Heteroatom Chemistry
Volume 12, Number 4, 2001

Unusual Formation of a Thiacyclopent-2-ene by the Reaction of 4,4′-Dimethoxythiobenzophenone with Tetracyanoethylene

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Received 12 December 2000; revised 22 January 2001

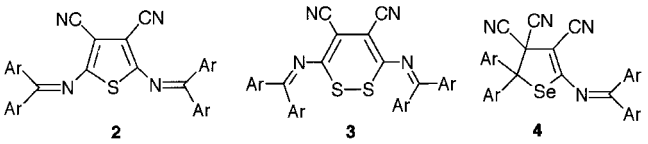
ABSTRACT: *The reaction of 4,4′-dimethoxythiobenzophenone (***1a***) with tetracyanoethylene (TCNE) afforded an unusual type of 2:1 adduct with the structure of thiacyclopent-2-ene (***5a***). On the other hand, the reaction of thiobenzophenone (***1b***) with TCNE afforded the corresponding thiophene, the normal 2:1 adduct (***2b***). The mechanism of the formation of* **5a** *is discussed.* © 2001 John Wiley & Sons, Inc. Heteroatom Chem 12:259–262, 2001

INTRODUCTION

Tetracyanoethylene (TCNE) has played an important role in extensive applications in organic synthesis owing to its anomalous reactivity [1]. Previously, we reported the reaction of tropothione with TCNE to afford 8,8-dicyanoheptafulvene via a [2 + 2]-type cycloaddition [2]. Huisgen et al. reported that thiobenzophenone (**1**) reacted with TCNE to give 2:1 adducts of thiophene derivatives (**2**) and six-membered dithiins (**3**) in moderate yields [3]. We have isolated selenobenzophenones, which reacted with olefins to afford several types of the corresponding cycloadducts [4]. In a previous article, we have reported an unusual reaction of selenobenzophenones with TCNE to give a novel type of cycloadducts, selenacyclopent-2-enes (**4**), sharply different from the above result with thiobenzophenone (Scheme 1) [5]. These results prompted us to investigate the possibility to form thiacyclopent-2-enes from thiobenzophenones. This article describes a precise reaction of thiobenzophenones with TCNE.

RESULTS AND DISCUSSION

4,4′-Dimethoxythiobenzophenone (**1a**) reacted with 2 equiv. of TCNE in refluxing benzene to afford yellow crystals (**5a**) along with **2a** (25%) (Scheme 2). The structure of **5a** (8%) was found to be 5,5-di-(4-methoxyphenyl)-2-[di-(4-methoxyphenyl)methylene]amino-3,4,4-tricyano-thiacyclopent-2-ene by its spectroscopic analysis. Mass spectrum and elemental analysis suggested that we are dealing with a 2:1 (**1a**: TCNE) adduct. The ^{1}H NMR spectrum of **5a**



SCHEME 1

Dedicated to Prof. Naoki Inamoto on the occasion of his 72nd birthday.

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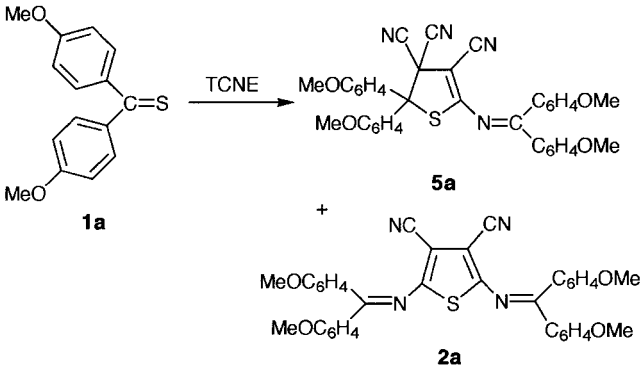
Contract Grant Sponsor: Scientific Research from the Ministry of Education, Science, Culture, and Sports, Japan.
Contract Grant Number: Grant-in-Aid 06640706.



SCHEME 2

shows only two different 4-methoxyphenyl protons. The ^{13}C NMR spectrum of **5a** shows four methoxy, three cyano, two aliphatic (quaternary), one C=N, two olefinic, and aromatic carbons.

This result is quite different from that reported by Huisgen et al. [3,6]. They have reported that the reaction of **1a** with TCNE in refluxing chloroform afforded only **2a** in 78% yield, and the reaction of thiobenzophenone (**1b**) with TCNE in refluxing benzene afforded **2b** (Ar = Ph) and **3b** (Ar = Ph) in 52% and 29% yields, respectively. The difference in the reactivity might be mainly due to the reaction temperature. To confirm this possibility, the reaction was carried out at an elevated temperature. When the reaction of **1a** with TCNE was carried out in refluxing xylene for 8 hours, the yields of **5a** and **2a** were improved to 32% and 33%, respectively. Thus, the reaction temperature plays an important role in the formation of **5a**.

