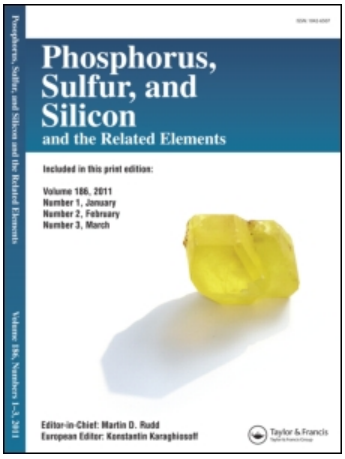


Phosphorus, Sulfur, and Silicon and the Related Elements
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713618290

REACTIONS WITH HYDRAZIDOYL HALIDES II [1]: SYNTHESIS AND REACTIONS OF 2-BROMOTHIENYLGLYOXAL-2-PHENYLHYDRAZONE

Abdou O. Abdelhamid[a]; Fathia H.H. El Shiaty[a]
[a] Chemistry Department, Faculty of Science, Cairo University, Giza, A. R. Egypt

To cite this Article Abdelhamid, Abdou O. and Shiaty, Fathia H.H. El(1988) 'REACTIONS WITH HYDRAZIDOYL HALIDES II [1]: SYNTHESIS AND REACTIONS OF 2-BROMOTHIENYLGLYOXAL-2-PHENYLHYDRAZONE', Phosphorus, Sulfur, and Silicon and the Related Elements, 39: 1, 45 — 49
To link to this Article: DOI: 10.1080/03086648808072853
URL: http://dx.doi.org/10.1080/03086648808072853

Phosphorus and Sulfur, 1988, Vol. 39, pp. 45–49
Reprints available directly from the publisher
Photocopying permitted by license only

REACTIONS WITH HYDRAZIDOYL HALIDES II [1]: SYNTHESIS AND REACTIONS OF 2-BROMOTHIENYLGLYOXAL-2-PHENYLHYDRAZONE

ABDOU O. ABDELHAMID* and FATHIA H. H. EL SHIATY
Chemistry Department, Faculty of Science, Cairo University, Giza, A. R. Egypt

(Received January 12, 1988)

2-Bromoacetylthiophene reacted with dimethylsulfide in ethanol to afford dimethylsulfonium bromide **2**, which reacted with *N*-nitrosoacetanilide to give 2-bromo-thienylglyoxal-2-phenylhydrazone (**3**). **3** reacted with pyridine and with triphenylphosphine to give **4a** and **4b**, respectively. **3** reacted also with morpholine, sodium thiophenolate or potassium cyanide to afford the corresponding hydrazones **5a—c**, respectively. **3** reacted also with potassium thiocyanate and with potassium selenocyanate to give the thiadiazoline **6a** and selenadiazoline **6b**. **3** is utilized also for the synthesis of several heterocycles via its reactions with malononitrile, benzoylacetonitrile, dibenzoylmethane, ω-benzenesulfonylacetophenone, *N*-arylmaleimides and benzalaniline. Structural assignments have been made on the basis of elemental analyses, spectral data and independent synthesis wherever possible.

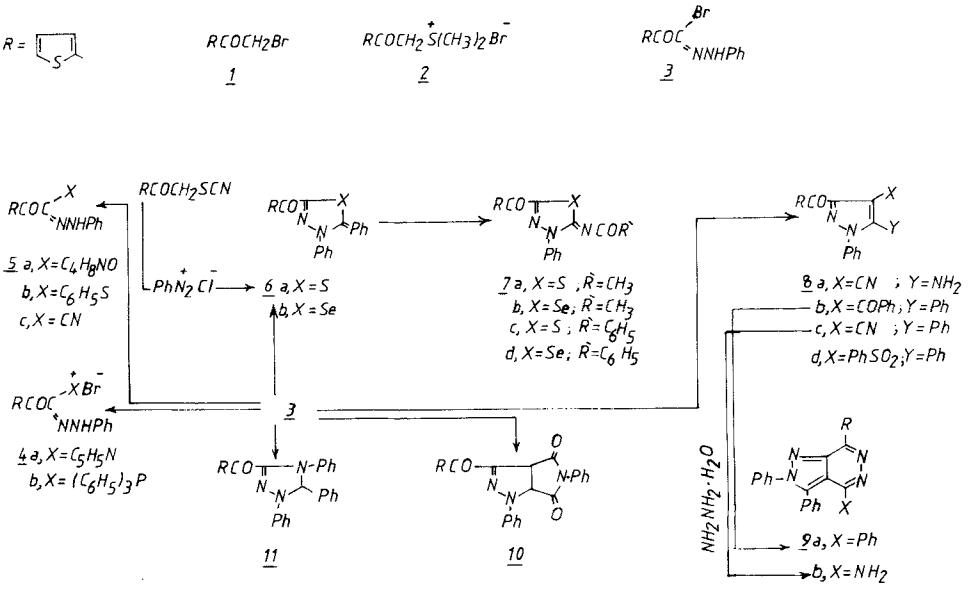
Key words: Hydrazidoyl bromides; hydrazones; pyrazoles; pyrrolo[4,5-d]pyrazole; pyrazolo[3,4-d]-pyridazine.

