[6] by cyclisation of *N,N*-dimethyl-2-chloro-5-nitrobenzohydrazide in high yield in contrast to the small quantity produced in this work. This earlier characterisation of **13b** helped to confirm our isolation of this small amount and our analytical and spectral data are given for comparison. Cyclisation by this alternative method has been extended by the same group of workers[7] to produce other indazol-1-ium-3-olates and they have used them in the synthesis[8,9] of 1-substituted indazolols which show remarkable cytostatic activity. It is hoped that this new method of preparation of indazol-1-ium-3-olates may assist with this work.

Experimental

Melting points were determined on an Electrothermal 1900 capillary apparatus and are uncorrected. ^{1}H NMR spectra were recorded at 80 MHz using a Bruker WP-80 instrument. ^{13}C NMR spectra were taken on a Bruker AMX spectrometer at 600 MHz. *J* Values are given in Hz. IR spectra were taken on a Perkin-Elmer 1600 FT-IR machine. Mass spectra were obtained by EI at 70 eV using the Kratos MS 50 RF with the DS 90 data system. 'Ether' refers to diethyl ether. Boiling points refer to those obtained by bulb-to-bulb distillation.

Methyl 3-methyl-2-methylaminobenzoate

Methyl 2-amino-3-methylbenzoate **1b** (22.3 g, 0.135 mol) was heated under reflux for 24 h with methyl iodide (15 cm³) and methanol (50 cm³). A crust of the hydriodide salt of the product formed around the top of the solution. After rotary evaporation of the mixture, water (100 cm³) was added to dissolve the residue and the hydriodic acid was neutralised by the slow addition of a suspension of sodium hydrogen carbonate (11.5 g, 0.136 mol) in water (25 cm³). The solution was extracted with ether (200 cm³) in four portions, and the organic extracts were dried with sodium sulfate and evaporated to give the monomethylated product, (21.0 g, 87%) which was distilled, bp 130–134 °C/18 mmHg (Found: C, 67.1; H, 7.0; N, 8.1. $C_{10}H_{13}NO_2$ requires C, 67.0; H, 7.3; N, 7.8%); ν_{max}(film)/cm⁻¹ 3352 (NH), 3058 (ArCH), 2946 (CH), 1690 (CO), 1598 and 1510 (Ar conj.); δ_H(CDCl₃) 7.84 (1 H, dd, *J* 8 and 2, ArH), 7.28 (1 H, dd, *J* 8 and 2, ArH), 6.76 (1 H, t, *J* 8, ArH), 6.67 (1 H, br s, NH), 3.87 (3 H, s, OCH₃), 2.90 (3 H, s, NCH₃) and 2.36 (3 H, s, ArCH₃).

Methyl 2-methylaminobenzoate can be prepared similarly in equally high yield, which is preferable to the method of Willstatter and Kahn.[10]

Methyl 2-dimethylamino-3-methylbenzoate 2b

Methyl 3-methyl-2-methylaminobenzoate (21.0 g, 0.117 mol) was heated under reflux for 24 h with methyl iodide (15 cm³) and methanol (50 cm³) and then worked up by the same procedure as for the monomethylation. The yield of the dimethylamine **2b**, bp 141–143 °C/16 mmHg, was 18.5 g (82%) (Found: C, 68.4; H, 7.85; N, 7.3. $C_{11}H_{15}NO_2$ requires C, 68.4; H, 7.8; N, 7.25%); ν_{max}(film)/cm⁻¹ 3048 (ArCH), 2975, 2942, 2918, 2863 and 2790 (CH), 1725 (CO), 1590 and 1492 (Ar conj.); δ_H(CDCl₃) 7.94 (2 H, m, 2ArH), 7.56 (1 H, t, *J* 8.5, ArH), 4.21 (3 H, s, OCH₃), 3.01 [6 H, s, N(CH₃)₂] and 2.50 (3 H, s, ArCH₃).

For the preparation of methyl 2-dimethylaminobenzoate **2a**, this method gives a much higher yield than previously found.[10]

Methyl 2-ethylaminobenzoate

Methyl 2-aminobenzoate **1a** (45 g, 0.29 mol) was heated under reflux for 7 days with ethyl bromide (36 g, 0.33 mol) and ethanol (100 cm³). The reaction mixture was worked up in a similar manner to the preparation of methyl 3-methyl-2-methylaminobenzoate to yield the oily methylamino ester (48.3 g, 91%), which was distilled, bp 145 °C/16 mmHg (Found: C, 66.9; H, 7.0; N, 7.6. $C_{10}H_{13}NO_2$ requires C, 67.0; H, 7.3; N, 7.8%); ν_{max}(film)/cm⁻¹ 3368 (NH), 3088 (ArCH), 2971, 2963 and 2874 (CH), 1683 (CO), 1607, 1581 and 1510 (Ar conj.); δ_H(liquid) 7.68 (1 H, dd, *J* 8 and 2, ArH), 7.48 (1 H, br s, NH), 7.03 (1 H, td, *J* 8 and 2, ArH), 6.31 (2 H, m, 2ArH), 3.42 (3 H, s, OCH₃), 2.75 (2 H, q, *J* 7, CH₂) and 0.83 (3 H, t, *J* 7, CH₃).

