Monatshefte für Chemie 128, 687–696 (1997)

Monatshefte für Chemie
Chemical Monthly

Printed in Austria

Syntheses with Heterocyclic β-Enaminonitriles: An Expeditious Synthetic Approach to Polyfunctionally Substituted 5-Phenylsulfonylthiophenes and their Fused Derivatives

S. M. Sherif[1,*] and **A. M. Hussein**[2]

[1] Department of Chemistry, Faculty of Science, Cairo University, Giza, Egypt
[2] Department of Chemistry, Faculty of Science, Al-Azhar University, Assiut 71511, Egypt

Summary. Phenylsulfonylacetophenones **1** react with a mixture of elemental sulfur and malononitrile to yield the corresponding 2-amino-4-aryl-5-phenylsulfonylthiophene-3-carbonitriles **2.** Compound **2a** could be annelated to the corresponding thieno[2,3-*d*]pyrimidine and thieno[2,3-*c*]-pyrazole derivatives **3** and **5** upon reaction with nitrogen nucleophiles (cyanamide and hydroxylamine hydrochloride), respectively. The applicability and synthetic potency of **5** to develop a facile convenient route to the polyfunctionally substituted thieno[2′,3′ : 3, 4]pyrazolo[1,5-*a*]pyrimidines **8, 14, 17, 20,** and **21** is reported. Chemical and spectroscopic evidences for the structures of the new compounds are presented.

Keywords. Arylsulfonylacetophenones; Thiophenes; β-Enaminonitriles; Thienopyrazolopyrimidines.

Synthesen mit heterocyclischen β-Enaminonitrilen: Ein rascher synthetischer Zugang zu polyfunktionell substituierten 5-Phenylsulfonylthiophenen und ihren kondensierten Derivaten

Zusammenfassung. Die Phenylsulfonylacetophenone **1** reagieren mit einem Gemisch aus elementarem Schwefel und Malonsäurenitril zu den entsprechenden 2-Amino-4-aryl-5-phenylsulfonylthiophen-3-carbonitrilen **2.** Durch Umsetzung mit Stickstoffnucleophilen wie Cyanamid und Hydroxylaminhydrochlorid konnten aus Verbindung **2a** die entsprechenden Thieno[2,3-*d*]pyrimidin- und Thieno[2,3-*c*]pyrazolderivate erhalten werden. Das synthetische Potential und die Anwendbarkeit von **5** zur Synthese polyfunktionell substituierter Thieno[2′,3′:3,4]pyrazolo[1,5-*a*]pyrimidine (**8, 14, 17, 20, 21**) werden beschrieben. Die Strukturen der neuen Verbindungen wurden durch chemische und spektroskopische Methoden abgesichert.

Introduction

A literature survey reveals that – although arylsulfonylacetophenones have proven to be a valuable synthon for the synthesis of a wide variety of heterocyclic systems

[1–3] – no reports, if any, describe its applicability for the synthesis of thiophenes [4–6]. As an extension of our efforts directed towards the development of convenient synthetic approaches for the synthesis of thiophenes [7–10] with an expected broad spectrum of biological activity, we wised to broaden the scope of the *Gewald* reaction utilizing phenylsulfonylacetophenones (**1**) as a key precursor for the synthesis of some hitherto unreported polyfunctionally substituted 2-amino-5-phenylsulfonylthiophene-3-carbonitrile derivatives (**2**). The latter, in turn, could be successfully annelated to polyfunctionally substituted thieno[2,3-*c*]pyrazole, thieno-[2,3-*d*]pyrimidine, and theino[2′,3′:3,4]pyrazolo[1,5-*a*]pyrimidine derivatives. The importance of these compounds is due to their potential biological and physiological activities [11, 12].

