Reaction of α-Bromocarbonyl Compounds with 1-Amino-4,6-diphenyl-2-thioxo-1,2-dihydropyridine: Synthesis of Pyrazolo[1,5-*a*]pyridines[1]

P. MOLINA*, A. ARQUES, A. FERAO

Departamento de Quimica Orgánica, Facultad de Ciencias, Universidad de Murcia, Murcia, Spain

It is well known that the cyclocondensation reaction of α-halocarbonyl compounds with thiosemicarbazide derivatives[2,3,4] or thiobenzoic and phenylthioacetic acid hydrazides[5], is a simple and convenient preparative method for 6*H*-1,3,4-thiadiazines. There is some evidence that these compounds can be desulphurised to pyrazoles by the action of triphenylphosphine or triethyl phosphite[6].

The structural similarity between the thiosemicarbazide and 1-amino-4,6-diphenyl-2-thioxo-1,2-dihydropyridine **(1)** is such that this *N*-aminoheterocycle might be expected to be a suitable starting material for the preparation of fused derivatives of the 2*H*-1,3,4-thiadiazine ring system. On this basis, we report here an apparently widely applicable route to 2-substituted 5,7-diphenylpyrazolo[1,5-*a*]pyridines **5** through conversion of **1** into 2*H*-1,3,4-thiadiazino[3,2-*a*]pyridinium salts **3** followed by basic treatment to give the ylids **4**, which on reaction with *m*-chloroperbenzoic acid, undergo sulphur extrusion to give the corresponding pyrazolo[1,5-*a*]pyridines **5.**

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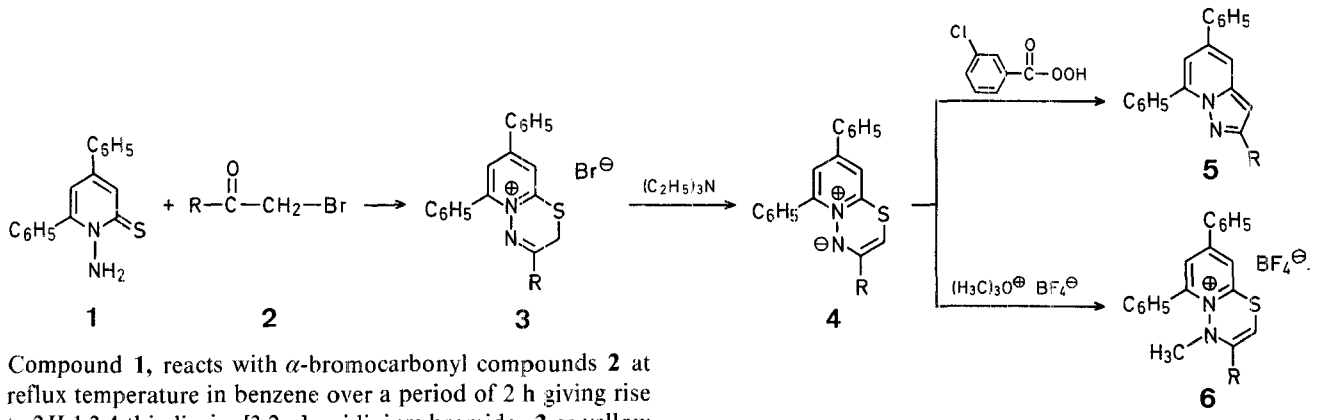

Compound **1**, reacts with α-bromocarbonyl compounds **2** at reflux temperature in benzene over a period of 2 h giving rise to 2*H*-1,3,4-thiadiazino[3,2-*a*]pyridinium bromides **3** as yellow crystalline solids in high yields.

