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SYNTHESIS OF PYRIDAZINE AND 1,3-THIAZINE DERIVATIVES VIA CT-COMPLEXATION BETWEEN THIOSEMICARBAZIDES AND TETRACYANOETHYLENE

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SYNTHESIS OF PYRIDAZINE AND 1,3-THIAZINE DERIVATIVES VIA CT-COMPLEXATION BETWEEN THIOSEMICARBAZIDES AND TETRACYANOETHYLENE

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Intermolecular charge transfer (CT) complexes of aromatic aldehyde thiosemicarbazones with some π -acceptors such as 7,7,8,8-tetracyanoquinodimethane, 2-(dicyanomethylene)indane-1,3-dione and 9-dicyanomethylene-2,4,7-trinitrofluorene have been studied spectrophotometrically. Aromatic aldehyde thiosemicarbazones, and thiosemicarbazide reacted with tetracyanoethylene via CT-complex formation to give 1,3-thiazine and pyridazine derivatives.

Key words: Pyridazines, 1,3-thiazines, thiosemicarbazides, π -acceptors, CT-complexes.

The charge transfer (CT) interactions play an important role in biologically active systems.¹ Thiosemicarbazide and its derivatives are versatile compounds which are biologically active^{2,3} and have been extensively used in the preparation of heterocyclic ring systems. In continuation of our work on synthesis of heterocyclic compounds via CT-complexation between simple organic electron donors and π -acceptors,^{4–9} we report in the present investigation the behavior of the aromatic aldehyde thiosemicarbazones 1a–e towards some π -acceptors which can be divided into two types based on the electron affinity of these acceptors:

i) With acceptors of high electron affinity (e.g. tetracyanoethylene (TCNE)),¹⁰ an initial CT-complex was formed which was then transformed immediately to reaction products 3–5 (Figures 2 and 3).

ii) With acceptors of moderate electron affinity [e.g. 2-dicyanomethylene)indane-1,3-dione(CNIND), 9-dicyanomethylene-2,4,7-trinitrofluorene(DTF) and 7,7,8,8-tetracyanoquinodimethane (TCNQ)]¹⁰ an initial CT-complex was formed, and its absorbance did not change under the experimental conditions required for determination of the association constants.

Table I contains the wavelengths of the absorption maxima of the CT-complexes between 1 and each of CNIND, DTF as well as TCNQ in the visible region, which is attributable to neither component of the complex alone, but to a new molecular species. Taking into consideration the λ_{max} values for CT-complexes as a measure of the base strength,¹¹ the basicity of the electron donors 1a–e could be arranged as follows, 1c > 1e > 1b > 1a > 1d.

The association constants (K_{CT}) of complex formation and molar extinction coef-

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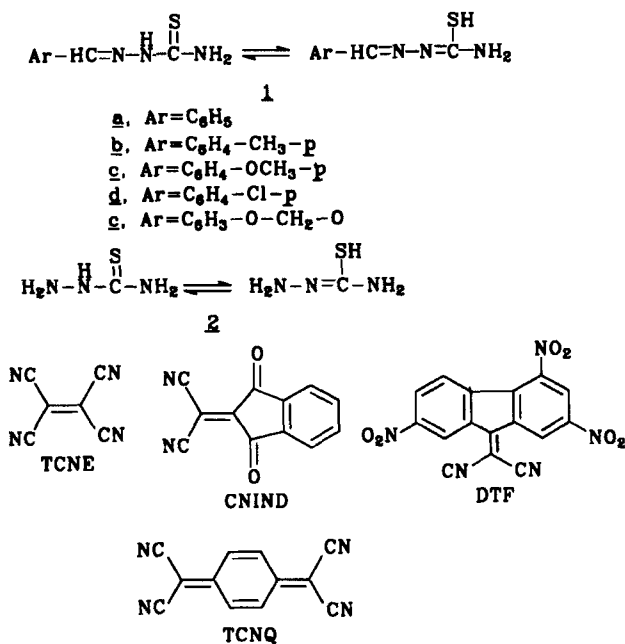


