3-Diphenylmethylpyrido[1,2-*a*][1,3,5]triazine-2,4-dione

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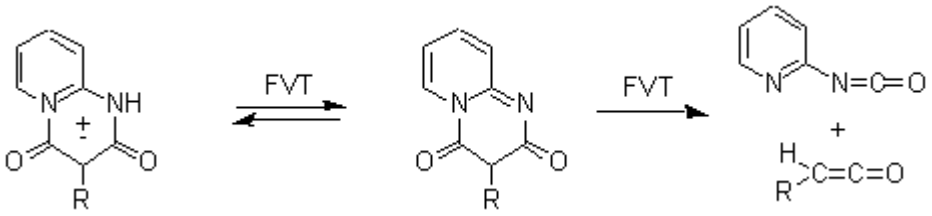
Abstract

3-Substituted pyrido[1,2-*a*][1,3,5]triazine-2,4-dione 8 was obtained unexpectedly in a reaction between 2-picolinoyl azide and diphenylacetyl chloride intended to furnish a cycloaddition product of 2-pyridyl isocyanate and diphenylketene, viz. 3,3-diphenylpyrido[1,2-*a*]pyrimidin-2,4-dione 7. Triazine 8 was also synthesised by cycloaddition between diphenylmethyl isocyanate (9) and 2-pyridyl isocyanate (3), both generated *in situ* from the respective azides (2 and 12). Flash vacuum thermolysis of compound 8 regenerates 2-pyridyl isocyanate (3) and diphenylmethyl isocyanate (9), both characterized by FTIR spectroscopy.

Keywords: Pyridopyrimidinediones, 2-picolinoyl azide, diphenylketene

Introduction

We have recently found that mesoionic pyridopyrimidinediones undergo cycloreversion to 2-pyridyl isocyanate and a ketene on flash vacuum thermolysis (FVT).[1]