Methyl 2-diethylaminobenzoate 2c

Methyl 2-ethylaminobenzoate (15 g, 84 mmol) was heated under reflux with ethyl bromide (20 g, 0.184 mol) and ethanol (100 cm³) for 24 h. The methyl 2-diethylaminobenzoate **2c** was isolated in a similar way to the mono ethyl compound, to give an oil (16.3 g, 93%) which was distilled, bp 157 °C/15 mmHg (Found: C, 69.6; H, 8.2; N, 6.55. $C_{12}H_{19}NO_2$ requires C, 69.5; H, 8.3; N, 6.8%); ν_{max}(film)/cm⁻¹ 3065 (ArCH), 2913, 2871 and 2836 (CH), 1723 (CO), 1596, 1568 and 1489 (Ar conj.); δ_H(liquid) 7.45 (1 H, dd, *J* 7 and 2, ArH), 7.15 (1 H, td, *J* 7 and 2, ArH), 6.66 (1 H, td, *J* 7 and 2, ArH), 6.13 (1 H, dd, *J* 7 and 2, ArH), 3.34 (3 H, s, OCH₃), 2.63 (4 H, q, *J* 7, 2CH₂) and 0.60 (6 H, t, *J* 7, 2CH₃).

Reaction of dialkylamino esters 2 with hydrazine hydrate

The dialkylamino esters **2** (0.1 mol) were heated under reflux with hydrazine hydrate (8.5 cm³, 0.15 mol) for 72 h after which the mixture was concentrated by evaporation under reduced pressure. The resulting viscous oils were successively extracted with hot light petroleum (bp 100–120 °C, 1 dm³) leaving behind small amounts of red oil and evaporation of the extracts gave the crude hydrazides. 2-Dimethylamino-3-methylbenzohydrazide was produced in 100% yield, mp 72–76 °C, which was recrystallised for analysis from light petroleum (bp 100–120 °C) to give the pure hydrazide, mp 80–81 °C (Found: C, 62.3; H, 7.8; N, 21.5. $C_{10}H_{15}N_3O$ requires C, 62.15; H, 7.8; N, 21.7%); ν_{max}(KBr)/cm⁻¹ 3290, 3257 and 3195 (NH), 2979, 2923, 2868 and 2789 (CH), 1634, 1586 and 1513 (CO, NH and Ar conj.); δ_H[(CD₃)₂SO] 9.44 (1 H, br s, NH), 7.06 (3 H, m, ArH), 4.40 (2 H, br s, NH₂), 2.70 [6 H, s, N(CH₃)₂] and 2.28 (3 H, s, ArCH₃). 2-Diethylaminobenzohydrazide was produced as a very viscous oil which could not be purified. It was converted into its dihydrochloride for analysis and subsequent reactions.

Preparation of hydrazide dihydrochlorides 3

The hydrazides (0.1 mol) were dissolved and warmed in ethanol (150 cm³) which had been saturated with HCl gas, which gave the dihydrochlorides as white crystalline powders.

2-Dimethylamino-3-methylbenzohydrazide dihydrochloride 3b.
(73%), Mp 186–188 °C (EtOH) (Found: Cl, 26.3. $C_{10}H_{15}N_3O\cdot$2HCl requires Cl 26.6%); ν_{max}(KBr)/cm⁻¹ 2950, 2912, 2847 and 2720 (CH), 2649 and 2578 (NH⁺), 1686, 1649 and 1590

(CO, NH and Ar conj.); δ_H[(CD$_3$)$_2$SO] 7.28 (3 H, m, 3ArH), 7.20 (4 H, vbr s, 4NH), 2.85 (6 H, s, 2NCH$_3$) and 2.35 (3 H, s, ArCH$_3$).

2-Diethylaminobenzohydrazide dihydrochloride 3c. (71%), Mp 186–188 °C (dec., EtOH) (Found: C, 47.1; H, 6.7; N, 14.8; Cl, 25.6. C$_{11}$H$_{17}$N$_3$O·2HCl requires C, 47.15; H, 6.8; N, 15.0; Cl, 25.3%); ν_{max}(KBr)/cm^{-1} 3375 (br NH), 2947, 2840 and 2721 (CH), 1662, 1611, 1560, 1532 and 1483 (CO, NH and Ar conj.); δ_H[(CD$_3$)$_2$SO] 7.82 (4 H, m, 4ArH), 6.16 (4 H, br s, 4ArH), 3.57 (4 H, q, J 7, 2CH$_2$) and 0.98 (6 H, t, J 7, 2CH$_3$).