FIGURE 1

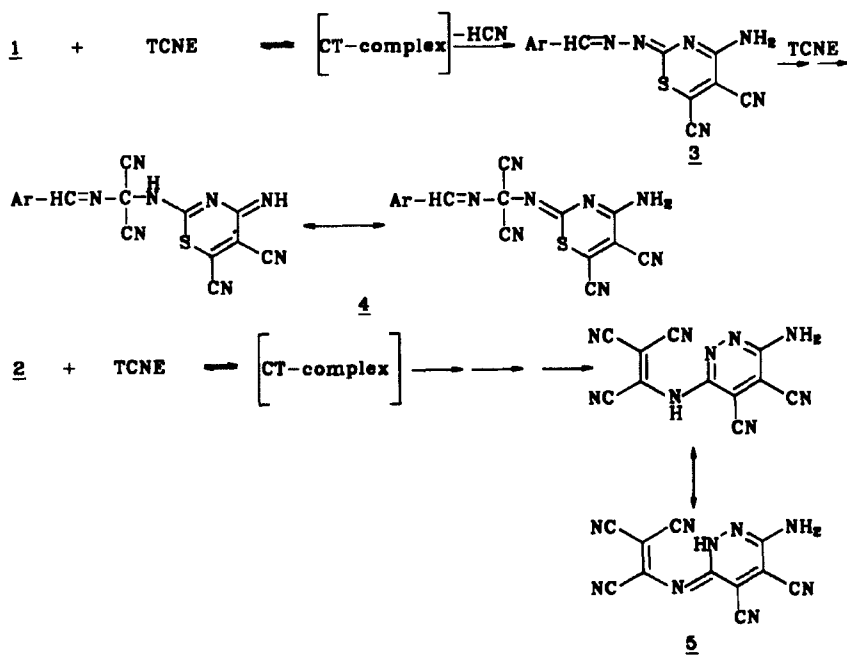


FIGURE 2

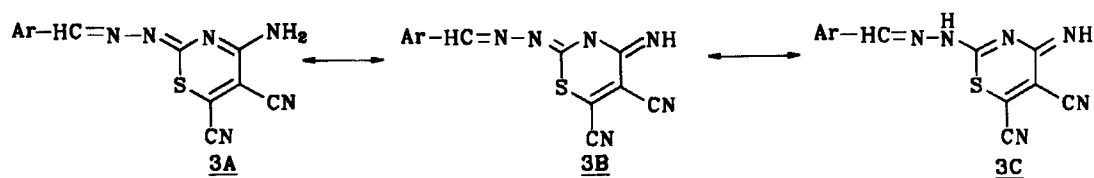


FIGURE 3

TABLE I

Spectral data for the CT-complexes of 1a–e with CNIND, DTF and TCNQ in ethyl acetate at 22°C

Donor	Acceptor	γ_{\max} [nm]	K_{ct} [$l \cdot mol^{-1}$]	ϵ_{\max} [$l \cdot mol^{-1} cm^{-1}$]	E [eV]
<u>1a</u>	CNIND	465	2.75	454	2.66
<u>1b</u>	CNIND	472	3.25	769	2.63
<u>1c</u>	CNIND	477	4.50	444	2.59
<u>1d</u>	CNIND	460	2.50	666	2.70
<u>1e</u>	CNIND	474	4.00	400	2.62
<u>1a</u>	DTF	520	3.57	500	2.38
<u>1b</u>	DTF	530	4.20	250	2.34
<u>1c</u>	DTF	541	6.00	333	2.39
<u>1d</u>	DTF	500	2.90	666	2.48
<u>1e</u>	DTF	535	4.83	444	2.32
<u>1a</u>	TCNQ	585	7.00	17	2.12
<u>1b</u>	TCNQ	610	10.80	77	2.03
<u>1c</u>	TCNQ	Sh(620)	—	—	—
<u>1d</u>	TCNQ	570	6.66	50	2.18
<u>1e</u>	TCNQ	Sh(615)	—	—	—

ficients (ϵ) were determined according to the Benesi-Hildebrand's method.¹² Values of K_{CT} and ϵ determined by this method are compiled in Table I. The sequence of K_{CT} values further supports the relative basicity of the donors 1a–e.

On addition of double molar amounts of TCNE to a solution of aromatic aldehyde thiosemicarbazones 1a–e in ethyl acetate a blue color, which may be due to a transient CT-complex¹³ formation, changed quickly to a characteristic pink color, from which the products 3 and 4 could be separated chromatographically (Figure 2). Compound 3 can theoretically exist in three different tautomeric forms 3A–C (Figure 3). It has been concluded that compound 3 existed in the form 3B in DMSO solution as evidenced from the 1H NMR spectrum, which indicated that the imino group resonates at δ in the range from 9.25 to 9.35 ppm, whereas the thiazine ring NH appears in the range from 11.35 to 11.40 ppm (see experimental). The N—NH proton in 3C should appear upfield relative to NH ring in 3B.

On the other hand, mixing a solution of TCNE in ethyl acetate with thiosemicarbazide 2 in the same solvent results in an initial formation of a green color which changed rapidly to red. This may be interpreted in terms of formation of an unstable CT-complex which ultimately gave the pyridazine derivative 5.