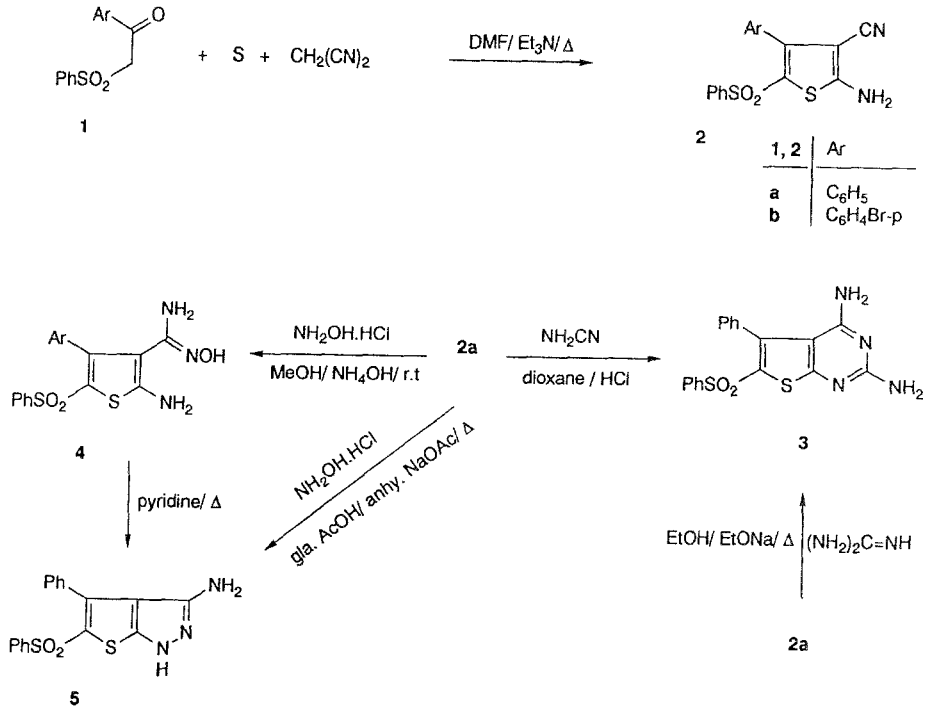
Results and Discussion

The reaction of equimolar amounts of each of the phenylsulfonylacetophenones **1a,b,** elemental sulfur, and malononitrile in dry *DMF* containing a catalytic amount of anhydrous Et_3N furnishes upon heating under reflux exclusively and in reasonable good yields products that could be formulated as 2-amino-4-aryl-5-phenylsulfonylthiophene-3-carbonitriles (**2a,b** Scheme 1). The elemental and spectroscopic data of **2** are consistent with the assigned structure.

Thus, as a representive example, the mass spectrum of **2a** reveals a molecular ion peak at $m/z = 340$ with 26% relative abundance corresponding to the molecular formula $C_{17}H_{12}N_2O_2S_2$. Its IR spectrum contains absorption peaks at $\nu = 3450$–3380 and 2218 cm^{-1}, demonstrating the presence of NH_2 and CN functions, respectively. Its ^1H NMR spectrum (*DMSO*-d_6) shows the presence of a D_2O exchangeable broad singlet at $\delta = 5.65$ ppm (2H) which can be attributed to the NH_2 protons and a multiplet at $\delta = 7.12$–7.65 ppm (10H) corresponding to the aromatic protons.

The synthetic potency of β-enaminonitriles as versatile reagents in heterocyclic synthesis is well documented [13]. In our hand, the β-enaminonitrile moiety in **2** proved to be highly reactive towards nitrogen nucleophiles. Thus, compound **2a** reacted with an equimolar amount of cyanamide in dioxane solution saturated with HCl gas to yield a single product that could be formulated as 2,4-diamino-5-phenyl-6-phenylsulfonylthieno[2,3-*d*]pyrimidine (**3**) based on elemental analysis and spectroscopic data. Alternatively, compound **2a** reacted with guanidine in EtOH/EtONa solution under reflux to afford a single product which was found to be identical in all aspects (m.p., mixed m.p., and IR spectrum) with **3**. To our knowledge, 2,4-diaminopyrimidine derivatives have been reported to exhibit a broad spectrum of biological activity [14, 15].

The reaction of **2a** with an equimolar amount of hydroxylamine hydrochloride in MeOH containing NH_4OH at room temperature provided 3-amidoximo-2-amino-4-phenyl-5-phenylsulfonylthiophene (**4**) in 52% yield. Compound **4** underwent an intramolecular cyclization to the corresponding 3-amino-4-phenyl-5-phenylsulfonyl-1*H*-thieno[2,3-*c*]pyrazole **5,** *via* loss of H_2O molecule upon prolonged heating in pyridine solution. The analytical and spectroscopic data of **5** are entirely consistent with its proposed structure. Its ^1H NMR spectrum (*DMSO*-d_6) reveals two types of exchangeable protons $\delta = 5.00$ (2H) and 8.53 (1H) ppm attributable to NH_2 and NH protons, respectively. Alternatively, compound **2a** reacted with an equimolar amount of hydroxylamine hydrochloride in glacial AcOH in the