Preparation and decomposition of 2-dialkylaminobenzoyl azides 4

The hydrazide dihydrochlorides 3 (10 mmol) were dissolved in water (5 cm^3), covered with ether (50 cm^3) and cooled to −10 °C. Sodium nitrite (1.52 g, 11 mmol) in water (3 cm^3), also cooled to −10 °C, was added dropwise to the stirred mixture over 10 min keeping the temperature below −5 °C. Even at this stage the already formed azides started to decompose, causing bubbles of nitrogen to evolve and cloudiness to appear in the ether solution. The reaction was allowed to continue for a further 20 min at −10 °C, after which a solution of sodium hydroxide (0.44 g, 11 mmol) in water (2 cm^3) at −10 °C was added over a period of 2 min. The ether solution was separated from the aqueous solution which was extracted with more cold (−10 °C) ether (2 × 25 cm^3). **CAUTION**. Isolation of the oily azides by evaporation of this ether solution at low temperatures must not be attempted as they explode spontaneously below 0 °C. To the combined ether solutions was added benzene (30 cm^3), the ether was distilled off at 50 °C and heating of the benzene solution was continued for 30 min to complete the decomposition of the azide. White crystals of the zwitterions 7 were filtered off from the cooled benzene solution and a further small quantity of 7 was obtained by extraction of the evaporated filtrate with boiling acetone. The combined amounts were purified together.

1,1-Dimethylindazol-1-ium-3-olate trihydrate 7a. Recrystallised from acetone containing a little water (31%), mp softens 60–70 °C, melts 218–220 °C (Found: C, 50.3; H, 7.8; N, 12.95. C$_9$H$_{10}$N$_2$O·3H$_2$O requires C, 50.0; H, 7.5; N, 13.0%); ν_{max}(KBr)/cm^{-1} 3424, 3380 and 3233 (OH), 3047 (ArCH), 1655 and 1566 ($^-$OCN) and 1634 (Ar conj.); δ_H[(CD$_3$)$_2$SO] 7.97 (1 H, m, ArH), 7.51 (3 H, m, 3ArH), 3.42 [6 H, s, N(CH$_3$)$_2$] and 3.34 (6 H, s, 3H$_2$O); δ_C[(CD$_3$)$_2$SO] 171.78 (CO$^-$), 154.61, 130.98, 130.53, 129.90, 123.19 and 116.67 (Ring C) and 56.71 [N(CH$_3$)$_2$].

1,1,7-Trimethylindazol-1-ium-3-olate monohydrate 7b. Recrystallised from acetone–methanol (81%), mp softens 60–70 °C, melts 226–228 °C (Found: C, 61.75; H, 7.1; N, 14.3. C$_{10}$H$_{12}$N$_2$O·H$_2$O requires C, 61.8; H, 7.3; N, 14.4%); ν_{max}(KBr)/cm^{-1} 3480, 3419 and 3312 (OH), 3042 (ArCH), 1666 and 1573 ($^-$OCN) and 1634 (Ar conj.); δ_H[(CD$_3$)$_2$SO] 7.38 (3 H, m, 3ArH), 3.40 [6 H, s, N(CH$_3$)$_2$], 3.32 (2 H, s, H$_2$O) and 2.60 (3 H, s, ArCH$_3$); δ_C[(CD$_3$)$_2$SO] 117.30 (CO$^-$), 152.06, 133.16, 131.21, 131.01, 127.02 and 121.02 (Ring C), 54.86 [N(CH$_3$)$_2$] and 17.55 (ArCH$_3$).

1,1-Diethylindazol-1-ium-3-olate 7c. Obtained as slightly hygroscopic crystals (79%), mp 205–206 °C (acetone) (Found: C, 69.3; H, 7.3; N, 14.8. C$_{11}$H$_{14}$N$_2$O requires C, 69.4; H, 7.4; N, 14.7%); ν_{max}(KBr)/cm^{-1} 3086, 3047 and 3014 (ArCH), 2994, 2981 and 2942 (CH), 1633 and 1463 ($^-$OCN) and 1584 (Ar conj.); δ_H[(CD$_3$)$_2$SO] 7.85 (1 H, m, ArH), 7.53 (3 H, m, 3ArH), 3.87 (4 H, q, J 7, 2CH$_2$) and 0.78 (6 H, t, J 7, 2CH$_3$).

Evaporation of the above benzene filtrate produced brown solids which were recrystallised from ethanol to yield the symmetrically substituted ureas 6 as white crystals.

N,N'-Bis(2-dimethylaminophenyl)urea 6a. (53%), Mp 202–203 °C (Found: C, 68.5; H, 7.3; N, 18.5. C$_{17}$H$_{22}$N$_4$O requires C, 68.4; H, 7.4; N, 18.8%); ν_{max}(KBr)/cm^{-1} 3231 (NH), 3056 (ArCH), 2972, 2936, 2854, 2827 and 2787 (CH), 1660 and 1522

(CONH) and 1589 (Ar conj.); δ_H[(CD$_3$)$_2$SO] 8.85 (2 H, br s, 2NH), 7.92 (2 H, dd, J 7 and 4, 2ArH), 6.99 (6 H, m, 6ArH) and 2.62 [12 H, s, 2N(CH$_3$)$_2$].

