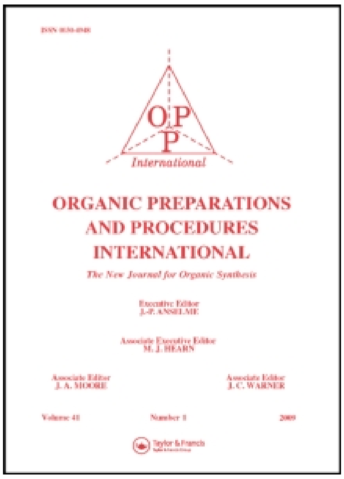


Organic Preparations and Procedures International
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t902189982

SYNTHESIS AND REACTIONS OF C-(2-THENOYL)-N-ARYLFORMHYDRAZIDOYL BROMIDES

Ahmed M. Farag[a]; Mohamed S. Algharib[b]
[a] Department of Chemistry, Faculty of Science, University of Cairo, Giza, EGYPT [b] Faculty of Engineering and Technology, University of Suez Canal, Port Said, EGYPT

To cite this Article Farag, Ahmed M. and Algharib, Mohamed S.(1988) 'SYNTHESIS AND REACTIONS OF C-(2-THENOYL)-N-ARYLFORMHYDRAZIDOYL BROMIDES', Organic Preparations and Procedures International, 20: 5, 521 — 526

To link to this Article: DOI: 10.1080/00304948809356298

URL: http://dx.doi.org/10.1080/00304948809356298

ORGANIC PREPARATIONS AND PROCEDURES INT. 20(5), 521-526 (1988)

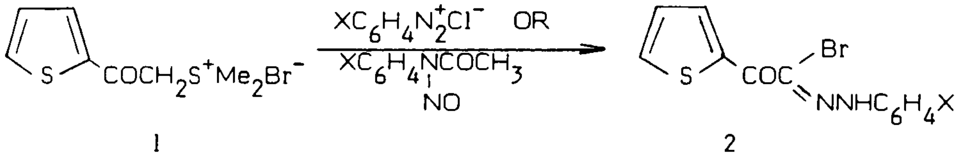
SYNTHESIS AND REACTIONS OF C-(2-THIENOYL)-N-ARYLFORMHYDRAZIDOYL BROMIDES

Ahmed M. Farag*
Department of Chemistry, Faculty of Science, University of Cairo, Giza,
EGYPT

Mohamed S. Algharib
Faculty of Engineering and Technology, University of Suez Canal
Port Said, EGYPT

As part of our program directed towards exploring the utility of hydrazidoyl halides[1] in heterocyclic synthesis[2], we now report the synthesis and some reactions of C-(thienoyl)-N-arylformhydrazidoyl bromides (2). By virtue of their structural relationship with the C-aroyl analogues, these compounds would be expected to show bacteriostastic and fungistatic activity.

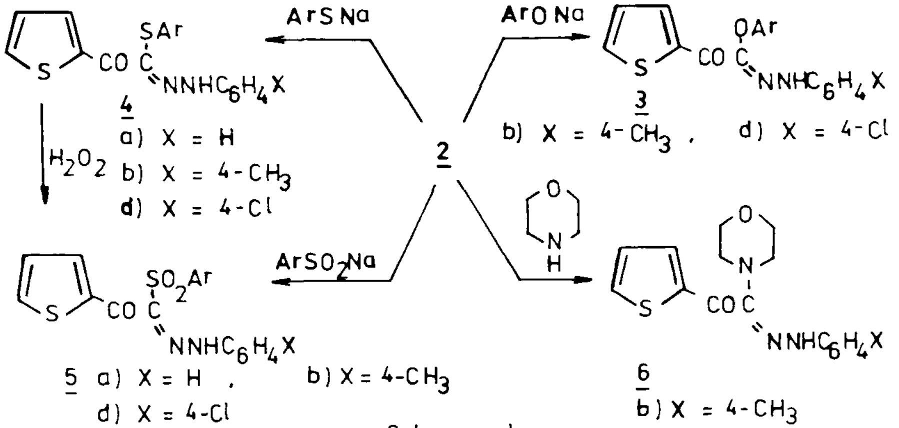
The new hydrazidoyl bromides 2a-2e were prepared by coupling 1-thienylethanone-2-dimethylsulfonium bromide (1) with diazotized anilines in ethanol solution buffered with sodium acetate or with N-nitrosoacetarylamides[3] in ethanol. Attempts at direct coupling of 2-bromoacetylthiophene with arenediazonium salts and N-nitrosoacetarylamides were unsuccessful.



