Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry
Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/lsyc20

s-Triazolo[3,4-α]Phthalazines From 1-Phthalazinylhydrazones by Thianthrene Cation Radical Perchlorate

Koon Ha Park [a] , Kun Jun [b] , Seung Rim Shin [b] & Sea Wha Oh [b]

[a] Department of Chemistry , Chungnam National University , Taejon, 305-764, Korea

[b] Research Institute of Chemical Technology , P.O. Box 107, Yusung, Taejon, 305-606, Korea

Published online: 17 Sep 2007.

To cite this article: Koon Ha Park , Kun Jun , Seung Rim Shin & Sea Wha Oh (1999) s-Triazolo[3,4-α]Phthalazines From 1-Phthalazinylhydrazones by Thianthrene Cation Radical Perchlorate, Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry, 29:4, 583-589, DOI: 10.1080/00397919908085806

To link to this article: http://dx.doi.org/10.1080/00397919908085806

SYNTHETIC COMMUNICATIONS, 29(4), 583-589 (1999)

s-TRIAZOLO[3,4-*a*]PHTHALAZINES FROM 1-PHTHALAZINYLHYDRAZONES BY THIANTHRENE CATION RADICAL PERCHLORATE

Koon Ha Park[a*], Kun Jun[b], Seung Rim Shin[b], and Sea Wha Oh[b]

[a]Department of Chemistry, Chungnam National University, Taejon 305-764, Korea

[b]Korea Research Institute of Chemical Technology, P.O. Box 107, Yusung, Taejon 305-606, Korea

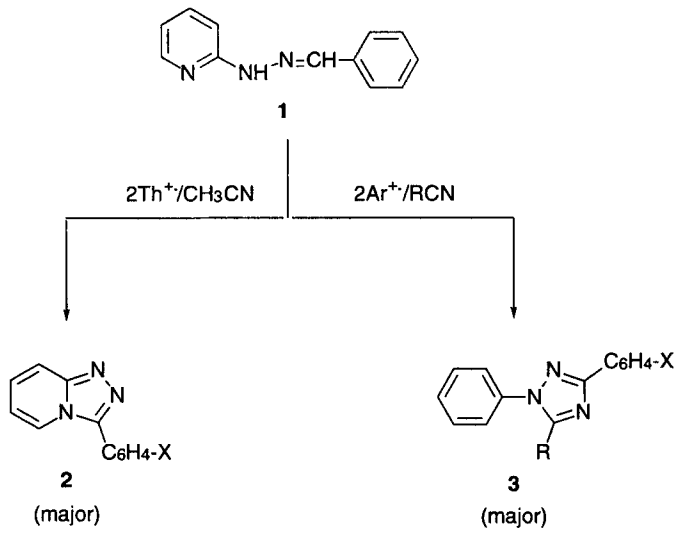
Abstract: 1-Phthalazinylhydrazones **4** gave *s*-triazolo[3,4-*a*]phthalazines **5** in 94-98% yields by thianthrene cation radical perchlorate ($Th^{+\cdot}ClO_4^-$).

In our continuing investigations on the chemistry of cation radicals with heterocyclic hydrazones and Schiff's bases,[1] we have found out that the major product depended not only on the organic substrate but also on the radical used.[2] For instance, reaction of thianthrene cation radical perchlorate ($Th^{+\cdot}ClO_4^-$)[3-5] with phenolic Schiff's bases in acetonitrile solvent provided a convenient new method for the synthesis of arylbenzoxazoles by intramolecular cyclization.[6]

* To whom correspondence should be addressed

Reactions of arenealdehyde 2-pyridylhydrazones **1** with either $Th^{+\cdot}ClO_4^-$ or tris(2,4-dibromophenyl)aminium hexachloroantimonate ($Ar_3N^{+\cdot}SbCl_6^-$) afforded *s*-triazolo[4,3-*a*]pyridine **2** by intramolecular cyclization and 1-(2-pyridyl)-1,2,4-triazoles **3** by intermolecular cycloaddition respectively (Scheme 1).[2]

Scheme 1



Herein we report reactions of $Th^{+\cdot}ClO_4^-$ with 1-phthalazinylhydrazone **4** in acetonitrile (eq. 1).

