Synthesis of Methyl 3-arylamino-4,6-Dinitrobenzo[b]thiophene-2-carboxylates. Smooth Dehydrogenation of 2,3-Dihydrobenzo[b]thiophene Derivatives.

Valentina I. Gulevskaya, Alexander M. Kuvshinov and Svyatoslav A.Shevelev*
N. D. Zelinsky Institute of Organic Chemistry, Russian Academy of Scienses, Leninsky prospekt 47, 119992, Moscow, Russia. Fax +7(095) 135 5328; E-mail: shevelev@cacr.ioc.ac.ru

Abstract: Interaction of C–(2,4,6-trinitrophenyl)-N-arylazomethines (**1**) with methyl thioglycolate (**2**) in the presence of K_2CO_3 in MeCN resulted in the *ortho*-NO_2 group substitution in **1** by the SCH_2CO_2Me fragment. Thus obtained sulfides **3** undergo intramolecular cyclisation with the further *in situ* dehydrogenation of the cyclisation product to form previously unknown methyl 3-arylamino-4,6–dinitrobenzo[b]thiophene-2-carboxylates. In the case of C-(2,4,6-trinitrophenyl)-N-hetarylazomethines (hetaryl=1,3,5-pyrazolyl-4, thiazolyl-2), under the same conditions, we observed the elimination of a hetarylamine. Dehydrogenation in this case either did not occur at all or proceeded in very low yield.

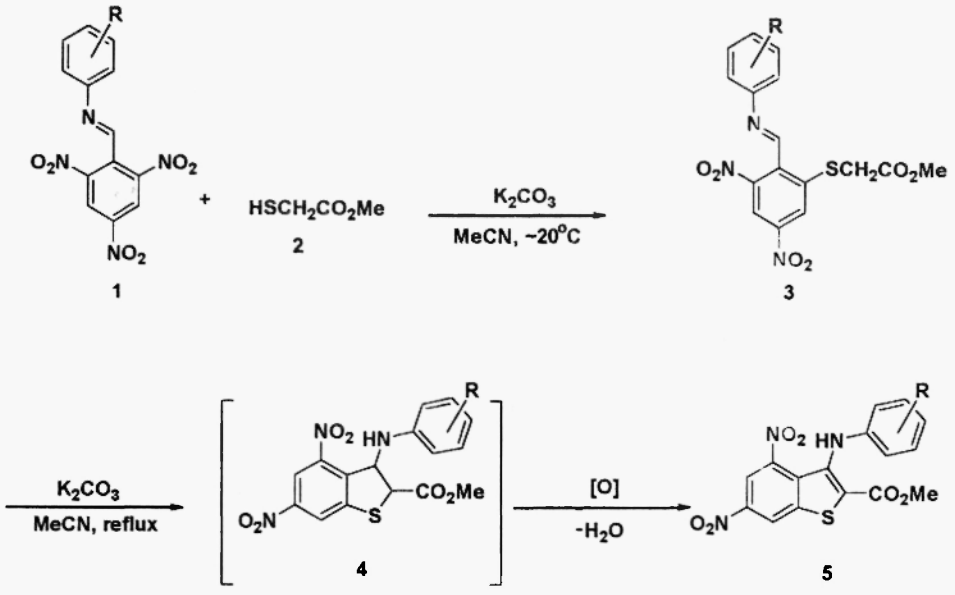
Key words: azomethines, aromatic nitro compounds, benzo[b]thiophenes, aromatic nucleophilic substitution, dehydrogenation.

Introduction.

Previously we have shown, that the *ortho*-nitro group in C-(2,4,6-trinitrophenyl)-N-R-azomethines can be easily substituted by the action of NaN_3 with the formation of corresponding azides[1]. This allowed further intermolecular cyclisation to give 2-substituted 4,6-dinitroindazoles. In the present paper we describe thiolate substitution (cf.[2]).

Results and Discussions.

