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Photodesulfurization of 2,4-Diaryl-1,2,4-triazole-3-thiones

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ABSTRACT: *Irradiation of triazole thiones in thin-film reactor furnished the corresponding desulfurized triazoles in good yield. The required triazole thiones were synthesized from the respective acid hydrazide and isothiocyanate.* © 2003 Wiley Periodicals, Inc. Heteroatom Chem 14:269–272, 2003; Published online in Wiley InterScience (www.interscience.wiley.com). DOI 10.1002/hc.10140

INTRODUCTION

1,2,4-Triazole derivatives are associated with diverse pharmacological activities; they act as anticonvulsants, antidepressants, tranquilizers, and plant growth regulators. Recently some new triazoles have been synthesized as possible antibacterial, antimicrobial, antiviral, antifungal, and antioxidant and antiradical agents [1–3].

The photochemistry of thiones has received much attention from both synthetic and mechanistic point of view [4]. There are a few reports [5–7] on the intramolecular photocyclization of amides and thioamides. Synthesis of heterocyclic systems via photodesulfurization has also been reported [8–10]. Photoinduced desulfurization of episulfide [11] and indoline-2-thiones to indole too are known [12].

In continuation of our work on the photochemistry of thioamide systems [13–15], we have earlier reported the synthesis of triazolo benzothiazole [16] via intramolecular dehydrohalogenation of 4-(2-chlorophenyl)-5-phenyl-1,2,4-triazole-3-thiones. In this line, we are interested in the synthesis of such ring systems by the oxidative photodehydrogenation of substituted 1,2,4-triazole-3-thiones lacking halogen in the o-position of 4-aryl substituent. Synthesis of 2-substituted benzothiazoles via oxidative photocyclization in alcohol has also been reported earlier [17,18].

RESULTS AND DISCUSSION

Triazolethiones **1a–e** were prepared in good yield from the corresponding acid hydrazides and isothiocyanates. Their irradiation in methanol, using a thin-film reactor (TFR, 254 nm) under nitrogen atmosphere gave the corresponding desulfurized triazoles **2a–e** (Scheme 1, Table 1). A trace amount of sulfur was also isolated.

Recently, a straightforward synthesis of 1,2,4-triazole-3-thiones via the irradiation of the corresponding 2-methyl-4-phenyl substituted benzaldehyde thiosemicarbazones has been reported [19]. On the other hand, in the present work, an efficient desulfurization of triazolethiones has been observed under similar condition. So it may be concluded that thioenolization may facilitate the desulfurization.

The structure of **1a–e** and **2a–e** was confirmed by spectral and analytical data. The thione and thiol forms of **1** are assigned by ^{1}H NMR as a singlet around δ 12 due to SH, while the ^{13}C NMR shows the presence of C=S by a signal around δ 169. IR spectra were comparable with those reported in literature [20,21]. A strong band in the region 1300 cm^{-1}

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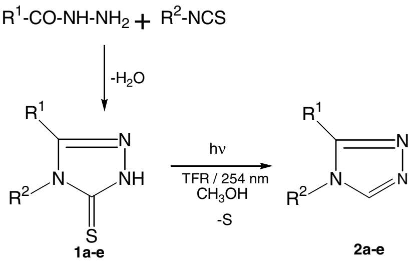


SCHEME 1

shows the presence of thione form and a weak band around 2700 cm^{-1} indicates the thiol form. The CH-ring member of **2** appears as a singlet around δ 8 in the ^1H NMR spectra and as a singlet around δ 141–145 in the ^{13}C NMR spectra. The mass spectral fragmentation pattern of **2e** is depicted in Scheme 2. The identity of **2a** was also confirmed by mixture mp and IR superimposable with that of the product from Raney Ni/EtOH desulfurization [22] of **1a**.

Photoreactions described here would provide a facile method for the synthesis of 1,2,4-triazole; the irradiation of triazole-3-thiones without ortho halogen on the aryl ring of position 4 leads to smooth desulfurization instead of photocyclization.