Compounds **3** display in the I.R. spectra a clear absorption at $\nu = 1630$–1620 cm^{-1} which is assigned to the C=N stretching vibration. The N.M.R. spectra of **3** show signals for $-CH_2-$ at $\delta = 5.5$–4.7 ppm, and the $M^+ - BrH - 32$ peak is the base in the mass spectra. When ethanolic solutions of the salts **3** were treated with triethylamine, the colour of the reaction mixture turned deep red indicating the formation of the peripheral ylids, anhydro-4*H*-1,3,4-thiadiazino[3,2-*a*]pyridinium hydroxides **4**, which were isolated as crystalline solids in high yields. However, for **3f** (R = 4-O_2N—C_6H_4) the reaction product was found to be **5e**, 3-*p*-nitrophenyl-5,7-diphenylpyrazolo[1,5-*a*]pyridine. Compounds **4** have a C=N stretching vibration at $\nu = 1635$–1630 cm^{-1} in their I.R. spectra, no signal for methylene hydrogens were revealed in the N.M.R. spectra, and the $M^+ - 32$ peak is the base in the mass spectra. Upon reaction with trimethyloxonium tetrafluoroborate, compounds **4a** and **4d** gave the *N*-methyl derivatives **6a** and **6b**. However, they did not react with acyl chlorides in presence of aluminium trichloride.

Although the mass spectra of compounds **4** clearly show the ability of these heterocycles to eliminate sulphur, extrusion of sulphur from **4** does not occur at temperatures up to 200 °C even in the presence of triphenylphosphine or triethyl phosphite, which normally promote this type of reaction in other cases[7]. However, compounds **4** react with *m*-chloroperbenzoic acid in chloroform at reflux temperature to give the corresponding pyrazolo[1,5-*a*]pyridines **5** in moderate yields. Attempts to apply this transformation to **4f** resulted in unaltered starting material being recovered. We believe that the reaction involves the initial formation of the *S*,*S*-dioxides as intermediates which undergo then easily sulphur dioxide extrusion to give the products **5** isolated. Attempts to isolate the *S*,*S*-dioxides were unsuccessful.

3-Substituted 5,7-Diphenyl-2*H*-1,3,4-thiadiazino[3,2-*a*]pyridinium Bromides 3; General Procedure:

The 1-amino-4,6-diphenyl-2-thioxo-1,2-dihydropyridine (**1**; 2.78 g, 10 mmol) is dissolved in dry benzene (75 ml). The α-bromocarbonyl compound **2** (10 mmol) is added and the solution is heated at reflux temperature for 2 h. The mixture is then allowed to stand at room temperature to precipitate a yellow crystalline solid which is isolated and recrystallised from ethanol (Table).

3-Substituted Anhydro-5,7-diphenyl-4*H*-1,3,4-thiadiazino[3,2-*a*]pyridinium Hydroxides 4; General Procedure:

To a solution of the 2*H*-1,3,4-thiadiazino[3,2-*a*]pyridinium bromide **3** (10 mmol) in dry ethanol (100 ml), triethylamine (10 mmol) is added. A deep red colouration immediately develops; after 3 h under gentle reflux, the solution is set aside at room temperature. The precipitated solid is filtered off and recrystallised from ethanol to give **4** (Table).

Table. Compounds **3**, **4**, **5**, and **6** prepared

Product No.	R	Yield[a] [%]	m.p.[b] [°C]	Molecular formula[c]	I.R. (nujol)[d] ν [cm^{-1}]	^{1}H-N.M.R. (DMSO-d_6)[e] δ [ppm]	M.S. *m/e*
3a	C_6H_5	83	227°	$C_{25}H_{19}BrN_2S$ (459.4)	1620, 1540, 1455, 1355, 1340, 1255, 1020, 910, 770, 705, 690	8.45–7 (m, 17 H); 5.1 (s, 2 H)	378, 346 (100), 345, 269, 263, 241, 215, 203, 139, 77
3b	4-H_3CO—C_6H_4	75	193°	$C_{26}H_{21}BrN_2OS$ (489.4)	1625, 1610, 1540, 1440, 1345, 1270, 1200, 840, 775, 705	8.8–6.9 (m, 16 H); 4.7 (s, 2 H); 3.8 (s, 3 H)	408, 377, 376, 363 (100), 333, 332, 230, 203, 189, 77
3c	4-Cl—C_6H_4	98	185°	$C_{25}H_{18}BrClN_2S$ (493.8)	1625, 1600, 1535, 1410, 1335, 1260, 1095, 1015, 835, 765, 690	8.5–7 (m, 16 H); 4.8 (s, 2 H)	414, 412, 382, 381, 380 (100), 379, 263, 203, 172, 103, 77
3d	4-C_6H_5—C_6H_4	96	190°	$C_{31}H_{23}BrN_2S$ (535.5)	1625, 1580, 1540, 1415, 1340, 1260, 850, 760, 735, 705	8.3–7.2 (m, 21 H); 5.1 (s, 2 H)	454, 453, 422 (100), 421, 345, 263, 203, 202, 153, 77
3e	4-Br—C_6H_4	93	221°	$C_{25}H_{18}Br_2N_2S$ (538.3)	1630, 1595, 1540, 1420, 1270, 1025, 835, 790, 775, 700	8.4–7.2 (m, 16 H); 4.9 (s, 2 H)	458, 456, 426 (100), 425, 424 (100), 263, 261, 247, 219, 173, 77
3f	4-O_2N—C_6H_4	94	208°	$C_{25}H_{18}BrN_3O_2S$ (504.4)	1620, 1530, 1355, 1340, 1030, 870, 860, 850, 785, 775, 720, 695	8.45–7.4 (m, 16 H); 5.3 (s, 2 H)	423, 391, 277, 276, 263, 230, 219, 203, 202, 163, 150, 96, 94, 77 (100)
3g	$COOC_2H_5$	91	177°	$C_{22}H_{18}BrN_2O_2S$ (454.4)	1770, 1620, 1560, 1270, 1230, 1200, 1130, 850, 775, 710, 695	8.35–7.3 (m, 12 H); 5.5 (s, 2 H); 4.3 (q, 2 H); 1.3 (t, 3 H)	374, 342, 313, 270 (100) 263, 230, 219, 203, 202, 191 115, 77