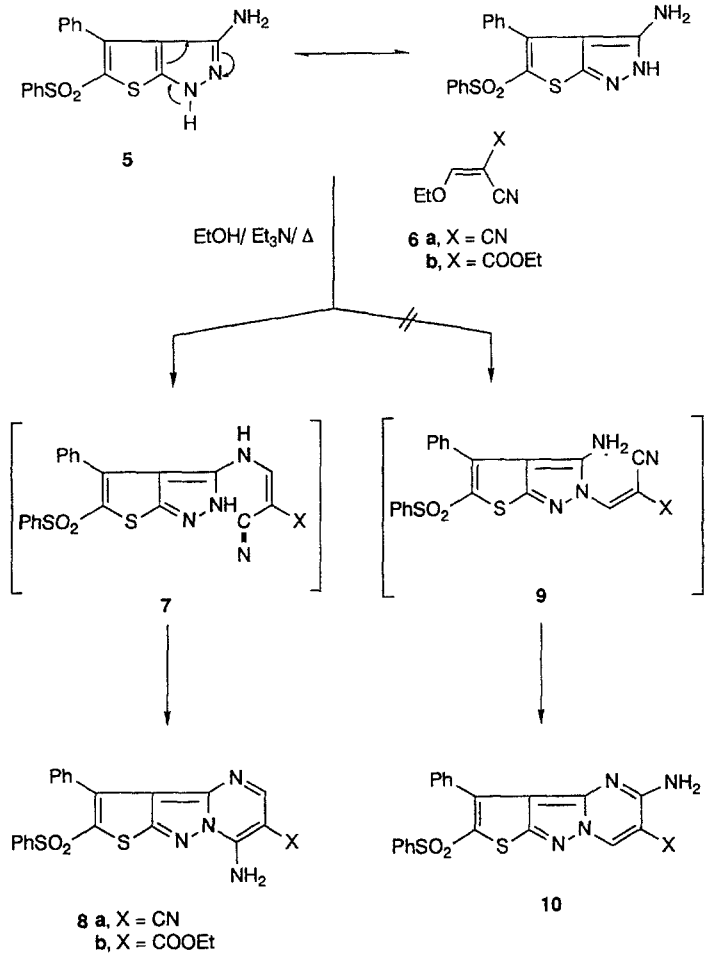
Scheme 1

presence of anhydrous AcONa under reflux to a single product identical in all aspects (m.p., mixed m.p., and IR spectrum) with **5**.

Next, we moved to investigate the applicability and synthetic potency of **5** to develop a facile and convenient route to polyfunctionally substituted thienopyrazolopyrimidine derivatives of an expected wide spectrum of bioresponses. For instance, some pyrazolo[1,5-*a*]pyrimidine derivatives proved to be a good CAMP phosphodiesterase inhibitor with an excellent antianxiety profile in animals [16, 17]. Other derivatives showed antipyritic [18], antitumor [19], and herbicidal activities [20].

Encouraged by such properties, we investigated the behaviour of **5** towards acrylic acid derivatives. Thus, compound **5** reacted with 2-cyano-3-ethoxyacrylonitrile (**6a**) in refluxing EtOH/Et_3N solution to yield a single product analyzed as $C_{21}H_{13}N_5O_2S_2$ *via* EtOH elimination. Several isomeric structures seemed to be possible for this product (structures **7–10**, Scheme 2). The acyclic structures **7** and **9** were ruled out based on the IR spectrum which revealed the presence of only one CN absorption band at 2210 cm^{-1}. On the other hand, the ^1H NMR spectrum (*DMSO*-d_6 showed a broad exchangeable singlet signals $\delta = 9.55$ ppm (2H) assigned to the NH_2 protons, together with a multiplet signal at $\delta = 7.15$–7.76 ppm (11H) for the aromatic protons and the pyrimidine H-4. Consequently, we assigned the 7-aminothieno[2′,3′:3,4]pyrazolo[1,5-*a*]pyrimidine structure (**8a**) to this reaction product. If the structure of such a product were the isomeric **10a**, the NH_2 signal should have been observed at $\delta = 4$–6 ppm. Deshielding of the NH_2 protons of pyrazolo[1,5-*a*]pyrimidin-7-amine by ring nitrogen anisotropy has been reported previously [21]. Similarly, compound **5** reacted with ethyl 2-cyano-3-ethoxyacry-

late (**6b**) to furnish the corresponding ethyl 7-amino-thieno[2′,3′:3,4]pyrazolo-[1,5-*a*]pyrimidine-6-carboxylate derivative **8b**.