EXPERIMENTAL

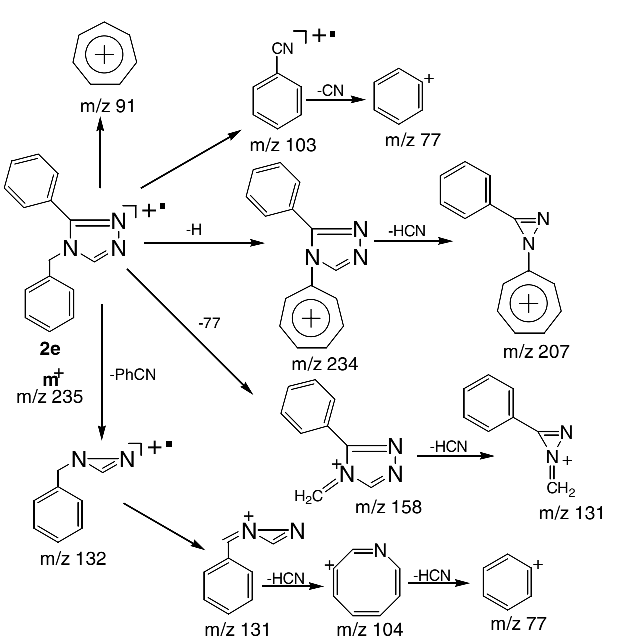
Melting points are uncorrected. UV spectra were recorded with Shimadzu 1601 spectrophotometer, and IR spectra with FTIR-8300 Shimadzu spectrophotometer. ^1H and ^{13}C NMR spectra were recorded with Bruker-DPX 200 (200 MHz) and Jeol-GSX 400 (400 MHz) instruments with TMS as internal standard (chemical shift δ in ppm). The mass spectra were recorded with Jeol-JMS-DX 303 HF and GCMS QP 5000 Shimadzu instruments. The photochemical reactions were carried out in quartz vessel in Applied Photophysics thin-film reactor (254 nm).

General Procedure for 4,5-Diaryl-1,2,4-triazole-3-thiones **1a–d**

A mixture of acid hydrazide (7 mmol) and isothiocyanate (7 mmol) was refluxed in aqueous K_2CO_3 solution (100 ml, 10%) for 6–8 h, cooled, filtered, and the filtrate washed with ether. The aqueous layer was neutralized with cold dil. HCl (in the case of **1d** pH 7 was maintained). The separated solid was filtered and washed with water to get the triazole-3-thione **1**. The use of NaOH [16], instead of K_2CO_3 gave **1** in lower yields (40–45%).

TABLE 1 Irradiation Time and Yield of the Triazoles **2a–e**

	R¹	*R²*	*Time (h)*	*Yield (%)*
1a	Phenyl	*p*-Tolyl	1	50
1b	*p*-Tolyl	*p*-Tolyl	1.5	68
1c	*o*-Tolyl	1-Naphthyl	1	82
1d	4-Pyridyl	*p*-Tolyl	1.5	34
1e	Phenyl	Benzyl	1	59



SCHEME 2 Mass spectral fragmentation pattern of **2e**.

5-Phenyl-4-(p-tolyl)-1,2,4-triazole-3-thione (**1a**). Yield: 65%; mp 210–212°C ($CHCl_3$); IR (KBr) 3112, 2931, 2750, 1506 (C=N), 1330 cm^{-1}; UV (MeOH) 206, 262 nm; ^1H NMR (200 MHz, $CDCl_3$) δ 2.42 (s, 3H, CH_3), 7.17–7.43 (m, 9H, ArH), 12.08 (s, 1H, SH); ^{13}C NMR (50 MHz, $CDCl_3$) δ 21.78, 124.50, 128.33, 128.64, 129.07, 130.81, 131.01, 132.13, 140.47, 155.00 (C=N), 169.20 (C=S); ^{13}C NMR-DEPT 135 (50 MHz, $CDCl_3$)δ; 21.78 (CH_3), 128.33, 128.64, 129.07, 130.81, 131.01, MS *m/z* (%) 267 (M^+,100), 234 (2), 208 (8), 194 (4), 180 (2), 163 (14), 131 (6), 118 (10), 103 (8), 91 (18), 77 (12). Anal. Calcd for $C_{15}H_{13}N_3S$: C, 67.38; H, 4.90; N, 15.71. Found: C, 67.45; H, 4.98; N, 15.63.