Reaction of C - (2,4,6-trinitrophenyl)-N-arylazomethines[1] (**1**) with methyl thioglycolate (**2**) in MeCN in the presence of K_2CO_3 at room temperature results in the formation of the corresponding sulfides **3** (Scheme 1).



Scheme 1

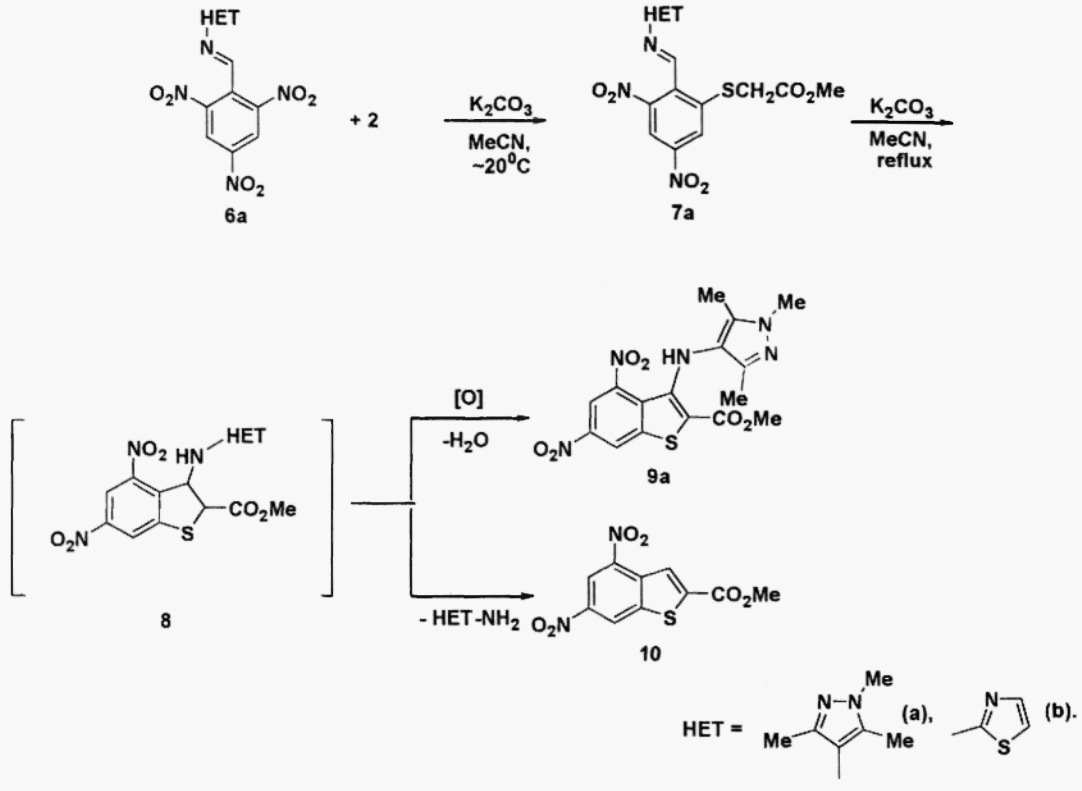
When the reaction is carried out in boiling MeCN, according to the structure of the obtained product, sulfides **3** undergo intramolecular cyclisation through the addition of the active CH_2 group to the C=N bond. The initial product methyl 3-arylamino-4,6-dinitro-2,3-dinydrobenzo[b]thiophene-2-carboxylates (**4**) is readily aromatized to fully conjugated methyl 3-arylamino-4,6-dinitrobenzo[b]thiophene-2-carboxylates (**5**) in the yields of 65-70 %, Scheme 1, as a result of smooth dehydrogenation of **4**. The reaction can be a facile one-step method for the preparation of such dinitrothiophenes.

