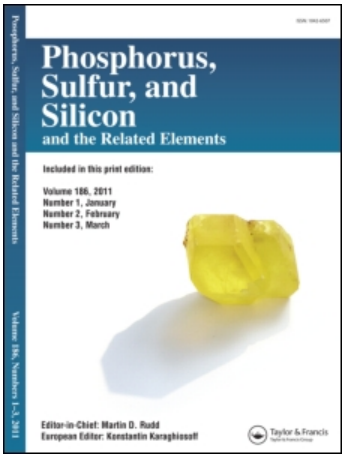


Phosphorus, Sulfur, and Silicon and the Related Elements
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713618290

ACTIVATED NITRILES IN HETEROCYCLIC SYNTHESIS: NOVEL SYNTHESIS OF PYRIDINE, BENZO[1,4]THIAZINE AND BENZO [1,3]THIAZOLE DERIVATIVES

Galal Eldin Hamza Elgemeie[a]; Ahmed Hafez Hussein Elghandour[b]
[a] Chemistry Department, Faculty of Science, Bani Suef, Egypt [b] Chemistry Department, Faculty of Science, Cairo University, Giza, Egypt

To cite this Article Elgemeie, Galal Eldin Hamza and Elghandour, Ahmed Hafez Hussein(1990) 'ACTIVATED NITRILES IN HETEROCYCLIC SYNTHESIS: NOVEL SYNTHESIS OF PYRIDINE, BENZO[1,4]THIAZINE AND BENZO [1,3]THIAZOLE DERIVATIVES', Phosphorus, Sulfur, and Silicon and the Related Elements, 48: 1, 281 — 284
To link to this Article: DOI: 10.1080/10426509008045911
URL: http://dx.doi.org/10.1080/10426509008045911

Phosphorus, Sulfur, and Silicon, 1990, Vol. 48, pp. 281–284

Reprints available directly from the publisher
Printed in the United Kingdom
Photocopying permitted by license only

Communication

ACTIVATED NITRILES IN HETEROCYCLIC SYNTHESIS: NOVEL SYNTHESIS OF PYRIDINE, BENZO[1,4]THIAZINE AND BENZO[1,3]THIAZOLE DERIVATIVES

GALAL ELDIN HAMZA ELGEMEIE†
Chemistry Department, Faculty of Science, Bani Suef, Egypt

AHMED HAFEZ HUSSEIN ELGHANDOUR
Chemistry Department, Faculty of Science, Cairo University, Giza, Egypt

(Received August 21, 1989, in revised form October 24, 1989)

A novel synthesis of pyridine, benzo[1,4]thiazine and benzo[1,3]thiazole derivatives utilizing o-aminobenzenethiol and α,β-unsaturated nitriles as starting components is reported.

Key words: α,β-Unsaturated nitriles, o-aminobenzenethiol, 4H-benzo[1,4]thiazines, 2-aryl-benzo[1,3]thiazoles.

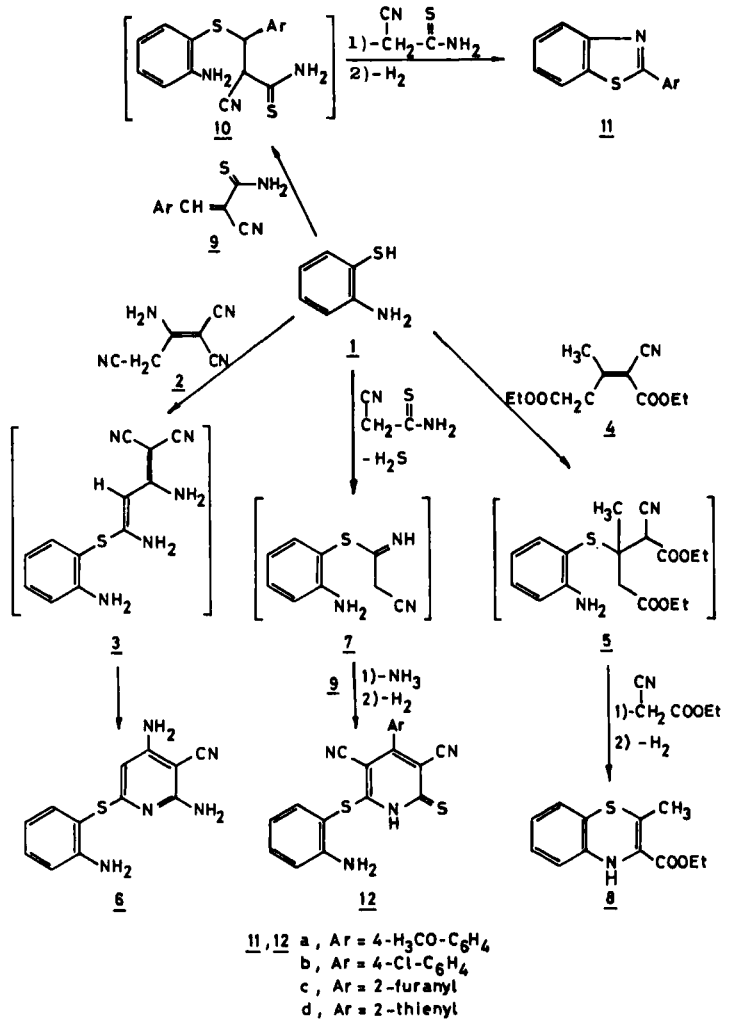
INTRODUCTION

In the last few years we were involved in a programme aiming to develop synthetic approaches for polyfunctionally substituted heterocycles utilizing readily obtainable nitriles as starting materials.[1–4] In a previous paper, we reported on the synthesis of thiazolopyridines utilizing o-aminobenzenethiol.[5]