INTRODUCTION

For the last ten years we have published reports dealing with the utilization of hydrazidoyl halides in heterocyclic synthesis.[1–12] In conjunction with our previous work we report here on the synthesis and utilization of 2-bromothienylglyoxal-2-phenylhydrazone **3** in heterocyclic synthesis. The newly synthesised derivatives bear latent functional substituents and appear promising for biological activity studies as well as for further chemical transformations.

RESULTS AND DISCUSSION

It has been found that reaction of **2** with N-nitrosoacetanilide[13] in ethanol (or any organic solvent) gave 2-bromothienylglyoxal-2-phenylhydrazone (**3**). Structure of **3** was established by elemental analysis and spectral data. IR spectrum (KBr) of **3** revealed bands at (cm^{-1}) 1660 (CO) and 3240 (NH). ^{1}H-NMR ($CDCl_3$) revealed signals at (δ ppm) 6.5–7.5 (m, 8H, ArH's and thiophene protons) and 8.2 (s, 1H, NH). The synthetic potential of **3** was demonstrated via its reactions with different reagents. Thus, **3** reacted with pyridine, triphenylphosphine, morpholine, sodium thiophenolate or potassium cyanide in ethanol to give **4a,b** and **5a–c**, respectively. The structures of **4** and **5** were confirmed based on elemental analyses and spectral data (see Experimental). **3** reacted with potassium



thiocyanate and with potassium selenocyanate in ethanol to give 2-imino-2,3-dihydro-1,3,4-thiadiazole **6a** and 2-amino-2,3-dihydro-1,3,4-selenadiazole **6b**, respectively. The structure of **6a,b** was elucidated on the basis of elemental analyses, spectral data and the reaction with acetic anhydride (or benzoyl chloride or nitrous acid). The IR spectra (cm^{-1}) of **6a,b** showed bands at 3350 (NH) and 1660 (CO). ^{1}H-NMR spectra of **6a,b** showed the signals (δ ppm) at 7–8.5 for aromatic, thiophene, and NH protons. Compounds **6a,b** reacted with acetic anhydride to give the *N*-acetyl derivatives **7a,b**. The ^{1}H-NMR spectra of **7a,b** revealed signals at 2.3 (s, 3H, CH_3CON=) and 7.1–7.8 (m, 8H, ArH's and thiophene protons). The IR spectra of **7a,b** showed bands at 1660 and 1630 for two CO groups. Compound **6a** was also obtained by coupling of 2-thiocyanatoacetylthiophene with benzenediazonium chloride in ethanolic sodium acetate solution.[14] When **3** was treated with malonitrile, dibenzolymethane, benzoylacetonitrile or ω-benzenesulfonylacetophenone in ethanolic sodium ethodixe solution, it afforded the pyrazole derivatives **8a–d,** respectively. The structure of the pyrazole derivatives was assigned based on spectral data and elemental analyses together with chemical reactions. The ^{1}H-NMR spectrum of **8a** ($CDCl_3$) revealed signals (δ ppm) at 5.6 (s, br., 2H, NH_2) and 7.1–7.8 (s, 8H, ArH's and thiophene protons). Upon shaking with D_2O the signal at 5.6 ppm disappeared and a new signal appeared at 4.7 ppm for H_2O. IR (KBr, cm^{-1}) for **8a** showed peaks at 3420, 3320, (NH_2); 2200 (CN) and 1650 (CO). **8b** and **8c** reacted with hydrazine hydrate in ethanol under reflux to give **9a,b** respectively. The structure of the pyrazolo[3,4-d]pyridazine derivatives **9a,b** was elucidated by spectral and elemental analyses (see Experimental). **3** reacted also with *N*-phenylmaleimide and with benzalaniline in benzene solution containing triethylamine to give the pyrrolo[3,4-d]pyrazole derivative **10** and the triazole derivative **11,** respectively. The structures of **10** and **11** were confirmed by elemental analyses and spectral data. ^{1}H-NMR of **10** showed signals (δ ppm) at 5.2 (d, 1H,