When the same reaction is carried out under in the absence of the atmospheric oxygen dinitrothiophenes **5** are formed in poorer yields. It is likely that the main oxidizers, causing dehydrogenation, are the starting nitro compounds. In view of reports, such a possibility for the reactions of oxidative nucleophilic substitution of hydrogen is known[3,4].

The work was extended to hetarenes and we used azomethines (**6**) bearing 1,3,5-trimethylpyrazolyl-4 (**6a**) and thiazolyl-2 (**6b**) functionalities.

Sulfide substitution proceeded as above at room temperature and **6**a gives the product of the *ortho*-nitro group substitution-sulfide **7**a. In boiling solvent we detected the formation of methyl 3-(1,3,5-pyrazolyl-4)-amino-4,6 -dinitrobenzo[b]thiophene-2-carboxylate (**9**) as a result of the oxidation of **8**, in respective yield of 7%, Scheme 2. But the major reaction product was methyl 4,6-

dinitrobenzo[b]thiophene-2-carboxylate (**10**), obtained in the yield of 40% as a result of the elimination of 4-amino-1,3,5-trimethylpyrazole, Scheme 2.



Scheme 2

It is interesting to note that **6b,** under the same conditions, gave only the product of 2-aminothiazole elimination **10**.

Compound	Yield, %	mp, °C (EtOH)	^{1}H NMR	MS (EI), *m/z*
3a	70	157-158	3.67 (s, 3H, OMe), 4.26 (s, 2H, CH_2S), 7.25-7.56 (m, 5H, Ph), 8.62 (s, 1H, H_{arom}), 8.67 (s, 1H, NH), 8.91 (s, 1H, H_{arom}).	[M+, 375 (13)], 343 (19), 302 (44), 251 (7), 224 (5), 210 (11), 177 (6), 43 (100).
3b	65	163-164	3.66 (s, 3H, OMe), 3.8 (s, 1H, OMe), 4.22 (s, 2H, CH_2S), 7.05 (d, 2H, *p*-MeOPh, ^3J = 8.8Hz), 7.35 (d, 2H, *p*-MeOPh, ^3J = 8.8Hz), 8.57 (s, 1H, H_{arom}), 8.59 (s, 1H, NH), 8.91 (s, 1H, H_{arom}).	[M+, 405 (41)], 373 (18), 332 (99), 302 (9), 252 (7), 240 (25), 208 (7), 158 (13).
5a	65	229-230	3.99 (s, 3H, MeO), 6.75-7.31(m, 5H, Ph), 8.47 (d, 1H, H_{arom}, ^4J = 2 Hz), 8.73 (s, 1H, NH), 8.91 (d, 1H, H_{arom}, ^4J = 2 Hz).	[M+, 373 (100)], 294 (11), 265 (20), 253 (10), 248 (11), 177 (33), 69 (16), 45 (12),