N,N'-Bis(2-dimethylamino-3-methylphenyl)urea 6b. (11%), Mp 213–215 °C (Found: M$^+$, 326.2107. C$_{19}$H$_{20}$N$_4$O requires M, 326.2107); ν_{max}(KBr)/cm^{-1} 3228 (NH), 2960, 2921, 2852, 2827 and 2785 (CH), 1654, 1597, 1582 and 1522 (CONH and Ar conj.); δ_H[(CD$_3$)$_2$SO] 7.16 (6 H, m, 6ArH), 6.79 (2 H, br s, 2NH), 2.72 [12 H, s, 2N(CH$_3$)$_2$] and 2.28 (6 H, s, 2ArCH$_3$).

N,N'-Bis(2-diethylaminophenyl)urea 6c. (9%), Mp 189–190 °C (Found: M$^+$, 354.2418. C$_{21}$H$_{30}$N$_4$O requires M, 354.2420); ν_{max}(KBr)/cm^{-1} 3254 (NH), 3030 (ArCH), 2960, 2932, 2842 and 2820 (CH), 1654, 1595 and 1525 (CONH and Ar conj.); δ_H[(CD$_3$)$_2$SO] 8.64 (2 H, s, 2NH), 7.86 (2 H, m, 2ArH), 7.02 (6 H, m, 6ArH), 2.84 (4 H, q, J 7, 2CH$_2$) and 0.65 (6 H, t, J 7, 2CH$_3$).

Modifications of the decomposition reaction of azide 4b

(*a*) When sodium hydroxide was not used to neutralise the solution in the above procedure, much brown material was produced in the benzene solution and the product which precipitated from the decomposition reaction was the nitrate salt of the zwitterion **7b**[2] (22%) which was recrystallised from methanol, mp 170–171 °C with explosive decomposition. Since the compound exploded on heating, neither elemental nor mass spectral analysis was possible but the structure has been confirmed by X-ray diffraction:[2] ν_{max}(Nujol)/cm^{-1} 3048 (ArCH), 1738, 1618, 1582 and 1560 (Ar conj.) and 1373 (NO$_3^-$); δ_H[(CD$_3$)$_2$SO] 7.81 (3 H, s, 3ArH), 3.87 [6 H, s, N(CH$_3$)$_2$] and 2.72 (3 H, s, ArCH$_3$); δ_C[(CD$_3$)$_2$SO] 168.68 (CO$^-$), 151.36, 136.94, 132.49, 128.30, 124.57 and 122.10 (Ring C), 54.74 [N(CH$_3$)$_2$] and 17.11 (ArCH$_3$). (*b*) When the above azide formation procedure was used but with only 10 min reaction time with the nitrous acid, some of the azide produced decomposed as usual but the majority reacted with unchanged hydrazide to yield N,N'-*bis*(2-*dimethylamino*-3-*methylbenzo*)*hydrazide* (49%) which was soluble in the warm benzene and so easily separated from the insoluble zwitterion **7b** (38%). The bishydrazide was recrystallised from methanol for analysis, mp 203–204 °C (Found: C, 67.8; H, 7.4; N, 15.9 and M$^+$, 354.2059. C$_{20}$H$_{26}$N$_4$O$_2$ requires C, 67.8; H, 7.4; N, 15.8% and M, 354.2058); ν_{max}(KBr)/cm^{-1} 3275 (NH), 3070 (ArCH), 2936, 2901, 2863 and 2800 (CH), 1619, 1578 and 1472 (CONH and Ar conj.); δ_H[(CD$_3$)$_2$SO] 7.54 (2 H, br s, 2NH), 7.22 (6 H, m, 6ArH), 2.67 [12 H, s, 2N(CH$_3$)$_2$] and 2.31 (6 H, s, 2ArCH$_3$).

2-Dimethylamino-3-nitrobenzoic acid 9a

2-Bromo-3-nitrobenzoic acid (17.2 g, 70 mmol) was dissolved in a solution of sodium hydroxide (2.8 g, 70 mmol) in water (50 cm^3) and aqueous dimethylamine (40 cm^3, 40% solution) was added. The solution was heated at 90 °C for 3 d, when a further amount of dimethylamine (20 cm^3, 40% solution) was added and heating continued for 2 more days. 2-Dimethylamino-3-nitrobenzoic acid **9a** was precipitated from solution after the addition of concentrated hydrochloric acid (21 cm^3) as greenish–yellow needles (11.1 g, 76%), mp 109–110 °C (EtOH–H$_2$O) (Found: C, 51.35; H, 4.7; N, 13.0. C$_9$H$_{10}$N$_2$O$_4$ requires C, 51.4; H, 4.8; N, 13.3%); ν_{max}(KBr)/cm^{-1} 3080 (ArCH), 2942, 2915 and 2847 (CH), 1708 (CO), 1598, 1578 and 1496 (Ar conj.), 1532 and 1355 (NO$_2$); δ_H[(CD$_3$)$_2$SO] 7.63 (2 H, m, 2ArH), 7.03 (1 H, t, J 7, ArH), 5.52 (1 H, br s, CO$_2$H) and 2.67 (6 H, s, 2CH$_3$).