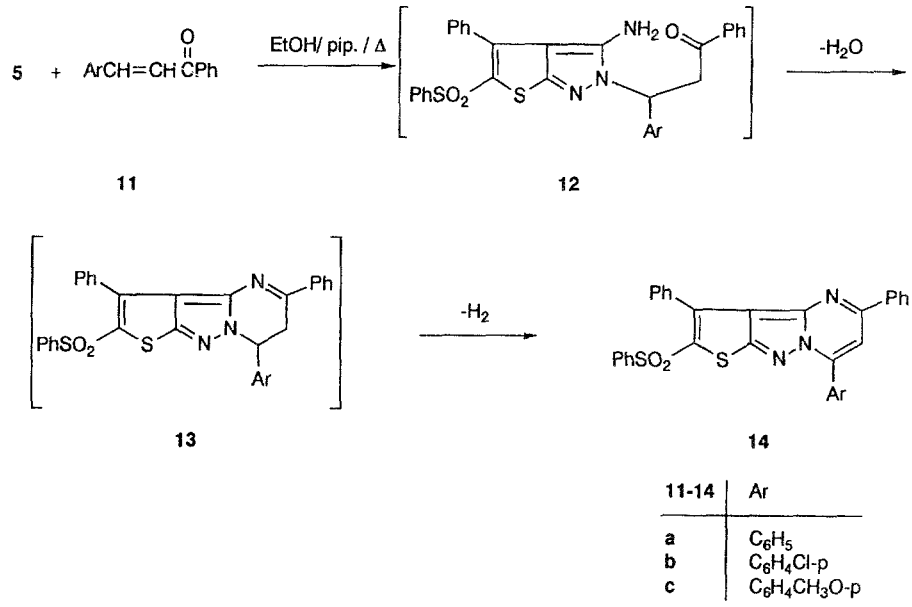
Scheme 2

The behaviour of **5** towards α,β-unsaturated ketones has also been investigated. Thus, compound **5** reacted with chalcones **11a–c** in absolute EtOH containing a catalytic amount of piperidine, under reflux, to yield the corresponding thieno-[2′,3′:3,4]pyrazolo[1,5-*a*]pyrimidine derivatives **14a–c** in acceptable yields. Structure **14** was established based on elemental analyses and spectroscopic studies (Scheme 3).

Thus, the mass spectrum of **14a** reveals a molecular ion peak at $m/z = 543$ (15%) corresponding to the molecular formula $C_{32}H_{21}N_3O_2S_2$. Its ^{1}H NMR spectrum (*DMSO*-d_6) shows a multiplet signal at $\delta = 7.13$–8.20 ppm (21H) attributed to the aromatic protons and the pyrimidine H-5.

Formation of **14** is assumed to be proceed *via* a *Michael* type addition on the most basic ring-N in **5**, intramolecular cyclodehydration, and spontaneous autoxidation under the reaction conditions. Similar autoxidations have been reported previously [22, 23]. It should be pointed out that the reaction of **5** with **11** may involve the exocyclic 3-amino group. However, the involvement of the endocyclic

pyrazole-N was considered based on literature reports [24–26] which revealed that the ring H in 3(5)-aminopyrazoles is the most reactive centre in the molecule.



Scheme 3

Finally, our study was extended to investigate the behaviour of **5** towards α-cinnamonitriles **15a–d**. Thus, compound **5** reacted with an equimolar amount of benzylidenemalononitrile (**15a**) in refluxing pyridine solution to provide a product of composition $C_{27}H_{17}N_5O_2S_2$ (*m/z* = 507, 12%). Two possible isomeric structures could be considered. To our knowledge, 3(5)-aminopyrazoles react with α,β-unsaturated nitriles *via* a *Michael* type addition of the endocyclic pyrazole NH proton to the electron deficient carbon in the α,β-unsaturated system [26, 27]. Consequently, structure **17a** was considered for such a reaction product (Scheme 4). Spectroscopic data are in accordance with the proposed structure.

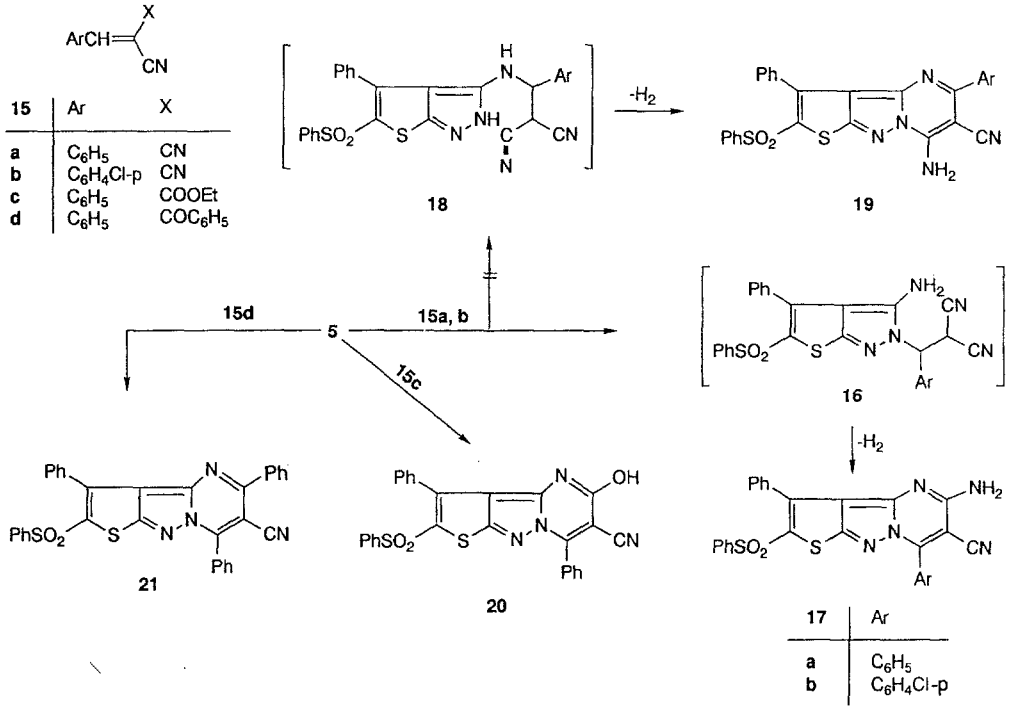
Thus, ^{1}H NMR spectrum (*DMSO*-d_6) of the product reveals the presence of a D_2O-exchangeable singlet at δ = 4.65 ppm (2H) attributed to the NH_2 protons. If the product structure were **19a** these NH_2 protons should be deshielded by the endocyclic ring nitrogen anisotropic effect and, consequently, appear at lower field (δ 9 ppm) [21].