The reaction of thiobenzophenone (**1b**) with TCNE was carried out in a similar manner. However, the corresponding thiacyclopent-2-ene (**5b**) was not obtained even in refluxing xylene for 8 hours (Table 1).

As to the formation of **5**, we thought as follows: the reaction between thiobenzophenone and TCNE proceeded through the initial attack of the thiocarbonyl sulfur on the nitrile carbon via a [2 + 2] manner. The four-membered intermediate is easily converted into the ring-opened thioamide (**6**). Another molecule of 4,4′-dimethoxythiobenzophenone (**1a**) reacted with **6** via a [4 + 2] manner to afford the six-membered cyclic disulfide (**7**), which finally extruded sulfur to give **5a**. The formation mechanism of **2** had already been suggested by Huisgen et al. [6]. The thioamide **6** was further attacked by another molecule of thiobenzophenone (**1a**) to yield maleonitrile and/or fumaronitrile derivatives (**8**). Ring closure of **8** and the final sulfur extrusion formed the five-membered cyclic thiophene derivatives (**2**) (Scheme 3).

TABLE 1 The Reaction of Thiobenzophenones with TCNE

Thiobenzophenone (Ar)		*Conditions*			*Products (% Yield)*			
		Solvent	*TCNE (equiv.)*	*Time (h)*				
1a	*p*-$MeOC_6H_4$	Benzene	1	1	**2a**	25	**5a**	8
		Toluene	2	2		55		15
		Xylene	2	8		33		32
1b	C_6H_5	Benzene	1	8	**2b**	63	**5b**	0
		Toluene	2	8		45		0
		Xylene	2	8		5		0

Since **5b** could not be obtained by using thiobenzophenone **1b**, the electron-donating group (MeO) of **1** might affect the formation of **5a**. To confirm this assumption, we then tried the reaction of 4,4′-difluorothiobenzophenone (**1c**) with TCNE. In this case, the product was not a thiacyclopent-2-ene but a thiophene derivative (**2c**) obtained in 50% yield (Scheme 4). Thus, the electron-donating group evidently plays an important role for the formation of **5**.

Thiacyclopent-2-enes were previously prepared in many ways: for example, in five steps from α-acetyl γ-lactones [7], in five steps from cysteine [8], by the partial hydrogenolysis of thiophene [9], by Michael reaction of a sulfonium ylide with an unsaturated thioamide [10], by a free radical intramolecular cyclization of enynes [11], and by the the reaction of *S*-3,3-bis(phenylthio)propylthioalkanoates with a low-valent titanium species [12]. The present result offers the formation of a thiacyclopent-2-ene from TCNE by novel types of [2 + 2] and [4 + 2] sequential cycloadditions.

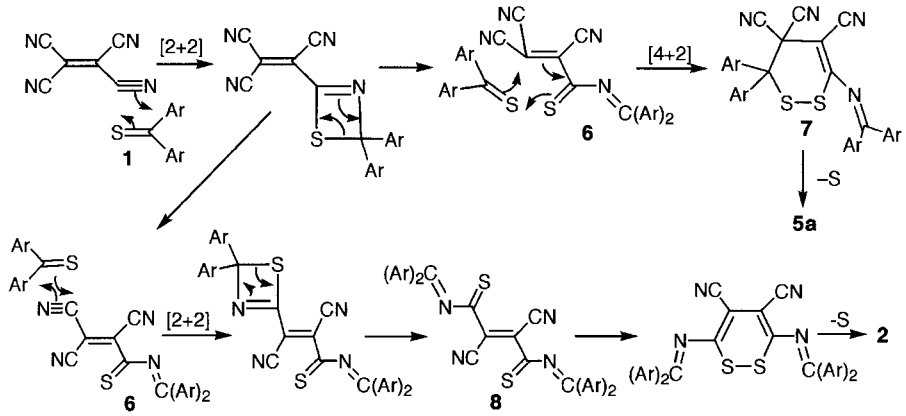
EXPERIMENTAL

General

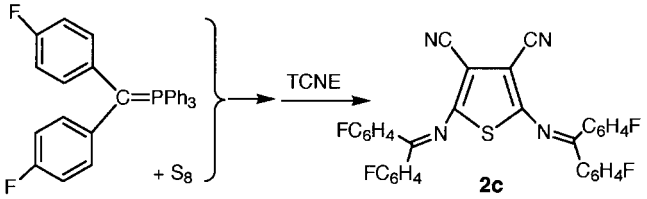
All chemicals were obtained from commercial suppliers and were used without further purification. Analytical TLC was carried out on precoated plates (Merck silica gel 60, F254) and flash column chromatography was performed with silica gel (Merck, 70–230 mesh). NMR spectra (^1H at 400 MHz; ^{13}C at 100 MHz) were recorded in $CDCl_3$ solvent, and chemical shifts are expressed in ppm relative to internal TMS.