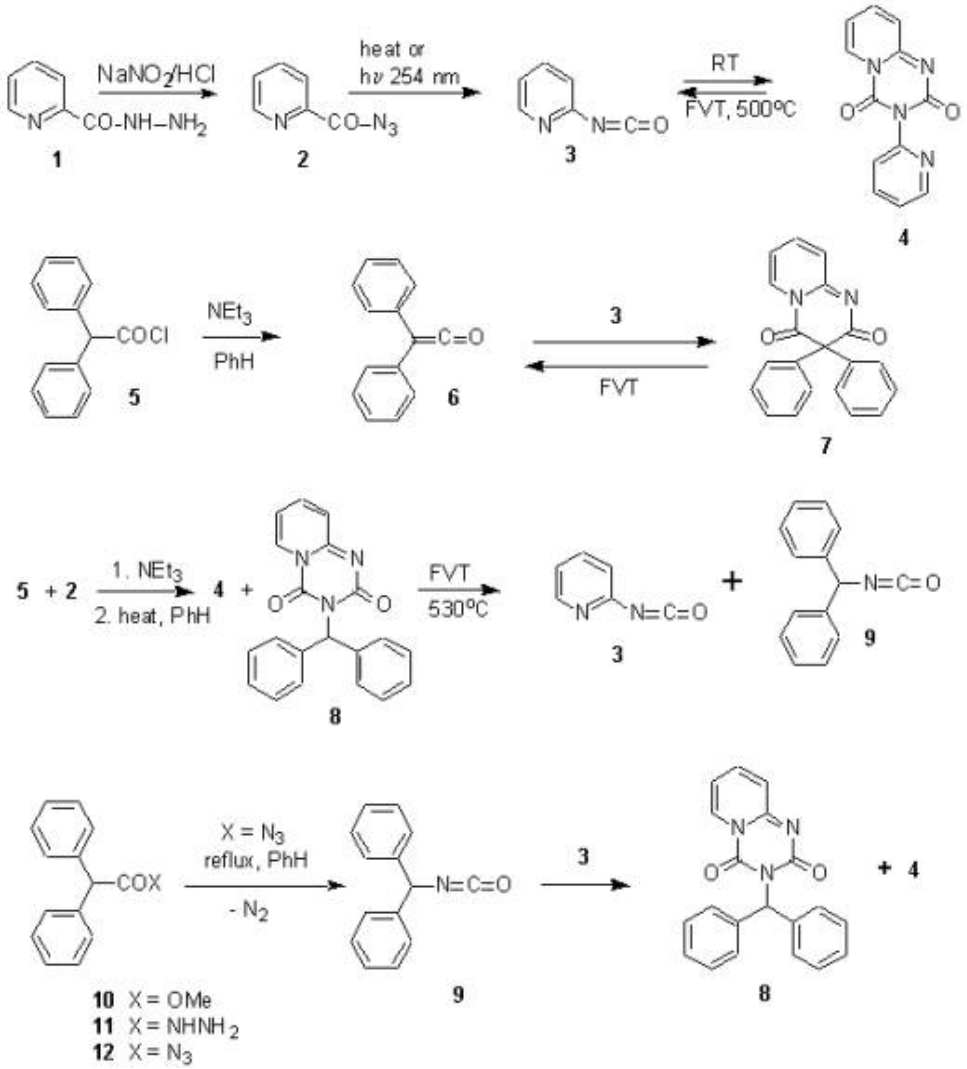


For this reason we became interested in the possibility of the reverse reaction, the synthesis of pyridopyrimidinediones by cycloaddition between 2-pyridyl isocyanate (3) and ketenes. One such reaction has been reported, viz. the reaction between 3 and ketene itself.[2] Such reactions are hampered by the fact that, of the three possible pyridyl isocyanates, only the 3-isomer is isolable in pure form. It was prepared by a Curtius rearrangement of nicotinoyl azide.[3] 3 can be generated in solution by the same method, but attempted isolation leads to the formation of its dimer (4).[1, 2,]

[4, 5] FVT of either 2 or 4, or matrix photolysis of 2, leads to the monomeric isocyanate 3 (Scheme 1).[1]

Results and Discussion

2-Pyridyl isocyanate (3) was generated *in situ* in a Curtius rearrangement of picolinoyl azide (2), itself obtained from the hydrazine 1.[1, 2, 4] Diphenylketene 6 was also generated *in situ* by dehydrohalogenation of the acid chloride 5 with triethylamine as described elsewhere.[6] However, reaction between the two solutions gave only a small amount of the expected cycloaddition product 7, as evidenced by the results of FVT. Thermal cycloreversion of 7 would regenerate 3 and 6, but in fact the IR spectrum of the matrix isolated products of such FVT demonstrated formation of the isocyanate 3 but only a weak peak due to diphenylketene 6 (2107 cm^{-1} in Ar matrix).