Formation of **17a** is assumed to proceed *via* acyclic intermediate **16a**, intramolecular cyclization (*Michael* type addition of the NH_2 protons to the C≡N function) and spontaneous autoxidation. Similarly, compound **5** reacted with **15b** to yield **17b**.

Compound **5** reacted with an equimolar amount of ethyl benzylidenecyanoacetate (**15c**) under the same experimental conditions to yield the corresponding 5-hydroxy-7-phenylthieno[2′,3′:3,4]pyrazolo[1,5-*a*]pyrimidine derivative **20** *via* an initial *Michael* type addition of the pyrazole NH function to the α,β-unsaturated centre, cyclization *via* EtOH elimination, and subsequent autoxidation. Likewise, **5** reacted with benzylidene-ω-cyanoacetophenone (**15d**) to yield **21**. The analytical

and spectroscopic data of **20** and **21** are entirely consistent with the proposed structures.

In conclusion, the result presented in the article indirectly extend and broaden the knowledge in the area of thiophene-β-enaminonitriles and explore their synthetic applicability for the construction of polyfunctionally substituted condensed thiophene ring systems obtainable only with difficulty otherwise. It seemed that, due to the availability of the starting materials, the simplicity of the experimental procedures, and the comparatively reasonable yields of the products, this synthetic methodology might be convenient for the synthesis of such ring systems.



Scheme 4

Experimental

Melting points are uncorrected; IR spectra (KBr): Pye Unicam SP-1000, cm^{-1}; ^1H NMR spectra (*DMSO*-d_6): Varian Gemini 200 MHz spectrometer, *TMS* as internal standard, chemical shifts in ppm; mass spectra; AEI MS 30 mass spectrometer operating at 70 eV; microanalytical data: microanalytical Data Unit at Cairo University.

2-Amino-4-aryl-5-phenylsulfonylthiophene-3-carbonitriles (**2a,b**; *general procedure*)

A mixture of **1a,b** (0.01 mol), elemental sulfur (0.32 g, 0.01 mol), and malononitrile (0.66 g, 0.01 mol) in dry *DMF* (40 ml) containing anhydrous Et_3N (5 drops) was boiled under reflux for 6 h. The reaction mixture was poured into cold H_2O and neutralized with dilute HCl ($pH = 7$). The resulting precipitated solid was collected by filtration, washed with H_2O, dried, and crystallized from the appropriate solvent.

2-Amino-4-phenyl-5-phenylsulfonylthiophene-3-carbonitrile (**2a**)

Yield: 2.31 g (68%); m.p.: 296°C(dioxane); $C_{17}H_{12}N_2O_2S_2$ (340.42); calc.: C 59.98, H 3.55, N 8.22, S 18.83; found: C 59.9, H 3.3, N 8.1, S 18.8; IR: 3450–3380 (NH_2), 2218 (CN); ^{1}H NMR: 5.65 (br s, 2H, NH_2, exchangeable), 7.12–7.65 (m, 10H, arom. protons); MS $m/z = 340$ (M^+, 26%).

2-Amino-4-(4-bromophenyl)-5-phenylsulfonylthiophene-3-carbonitrile (**2b**)

Yield: 2.5g (62%); m.p: > 320°C (*DMF*); $C_{17}H_{11}BrN_2O_2S_2$ (419.32); calc.: C 48.69, H 2.64, N 6.68, S 15.29; found: C 48.5, H 2.6, N 6.6, S 15.0; IR: 3450–3374 (NH_2), 2220 (CN); ^{1}H NMR: 5.52 (br s, 2H, NH_2, exchangeable), 7.25–7.60 (m, 9H, arom. protons).

2,4-Diamino-5-phenyl-6-phenylsulfonylthieno[2,3-d]pyrimidine (**3**)

Method A. A mixture of **2a** (1.02 g, 0.003 mol) and cyanamide (0.16 g, 0.004 mol) was dissolved in dioxane (30 ml). The solution was continuously saturated with HCl gas at room temperature for 6 h. The mixture was boiled under reflux for 12 h, poured into ice/H_2O and neutralized with NaOH (10%). The precipitated product was collected by filtration and crystallized from benzene.