*Reaction of 4,4′-Dimethoxythiobenzophenone (**1a**) with TCNE*

To a refluxing solution of **1a** (0.258 g, 1.0 mmol) in benzene (25 mL) was added a solution of TCNE (0.25



SCHEME 3



SCHEME 4

g, 2.0 mmol) in benzene (10 mL). After refluxing for 1 hour, the reaction mixture was filtered and evaporated to give dark purple crystals, which were chromatographed over silica gel by elution with dichloromethane to afford **5a** (0.025 g, 8%) and **2a** (0.077 g, 25%). Thiobenzophenone **1a** was recovered in 35% yield (0.090 g). **5a**: Yellow crystals; m.p. 89–90°C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ = 3.83 (s, 6H, MeO), 3.88 (s, 6H, MeO), 6.86 (d, 4H, J = 9 Hz, Ar), 6.93 (d, 4H, J = 9 Hz, Ar), 7.29 (d, 4H, J = 9 Hz, Ar), 7.51 (d, 4H, J = 9 Hz, Ar). ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 53.8 (Ar_2C-S), 55.3 (MeO), 55.3 (MeO), 55.5 (MeO), 55.6 (MeO), 73.7 ($\underline{C}(CN)_2$), 82.0 (C=$\underline{C}$CN), 111.6 (2 CN), 112.7 (CN), 114.0, 114.1, 127.9, 129.2, 130.8, 132.2, 160.2, 162.9, 170.9 (S–C=), 174.1 (C=N). Exact Mass: Found: 612.1822 (M^+). Calcd for $C_{36}H_{28}N_4O_4S$: 612.1831. Anal. Found: C, 70.38; H, 4.65; N, 9.15. Calcd for $C_{36}H_{28}N_4O_4S$: C, 70.57; H, 4.61; N, 9.14. **2a**: Orange crystals; m.p. 227–229°C. (lit. [6] m.p. 227–229°C).

*Reaction of Thiobenzophenone (***1b***) with TCNE*

To a refluxing solution of **1b** (0.198 g, 1.0 mmol) in benzene (25 mL) was added a solution of TCNE (0.25 g, 2.0 mmol). After refluxing for 8 hours, the reaction mixture was filtered and evaporated to give dark purple crystals, which were chromatographed over silica gel by elution with dichloromethane to afford **2b** (0.155 g, 63%); m.p. 298–300°C (lit. [6] 304–305°C).

Reaction of 4,4′-Difluorothiobenzophenone with TCNE

To a suspension of 4,4′-difluorobenzhydriltriphenylphosphonium fluoroborate (0.509 g, 1.0 mmol) in benzene (50 mL) was added butyllithium (0.70 mL, 1.6 M in hexane, 1.1 mmol) dropwise at room temperature (rt). After the mixture had been stirred for 1 hour, powder of elemental sulfur (0.11 g, 3.5 mg atom) was added to the red suspension, and the reaction mixture was refluxed for 1 hour to give a deep purple suspension of 4,4′-difluorothiobenzophenone **1c**. TCNE (0.13 g, 1.0 mmol) in benzene (10 mL) was added dropwise to the resulting suspension. After the mixture had been refluxed for 1 hour, TCNE (0.13 g, 1.0 mmol) was further added to this suspension portionwise. After refluxing for 8 hours, the reaction mixture was poured into water, and the organic layer was separated, dried over $MgSO_4$, and evaporated to give dark reddish oily crystals. Chromatography on silica gel by elution with dichloromethane–hexane (1:1) afforded the thiophene derivative (**2c**, 0.141 g, 50%). Orange crystals, m.p. > 300°C. ^{1}H NMR ($CDCl_3$) δ = 7.00–7.20 (br, 12H, Ar), 7.76 (br s, 4 H, Ar); All of aromatic protons in coalescence. ^{13}C NMR ($CDCl_3$) δ = 106.7 (C-3/C-4 of thiophene), 112.4 (CN), 115.8 (C-2/C-5 of C_6H_4F, J_{CF} = 23 Hz), 117.1 (C-2/C-5 of C_6H_4F, J_{CF} = 23 Hz), 129.1 (C-1 of C_6H_4F), 130.4 (C-3/C-4 of C_6H_4F), 132.3 (C-3/C-4 of C_6H_4F), 155.3 (C-2/C-5 of thiophene), 166.9 (C=N). Anal. Found: C, 68.28; H, 2.65; N, 9.81. Calcd for $C_{32}H_{16}F_4N_4S$: C, 68.08; H, 2.86; N, 9.92.

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