Scheme 1

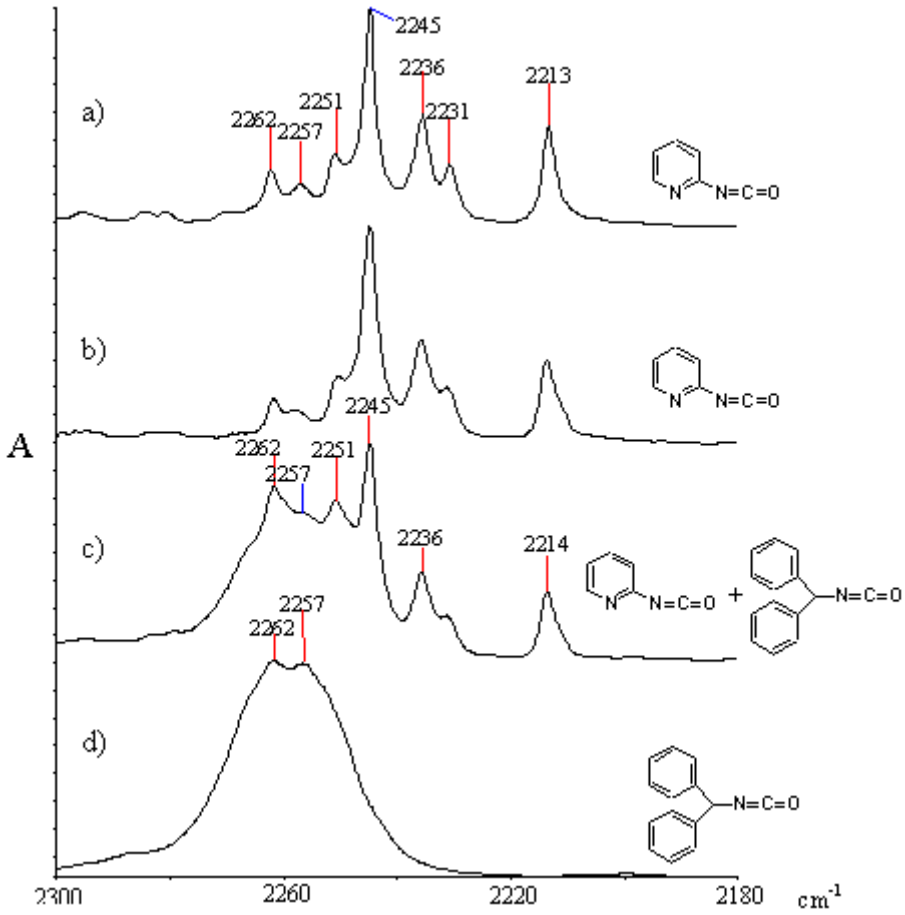


Figure 1. IR of Ar matrix isolated isocyanates 3 and 9.(a) Product of matrix photolysis of picolinoyl azide(2). (b) Product of FVT of dimer 4. (c) Product of FVT of 8.(d) Product of FVT of Ph_2CH-CO-N_3 (12).

Instead,FVT of the reaction product afforded a mixture of the two isocyanates 3 and 9 as described below. Accordingly, the original reaction product appeared to be the 3-substituted pyrido[1,2-*a*][1,3,5]triazine-2,4-dione 8. The isocyanate dimer 4 always accompanied the formation of 8. The structure of compound 8 was ascertained by its spectroscopic data, including [a] HMBC ^{1}H-^{13}C NMR correlation.

An authentic sample of diphenylmethyl isocyanate 9 was prepared by Curtius rearrangement of azide 13. Reaction of this material with 2-pyridyl isocyanate 3 afforded the expected cycloaddition product 8, which in all respects was identical with the material described above. Moreover, FVT of 8 led to the formation of the two isocyanates 3 and 9 resulting from cycloreversion, as proved by the IR spectra of the materials isolated in Ar matrices (Figure 1). Further studies of these reactions would be required before a discussion of the origin of the triazine would be warranted. As no mechanistic studies have been performed, we do not claim to

know the reaction pathways, and they may not be as suggested in the reaction schemes. Further work on the desired ketene–isocyanate cycloaddition reaction will be carried out.

Experimental Section

General Procedures. ^{1}H NMR and ^{13}C NMR were recorded on a Varian XL-200 instrument at 200 MHz and 50.3 MHz, respectively, unless otherwise indicated. Microanalyses were performed on a C, H, N-Automat Carlo Erba 1106. Mass spectra were obtained using 70 eV electron ionization on a Kratos MS25RFA instrument, and HRMS on a Finnigan 2001 FTMS. GC-MS employed a BP-4 capillary column (30 m x 0.25 mm; He carrier gas at 20 psi head pressure; injector 200 ^{o}C; detector 280 ^{o}C; column temperature 100-270 ^{o}C, programmed at 16 ^{o}C/min) using a Hewlett Packard 5890 GC and a HP 5970 MS detector. Column chromatography was performed on silica gel (Merck 0.063-0.2 mm). FTIR spectra were recorded on a Perkin Elmer 2000 FTIR spectrometer, UV spectra on a Varian Cary 1 UV-Vis spectrometer, and fluorescence spectra on a Perkin Elmer LS 50B luminesence spectrometer. Melting points are uncorrected. TLC: Kieselgel 60 F_{254}, (0.25 mm) (Merck); eluent: 40% ethyl acetate in hexane unless otherwise indicated. Conditions for FVT, matrix isolation and photolysis were as previously reported.[7] BaF_2 disks were used for matrix deposition.