1 2

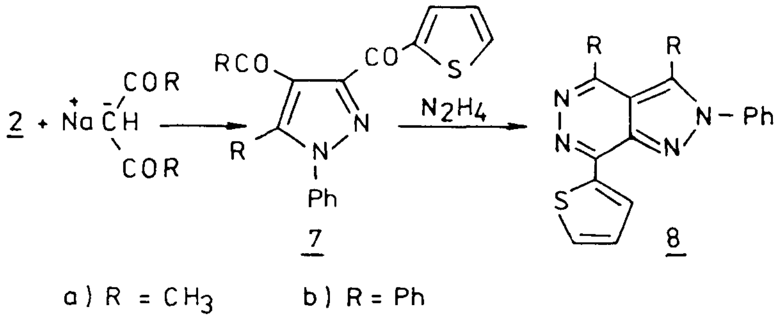
a) X = H, b) X = 4-CH_3, c) X = 4-OCH_3, d) X = 4-Cl, e) X = 4-NO_2

Treatment of 2 with nucleophiles gave the corresponding hydrazonates 3, thiohydrazonates 4, the hydrazonylsulfones 5 and amidrazone 6 respectively (scheme 1). Oxidation of the thiohydrazonate 4 with hydrogen peroxide in acetic acid afforded products identical in all respects with 5. The identity of the oxidation products of 4 with the products obtained from reaction of 2 with sodium benzenesulfinate supports the assigned structures of 4 and 5.



Scheme 1

Treatment of 2a with the sodium salt of acetylacetone, and dibenzoylmethane in ethanol gave 1-phenyl-3-(2-thienoyl)-4-acetyl-5-methyl pyrazole (7a) and 1,5-diphenyl-3-(2-thienoyl)-4-benzoylpyrazole (7b) respectively. Only one product was obtained in each case. Thin layer chromatography of the reaction mixture did not show the presence of the isomeric products (scheme 2). The structural assignment was confirmed by reaction with hydrazine which gave 2-H-pyrazolo-[3,4-d]pyridazines 8 in nearly quantitative yields.



Scheme 2

EXPERIMENTAL SECTION

Mps were determined on a Gallenkamp melting point apparatus and are uncorrected. The infrared spectra (KBr) were recorded on a Unicam SP 1000 infrared spectrophotometer. The microanalysis were performed by the Microanalytical Laboratory of Cairo University, Giza, EGYPT.

1-Thienylethanone-2-dimethylsulfonium bromide (1).- A mixture of 2-bromoacetylthiophene[4] (20.51 g, 0.1 mole) and dimethyl sulfide (7.5 ml, 0.1 mole) was refluxed in methanol (50 ml) for 30 min. The crystalline product which precipitated from the hot reaction mixture was collected and recrystallized from ethanol to afford 24.6 g (92 %) of pure product, mp. 145° (dec.). IR: 1660 cm^{-1}, 3105 cm^{-1} and 3060 cm^{-1}.

Anal. Calcd for $C_8H_{11}BrOS_2$: C,35.95; H,4.15; Br,29.90; S,23.99

Found: C,36.13; H,4.13; Br,29.85; S,24.12

C-Thienoyl-N-arylformhydrazidoyl Bromides 2a-e.

A. Coupling of 1 with Diazonium Salts. General Procedure.- A solution of 1 (0.01 mole) in ethanol (50 ml) was stirred with sodium acetate (3 g) and the mixture was then chilled in ice to 0-5°C. A cold aqueous solution (0-5°C) of the diazonium salt[3] (0.01 mole) was added dropwise with stirring over 45 min. After addition, the mixture was stirred for further 30 min. and then left for 2 hrs in an ice-chest. The precipitated yellow product was collected, washed with water and recrystallized from glacial acetic acid. Compounds 2a-e (Table 1) showed IR bands at 1640-1630 cm^{-1}, 3100-3010 cm^{-1} and 3280-3260 cm^{-1}.