4,5-Di-(p-tolyl)-1,2,4-triazole-3-thione (**1b**). Yield: 78%; mp 220–222°C ($CHCl_3$); IR (KBr) 3085, 2931, 2752, 1512, 1328 cm^{-1}; UV (MeOH) 217 nm; ^1H NMR (200 MHz, $CDCl_3$) δ 2.32 (s, 3H, CH_3), 2.42 (s, 3H, CH_3), 7.06–7.31 (m, 8H, ArH), 12.06 (s, 1H, SH); ^{13}C NMR (50 MHz, $CDCl_3$) δ 21.99 (2CH_3), 123.22, 128.50, 128.70, 129.90, 130.90, 132.47, 140.57, 141.57, 152.10 (C=N), 169.93 (C=S); ^{13}C NMR-DEPT 135 (50 MHz, $CDCl_3$) δ; 22.0 (2CH_3), 128.5, 128.7, 129.9, 130.9, MS *m/z* (%) 281 (M^+, 20), 280 (4), 163 (4), 132 (3), 131 (4), 91 (4), 77 (10). Anal. Calcd for $C_{16}H_{15}N_3S$: C, 68.29; H, 5.37; N, 14.43. Found: C, 67.84; H, 5.40; N, 14.92.

*4-(1-Naphthyl)-5-(o-tolyl)-1,2,4-triazole-3-thione (***1c***).* Yield: 62%; mp 244–246°C ($CHCl_3$); IR (KBr) 3078, 2921, 2748, 1508, 1330 cm^{-1}; UV (MeOH) 222, 258 nm; ^1H NMR (200 MHz, $CDCl_3$) δ 2.3 (s, 3H, CH_3), 6.9–7.9 (m, 11H, ArH), 12.3 (s, 1H, SH); ^{13}C NMR (50 MHz, $CDCl_3$)δ 20.23 (CH_3), 123.40, 124.71, 125.12, 125.42, 126.88, 127.14, 127.58, 128.55, 128.73, 129.61, 129.70, 130.19, 130.49,130.67, 134.16, 138.12, 152.17 (C=N), 169.03 (C=S), MS *m/z* (%) 317 (M^+, 100), 284 (20), 258 (3), 185 (4), 140 (16), 132 (7), 127 (12), 117 (4), 116 (12), 91 (9), 77 (10). Anal. Calcd for $C_{19}H_{15}N_3S$: C, 71.89; H, 4.76; N, 13.23. Found: C, 71.73; H, 4.92; N, 13.26.

*5-(4-Pyridyl)-4-(p-tolyl)-1,2,4-triazole-3-thione (***1d***).* Yield: 40%; mp 238–240°C (EtOH); IR (KBr) 3136, 2931, 2738, 1602, 1574, 1427 cm^{-1}; UV (MeOH) 260, 312 nm; ^1H NMR (200 MHz, CH_3OH-d_4) δ 2.44 (s, 3H, CH_3), 7.21–7.39 (m, 6H, ArH), 8.49–8.52 (m, 2H, ArH); ^{13}C NMR (50 MHz, CH_3OH-d_4) δ 20.29, 122.55, 128.35, 130.46, 132.13, 135.20, 141.12, 149.75, 157.00 (C=N), 170.10 (C=S); ^{13}C NMR-DEPT 90 (50 MHz, $CDCl_3$) δ 119.20, 122.55, 128.36, 130.46, 149.75, MS *m/z* (%) 268 (M^+, 100), 267 (85), 235 (2), 209 (15), 181 (7), 163 (15), 131 (10), 119 (8), 105 (15), 104 (12), 91 (24), 78 (10), 77 (5). Anal. Calcd for $C_{14}H_{12}N_4S$: C, 62.66; H, 4.50; N, 20.87. Found: C, 62.87; H, 4.72; N, 20.89.