Table. (*Continued*)

Product No.	R	Yield[a] [%]	m.p.[b] [°C]	Molecular formula[c]	I.R. (nujol)[d] ν [cm^{-1}]	^{1}H-N.M.R. (DMSO-d_6)[e] δ [ppm]	M.S. *m/e*
4a	C_6H_5	97	192°	$C_{25}H_{18}N_2S$ (378.5)	1630, 1535, 1455, 1435, 1070, 1020, 860, 755, 690	8.19–6.84 (m, 18 H)	378 (M^+), 377, 346 (100), 345, 276, 274, 230, 203, 103, 102, 91, 77
4b	4-H_3CO—C_6H_4	91	125°	$C_{26}H_{20}N_2OS$ (408.5)	1630, 1615, 1540, 1440, 1250, 1180, 840, 765, 700	8.15–6.63 (m, 17 H); 3.7 (s, 3 H)	408 (M^+), 393, 377, 376 (100), 361, 332, 276, 274, 230, 203, 77
4c	4-Cl—C_6H_4	83	173°	$C_{25}H_{17}ClN_2S$ (412.9)	1635, 1600, 1540, 1510, 1460, 1440, 1380, 1090, 1015, 835, 765, 730, 700	8.17–6.51 (m, 17 H)	414 (M^++2), 412 (M^+), 380 (100), 325, 230, 203, 202, 77
4d	4-C_6H_5—C_6H_4	87	256°	$C_{31}H_{22}N_2S$ (454.6)	1630, 1530, 1500, 1205, 760, 745, 735, 700	8.17–6.51 (m, 22 H)	454 (M^+), 422 (100)
4e	4-Br—C_6H_4	87	186°	$C_{25}H_{17}BrN_2S$ (457.4)	1635, 1540, 1500, 1490, 1215, 1015, 830, 770, 700	8.2–6.48 (m, 17 H)	458 (M^++2), 456 (M^+), 426 (100), 424 (100)
4f	$COOC_2H_5$	82	94°	$C_{22}H_{18}N_2O_2S$ (374.4)	1730, 1635, 1530, 1450, 1245, 1230, 1205, 1070, 870, 760, 700	8.03–6.6 (m, 13 H), 4.2 (q, 2 H), 1.2 (t, 3 H)	374 (M^+)
5a	C_6H_5	66	311°	$C_{25}H_{18}N_2$ (346.4)	1625, 1525, 1490, 1450, 1320, 1215, 1070, 1010, 850, 755, 720, 685		346 (M^+, 100), 345, 313, 239, 236, 230, 215, 203, 202, 189, 175, 129, 98, 77
5b	4-H_3CO—C_6H_4	63	273°	$C_{26}H_{20}N_2O$ (376.5)	1615, 1530, 1460, 1440, 1310, 1260, 1185, 1035, 840, 765, 700		376 (M^+, 100), 375, 360, 359, 330, 274, 273, 230, 229, 203, 202, 189, 130, 103, 89, 76
5c	4-Cl—C_6H_4	49	328°	$C_{25}H_{17}ClN_2$ (380.9)	1630, 1600, 1535, 1495, 1325, 1090, 1015, 950, 840, 770, 700		382 (M^++2), 380 (M^+, 100), 379, 344, 318, 304, 275, 242, 230, 215, 203, 174, 111, 76
5d	4-Br—C_6H_4	56	317°	$C_{25}H_{17}BrN_2$ (425.3)	1630, 1540, 1500, 1455, 1325, 1240, 1075, 1015, 860, 835, 765, 695		426 (M^++2, 100), 424 (M^+, 100), 344, 342, 242, 241, 240, 230, 218, 203, 189, 183, 181, 171, 170, 157, 155, 115, 103, 76
5e	4-O_2N—C_6H_4	88	227°	$C_{25}H_{17}N_3O_2$ (391.4)	1630, 1600, 1515, 1495, 1440, 1330, 870, 855, 765, 710, 700		391 (M^+), 345, 344, 267, 266, 256, 241, 215, 203, 148, 102 (100), 90, 77, 76
6a	C_6H_5	73	186°	$C_{26}H_{21}BF_4N_2S$ (480.3)	1630, 1535, 1455, 1400, 1060, 1020, 865, 765, 695		392, 377, 346 (100), 345, 276, 274, 230, 203, 202, 103, 77
6b	4-C_6H_5—C_6H_4	81	185°	$C_{32}H_{25}BF_4N_2S$ (556.4)	1630, 1610, 1540, 1060, 1010, 850, 770, 700		468 (100), 453, 422, 421, 276, 274, 236, 230, 203, 194, 179, 153, 152, 77