The yields% and mp's of the products **5** obtained in eq. 1 are compared with those of reported values in Table 1 which shows much improvement in yields (>94%). Particularly noteworthy in our reactions is an exclusive formation of intramolecular cyclization product instead of the expected intramolecular and intermolecular

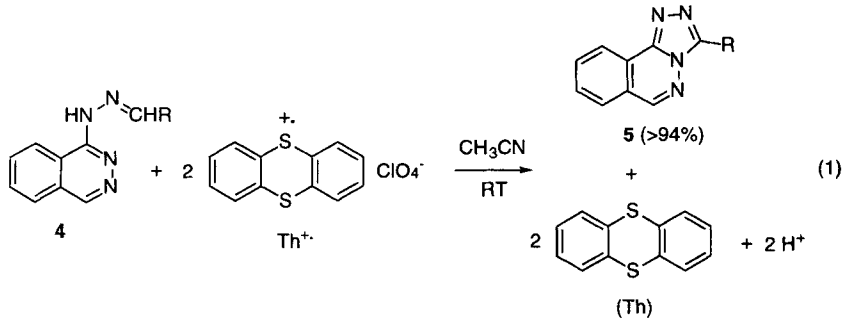


Table 1. Comparisons of Yield%[a] and mp of **5** Obtained from the Reaction of **4** and $Th^{+\cdot}ClO_4^-$ with those of Reported Values

4	**5** (Yield%)		mp	
R	observed	reported	observed	reported
Ph	98.2	15[b]	208-210	215-216[b]
				208-209[c]
p-MeOPh	94.2	16[b]	201-202	203-205[b]
p-BrPh	98.0		232-233[d]	
2-Styryl	97.8		191-193[e]	

[a]The yield was quantitatively determined. [b]ref. 7. [c]ref. 8. [d,e]These *s*-triazolo[3,4-*a*]phthalazines are new compounds.

cyclization products. In order to study the participation of liberated acid in the formation of product **5**, the following reactions were performed. *i.e.* in the reaction of **4** (R=Ph) with 70% $HClO_4$ in acetonitrile, any cyclized product was not

detected. This observation indicated that the products obtained in our reactions were not derived from the acid liberated during the reaction.

The product **5** in eq.1 is believed to be formed through two successive one electron oxidations by $Th^{+\cdot}ClO_4^-$ and deprotonations as reported previously for the formation of **2**.[2] The different behaviors of **1** and **4** towards $Th^{+\cdot}ClO_4^-$ might be explained as follows. *i.e.* One of the two ring nitrogens can capture the liberated acid formed during the reaction, permitting the second ring nitrogen more favorably for nucleophilic attack compared with the pyridylhydrazones **1** having only one ring nitrogen. Therefore **4** could have more chance to undergo intramolecular cyclization by the second ring nitrogen.

In conclusion, oxidative intramolecular cyclization of **4** to **5** was achieved by thianthrene cation radical perchlorate in a quantitative yield in mild conditions.

EXPERIMENTAL

Preparation of Hydrazone (General procedure for Benzaldehyde 1-Phthalazinylhydrazone)

A solution of 3.50 g (17.0 mmol) of 4-bromobenzaldehyde, 5.00 g (25.5 mmol) of 1-hydrazinophthalazine hydrochloride and 4.2 g (30.4 mmol) of sodium acetate trihydrate in 20 mL of ethanol and 10 mL of water was heated for 3h at 40 °C. After cooling, 30 g of ice water was added to the reaction mixture. The formed pale yellow solid was collected by filtration. Hydrazone was then dried in a vacuum oven. The product was crystallized from methylene chloride to give 3.3 g (10.1 mmol, 59.2%) of pale yellow crystals with mp 199-201.5 °C .

^{1}H NMR (300MHz, $CDCl_3$): δ 7.53-7.56 (m, 3H), 7.65-7.70 (m, 4H), 7.89 (s, 1H), 8.39-8.42 (m, 1H), 8.47 (s, 1H), 10.63 (s, 1H).

GC/MS:m/e (relative intensity), 328 (M+2, 42.7), 326 (M^+, 53.5), 171

(100), 129 (10.1), 103 (34.7), 89 (41.1), 76 (29.4), 63 (45.9), 50 (11.3).

HRMS. Calcd. for $C_{15}H_{11}N_4Br$:326.0187; Found: 326.0189.