pyrazoline H-4), 5.4 (d, 1H, pyrazoline H-5) and 6.8–8.2 (m, 13H, ArH's and thiophene protons). IR spectrum of **10** revealed absorption bands at 1790–1720 and 1710–1690 cm^{-1} attributed to the presence of the (—CO—NR—CO—) grouping and 1650 for (CO). The ^{1}H-NMR of **11** exhibited a singlet at δ 6.4 (1H, 5-CH) and 6.8–8.6 (m, 18H, ArH's and thiophene protons). IR for **11** revealed bands characteristic for the triazole ring in the 1110–1040 cm^{-1} [15] in addition to a strong band at 1650 assignable to 3-thienoyl group.

EXPERIMENTAL

All melting points are uncorrected. IR spectra were recorded on a Pye-Unicam SP_3-300 spectrophotometer. ^{1}H-NMR on a Varian EM-360-90 MHz spectrometer using TMS as internal indicator and chemical shifts are expressed as δ ppm. The microanalyses were performed by the microanalytical Centre at Cairo University. 2-Bromo-acetylthiophene was prepared according to literature procedure.[16]

Synthesis of thienoylmethanedimethylsulfonium bromide (**2**)

A mixture of **1** (21.7 g, 0.1 mol) and dimethylsulfide (6.2 g, 0.1 mol) in ethanol (100 ml) was refluxed for 30 min. The reaction mixture was cooled and the solid was collected by filtration. The crude solid product was crystallized from ethanol to give dimethylsulfonium bromide **2** (cf. Table I).

Synthesis of 2-bromothienylglyoxal-2-phenylhydrazone **3**

A mixture of **2** (0.1 mol) and N-nitrosoacetanilide (0.12 mol) was stirred in ethanol (100 ml) for 2h. at room temperature. The solid, so formed, was collected and crystallized from ethanol to give **3** (cf. Table I).

Synthesis of the pyridinium and phosphonium bromides **4a,b**

Hydrazidoyl bromide **3** (1.5 g, 0.005 mol) and pyridine or triphenylphosphine (0.005 mol) were refluxed in ethanol (15 ml) for 1 h. The reaction mixture was cooled and diluted with ether to precipitate the product. The solid so formed was collected, washed with ether and crystallized from ethanol-ether to give thienylglyoxal-2-phenylhydrazone-2-(N)pyridenium bromide (**4a**) and thienylglyoxal-2-phenylhydrazone-2-(P)-triphenylphosphonium bromide (**4b**), respectively (cf. Table I).

Reactions of **3** *with Nucleophiles, General procedure*

Equimolecular quantities of **3** and the appropriate neucleophile (morpholine, NaSPh, KCN, KSCN or KSeCN) were stirred for 0.5–2 h. at 40°C and left overnight, washed with water and crystallized from ethanol to give 2-morphelinothienylglyoxal-2-phenylhydrazone (**5a**), 2-thiophenothienylglyoxal-2-phenylhydrazone (**5b**), 2-cyanothienoyl-glyoxal-2-phenylhydrazone (**5c**), 2,3-dihydro-2-imino-3-phenyl-5-thienoyl-1,3,4-thiadiazole (**6a**) and 2,3-dihydro-2-imino-3-phenyl-5-thienoyl-1,3,4-selenadiazole (**6b**), respectively (cf. Table I).

Acylation of **6a,b**

Each of compounds **6a,b** (1 g) was stirred in acetic anhydride (20 ml) for 10 min. and poured onto crushed ice. The crude solid which precipitated was collected and crystallized from ethanol to give