				40 (22).
5b	70	212-213	3.67 (s, 3H, MeO), 3.90 (s, 3H, MeO), 6.67 (d, 2H, *p*-MeOPh, ^3J = 9Hz), 6.72 (d, 2H, *p*-MeOPh, ^3J = 9 Hz), 8.45 (d, 1H, H-5, ^4J = 2 Hz), 8.55 (s, 1H, NH), 9.48 (d, 1H, H-7, ^4J = 2 Hz).	[M+, 403 (100)], 388 (9), 371 (35), 296 (27), 282 (12), 248 (13), 237 (13), 208 (44), 43 (69).
5c	66	274-275	3.88 (s, 3H, MeO), 6.69 (m, 2H, *p*-FPh), 6.95 (m, 2H, *p*-FPh), 8.53 (d, 1H, H_{arom}, ^4J =2 Hz), 8.55 (s, 1H, NH), 9.5 (d, 1H, H_{arom}, ^4J =2 Hz).	[M+, 391 (100)], 361 (27), 359 (37), 313 (44), 267 (46), 239 (66), 195 (61), 59 (24).
7a	70	161-163	2.29 (s, 3H, Me), 2.32 (s, 3H, Me), 3.66 (s, 3H, NMe_{pyr}), 3.68 (s, 3H, OMe), 4.20 (s, 2H, CH_2S), 8.52 (s, 1H, H_{arom}), 8.54 (s, 1H, CH=N), 8.83 (s, 1H, H_{arom}).	[M+, 407 (22)], 334 (100), 288 (15), 242 (17), 124 (69), 69 (10), 56 (65), 43 (77).
9a[1]	7	207-208	1.55 (s, 3H, Me), 1.90 (s, 3H, Me), 3.61 (s, 3H, NMe), 3.97 (s, 3H, OMe), 8.33 (d, 1H, H-5, ^4J = 2 Hz), 8.39 (s, 1H, NH), 9.17 (d, 1H, H-7, ^4J = 2 Hz).	[M+, 405 (100)], 343 (21), 125 (48), 43 (50).
10	40* 50**	160-162	3.98 (s, 3H, MeO), 8.65 (s, 1H, H_{het}), 8.96 (d, 1H-5, H_{arom}, ^4J =2 Hz), 9.65 (s, 1H-7, H_{arom}, ^4J =2 Hz).	[M+, 282, (100)], 252 (35), 251 (82), 205 (28), 189 (30), 159 (70), 87 (40), 59 (16).

Table. Yields, mps, ^{1}H NMR and mass spectra of compounds **3** and **5**. NMR spectra were recorded in DMSO-d_6 with TMS as internal standard, δ, *ppm*, *J/Hz*.[1]Spectrum recorded in acetone-d^6. *for **6a**; ** for **6b**.

Conclusion.

The interaction of C-(2,4,6-trinitrophenyl)-N-R-azomethines with S-anion, generated from $HSCH_2CO_2Me$ in MeCN leads to the substitution of the *ortho*-nitro to give the corresponding sulfide which subsequently undergoes cyclisation. The dehydrohetarene is readily dehydrogenated. In the case of **1**, where R = Het, an unexpected elimination of a hetarylamine substituent led to aromatization.

Spectroscopic data is in accord with the structures assigned to the products.

Experimental.

Melting points were measured using a Boetius apparatus and are uncorrected. All reactions were monitored by TLC, using Silufol (UV-254) precoated aluminiun plates. ^{1}H NMR spectra were recorded on a Bruker AC 200 spectrometer. Chemical shifts are reported in ppm downfield from

TMS. Mass spectra were recorded on MS-30 (Kratos) spectrometer using electron ionization technique. Organic solvents and reagents were purified by the standard literature procedures. Satisfactory microanalyses were obtained for all new compounds.

2-(Methoxycarbonylmethylenethio)-4,6-dinitro-N-arylazomethines (3); General Procedure.

To a stirred mixture of methyl thioglycolate (1 mmol) and K_2CO_3 (1 mmol) in MeCN (10 mL) a solution of an azomethine (**1**) was added at rt. The mixture was left to stir (TLC control). After evaporation of the solvent, the residue was washed with water and purified by column chromatography on silica gel (EtOAc/CCl_4, 4:10). Recrystallisation from EtOH gave sulfides **3** and **7a**.

Methyl 3-arylamino-4,6-dinitrobenzo[b]thiophene-2-carboxylates 5; General Procedure.

To a stirred mixture of methyl thioglycolate (1 mmol) and K_2CO_3 powder (2 mmol) in MeCN (15 mL) the solution of an azomethine (1 mmol) in MeCN (5 mL) was added in one portion. After stirring at reflux (TLC), the resulting suspension was filtered through a pad of Celite, and the filtrate was concentrated on a rotary evaporator. Purification of the residue by flash column chromatography on silica gel (EtOAc/CCl_4, 4:10) with the further recrystallisation gave thiophenes **5**. Azomethines **6** gave thiophenes **9a** and **10** correspondingly.

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