Yield: 0.62 g (54%); m.p.: 283°C; $C_{18}H_{14}N_4O_2S_2$ (382.46); calc.: C 56.52, H 3.68, N 14.64, S 16.76; found: C 56.4, H 3.6, N 14.5, S 16.5; IR: 3455–3300 (NH_2); ^{1}H NMR: 6.55, 6.93 (2s, 4H, $2NH_2$, exchangeable), 7.20–7.65 (m, 10H, arom. protons); MS : $m/z = 382$ (M^+, 15%).

Method B. Guanidine nitrate (0.5 g, 0.004 mol) in EtOH/EtONa solution (prepared by dissolving Na (0.09 g, 0.004 gatom) in absolute EtOH (30 ml)) was stirred for 1 h and then treated with **2a** (1.36 g, 0.004 mol). The reaction mixture was refluxed for 24 h, left to cool at room temperature and then poured into ice/H_2O. The solid product was collected by filtration, washed with H_2O, dried, and crystallized from benzene. Yield: 0.90 g (59%); identical (m.p., mixed m.p, IR spectrum) with authentic sample prepared according to method *A*.

3-Amidoximo-2-amino-4-phenyl-5-phenylsulfonylthiophene (**4**)

To a solution of **2a** (1.7 g 0.005 mol) in MeOH (40 ml) containing NH_4OH (2 ml), hydroxylamine hydrochloride (0.35 g, 0.005 mol) was added and the mixture was stirred at room temperature for 24 h. The solid product precipitated upon pouring the solution into cold H_2O was collected by filtration, dried, and crystallized from EtOH.

Yield: 0.87 g (52%); m.p.: 274°C; $C_{17}H_{15}N_3O_3S_2$ (373.45); calc.: C 54.67, H 4.04, N 11.25, S 17.17; found: C 54.5, H 4.0, N 11.2, S 17.0; IR: 3550 (OH), 3440–3300 (NH_2); ^{1}H NMR: 4.05 (br s, 2H, NH_2, exchangeable), 6.15 (br s, 2H, NH_2, exchangeable), 7.00–7.59 (m, 10H, arom. protons), 9.85 (s, 1H, OH, exchangeable).

3-Amino-4-phenyl-5-phenylsulfonyl-1H-thieno[2,3-c]pyrazole (**5**)

Method A. A solution of **4** (1.12 g, 0.003 mol) in dry pyridine (25 ml) was heated under reflux for 5 h. The solvent was then evaporated under reduced pressure, and the reaction mixture was triturated with cold H_2O. The solid product formed was filtered off, dried, and crystallized from dioxane.

Yield: 0.68 g (64%); m.p.: > 320°C; $C_{17}H_{13}N_3O_2S_2$ (355.43); calc.: C 57.44, H 3.68, N 11.82, S 18.04; found: C 57.4, H 3.5, N 11.8, S 18.0; IR: 3470–3250 (NH, NH_2); ^{1}H NMR: 5.00 (s, 2H, NH_2, exchangeable), 7.23–7.56 (m, 10H arom. protons), 8.53 (s, 1H, NH, exchangeable); MS: $m/z = 355$ (M^+, 18%).

Method B. A mixture of **2a** (1.02 g, 0.003 mol) and hydroxylamine hydrochloride (0.21 g, 0.003 mol) in glacial AcOH (30 ml) containing anhydrous AcONa (1 g) was boiled under reflux for 6 h. The reaction mixture was left overnight at room temperature and then poured onto H_2O. The solid precipitate was filtered off, washed with H_2O, and crystallized from dilute dioxane.

Yield: 0.63 g (59%); identical (m.p., mixed m.p., IR spectrum) with authentic sample prepared according to method *A*.

7-Aminothieno[2',3':3,4]pyrazolo[1,5-a]pyrimidines (**8a**,b; *general procedure*)

A solution of **5** (1.06 g, 0.003 mol) and the appropriate **6a**,**b** (0.003 mol) in EtOH (30 ml) containing a catalytic amount of Et_3N (5 drops) was heated under reflux for 3 h. The reaction mixture was evaporated *in vacuo*, triturated with cold H_2O, and neutralized with dilute HCl. The solid product was collected by filtration, dried, and crystallized from the appropriate solvent.

7-Amino-3-phenyl-2-phenylsulfonylthieno[2',3':3,4]pyrazolo[1,5-a]-pyrimidine-6-carbonitrile (**8a**)

Yield: 0.78 g (61%); m.p.: > 320°C (dilute *DMF*); $C_{21}H_{13}N_5O_2S_2$ (431.49); calc.: C 58.45, H 3.03, N 16.23, S 14.86; found: C 58.4, H 2.9, N 16.2, S 14.6; IR: 3452–3315 (NH_2), 2210 (CN); ^{1}H NMR: 7.15–7.76 (m, 11H, arom. protons + pyrimidine H-4), 9.55(br s, 2H, NH_2 exchangeable); MS: $m/z = 431(M^+, 12\%)$.