*4-Benzyl-5-phenyl-1,2,4-triazole-3-thione (***1e***).* A mixture of benzoic hydrazide (0.45 g, 3.3 mmol) and benzyl isothiocyanate (0.5 g, 3.3 mmol) was refluxed in ethanol (50 ml) for 4 h to afford the corresponding thiosemicarbazide (0.8 g, 86%) as per the reported procedure [3]. The separated thiosemicarbazide (0.78 g, 2.7 mmol) was refluxed in K_2CO_3 solution (60 ml, 10%) for 8 h, cooled, filtered, and the filtrate washed with ether. The aqueous layer was neutralized with cold dil. HCl. The separated solid was filtered and washed with water to get **1e** (0.6 g, 82%). The one-pot reaction used as in the case of **1a–d** gave **1e** in less than 25% yield: mp 278–280°C ($CHCl_3$); IR (KBr) 3087, 2931, 2752, 1506, 1353 cm^{-1}; UV (MeOH) 258 nm; ^1H NMR (200 MHz, $CDCl_3$)δ 5.34 (s, 2H, CH_2), 7.11–7.55 (m, 10H, ArH), 12.47 (s, 1H, SH); ^{13}C NMR (50 MHz, $CDCl_3$) δ 48.46 (CH_2), 126.13, 127.49, 128.43, 129.18, 129.23, 129.40, 131.49, 135.55, 153.02 (C=N), 169.06 (C=S); ^{13}C NMR-DEPT 135 (50 MHz, $CDCl_3$) δ 43.46 (CH_2), 125.49, 128.43, 129.18, 129.24, 129.41, 131.50, MS *m/z* (%) 267 (M^+, 52), 266 (100), 234 (40), 233 (40), 207 (3), 131 (20), 103 (75), 91 (90), 77(50). Anal. Calcd for $C_{15}H_{13}N_3S$: C, 67.38; H, 4.90; N, 15.71. Found: C, 67.42; H, 4.97; N, 15.80.

General Procedure for 4,5-Diaryl-1,2,4-triazoles **2a–e**

A solution of triazole-3-thione **1** (250–500 mg) in absolute methanol (180 ml) was irradiated in a thin-film reactor (equipped with one lamp) at 254 nm for 1–1.5 h. The solution was pumped from a three-necked RB flask through a jet, which allows a thin-film to fall over a quartz tube surrounding the lamp. A thin stream of nitrogen gas was passed through the reaction mixture during the reaction. After the completion of the reaction (monitored by TLC), the solvent was evaporated under vacuum and the residue chromatographed and eluted with ethyl acetate/petroleum ether mixture (2:3–4:1) to give the triazole **2**.

*5-Phenyl-4-(p-tolyl)-1,2,4-triazole (***2a***).* mp 142–144°C ($CHCl_3$) (Lit. [22] mp: 140°C); UV (MeOH) 209 nm; IR (KBr) 1517 cm^{-1}; ^1H NMR (200 MHz, CD_3CN) δ 2.37 (s, 3H, CH_3), 7.15–7.45 (m, 9H, ArH), 8.38 (s, 1H, CH); ^{13}C NMR (50 MHz, CD_3CN) δ 20.56, 126.33, 127.59, 128.87, 129.02, 130.09, 130.55, 132.73, 140.01, 145.54 (C_3—CH), 156.30; ^{13}C NMR-DEPT 90 (50 MHz, $CDCl_3$) δ 126.33, 128.88, 129.02, 130.09, 130.55, 145.55 (C_3—CH).