TABLE I

The newly synthesised compounds

Comp.	Yield %	Color	M.p. °C	Mol. formula Mol. Wt.	Analysis % C	H	N	S
2	85	pale yellow	160	$C_{18}H_{11}BrS_2O$ (267.18)	35.96 36.10	4.14 4.00	23.98 24.10	29.91 30.20
3	72	yellow	140–1	$C_{12}H_9N_2BrSO$ (309.18)	46.61 46.40	2.93 2.81	9.06 8.90	10.36 10.20
4a	83	yellow	190–1 dec.	$C_{17}H_{14}N_3BrSO$ (388.28)	52.85 52.70	3.63 3.50	10.82 10.60	8.25 8.10
4b	91	yellow	176–7 dec.	$C_{30}H_{24}PN_2BrSO$ (571.49)	63.05 62.90	4.23 4.10	4.90 4.80	5.60 5.40
5a	78	orange	148	$C_{16}H_{17}N_3SO_2$ (315.37)	60.93 60.70	5.43 5.10	13.32 13.10	10.16 10.00
5b	72	redish-yellow	124	$C_{18}H_{15}N_2S_2O$ (339.42)	63.69 63.40	4.45 4.60	8.25 8.30	18.88 19.10
5c	65	brown	193–5[a]	$C_{13}H_9N_3SO$ (255.28)	61.16 61.30	3.55 3.10	16.46 16.30	12.55 12.20
6a	92	yellow	149–50	$C_{13}H_9N_3S_2O$ (287.32)	54.34 54.50	3.15 3.30	14.62 14.40	22.30 23.10
6b	94	yellowish brown	140	$C_{13}H_9N_3SeOS$ (334.24)	46.71 46.60	2.71 2.90	12.57 12.70	9.58 9.70
7a	84	pale yellow	175–6	$C_{15}H_{11}N_3S_2O$ (329.36)	54.70 54.90	3.36 3.10	12.75 12.90	19.46 19.60
7b	87	yellow	155[a]	$C_{15}H_{11}N_3SSeO_2$ (378.28)	47.88 47.90	2.94 3.1	11.16 11.20	8.51 8.30
7c	85	yellow	260–2[b]	$C_{20}H_{13}N_3S_2O$ (391.43)	61.36 61.60	3.34 3.50	10.74 10.90	16.37 16.70
7d	82	yellowish brown	255[b]	$C_{20}H_{13}N_3SSeO_2$ (438.35)	54.80 54.70	2.98 2.90	9.58 9.70	7.31 7.30
8a	72	yellowish brown	195–7[a]	$C_{15}H_{10}N_4SO$ (294.31)	61.21 61.40	3.42 3.50	19.03 18.80	10.88 10.70
8b	95	colorless	204[a]	$C_{27}H_{18}N_2O_2S$ (434.50)	74.63 74.50	4.17 3.90	6.44 6.70	7.37 7.60
8c	78	pale yellow	219–20[a]	$C_{21}H_{13}N_3SO$ (355.40)	70.97 71.00	3.68 3.90	11.82 11.70	9.01 8.80
8d	65	orange	210–212	$C_{26}H_{18}N_2S_2O_3$ (470.53)	66.36 66.20	3.85 3.70	5.95 5.60	13.62 13.80
9a	87	yellow	259–60[b]	$C_{27}H_{18}N_4S$ (430.51)	75.32 75.10	4.21 4.00	13.01 12.80	7.44 7.10
9b	79	yellowish brown	227	$C_{21}H_{15}N_5S$ (369.43)	68.27 68.30	4.09 3.80	18.95 19.10	8.67 8.40
10	68	yellow	270–1[b]	$C_{22}H_{10}N_3SO_3$ (396.38)	66.66 66.90	2.54 2.70	10.60 10.70	8.08 8.70
11	62	yellowish brown	125	$C_{25}H_{18}N_3SO$ (408.48)	73.50 73.70	4.44 4.10	10.28 10.00	7.84 8.00

[a] acetic acid.
[b] dimethylformamide.

2-acetylimino-2,3-dihydro-3-phenyl-5-thienoyl-1,3,4-thiadiazole (**7a**) and 2-acetylimino-2,3-dihydro-3-phenyl-5-thienoyl-1,3,4-selenadiazole (**7b**), respectively. Benzoylation was effected by stirred equimolecular amounts of each **6a,b** and benzoylchloride in pyridine (6 ml/mmol) for 10 min. The reaction mixture was cooled and poured onto ice. Recrystallization from dimethylformamide gave 2-benzoylimino-2,3-dihydro-3-phenyl-5-thienoyl-1,3,4-thiadiazole (**7c**) and 2-benzoylimino-2,3-dihydro-3-phenyl-5-thienoyl-1,3,4-selenadiazole (**7b**), respectively (cf. Table I).