Ethyl 7-amino-3-phenyl-2-phenylsulfonylthieno[2',3':3,4]pyrazolo[1,5-a]-pyrimidine-6-carboxylate (**8b**)

Yield: 0.78 g (55%); m.p.: 305°C (dilute *DMF*); $C_{23}H_{18}N_4O_4S_2$ (478.54); calc.: C 57.72, H 3.79, N 11.70, S 13.40; found: C 57.6, H 3.7, N 11.5, S 13.4; IR: 3472–3318 (NH_2), 1695 (CO); ^{1}H NMR; 1.42 (t, 3H, $J = 8.25$ Hz, CH_3), 4.23(q, 2H, $J = 8.45$ Hz, CH_2) 7.20–7.93 (m, 11H, arom. protons + pyrimidine H-4), 8.85 (s, 2H, NH_2, exchangeable).

2-Phenylsulfonyl-3,5,7-triarylthieno[2',3':3,4]pyrazolo[1,5-a]pyrimidines (**14a–c**; *general procedure*)

A suspension of **5** (1.06 g, 0.003 mol) and the appropriate chalcone **11a-c** (0.003 mol) in absolute EtOH (30 ml) containing 3 drops of piperidine was refluxed for 12 h. The mixture was left to cool at room temperature, poured onto cold H_2O, and neutralized with dilute HCl. The solid product was filtered off and crystallized from the appropriate solvent.

2-Phenylsulfonyl-3,4,7-triphenylthieno[2'3':3,4]pyrazolo[1,5-a]pyrimidine (**14a**)

Yield: 0.79g (49%); m.p.: > 320°C (dilute *DMF*); $C_{32}H_{21}N_3O_2S_2$ (543.66); calc.: C 70.69, H 3.89, N 7.73, S 11.79; found: C 70.6, H 3.6, N 7.7, S 11.5; IR: 3050 (CH arom.); ^{1}H NMR: 7.13–8.20 (m, 21H, arom. protons + pyrimidine H-5); MS: m/z= 543 (M^+, 15%).

7-(4-Chlorophenyl)-3,5-diphenyl-2-phenylsulfonylthieno[2',3':3,4]-pyrazolo[1,5-a]pyrimidine (**14b**)

Yield: 0.9g (52%); m.p.: > 320°C (dilute *DMF*); $C_{32}H_{20}ClN_3O_2S_2$ (578.11); calc.: C 66.45, H 3.48, N 7.26, S 11.09; found: C 66.4, H 3.3, N 7.2, S 11.0; IR: 3050(CH arom.).

3,5-Diphenyl-7-(4-methoxyphenyl)-2-phenylsulfonylthieno[2',3':3,4]pyrazolo[1,5-a]-pyrimidine (**14c**)

Yield: 0.94 g (55%); m.p.: > 320°C (dilute *DMF*); $C_{33}H_{23}N_3O_3S_2$ (573.69); calc.: C 69.09, H 4.04, N 7.32, S 11.17; found: C 69.0, H 3.8, N 7.3, S 11.0; IR: 3055 (CH arom.), 2980(CH_3); ^{1}H NMR: 3.90 (s, 3H, CH_3), 7.22–7.91 (m, 20H, arom. protons + pyrimidine H-5).

Thieno[2',3':3,4]pyrazolo[1,5-a]pyrimidine-6-carbonitriles (**17a, b, 20, 21**; *general procedure*)

A suspension of **5** (0.71 g, 0.002 mol) and the appropriate α-cinnamonitrile derivative **15a–d** (0.002 mol) in dry pyridine(30 ml) was boiled under reflux for 6 h. Then the solvent was evaporated *in vacuo*. The reaction mixture was triturated with cold H_2O; the solid product was filtered off and crystallized from the appropriate solvent.

5-Amino-3,7-diphenyl-2-phenylsulfonylthieno[2',3':3,4]pyrazolo[1,5-a]-pyrimidine-6-carbonitrile (**17a**)

Yield: 0.49 g(49%); m.p.:298°C(dioxane); $C_{27}H_{17}N_5O_2S_2$ (507.59);calc.: C 63.89, H 3.37, N 13.79, S 12.63; found: C 63.8, H 3.2, N 13.5, S 12.6; IR: 3445–3320(NH_2), 2216 (CN); ^{1}H NMR: 4.65 (br s, 2H, NH_2, exchangeable), 7.18–7.83 (m, 15H, arom. protons); MS: m/z = 507 (M^+, 12%).