B. Coupling of 1 with N-nitrosoacetarylamides. General Procedure.- To a solution of 1 (0.01 mole) in ethanol (50 ml) was added the appropriate N-nitrosoacetylarylamide[5] (0.01 mole). The reaction mixture was warmed slightly and shaken to effect complete dissolution of the reactants, then stirred for 2 hrs. The precipitated crystalline product was collected, washed with methanol and recrystallized from acetic acid to afford compounds identical in all respects (mps, mixture mps and IR spectra) with compounds 2a-e.

TABLE 1. Compounds 2a-e

Comp.	mp (°C)	Yield (%)	Molecular formula	Analysis % Calcd (Found) Br	N	S
2a	149	65	$C_{12}H_9BrN_2OS$	25.85 (25.81)	9.06 (9.14)	10.37 (10.41)
2b	145	71	$C_{13}H_{11}BrN_2OS$	24.72 (24.80)	8.67 (8.66)	9.95 (10.04)
2c	137	56	$C_{13}H_{11}BrN_2O_2S$	23.56 (23.50)	8.26 (8.44)	9.45 (9.37)
2d	223	87	$C_{12}H_8BrClN_2OS$[a]		8.15 (8.26)	9.33 (9.56)
2e	256	94	$C_{12}H_8BrN_3O_3S$	22.56 (22.71)	11.86 (11.71)	9.06 (9.22)

[a] Calcd: Cl, 10.32 Found: Cl, 10.32

All attempts to couple 2-bromoacetylthiophene (2.05 g, 0.01 mole) in ethanol (50 ml) with arenediazonium chloride (0.01 mole) in the presence of sodium acetate (3 g), or with N-nitrosoacetarylamide (0.01 mole) in the absence of sodium acetate failed to give the corresponding compounds 2. IN all cases the starting 2-bromoacetylthiophene was recovered.

Reactions of 2 with Nucleophiles. Preparation of 3, 4, 5 and 6.- General Procedure.- Equimolecular quantities (0.01 mole) of 2 and the appropriate nucleophile (NaOAr, NaSAr, $NaSO_2Ph$ or morpholine) in ethanol were warmed and stirred for 30 min. then left overnight at room temperature. The precipitated product was collected, washed with water and recrystallized from ethanol (Table 2).

Oxidation of 4. General Procedure.- A solution of hydrogen peroxide (10 ml, 30 %) was added to a solution of 4 (0.01 mole) in acetic acid (15 ml). The reaction mixture was left at room temperature for 48 hrs then diluted with water. The precipitated product was collected and recrystallized from ethanol to afford compounds identical in all respects with 5 (mps, mixture mps).

TABLE 2. Compounds 3, 4, 5 and 6

Compd.	mp (°C)	Yield (%)	Molecular formula	Analysis % Calcd (Found)			
				C	H	N	S
3b	158	62	$C_{19}H_{16}N_2O_2S$	67.83 (68.05)	4.79 (4.81)	8.33 (8.25)	9.53 (9.64)
3d	169	68	$C_{18}H_{13}ClN_2O_2S$[a]	60.58 (60.77)	3.67 (3.70)	7.85 (7.86)	-- --
4a	125	78	$C_{18}H_{14}N_2OS_2$	63.87 (63.97)	4.17 (4.20)	8.28 (8.33)	18.95 (19.07)
4b	142	86	$C_{19}H_{16}N_2OS_2$	64.74 (65.03)	4.58 (4.61)	7.95 (8.01)	18.19 (18.15)
4d	169	91	$C_{18}H_{13}ClN_2OS_2$[b]	57.97 (58.14)	3.51 (3.60)	7.51 (7.45)	-- --
5a	205	84	$C_{18}H_{14}N_2O_3S_2$	58.36 (58.44)	3.81 (3.93)	7.56 (7.66)	16.68 (16.70)
5b	207	85	$C_{19}H_{16}N_2O_3S_2$	59.35 (59.00)	4.19 (4.23)	7.29 (7.12)	16.68 (16.55)
5d	216	91	$C_{18}H_{13}ClN_2O_3S_2$[c]	53.39 (53.67)	3.24 (3.38)	6.92 (7.15)	-- --
6b	148	97	$C_{17}H_{19}N_3O_2S$	61.98 (62.22)	5.81 (5.95)	12.76 (12.94)	9.73 (9.66)