Preparation of 2-dimethylaminobenzoyl chlorides 10

The 2-dimethylaminobenzoic acids 9 (60 mmol) were heated under reflux with thionyl chloride (20 cm^3) and benzene (100 cm^3) for 1 h. After the mixture was evaporated, the residue was dissolved in freshly sodium-dried benzene (20 cm^3) and again evaporated. The crude acid chlorides were produced in close to

100% yields and in each case recrystallised from light petroleum (bp 60–80 °C).

2-Dimethylamino-3-nitrobenzoyl chloride 10a. Mp 64–65 °C (Found: C, 47.3; H, 4.0; Cl, 15.2; N, 12.0. $C_9H_9ClN_2O_3$ requires C, 47.3; H, 4.0; Cl, 15.5; N, 12.25%); ν_{max}(KBr)/cm⁻¹ 3070 and 3005 (ArCH), 2935, 2880, 2870 and 2798 (CH), 1750 (CO), 1600 and 1505 (Ar conj.), 1522 and 1340 (NO₂); δ_H[(CD₃)₂CO] 8.16 (1 H, dd, J 8 and 1.5, ArH), 8.03 (1 H, dd, J 8 and 1.5, ArH), 7.29 (1 H, t, J 8, ArH) and 2.88 (6 H, s, 2CH₃).

2-Dimethylamino-5-nitrobenzoyl chloride 10b. Mp 74–75 °C (Found: C, 47.0; H, 4.1; Cl, 15.2; N, 11.9. $C_9H_9ClN_2O_3$ requires C, 47.3; H, 4.0; Cl, 15.5; N, 12.25%); ν_{max}(KBr)/cm⁻¹ 3110 (ArCH), 2975, 2918 and 2821 (CH), 1732 (CO), 1606, 1560 and 1500 (Ar conj.), 1526 and 1325 (NO₂); δ_H[(CD₃)₂CO] 8.87 (1 H, d, J 3, ArH), 8.26 (1 H, dd, J 9 and 3, ArH), 7.26 (1 H, d, J 9, ArH) and 3.22 (6 H, s, 2CH₃).

2-Dimethylamino-3,5-dinitrobenzoyl chloride 10c. Mp 105–106 °C (Found: C, 39.8; H, 3.0; Cl, 13.0; N, 15.1. $C_9H_8ClN_3O_5$ requires C, 39.5; H, 2.9; Cl, 13.0; N, 15.4%); ν_{max}(KBr)/cm⁻¹ 3092 (ArCH), 2923 (CH), 1741 (CO), 1604, 1578 and 1512 (Ar conj.), 1533 and 1328 (NO₂); δ_H(CDCl₃) 8.89 (1 H, d, J 2.5, ArH), 8.70 (1 H, d, J 2.5, ArH) and 2.98 (6 H, s, 2CH₃).

Preparation of 2-dimethylaminobenzoyl azides 11

The 2-dimethylaminobenzoyl chlorides **10** (40 mmol) were dissolved in acetone (200 cm³) and cooled to −15 °C. Sodium azide (6.5 g, 0.1 mol) in water (20 cm³), also cooled to −15 °C, was added dropwise to the stirred solution over 10 min. After the mixture was stirred for 15 min at −15 °C, sodium chloride had precipitated and ice (200 g) and ice–water (200 cm³) were added to precipitate the azides. The mixture was stirred without external cooling until nearly all the ice had melted (20–30 min) and the azides **11** were filtered off on a cold funnel and washed with a little cold aqueous acetone at −15 °C. The lemon-yellow crystals of 2-dimethylamino-3-nitrobenzoyl azide **11a**, because of their explosive nature near 0 °C, were not allowed to become dry but were used immediately in the decomposition reaction in benzene solution. A small amount was spread thinly on filter paper to dry in order to obtain the mp of 57 °C (dec.) which seemed reproducible. It was not possible to record any other physical constants of this compound because of its instability. In a similar way, moist yellow crystals of 2-dimethylamino-5-nitrobenzoyl azide **11b** were obtained, mp 70 °C (dec.). Again it was highly unstable. Deep yellow crystals of 2-dimethylamino-3,5-dinitrobenzoyl azide **11c** were filtered, washed with cold water and dried under reduced pressure at 0 °C over sulfuric acid. The yield was 97%, mp 75–76 °C (dec.). This compound was unstable above 20 °C.