5-Amino-7-(4-chlorophenyl)-3-phenyl-2-phenylsulfonylthieno[2',3':3,4]-pyrazolo[1,5-a]pyrimidine-6-carbonitrile (**17b**)

Yield: 0.55 g (51%); m.p.: > 320°C(dilute *DMF*); $C_{27}H_{16}ClN_5O_2S_2$ (542.03); calc.: C 59.83, H 2.97, N 12.92, S 11.83; found: C 59.7, H 2.9, N 12.7, S 11.8; IR: 3456–3312 (NH_2), 2220 (CN).

3,7-Diphenyl-5-hydroxy-2-phenylsulfonylthieno[2',3':3,4]pyrazolo-[1,5-a]pyrimidine-6-carbonitrile (**20**)

Yield: 0.46 g (46%); m.p.: > 320°C (dilute *DMF*); $C_{27}H_{16}N_4O_3S_2$ (508.58); calc.: C 63.76, H 3.17, N 11.01, S 12.61; found: C 63.7, H 3.0, N 10.9, S 12.4; IR : 3540 (OH), 2216 (CN); ^{1}H NMR: 7.00–7.86 (m, 15H, arom. protons), 11.58 (br s, 1H, OH).

2-Phenylsulfonyl-3,5-7-triphenyltheino[2',3':3,4]pyrazolo[1,5-a]pyrimidine-6-carbonitrile (**21**)

Yield: 0.44 g (39%); m.p.: > 320°C (dilute *DMF*); $C_{33}H_{20}N_4O_2S_2$ (568.67); calc.: C 69.69, H 3.45, N 9.85, S 11.27; found: C 69.5, H 3.5, N 9.7, S 11.0; IR: 2215 (CN); ^{1}H NMR: 7.15–7.96 (m, 20H, arom. protons).

References

[1] Sherif SM (1996) Monatsh Chem **127**: 557
[2] Ito S, Tanaka Y, Kakehi A, Miyazawa H (1977) Bull Chem Soc Jpn **50**: 2969
[3] Ito S, Kakehi A, Matsuno T, Yoshida J (1980) Bull Chem Soc Jpn **53**: 2007
[4] Litvinov VP, Sharanin YA, Babichev FS (1986) Sulfur Rep **6**: 97
[5] Campaigne E (1984) In: Katritzky AR, Rees CW (eds) Comprehensive Heterocyclic Chemistry, vol 4. Pergamon Press, New York, p 863
[6] Gronowitz S (1963) Adv Heterocycl Chem **1**: 1

[7] Sherif SM, Wardakhan WW, Mohareb RM (1996) J Chem Res (S) 356, (M) 1970
[8] Sherif SM, Mohareb RM, Shams HZ, Gaber HMM (1995) J Chem Res (S) 434, (M) 2658
[9] Sherif SM, Abdel-Sayed NI, El-Kousy SM, Mohareb RM (1995) Monatsh Chem **126**: 601
[10] Erian AW, Sherif SM (1995) Heterocycles **40**: 1195
[11] Houwing HA, van Leusen AM (1981) J Heterocycl Chem **18**: 1127
[12] Ram JV (1979) Arch Pharm (Weinheim) **312**: 19
[13] Erian AW (1993) Chem Rev **93**: 1991
[14] Shisho CJ, Jains KS (1992) J Heterocycl Chem **29**: 883
[15] Elslager EF, Hess C, Johnson J, Ortwine D, Chien V, Werbel LM (1981) J Med Chem **24**: 127
[16] Novinson T, Hanson R, Dimmitt MK, Simon LN, Robins RK, O'Brien DE (1974) J Med Chem **17**: 645
[17] Novinson T, Miller JP, Scholten M, Robins RK, Simon LN, O'Brien DE, Meyer RB (1975) J Med Chem **18**: 460
[18] Elnagdi MH (1974) Tetrahedron **30**: 2791
[19] Elnagdi MH, Fleita DH, Elmoghayar MRH (1975) Tetrahedron **31**: 63
[20] Doming BW (1974) US Pat. 3,833,582, CA 81: 973664
[21] Greenhill JV (1984) In: Katritzky AR, Rees CW (eds) Comprehensive Heterocyclic Chemistry, vol 5. Pergamon Press, New York, p 308
[22] Figueras J (1966) J Org Chem **31**: 803
[23] Soto JL, Seoane C, Zammorano P, Javier F (1981) Synthesis: 529
[24] Shawali AS, Sami M, Sherif SM, Parkanyi C (1980) J Heterocycl Chem **17**: 877
[25] Elgemeie GEH, Fathy NM, Fadah LM, Ebeide MY, Elsaid MK (1991) Arch Pharm (Weinheim) **324**: 149
[26] Elnagdi MH, Abd-Elaal FA, Elgemeie GEH (1985) Heterocycles **23**: 3121 and references cited therein
[27] Fathy NM, Abdel-Motti FM, Elgemeie GEH (1988) Arch Pharm (Weinheim) **321**: 509

Received January 10, 1997. Accepted January 22, 1997