*4,5-Di-(p-tolyl)-1,2,4-triazole (***2b***).* mp 185–187°C ($CHCl_3$); IR (KBr) 1515 cm^{-1}; UV (MeOH) 206 nm; ^1H NMR (400 MHz, $CDCl_3$) δ 2.32 (s, 3H, CH_3), 2.42 (s, 3H, CH_3), 7.06–7.41 (m, 8H, ArH), 8.26 (s, 1H, CH); ^{13}C NMR (50 MHz, $CDCl_3$) δ 21.7, 21.9, 124.2, 126.1, 129.0, 129.8, 131.0, 132.8, 140.1, 140.5, 145.3 (C_3—CH), 153.90 (C=N); ^{13}C NMR-DEPT 135 (50 MHz, $CDCl_3$) δ 21.7 (CH_3), 21.9 (CH_3), 126.1, 129.0, 129.8, 131.0, 145.3 (C_3—CH), MS *m/z* (%) 249 (M^+, 100), 248 (91), 221 (3), 132 (3), 131 (8), 118 (4), 117 (2), 104 (12), 91 (42), 90 (10), 77 (36). Anal. Calcd for $C_{16}H_{15}N_3$: C, 77.08; H, 6.06; N, 16.85. Found: C, 77.28; H, 5.97; N, 16.91.

*4-(1-Naphthyl)-5-(o-tolyl)-1,2,4-triazole (***2c***).* mp 164–166°C ($CHCl_3$); IR (KBr) 1598, 1487 cm^{-1}; UV (MeOH) 228, 282 nm; ^1H NMR (400 MHz, $CDCl_3$)δ 2.30 (s, 3H, CH_3), 6.97–7.95 (m, 11H, ArH), 8.43 (s, 1H, CH); ^{13}C NMR (50 MHz, DMSO-d_6) δ 15.7 (CH_3), 117.3, 121.2, 121.3, 121.8, 122.1, 122.9, 123.9, 124.3, 124.9, 125.6, 125.8, 126.1, 126.3, 129.4, 133.5, 141.5 (C_3—CH), 149.2 (C=N), ^{13}C NMR-DEPT 135 (50 MHz, DMSO-d_6) δ 15.7 (CH_3), 117.3, 121.2, 121.3, 121.8, 122.9, 123.9, 124.3, 125.6, 125.8, 126.3, 141.5 (C_3—CH), MS *m/z* (%) 285 (M^+, 100), 284 (50), 270 (8), 257 (10), 215 (20), 168 (2), 167 (2), 157 (4), 141 (10), 140 (15), 127 (8), 117 (4), 115 (8), 114 (6), 91 (6), 77 (8). Anal. Calcd for $C_{19}H_{15}N_3$: C, 79.97; H, 5.29; N, 14.72. Found: C, 79.81; H, 5.16; N, 14.85.

*5-(4-Pyridyl)-4-(p-tolyl)-1,2,4-triazole (***2d***)*. mp 162–164°C ($CHCl_3$); IR (KBr) 1602, 1514 cm^{-1}; UV (MeOH) 244 nm; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.45 (s, 3H, CH_3), 7.15–7.45 (m, 6H, ArH), 8.35 (s, 1H, CH), 8.6–8.8 (m, 2H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.17 (CH_3), 121.97, 125.44, 130.85, 131.25, 133.83, 140.40, 145.76 (C_3—CH), 150.18, 150.78 (C=N), MS *m/z (%)* 236 (M^+, 25), 235 (100), 234 (95), 207 (10), 132 (14), 131 (60), 118 (14), 104 (10), 91 (70), 90 (8), 78 (15), 77 (30). Anal. Calcd for $C_{14}H_{12}N_4$: C, 71.16; H, 5.11; N, 23.71. Found: C, 71.21; H, 5.20; N, 23.69.