Decomposition of 2-dimethylaminobenzoyl azides 11a and 11b

Benzene (300 cm³) at 5 °C was added to the moist azides (≈40 mmol) and when the azides had dissolved completely, the rapidly warming benzene solution was decanted from small drops of water. The solution temperature rose to 30 °C over 30 min and the solution was then heated to 50 °C for a further 15 min, by which time decomposition was complete. Deep yellow crystals of the zwitterions **13a** and **13b** were filtered off from the cold benzene solution and the yellow isocyanates **12a** and **12b** were obtained on evaporation of the benzene filtrate.

1,1-Dimethyl-7-nitroindazol-1-ium-3-olate 13a. (77% From **10a**), mp 218–220 °C (MeOH) (Found: C, 52.5; H, 4.4; N, 20.0. $C_9H_9N_3O_3$ requires C, 52.2; H, 4.4; N, 20.3%); ν_{max}(Nujol)/cm⁻¹ 3050 and 3008 (ArCH), 1631 (⁻OCN), 1605 (Ar conj.), 1543 and 1345 (NO₂); δ_H[(CD₃)₂CO] 8.48 (1 H, dd, J 6 and 2.5, ArH), 8.07 (2 H, m, 2ArH) and 3.79 (6 H, s, 2CH₃); δ_C[(CD₃)₂SO] 168.73 (CO⁻), 145.27, 139.41, 134.86, 133.60, 130.22 and 127.40 (Ring C) and 55.77 [N(CH₃)₂].

1,1-Dimethyl-5-nitroindazol-1-ium-3-olate 13b. (0.7% From **10b**), mp 192–194 °C (MeOH) (lit.,[6] 188–190 °C) (Found: M⁺,

207.0642. $C_9H_9N_3O_3$ requires M, 207.0644); ν_{max}(KBr)/cm⁻¹ 3098, 3039 and 3006 (ArCH), 2923 (CH), 1644 (⁻OCN), 1610 and 1595 (Ar conj.), 1543 and 1350 (NO₂); δ_H[(CD₃)₂SO] 8.59 (1 H, dd, J 9 and 2.5, ArH), 8.39 (1 H, d, J 9, ArH), 8.22 (1 H, d, J 2.5, ArH) and 3.53 (6 H, s, 2CH₃).

2-Dimethylamino-3-nitrophenyl isocyanate 12a. (7% From **10a**), mp 69–70 °C (benzene–light petroleum, bp 60–80 °C) (Found: M⁺, 207.0643. $C_9H_9N_3O_3$ requires M, 207.0644); ν_{max}(KBr)/cm⁻¹ 2974, 2936 and 2846 (ArCH), 1864 (NCO), 1603 (Ar conj.), 1541 and 1348 (NO₂); δ_H[(CD₃)₂CO] 7.67 (1 H, t, J 5, ArH), 7.40 (2 H, m, 2ArH) and 2.90 (6 H, s, 2CH₃).

2-Dimethylamino-5-nitrophenyl isocyanate 12b. (86% From **10b**), mp 130–131 °C (light petroleum, bp 60–80 °C) (Found: C, 52.4; H, 4.7; N, 20.5. $C_9H_9N_3O_3$ requires C, 52.2; H, 4.4; N, 20.3%); ν_{max}(KBr)/cm⁻¹ 3118, 3063 and 3005 (ArCH), 2955 (CH), 1796 (NCO), 1618 and 1586 (Ar conj.), 1526 and 1348 (NO₂); δ_H[(CD₃)₂CO] 8.10 (1 H, d, J 3, ArH), 7.95 (1 H, dd, J 8 and 3, ArH), 7.41 (1 H, d, J 8, ArH) and 2.97 (6 H, s, 2CH₃).

Decomposition of 2-dimethylamino-3,5-dinitrobenzoyl azide 11c

The dry azide **11c** (4.92 g, 17.5 mmol) was dissolved in dry benzene (50 cm³) at 20 °C and warmed slowly over 10 min to 40 °C and kept at that temperature for 1 h. 1,1-Dimethylamino-5,7-dinitroindazol-1-ium-3-olate **13c** was filtered from the cold solution and washed with dry benzene (1.36 g, 31%), mp 199–200 °C (MeOH) (Found: C, 42.75; H, 3.1; N, 22.4. $C_9H_8N_4O_5$ requires C, 42.9; H, 3.2; N, 22.2%); ν_{max}(KBr)/cm⁻¹ 3099 (ArCH), 2949 and 2863 (CH), 1641 (⁻OCN), 1544 and 1344 (NO₂); δ_H[(CD₃)₂SO] 9.06 (1 H, d, J 2, ArH), 8.55 (1 H, d, J 2, ArH) and 3.71 (6 H, s, 2CH₃); δ_C[(CD₃)₂SO] 167.05 (CO⁻), 150.21, 148.16, 139.77, 137.23, 123.42 and 122.36 (Ring C) and 56.03 [N(CH₃)₂]. 2-Dimethylamino-3,5-dinitrophenyl isocyanate **12c** was isolated from the evaporated benzene filtrate (2.86 g, 65%), mp 111–112 °C (benzene–light petroleum, bp 80–100 °C) (Found: C, 43.1; H, 3.4; N, 22.5. $C_9H_8N_4O_5$ requires C, 42.9; H, 3.2; N, 22.2%); ν_{max}(KBr)/cm⁻¹ 3068 (ArCH), 2966 (CH), 1848 (NCO), 1610 and 1585 (Ar conj.), 1543 and 1344 (NO₂); δ_H(CDCl₃) 8.61 (1 H, d, J 3.5, ArH), 8.29 (1 H, d, J 3.5, ArH) and 2.94 (6 H, s, 2CH₃).