General Reactions of Thianthrene Cation Radical ($Th^{+\cdot}$) with Heterocylic Hydrazones in Nitrile Solvents

Hydrazone (0.5 mmol) and $Th^{+\cdot}$ (1.0 mmol) were placed in a septum-capped flask under argon atmosphere, and nitrile solvent (20 mL) was added to the flask with a syringe. The mixture was stirred for 24h at room temperature and water (10 mL) was added, followed by neutralization with dilute sodium bicarbonate solution. The organic product mixture was extracted with methylene chloride (5x30 mL) and the solvent was dried over anhydrous sodium sulfate. After filtration, the combined organic layer was concentrated using a rotary evaporator. The solid residue was dissolved in methylene chloride (50 mL) and was used for identification of products by GC and GC/MS, and for quantitative analysis by GC. Authentic samples were used as controls. The products were separated by preparative TLC using methylene chloride/methanol (15:2, v/v) as the developing solvent, removed from the plate and extracted with methylene chloride.

Preparation of Authentic Compound 3-(4-Bromophenyl)-*s*-triazolo[3,4-*a*]phthalazine)

Bromine (0.4 mL, 7.69 mmol) in acetic acid (15 mL) was added to a suspension of powdered, anhydrous sodium acetate (3.7 g, 44.4 mmol) and benzaldehyde 1-phthalazinylhydrazone (2.01 g, 6.13 mmol) in 15 mL of acetic acid. The reaction mixture was heated under reflux for 3h and then 100 mL of water was added to the reaction mixture. On standing overnight, the precipitated solid was collected by filtration and dried. The product was crystallized from ethanol/acetone

(1:2, v/v) to give 0.51 g (1.56 mmol, 25.4%) of white crystals with mp 232-233.5 °C .

^{1}H NMR (300MHz, $CDCl_3$): δ 7.69 (d, 2H, *J*=8.7), 7.81-7.87 (m, 1H), 7.95-8.01 (m, 2H), 8.38 (d, 2H, *J*=8.7), 8.71-8.74 (m, 2H).

GC/MS:m/e (relative intensity), 326 (M+2, 73.9), 325 (M+1, 80.6), 324 (M^+, 100), 115 (22.1), 88 (32.5), 75 (15.8), 62 (27.4), 50 (17.3).

HRMS. Calcd. for $C_{15}H_9N_4Br$:324.0019; Found: 324.0020.

3-Styryl-*s*-triazolo[3,4-*a*]phthalazine

Similar procedure described for the preparation of 3-(4-bromophenyl)-*s*-triazolo[3,4-*a*]phthalazine was followed, using cinnamaldehyde 1-phthalazine (1.23 g, 4.5 mmol) and bromine (0.25 mL, 4.81 mmol). The product was crystallized from ethanol to give 0.32 g (1.18 mmol, 26.1%) of pale yellow crystals with mp 191-193 °C .

^{1}H NMR (300MHz, $CDCl_3$): δ 7.38-7.47 (m, 3H), 7.56 (d, 1H, *J*=16.6), 7.78 (d, 2H, *J*=7.4), 7.92-8.10 (m, 3H), 8.25 (d, 1H, *J*=7.8), 8.53 (d, 1H, *J*=7.8), 9.16 (s, 1H).

GC/MS:m/e (relative intensity), 272 (M^+, 31.3), 271 (M-1, 100), 128 (6.4), 116 (3.8), 102 (4.6).

Anal. Calcd. for $C_{17}H_{12}N_4$: C, 75.00; H, 4.41; N, 20.59. Found: C, 75.38; H, 4.38; N, 20.61.

Acknowledgments: We thank the Organic Chemistry Research Center sponsored by Korea Science Engineering and Foundation (1997) and the Ministry of Education through Basic Science Research Program (BSRI-97-3433) for financial support.

REFERENCES AND NOTES

1. Jun, K. *Ph. D. Thesis*, Chungnam National University, **1997**.
2. Park, K. H., Jun, K., Shin, S. R. and Oh, S. W. *Bull. Korean Chem. Soc.*, **1997**, *18*, 604.
3. Shine, H. J and Hoque, A. K. M. M. *J. Org. Chem.*, **1988**, *53*, 4349.
4. Chiou, S., Hoque, A. K. M. M. and Shine, H. J. *J. Org. Chem.*, **1990**, *55*, 3227.
5. Kovelesky, A. C. and Shine, H. J. *J. Org. Chem.*, **1988**, *53*, 1973.
6. Park, K. H., Jun, K., Shin, S. R. and Oh, S. W. *Tetrahedron Lett.*, **1996**, *37*, 8869.
7. Rekkas, S., Rodios, N. and Alexandrou, N. E. *Synthesis*, **1984**, 602.
8. Druey, J. and Ringier, B. H. *Helv. Chim. Acta*, **1951**, *34*, 195.

(Received in Japan 11 June 1998)