[a] Yield of isolated pure product.
[b] Uncorrected.
[c] The microanalyses were in good agreement with the calculated values (C ±0.22, H ±0.22, N ±0.29, S ±0.32).
[d] Recorded on a Perkin-Elmer 457 spectrometer.
[e] Recorded at 80 MHz a Varian FT-80 spectrometer with TMS as an internal standard.

2-Substituted 5,7-Diphenylpyrazolo[1,5-*a*]pyridines 5; General Procedure:

m-Chloroperbenzoic acid (1.38 g, 8 mmol) in dry chloroform (30 ml) is added dropwise during 1 h to a stirred solution of the ylid **4** (4 mmol) in dry chloroform (50 ml). The reaction mixture is heated at reflux temperature for 3 h and then allowed to stand at room temperature. The precipitated solid is filtered off and the filtrate is washed with 20% aqueous sodium hydrogen sulphite (3 × 80 ml), 10% sodium hydrogen carbonate (4 × 80 ml), and water (3 × 60 ml). The organic layer is dried with magnesium sulphate and evaporated in vacuo to leave the crude product, which is chilled with acetone (50 ml) and recrystallised from chloroform/benzene (1 : 1) to give the corresponding pyrazolo[1,5-*a*]pyridine **5** (Table).

3-Substituted 5,7-Diphenyl-4-methyl-4*H*-1,3,4-thiadiazino[3,2-*a*]pyridinium Tetrafluoroborates 6; Typical Procedure:

To a solution of **4a** (0.76 g, 2 mmol) in dry dichloromethane (40 ml), trimethyloxonium tetrafluoroborate (0.3 g, 2 mmol) is added under nitrogen. The reaction mixture is heated at reflux temperature for 6 h. After cooling at room temperature, the solvent is removed under reduced pressure to give a solid which is recrystallised from ethanol to give **6a** (Table).

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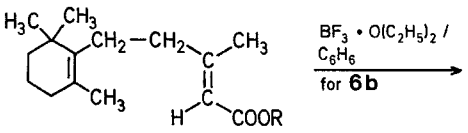
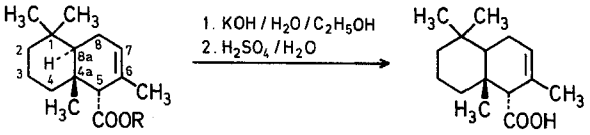
* Address for correspondence.