Derivatives of nitro isocyanates 12: (a) Symmetrical urea formation

The nitro isocyanates **12** (1 mmol) were boiled in water (5 cm³) for 5 min, cooled and filtered to give the symmetrical ureas in almost 100% yield.

N,N'-Bis(2-dimethylamino-3-nitrophenyl)urea. Mp 267–268 °C (CHCl₃–CCl₄) (Found: C, 52.3; H, 5.4; N, 21.4. $C_{17}H_{20}N_6O_5$ requires C, 52.6; H, 5.2; N 21.6%); ν_{max}(KBr)/cm⁻¹ 3247 (NH), 2989, 2935, 2881 and 2793 (CH), 1654 (CO), 1601 and 1578 (Ar conj. and NH), 1526 and 1363 (NO₂); δ_H[(CD₃)₂SO] 9.20 (2 H, br s, 2NH), 8.28 (2 H, dd, J 7.5 and 2, 2ArH), 7.39 (2 H, dd, J 7.5 and 2, 2ArH), 7.24 (2 H, t, J 7.5, 2ArH) and 2.81 (12 H, s, 4CH₃).

N,N'-Bis(2-dimethylamino-5-nitrophenyl)urea. Mp 234–235 °C (EtOH) (Found: C, 52.3; H, 5.3; N, 21.4. $C_{17}H_{20}N_6O_5$ requires C, 52.6; H, 5.2; N, 21.6%); ν_{max}(KBr)/cm⁻¹ 3272 (NH), 2990, 2978, 2920, 2865, 2842 and 2800 (CH), 1663 (CO), 1614, 1594, 1565 and 1521 (NH and Ar conj.), 1538 and 1338 (NO₂); δ_H(CF₃CO₂H) 9.42 (2 H, br s, 2NH), 8.54 (4 H, m, 4ArH), 8.14 (2 H, d, J 9.5, 2ArH) and 3.57 (12 H, s, 4CH₃).

N,N'-Bis(2-dimethylamino-3,5-dinitrophenyl)urea. Mp 252–253 °C (EtOH) (Found: C, 42.8; H, 4.0; N, 23.2. $C_{17}H_{18}N_8O_9$ requires C, 42.7; H, 3.8; N, 23.4%); ν_{max}(KBr)/cm⁻¹ 3366 and 3258 (NH), 3095 (ArCH), 2977, 2943, 2888 and 2807 (CH), 1712 and 1600 (CONH and Ar conj.), 1541 and 1350 (NO₂).

(b) Urea formation with aniline. The nitro isocyanates **12** (2 mmol) dissolved in dry benzene (20 cm³) were added to a stirred solution of redistilled aniline (0.186 g, 2 mmol) in dry benzene

(2 cm³) at room temperature and left for 1 h. The ureas precipitated from solution as yellow solids in 90% yields and were filtered off and washed with a little dry benzene.

N-(2-Dimethylamino-3-nitrophenyl)-*N'*-phenylurea. Mp 267–268 °C (dec.) (CHCl₃–CCl₄) (Found: C, 60.1; H, 5.4; N, 18.6. $C_{15}H_{16}N_4O_3$ requires C, 60.0; H, 5.4; N, 18.7%); $\delta_H[(CD_3)_2CO]$ 8.80 (1 H, br s, NH), 8.65 (1 H, dd, J 10 and 4, ArH), 8.55 (1 H, br s, NH), 7.58 (1 H, dd, J 8 and 2, ArH), 7.35 (4 H, m, 4ArH), 7.17 (1 H, dd, J 8 and 2, ArH) and 2.84 (6 H, s, 2CH₃).

N-(2-Dimethylamino-5-nitrophenyl)-*N'*-phenylurea. Mp 219–220 °C (dec.) (CHCl₃) (Found: C, 59.7; H, 5.4; N, 18.7. $C_{15}H_{16}N_4O_3$ requires C, 60.0; H, 5.4; N, 18.7); ν_{max}(Nujol)/cm⁻¹ 3275 (NH), 1639, 1606 and 1500 (CONH and Ar conj.), 1571 and 1320 (NO₂); $\delta_H(CF_3CO_2H)$ 8.40 (3 H, m, 2ArH and NH), 7.99 (1 H, d, J 9, ArH), 7.50 (1 H, br s, NH), 7.40 (5 H, m, 5ArH) and 3.49 (6 H, s, 2CH₃).