Materials. The following commercial materials were used: 2-picolinic acid, 2,2-diphenyl acetic acid, isobutyric acid (Aldrich,99%), hydrazine hydrate, $SOCl_2$, $NaNO_2$, Et_3N (BDH, >99 %), 1,4-dioxane (Riedel de Haen, Spectranal), other solvents: *p.a.*quality.

2-Picolinoylhydrazide(1) was prepared according to the literature.[8] Methyl 2-picolinoate (25.4 g, 0.185 mol) was added dropwise to a refluxing solution of hydrazine hydrate (85 %, 22 g, 0.37 mol) in ethanol (50 mL) and refluxed for 1 h. The solution was added benzene (15 mL) and evaporated. The crude solid product was recrystallized from ethanol/diethyl ether yielding 23.8 g (94 %) white crystals. R_f 0.15; m.p. 99-100 ^{o}C (lit.[8] 100 ^{o}C); ^{1}H NMR ($CDCl_3$/d_6-DMSO) d2.19 (s, 3H), 7.57 (ddd, 1H), 7.96 (dt, 1H) 8.26 (dd, 1H), 8.64 (ddd, 1H).

2-Picolinoyl Azide (2) and 3-(2-pyridyl)-pyrido[1,2-*a*][1,3,5]triazine-2,4-dione (4) were prepared according to the literature.[1-8]

2-Pyridyl Isocyanate (3) was obtained bymatrix isolation and photolysis of 2-picolinoyl azide (2) and by FVP of 2-pyridyl isocyanate dimer (4) as previously reported.[1]

Matrix isolation of diphenylketene (6) Freshly distilled diphenylketene[9] (IR[10] (neat film, cm^{-1}) 2097 (s),1596 (m), 1494 (m), 757 (m), 693 (m))was sublimed at 28 ^{o}C and deposited together with Ar on a cold head at 7 K. IR (Ar matrix, cm^{-1}); 2107 (s), 1674 (w), 1605 (w), 1497 (w), 1321 (w), 1282 (w), 1203 (w), 760 (w), 694 (w), 640 (w), 485 (w).

3-Diphenylmethylpyrido[1,2-*a*][1,3,5]triazine-2,4-dione (8)

Method A. Diphenylacetyl chloride (5, 0.6 g, 2.5 mmol) dissolved in anhydrous benzene (8 mL) was cooled to 5 ^{o}C and triethylamine (0.25 g, 2.5 mmmol) was added under N_2. The solution was

stirred for 15 min during which time it turned orange. Addition of a solution of 2-picolinoyl azide (2, ca 1 g, 6.8 mmol) in benzene (10 mL) to the ketene solution caused a change of the color to yellow. The reaction mixture was slowly heated and refluxed for 1 h until the N_2 evolution ceased. Off-white crystalline product (8, 120 mg, 15 % yield) was obtained after purification by column chromatography and crystallization from methanol/diethyl ether in addition to the major 2-pyridyl isocyanate dimer (4). Both compounds gave blue fluorescence on UV irradiation of a TLC plate.

Method B. To2-picolinoyl azide (2, ca 0.3 g, 2.2 mmol) in benzene (3 mL) was added diphenylacetyl azide (13, ca 0.3 g, 1.3 mmol) in benzene (3 mL) and the mixture was refluxed for 1 h until the N_2 evolution ceased. In addition to the dimer 4, the crystalline cycloaddition product 8 (150 mg, 35 % yield) was isolated by column chromatography and crystallization. The product co-eluted on TLC with the product obtained by method A, and m.p. and spectroscopic data (IR, MS and ^{1}H NMR) of the two samples were identical. R_f 0.4; m.p. 220 -222 ^{o}C (decomp.); ^{1}H NMR ($CDCl_3$) δ 6.69 (ddd, J = 7.2, 6.6 and 1.2 Hz, 1H, H7), 7.18 (ddd, J = 9.0, 1.7 and 0.7 Hz, 1H, H9), 7.25-7.42 (m, Ph-CH and methine-CH, 11H), 7.57 (ddd, J = 9.0, 6.6 and 1.7 Hz, 1H, H8), 8.54 (ddd, J = 7.2, 1.7 and 0.7 Hz, 1HH6); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 60.3 (methine-C), 112.5 (C7), 122.3 (C9), 126.7 (Ph-*p*-C), 127.3 (Ph-*o*-C), 127.9 (Ph-*m*-C and C6), 136.8 (Ph-C1'), 141.3 (C8), 147.2 (C(4)=O), 152.2 (C(2)=O), 153.6 (C9a); the assignments are based on the HMBC 2D ^{1}H–^{13}C correlation and a DEPT spectrum. IR (KBr, cm^{-1}) 1744 (m), 1672 (s), 1648 (m), 1540 (s) 1355 (w), 1289 (w), 764 (m), 709 (m); MS [m/z (% rel.int.)]: 329 (*M*, 26), 209 (74), 180 (63), 167 (26), 165 (100), 152 (17), 121 (84); UV (1,4-dioxane, λ_{max}, nm (ε_{max})) 221 (14500), 257 (14100), 266 (11300), 340 (5000), 353 (5200), 372 (2500); Fluorescence (0.19 mmol/10mL 1,4-dioxane, λ_{ex}, nm (int) 306 (65), 374 (66); λ_{em} nm (int) 406 (33), 428 (33). HRMS: calcd for $C_{20}H_{15}N_3O_2$, 329.1159; observed, 329.1154.