Synthesis of **8a–d**

The appropriate active methylene compound (malononitrile, dibenzoylmethane, benzoylacetonitrile and ω-benzenesulfonylacetophenone) (0.01 mol) was added to an ethanolic sodium ethoxide solution (prepared from sodium metal 0.23 g; 0.01 g-atom and 50 ml of ethanol). After stirring for 5 min, **3** (3.1 g, 0.01 mol) was added and stirring was continued for a further 30 min. The reaction mixture was left overnight at room temperature. The product was collected by filtration or dilution with water then crystallized from ethanol or acetic acid to give 5-amino-4-cyano-1-phenyl-3-thienoylpyrazole (**8a**), 4-benzoyl-1,5-diphenyl-3-thienoylpyrazole (**8b**), 1,5-diphenyl-4-cyano-3-thienoylpyrazole (**8c**) and 4-benzenesulfonyl-1,5-diphenyl-3-thienoyl-pyrazole (**8d**), respectively (cf. Table I).

Synthesis of the pyrazole[3,4-*d*]*pyridazines* **9a,b**

A mixture of the appropriate **8b,c** (0.005 mol) and hydrazine hydrate (0.01 mol) was refluxed in ethanol (10 ml) for 4 h. During this period the pyrazole dissolved and the corresponding pyrazolopyridazine derivatives **9a,b** precipitated. The product was collected, washed with water and crystallized from acetic acid or dimethylformamide to give 3-thienyl-1,6,7-triphenylpyrazole[3,4-d]pyridazine (**9a**) and 6-amino-1,7-diphenylpyrazolo[3,4-d]pyridazine (**9b**), respectively (cf. Table 1).

Synthesis of the pyrrolo[3,4-*d*]*pyrazole* **10** *and triazole derivative* **11**

A well stirred cold solution of equimolecular amounts (5 mmole each) of **3** and N-phenylmaleimide (or benzalaniline) in dry benzene (25 ml) was treated dropwise (5 min) with triethylamine (0.5 ml) in 10 ml of benzene. The mixture was then refluxed for 3 h and filtered. The oily residue left after removal of the solvent solidified on trituration with petroleum ether (40/60°C). Recrystallization from acetic acid gave 3-thienoyl-1,5-diphenylpyrrolidino[3,4-d]-Δ^2-pyrazoline-4,6-dione (**10**) and 3-thienoyl-1,4,5-triphenyl-1,2,4-triazole (**11**), respectively (cf. Table I).

REFERENCES

1. Part I: A. O. Abdelhamid and S. E. Abdou, *Sulfur letters,* **6,** 41 (1987).
2. A. O. Abdelhamid and M. M. Afifi, *Phosphorus and Sulfur,* **28,** 000 (1987).
3. A. S. Shawali and A. Osman, *Tetrahedron,* **27,** 2517 (1971).
4. A. S. Shawali and A. O. Abdelhamid, *Bull. Chem. Soc. Japan,* **49,** 321 (1976).
5. A. S. Shawali and A. O. Abdelhamid, *J. Heterocyclic Chem.,* **13,** 45 (1976).
6. A. S. Shawali and A. O. Abdelhamid, *J. Heterocyclic Chem.,* **13,** 989 (1976).
7. A. S. Shawali, A. O. Abdelhamid, H. M. Hassaneen and A. Shetta, *J. Heterocyclic Chem.,* **19,** 73 (1982).
8. H. M. Hassaneen, A. O. Abdelhamid, A. S. Shawali and R. Pagni, *Heterocycles,* **19,** 319 (1982).
9. A. O. Abdelhamid, H. M. Hassaneen, I. M. Abbas, and A. S. Shawali, *Tetrahedron,* **38,** 1527 (1982).
10. A. O. Abdelhamid, H. M. Hassaneen and A. S. Shawali, *J. Heterocyclic Chem.,* **20,** 719 (1983).
11. A. O. Abdelhamid, H. M. Hassaneen, A. S. Shawali and C. Párkányi, *J. Heterocyclic Chem.,* **20,** 639 (1983).
12. A. O. Abdelhamid, C. Parkanyi, A. S. Shawali and M. A. Abdalla, *J. Heterocyclic Chem.,* **21,** 1049 (1984).
13. O. Fischer, *Chem. Ber. Dtsch. Chem. Ges.,* **9,** 463 (1876); H. Wechester, *Liebigs Ann. Chem.,* **325,** 237 (1902).
14. A. O. Abdelhamid and F. A. Attaby, *Sulfur Letters,* (in press) (1987).
15. A. R. Katritzky, Physical Methods in Heterocyclic Chemistry Academic Press, N.Y. Vol. **2,** p. 231 (1963).
16. H. Brunswing, Ber. *Dtsch. Chem. Ges.,* **19,** 2891 (1886).