N-(2-Dimethylamino-3,5-dinitrophenyl)-*N'*-phenylurea. Mp 227–229 °C (dec.) (MeOH) (Found: C, 52.25; H, 4.4; N, 20.4. $C_{15}H_{15}N_5O_5$ requires C, 52.2; H, 4.4; N, 20.3%); ν_{max}(KBr)/cm⁻¹ 3384 and 3330 (NH), 3117 and 3091 (ArCH), 2966, 2883 and 2807 (CH), 1715 and 1597 (CONH and Ar conj.), 1534 and 1338 (NO₂); $\delta_H[(CD_3)_2SO]$ 9.64 (1 H, br s, NH), 9.27 (1 H, d, J 3, ArH), 8.73 (1 H, br s, NH), 8.21 (1 H, d, J 3, ArH), 7.53 (2 H, dd, J 7 and 2, 2ArH), 7.35 (2 H, t, J 7, 2ArH), 7.03 (1 H, tt, J 7 and 2, ArH) and 2.78 (6 H, s, 2CH₃).

(c) Reaction with methanol. The dinitro isocyanate **12c** (0.2 g, 0.8 mmol) was warmed with methanol (5 cm³) and the mixture was evaporated till crystallisation commenced. Yellow prisms of methyl *N*-(2-dimethylamino-3,5-dinitrophenyl)carbamate were obtained (0.21 g, 94%), mp 94–95 °C (MeOH) (Found: C, 42.0; H, 4.6; N, 19.8. $C_{10}H_{12}N_4O_6$ requires C, 42.3; H, 4.3; N, 19.7%); ν_{max}(KBr)/cm⁻¹ 3324 (NH), 3125 and 3088 (ArCH), 2954, 2886 and 2818 (CH), 1737 (CO), 1594 and 1490 (NH and Ar conj.), 1543 and 1366 (NO₂); $\delta_H[(CD_3)_2SO]$ 9.33 (1 H, br s, NH), 8.71 (1 H, d, J 3, ArH), 8.33 (1 H, d, J 3, ArH), 3.75 (3 H, s, OCH₃) and 2.75 [6 H, s, N(CH₃)₂].

(d) 2-Dimethylamino-3,5-dinitroaniline. The dinitro isocyanate **12c** (0.4 g, 1.6 mmol) dissolved in acetone (20 cm³) was added to acetone–water mixture (20 cm³, 50% v/v) which contained NaOH (2 mol dm⁻³; 0.8 cm³, 1.6 mmol) at room temperature for 30 min. The colour of the solution rapidly turned red. Evaporation of the mixture followed by extraction with dry acetone gave orange-red needles of 2-dimethylamino-3,5-dinitroaniline (0.36 g, 100%), mp 111–112 °C (acetone) (Found: C, 42.2; H, 4.6; N, 24.5. $C_8H_{10}N_4O_4$ requires C, 42.5; H, 4.45; N, 24.8%); ν_{max}(KBr)/cm⁻¹ 3454 and 3353 (NH), 3110 and 3000 (ArCH), 2932, 2885 and 2795 (CH), 1618, 1585 and 1501 (NH and Ar conj.), 1526 and 1325 (NO₂).

Acknowledgements

References

1 T. Curtius, *J. Pract. Chem.*, 1917, **95**, 340.
2 N. M. Waldron, M. Montevalli, S. Azam and P. C. Dasopoulos, *J. Chem. Soc., Chem. Commun.*, 1995, 81.
3 D. H. Williams and I. Fleming, *Spectroscopic Methods in Organic Chemistry*, 3rd edn., McGraw–Hill, Maidenhead., 1880, p. 54.
4 N. M. Waldron, Ph. D. Thesis, University of Leeds, 1952.
5 J. Martin, O. Meth-Cohn and H. Suschitzky, *J. Chem. Soc., Chem. Commun.*, 1971, 1319; *J. Chem. Soc., Perkin Trans. 1*, 1974, 2451.
6 J. R. Ruiz, V. J. Aran and M. Stud, *Tetrahedron Lett.*, 1988, **29**, 697.
7 V. J. Aran, J. L. Asensio, J. R. Ruiz and M. Stud, *J. Chem. Res. (S)*, 1993, 218; *J. Chem. Res. (M)*, 1993, 1319.
8 V. J. Aran, J. L. Asensio, J. R. Ruiz and M. Stud, *J. Chem. Soc., Perkin Trans. 1*, 1993, 1119.
9 V. J. Aran, M. Flores, P. Munoz, J. R. Ruiz, P. Sanchez-Verdu and M. Stud, *Leibigs Ann. Chem.*, 1994, **202**, 1.
10 R. Willstätter and W. Kahn, *Chem. Ber.*, 1904, **37**, 401.