a) Calcd: Cl, 9.94 Found: Cl, 10.00. b) Calcd: Cl, 9.51 Found: Cl, 9.58. c) Calcd: Cl, 8.76 Found: Cl, 8.89.

Pyrazoles 7. General Procedure.- The appropriate active methylene compound (acetylacetone or dibenzoylmethane) (0.01 mole) was added to an ethanolic solution of sodium ethoxide (prepared from sodium metal, 0.12 g, 0.005 g atom and 25 ml of absolute ethanol). After stirring for 15 min., compound 2a was added and stirring continued for a further hr, then the reaction mixture was left overnight at room temperature. The precipitated product was collected, washed with water and recrystallized from ethanol.

7a: mp 103°C, yield 75 %, IR 1680 cm^{-1} (acetyl C=O), 1635 cm^{-1}.

Anal. Calcd. for $C_{17}H_{14}N_2O_2S$: C, 65.77; H, 4.55; N, 9.03; S, 10.33

Found : C, 65.94; H, 4.51; N, 8.92; S, 10.21

7b: mp 199°C yield 81 %, IR 1670 cm^{-1} (benzoyl C=O) 1640 cm^{-1} (theinoyl C=O).

Anal. Calcd for $C_{27}H_{18}N_2O_2S$: C, 74.63; H, 4.17; N, 6.45; S, 7.38

Found: C, 74.40; H, 4.28; N, 6.38; S, 7.51

Pyrazolopyridazines 8. General Procedure.- A mixture of 7 (0.005 mole) and hydrazine hydrate (8 ml) was refluxed in ethanol (20 ml) for 1 hr then cooled and diluted with water. The precipitated product was collected, washed with water and recrystallized from ethanol.

8a: mp 260°C, yield 98 %. IR 3110 cm^{-1}, no carbonyl bands.

Anal. Calcd for $C_{17}H_{14}N_4S$: C, 66.46; H, 4.60; N, 18.29; S, 10.47

Found : C, 66.22; H, 4.42; N, 18.37; S, 10.46

8b: mp 256°C, yield 100 %, IR 3100; no carbonyl bands.

Anal. Calcd for $C_{27}H_{18}N_4S$: C, 75.32; H, 4.21; N, 13.01; S, 7.45

Found: C, 75.00; H, 4.18; N, 12.92; S, 7.51

REFERENCES

1. A. S. Shawali and C. Párkányi, J. Heterocyclic Chem., 17, 833 (1980); A. S. Shawali, Hetrocycles, 20, 2239 (1983).
2. A. M. Farag, A. A. Fahmi, A. O. Abdelhamid, M. S. Algharib and A. S. Shawali, J. Heterocyclic Chem., 24, 1341 (1987); M. K. A. Ibrahim, A. M. El-Reedy, M. S. Algharib and A. M. Farag, J. Ind. Chem. Soc., 64, 345 (1987); H. M. Hassaneen, A. M. Farag, A. S. Shawali and A. S. Algharib, J. Heterocyclic Chem., 24, 577 (1987).
3. H. Zollinger "Azo and Diazo Chemistry, Aliphatic and Aromatic Compounds", Intescience, New York, N.Y., 1961.
4. F. Kipnis, H. Soloway and J. Ornfelt, J. Am. Chem. Soc., 71, 10 (1949).
5. O. Fisher, Ber., 9, 463 (1876); H. H. Wechester, Ann., 325, 237 (1902).

(Received December 16, 1987; in revised form May 2, 1988)