DISCUSSIONS

In conjunction of this work we investigated the reaction of o-aminobenzenethiol **1** with malononitrile dimer **2**. In our laboratory, **1** reacted with **2** in refluxing ethanol containing catalytic amounts of triethylamine to yield 1:1 adducts. Two isomeric structures seemed possible (cf. structures **3** and **6**). Structure **6** seemed to be logic according to IR spectra which revealed one CN band at 2220 cm^{-1} and to ^1H NMR spectra which revealed three amino functions at δ 5.59, 6.08, 6.22 ppm[6] and a pyridine 5-H at δ 5.68 ppm.[7] Moreover, the reaction product could not be cyclized under a variety of conditions expected to effect such cyclization. This leads to the conclusion that it exists in the pyridine form **6**. The formation of **6** from **1** and **2** is assumed to proceed via addition of an SH function of the thiophenol to the CN group in **2** to give the intermediate **3**, which then cyclizes

† Author to whom all correspondence should be addressed.



under the reaction conditions to give the pyridine derivative **6**. Compound **1** reacts with **4** in refluxing ethanol containing catalytic amounts of triethylamine for 2 hrs to give the unexpected 4H-benzo[1,4]thiazine derivative **8**. Structure **8** finds support from the MS spectra which revealed a molecular formula $C_{12}H_{13}NO_2S$ ($M^+/e = 235$). The ^1H NMR spectra revealed a broad band at δ 7.82 ppm assigned to the NH group (D_2O exchangable) and signals for an ester and methyl groups. The formation of **8** from **1** and **4** is assumed to proceed via addition of an SH group of **1** to the double bond in **4** to give the intermediate **5**, which then cyclizes via ethyl cyanoacetate elimination and oxidation under the reaction conditions to give the benzothiazine derivative **8**. Similar oxidation have been previously reported by other groups[8,9] and a mechanism is suggested. The unexpected course of the reaction between **1** and **4** prompted us to investigate this reaction between **1** and other α,β-unsaturated nitriles under the same experimental reaction conditions. Thus, it has been found that **1** reacts with

arylmethylenecyanothioacetamide **9** to give also the unexpected 2-aryl-benzo[1,3]thiazole derivative **11**. The structure of **11** could be established and confirmed for the reaction products on the basis of their mass spectra and spectral data. The mass spectra for compound **11a** revealed a molecular formula $C_{14}H_{11}NOS$ ($M^+/e = 241$) and the ^1H NMR spectra revealed only the aromatic protones in the range $\delta = 6.9$–8.1 ppm. Compound **1** reacts with cyanothioacetamide and **9** in refluxing ethanol containing catalytic amounts of tri-ethylamine to give the pyridine-2(1H)-thione derivative **12**. The structure of **12** could be established for the reaction products on the basis of their elemental analysis and spectral data. The formation of **12** was assumed to proceed through the intermediacy of **7**, which adds to the double bond of **9** to give a Michael adduct. The latter then cyclizes via ammonia elimination and then aromatization under the reaction conditions[3,4,10] to give finally the pyridine-2(1H)-thione derivative **12**. These results when combined with our previous findings indicate that the reaction of o-aminobenzenethiol **1** with the suitable α,β-unsaturated nitriles can be utilized as an excellent route for synthesis of several, otherwise difficulty accessible medically important heterocyclic derivatives in most cases via initial Michael addition followed by elimination of byproducts. However, some exceptions to this generalization and to the type of by-products were observed. Thus, cautions should be made on suggesting structures for reaction products of similar reactions based on analogy to our results.

EXPERIMENTAL

All melting points are uncorrected. IR spectra were obtained (KBr) on a Pye Unicam Spectra-1000 spectrophotometer or on a Shimadzu IR 200. ^1H NMR spectra were measured on a Wilmad 270 MHz