FVT of 3-Diphenylmethylpyrido[1,2-a][1,3,5]triazine-2,4-dione (8). This product was sublimed (120 ^{o}C) and thermolyzed (530 ^{o}C) with deposition of the product in Ar matrix at 7 K. The matrix isolated product was characterized by IR as a mixture of 2-pyridyl isocyanate (3) and diphenylmethyl isocyanate (9). The IR spectrum was in accord with the sum of the IR spectra of the individual isocyanates 3 and 9 (Figure 1). IR (Ar matrix, cm^{-1}) 2262 (s), 2257 (m), 2251 (m), 2245 (s), 2236 (m), 2231 (w), 2213 (m), 1624, (m), 1608 (w), 1594 (m), 700 (m).

Diphenylacetyl Azide (12) was prepared according to the literature[12b] using the same procedure as for the preparation of azide 2, starting with diphenylacetylhydrazide[11] (11, 2.2 g, 10 mmol), hydrochloric acid (conc. 4 mL), ice (8g) diethylether (10 mL) and a solution of sodium nitrite (1.7 g, 25 mmol) in water (3 mL). The product, which was pure by TLC (R_f 0.9), was stored in the freezer in an about 1 g/10 mL benzene solution. IR (neat film, cm^{-1}) 2138 (s), 1711(m), 1358 (s), 1184 (w), 1141 (w), 1066 (m), 747 (w), 700 (m). IR of the compound after 4 weeks storage in the freezer indicated a partial conversion of the azide 12 to the isocyanate 9, as represented by a 40:60 % ratio of the intensities of the IR absorption bands of the azide and the isocyanate (2138 cm^{-1} and 2255 cm^{-1}, respectively).

Diphenylmethyl isocyanate (9). A solution of diphenylacetyl azide (12, ca 1 g, 4.2 mmol) in benzene (10 mL) was refluxed until gas evolution ceased. An oily product (0.85 g, 97 % yield) was obtained after evaporation of the solvent. The complete conversion of the azide to the isocyanate was confirmed by the absence of the azide signals in the IR and ^{1}H NMR spectra. ^{1}H NMR[12] ($CDCl_3$) δ 5.80 (s, 1H), 7.29-7.31 (m, 10 H); IR (neat film, cm^{-1}) 2255 (s), 1649 (w), 1494 (m), 1453 (m), 1393 (m), 697; GC-MS [m/z (% rel.int.)]: 209 (*M*, 72), 180 (53), 167 (52), 132 (34), 115 (8), 103 (36), 77 (100).
The azide was sublimed (70 ^{o}C) and thermolysed (500 ^{o}C) with deposition of the products with Ar on at 7 K. The matrix isolated product was identified by IR spectroscopy as diphenylmethyl isocyanate 9 (Fig. 1d). IR (Ar matrix, cm^{-1}) 2262 (s), 1607 (w), 1497 (w), 1457 (w), 1283 (w) 761 (w), 738 (w), 700 (m).

Acknowledgments

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