[1] Part II of the series: Bridgehead Nitrogen Heterocycles. Part I: A. Arques, H. Hernandez, P. Molina, M. J. Vilaplana, *Synthesis* **1981**, 910.
[2] H. Beyer, W. Lässig, G. Ruhlig, *Chem. Ber.* **86**, 764 (1953). H. Beyer, W. Lässig, E. Bulka, *Chem. Ber.* **87**, 1385 (1954).
[3] H. Beyer, *Z. Chem.* **9**, 361 (1969).
[4] D. W. Pfeiffer, E. Dilk, E. Bulka, *Z. Chem.* **17**, 173 (1977).
[5] E. Bulka, D. W. Pfeiffer, *J. Prakt. Chem.* **318**, 971 (1976).
[6] W. D. Pfeiffer, E. Bulka, *Synthesis* **1977**, 485.
[7] D. H. R. Barton, F. S. Guziec, I. Shahak, *J. Chem. Soc. Perkin Trans. 1* **1974**, 1794.

C. Schmidt, N. H. Chishti, T. Breining, *Synthesis* **1982** (5), 391-393:
The formula scheme for the reaction **6**→**7** (p. 391) should be:



6a R = H
6b R = CH_3
6c R = C_2H_5



7b R = CH_3 **7a** R = H

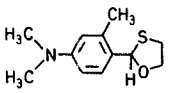
B. A. Arbuzov, N. N. Zobova, *Synthesis* **1982** (6), 433-450:
The correct name for compound **15** (p. 436) is *N'*-benzoyl-*N,N*-dimethyl-2-phenyl-2-butenamidine and for compound **30b** (p. 439) is 4-trifluoroacetylimino-2-trifluoromethyl-4*H*, 9a*H*-pyrido[2,1-*b*]-1,3,5-oxadiazine.

Chen-Chu Chan, Xian Huang, *Synthesis* **1982** (6), 452-454:
The last sentence on page 452 should read: However, under the normal conditions [20% aqueous sodium hydroxide in the presence of benzyltriethylammonium chloride (TEBA)] the ring underwent cleavage and the main product was dimethylmalonic acid in the case of methylation.

P. Molina, A. Arques, A. Ferao, *Synthesis* **1982** (8), 645-647:
Compounds **3,4,** and **6** are substituted pyrido[2,1-*b*][1,3,4]thiadiazinium salts.

Abstract 6431, *Synthesis* **1982** (9), 801
The correct name for the title compounds **3** is 2-oxoalkanehydroximic chlorides.

B. Burczyk, Z. Kortylewicz, *Synthesis* **1982** (10), 831-832:
In Table 1 (p. 832) the b.p. of product **6a** should be 113-114°C/0.3 torr; the structure and molecular formula of product **7d** should be



and $C_{12}H_{17}NOS$ (223.2); the b.p. and n_D^{20} of product **8a** should be 114-116°C/60 torr and 1.5346, respectively. In Table 2 (p. 832) the second term in the ^{1}H-N.M.R. spectrum of product **7b** should be 1.90 (s, 3H, CH_3).

K. D. Deodhar, A. D. D'Sa, S. R. Pednekar, D. S. Kanekar, *Synthesis* **1982** (10), 853-854:
The correct name for compounds **4a,b** (p. 854) is (*E*)- and (*Z*)-6-benzylidene-3-oxo-2,3,4,6-tetrahydro[1,2,4]triazino[3,4-*a*]isoindoles.

L. Lepage, Y. Lepage, *Synthesis* **1982** (10), 882-884:
The correct name for compound **10** (p. 884) is 2-acetyl-1,4-diphenyl-1,2,3,4-tetrahydro-1,4-epithiopentacene-7,12-quinone.

R. R. Schmidt, A. Wagner, *Synthesis* **1982** (11), 958-962:
It should be noted that the numbers in the products **5**-**16c** in Table 1 refer only to the ^{1}H-N.M.R. data in Table 2 and are not identical with the numbering used for the systematic nomenclature of the products.

T. Takajo, S. Kambe, W. Ando, *Synthesis* **1982** (12), 1080-1081:
The compounds **7** should be named 2,4,6,12-tetraaryl-2,5,6,7-tetrahydro-4*H*-3,6a-methanoindeno[1,2-*f*][1,3,5]triazocines.