TABLE I

List of compounds **6**, **8**, **11a–d** and **12a–d**

Compound	Solvent of cryst.	m.p. (°C)	Yield (%)	Mol. formula	Found Calcd (%) C	H	N
6	EtOH	193	75	$C_{12}H_{11}N_5S$	56.4	4.5	26.8
					56.0	4.3	27.2
8	EtOH	130	70	$C_{12}H_{13}NO_2S$	61.0	5.2	5.8
					61.3	5.5	6.0
11a	MeOH	117	80	$C_{14}H_{11}NOS$	69.3	4.8	5.8
					69.7	4.6	5.8
11b	MeOH	103	72	$C_{13}H_8ClNS$	63.9	3.6	5.5
					63.5	3.3	5.7
11c	EtOH-DMF	237	65	$C_{11}H_7NOS$	65.5	3.8	6.6
					65.7	3.5	7.0
11d	EtOH	175	60	$C_{11}H_7NS_2$	60.5	3.5	6.2
					60.8	3.2	6.5
12a	EtOH	164	77	$C_{20}H_{14}N_4S_2O$	61.5	4.0	14.2
					61.5	3.6	14.4
12b	Dioxane	152	58	$C_{19}H_{11}ClN_4S_2$	58.0	3.1	13.9
					57.8	2.8	14.2
12c	EtOH	182	50	$C_{17}H_{10}N_4S_2O$	58.6	3.2	15.8
					58.3	2.9	16.0
12d	MeOH	168	73	$C_{17}H_{10}N_4S_3$	55.3	3.1	15.0
					55.7	2.7	15.3

TABLE II

Spectroscopic data for the compounds listed in Table I

Compound	IR (cm^{-1}) (Selected bands)	^1H NMR (δ ppm)
6	3380, 3440 (NH_2); 2220 (CN)	5.21 (s, br, 2H, NH_2); 5.59 (s, 1H, pyridine 5-H); 6.08 (s, br, 2H, NH_2); 6.22 (s, br, 2H, NH_2); 6.5–6.88 (m, 2H, aromatic protons); 7.06–7.4 (m, 2H, aromatic protons)
8	3340 (NH); 1725 (CO)	1.25 (t, 3H, CH_3); 2.26 (s, 3H, CH_3); 4.12 (q, 2H, CH_2); 6.68–6.99 (m, 4H, C_6H_4); 7.8.1 (s, br, 1H, NH)
11a		3.92 (s, 3H, OCH_3); 6.84–7.18 (m, 2H, aromatic protons); 7.2–7.58 (m, 2H, aromatic protons); 7.77–8.13 (m, 4H, C_6H_4)
11b		7.28–7.58 (m, 4H, C_6H_4); 7.76–8.1 (m, 4H, C_6H_4)
12a	3330, 3400 (NH); 2220 (CN)	3.80 (s, 3H, OCH_3); 5.3 (s, br, 2H, NH_2); 6.62–7.88 (m, 8H, 2 C_6H_4); 13.2 (s, br, 1H, NH)
12b	3360, 3420 (NH) 2215 (CN)	5.42, (s, br, 2H, NH_2); 6.82–7.85 (m, 8H, 2 C_6H_4); 13.28 (s, br, 1H, NH)

in DMSO using TMS as internal standard and chemical shifts are expressed as δ ppm. Analytical data were obtained from the analytical data unit at Cairo University.
Compounds **2** and **4** were prepared following literature procedure.[11,12]

Preparation of **6**, **8** *and* **11a–c**. *General procedure*: A mixture of **1** (0.01 mole) and **2**, **4** or **9** (0.01 mole) are dissolved in ethanol (30 ml), 1 ml of triethylamine were then added. The mixture was refluxed for 3 hrs. The precipitated solid product was filtered off and crystallized from the proper solvent (cf. Table I).

Preparation of **12a–c**. *General Procedure:* A mixture of **1** (0.01 mole), cyanothioacetamide (0.01 mole) and arylmethylenecyanothioacetamide **9** (0.01 mole) in dry ethanol (30 ml), 1 ml of triethylamine were then added. The mixture was refluxed for 3 hrs. The precipitated solid product was filtered off and crystallized from the proper solvent (cf. Table I).

REFERENCES

1. G. H. Elgemeie and F. A. Aal, *Heterocycles*, 1986, **24**, 349.
2. G. H. Elgemeie, H. A. Elfahham and H. Nabey, *Bull. Chem. Soc. Japn.*, 1988, **61**, 4431.
3. G. H. Elgemeie, H. A. Elfahham and H. Nabey, *Sulfur Lett.*, 1989, **9**, 47.
4. G. H. Elgemeie, H. A. Elfahham and R. Mekhamer, *Sulfur Lett.*, 1988, **8**, 187.
5. G. H. Elgemeie and N. M. Fathy, *Sulfur Lett.*, 1988, **7**, 189.
6. S. Kambe, K. Saito, A. Sakurai and H. Midorikawa, *Synthesis*, 531.
7. A. R. Katritzky, Handbook of Heterocyclic Chemistry (structure of six-membered rings), Pergmon Press, 1985, p. 23.
8. R. P. Soni and M. L. Jain, *Tetrahedron Letters*, 1980, **21**, 3795.
9. T. Fujiwara, K. Hata and T. Kojima, *Chem. Letters*, 1973, 207.
10. J. Becher and C. E. Stidsen, *Sulfur Rep.*, 1988, **8**, 104.
11. F. Freeman, *Chem. Rev.*, 1969, **69**, 591.
12. J. Klosa, *Pharmazie*, 1952, **7**, 299.