*4-Benzyl-5-phenyl-1,2,4-triazole (***2e***)*. mp 130–132°C ($CHCl_3$); IR (KBr) 1504, 1444 cm^{-1}; UV (MeOH) 212 nm; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.2 (s, 2H, CH_2), 7.1–7.6 (m, 10H, ArH), 8.2 (s, 1H, CH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 48.64, 126.49, 126.80, 128.54, 128.80, 128.85, 129.20, 130.15, 134.86, 144.47 (C_3—CH),154.29 (C=N), MS *m/z (%)* 235 (M^+, 40), 234 (100), 207 (6), 158 (10), 132 (50), 131 (14), 104 (30), 103 (15), 91 (95), 90 (60), 89 (47), 77 (40). Anal. Calcd for $C_{15}H_{13}N_3$: C, 76.57; H, 5.56; N, 17.85. Found: C, 76.68; H, 5.71; N, 17.89.

REFERENCES

[1] Holla, B. S.; Poojary, K. N.; Kalluraya, B.; Gowda, P. V. Farmaco 1996, 51, 793.

[2] Dunaev, V. V.; Belenichev, I. F.; Kovalenko, S. I.; Vashkin, I. N.; Avramenko, N. A.; Mazur, I. A.; Knysh, E. G.; Tishkin, V. S. Ukr Biokhim Zh 1996, 68, 100.

[3] Iqbal, R.; Rama, N. H.; Ahmed, N.; Zamani, K.; Ebrahim, S.; Iqbal, N. Indian J Chem 1998, 37B, 506.

[4] (a) Ohno, A. Int J Sulfur Chem B 1971, 6, 183; (b) de Mayo, P. Acc Chem Res 1976, 9, 52; (c) Coyle, J. D. Tetrahedron 1985, 41, 5395; (d) Ramamurthy, V. In Organic Photochemistry; Padwa, A. (Ed.); Marcel Dekker: New York, 1985; Vol. 7, p. 231.

[5] Bowman, W. R.; Heaney, H.; Smith, P. H. G. Tetrahedron Lett 1982, 23, 5093.

[6] Arad-Yellin, R.; Green, B. S.; Muszkat, K. A. J Org Chem 1983, 48, 2578.

[7] Park, Y.-T.; Jung, C.-H.; Kim, K.-W.; Kim, H. S. J Org Chem 1999, 64, 8546.

[8] Grimme, S.; Mennicker, W.; Voegtle, F.; Nieger, M. J Chem Soc, Perkin Trans 2 1999, 3521.

[9] Yamato, T.; Miyazawa, A.; Tashiro, M. L. Chem Ber 1993, 126, 112505.

[10] Takehiko, N. J Chem Soc, Perkin Trans 1 1997, 885.

[11] Padwa, A.; Crumrine, D.; Shubber, A. J Am Chem Soc 1966, 3064.

[12] Nishio, T. J Org Chem 1988, 53, 1323.

[13] Paramasivam, R.; Palaniappan, P.; Ramakrishnan, V. T. J Chem Soc, Chem Commun 1979, 260.

[14] Muthusamy, S.; Ramakrishnan, V. T. Synth Commun 1992, 22, 519.

[15] Jayanthi, G.; Muthusamy, S.; Ramakrishnan, V. T. J Photochem Photobiol, A: Chem 1998, 116, 103.

[16] Jayanthi, G.; Muthusamy, S.; Paramasivam, R.; Ramakrishnan, V. T.; Ramasamy, N. K.; Ramamurthy, P. J Org Chem 1997, 62, 5766.

[17] Grellmann, K. H.; Tauer, E. Tetrahedron Lett 1967, 1909.

[18] Bellus, D.; Schaffner, K. Helv Chim Acta 1968, 51, 221.

[19] Buscemi, S.; Gruttadauria, M. Tetrahedron 2000, 56, 999.

[20] Dziewonska, M. Spectrochim Acta, A 1967, 23, 1195.

[21] Horsfall, J. G.; Rich, S. Indian Phytopathol 1953, 6, 1.

[22] Surendranath, T. G.; Husain, S.; Srinivasan, V. R. Indian J Chem, Sect B 1977, 15, 341.