EXPERIMENTAL

All melting points are uncorrected. UV/VIS spectra: Perkin-Elmer Lambda 2 spectrophotometer equipped with a thermostated cell. IR spectra: Shimadzu 470 and Nicolet 320 FT-IR spectrophotometers (KBr).

¹H NMR spectra: Bruker WP 80 (80 MHz) and Bruker WM 400 (400.1 MHz); the spectra were recorded in DMSO-*d*₆; the chemical shifts are expressed as δ (ppm) with TMS as the internal standard. Mass spectroscopy: Finnigan MAT 8430; 70 eV. Elemental analyses: were performed by microanalytical unit at Cairo University.

Materials: Tetracyanoethylene (TCNE, Merck) was recrystallized from chloro-benzene and sublimed, 7,7,8,8-Tetracyanoquinodimethane (TCNQ, EGA-Chemie, Germany) was used without further purification. 2-Dicyano-methyleneindane-1,3-dione (CNIND) was prepared according to the procedure described by Chatterjee¹⁴ and recrystallized from acetonitrile. 9-Dicyanomethylene-2,4,7-trinitrofluorene (DTF) was prepared from 2,4,7-trinitrofluorenone (Aldrich) and malononitrile according to Mukherjee.¹⁵ Thiosemicarbazide (**2**) (Merck) and thiosemicarbazones **1a–e** are well known and were prepared according to the published procedure.¹⁶ Ethyl acetate was used as organic solvent (purified following Vogel).¹⁷ Preparative layer chromatography: Ari-dried 1 mm layers of silica gel (Merck) PF 254 on plates 20 cm by 48 cm were employed for preparative TLC and bands were detected by indicator fluorescence quenching upon exposure to 254 nm UV/light.

The reaction of thiosemicarbazones 1a–e and thiosemicarbazide 2 with TCNE: To a solution of 256 mg (0.002 mol) TCNE in 10 ml of dry ethyl acetate, was added dropwise with stirring the thiosemicarbazones **1a–e** (0.001 mol) and thiosemicarbazide **2** (0.002 mol) in 20 ml dry ethyl acetate at room temperature. In case of the reaction of **1** with TCNE, the color of the reaction mixture changed quickly from blue to brown which gradually changed to red. The stirring was continued for 72 hours. The mixture was concentrated, and the residue was chromatographed on thin-layer plates (100 mg per plate) using toluene/ethyl acetate (2:1) as eluent to give two colored zones. The fastest migrating specie (which was characterized by orange color) contained compound **4**. The slowest migrating zone (which was characterized by a red color) contained compound **3**. Thiosemicarbazide and TCNE gave only an orange zone containing product **5**. The separated zones were rechromatographed for further purification. Recrystallization from suitable solvents afforded the pure compounds.

3a: Yield (109 mg) 53%, mp > 360°C, red crystals (ethanol). ¹H NMR (DMSO-*d*₆): δ 7.42–8.10 (m, 6 H, Ar-H and azomethine-CH), 9.30 (s, br, 1 H, NH); 11.40 (s, br, 1 H, thiazine ring NH). IR (KBr): ν = 3395–3316 (NH₂), 3155 (Ar-CH), 2925 (Al-CH), 2213 (CN), 1635 (Ar-C=C) cm⁻¹. MS (70 eV): m/z (%) = 280 (6) [M⁺], 212 (9), 211 (100), 210 (75), 193 (35), 104 (60), 77 (82). UV (methanol): λ_{\max} = 515 nm.

C₁₃H₈N₆S (280.312) Calcd. C 55.70; H 2.88; N 29.98; S 11.44.

Found C 55.39; H 3.17; N 30.21; S 11.22.

3b: Yield (101 mg) 49%, mp 347–49°C, red crystals (acetonitrile). ¹H NMR (DMSO-*d*₆): δ 2.35 (s, 3 H, CH₃), 7.35–8.05 (m, 5 H, Ar-H and azomethine-CH), 9.35 (s, br, 1 H, NH), 11.398 (s, br, 1 H, thiazine ring NH). IR (KBr): ν = 3420–3330 (NH₂), 3140 (Ar-CH), 2940 (Al-CH), 2210 (CN), 1630 (Ar-C=C) cm⁻¹. UV (methanol): λ_{\max} = 518 nm.

C₁₄H₁₀N₆S (294.339) Calcd. C 57.13; H 3.42; N 28.55; S 10.89.

Found C 56.97; H 3.28; N 28.77; S 11.03.

3c: Yield (100 mg) 47%, mp 225°C, dec., red crystals (acetonitrile). ¹H NMR (DMSO-*d*₆): δ 3.85 (s, 3 H, OCH₃), 7.38–8.00 (m, 5 H, Ar-H and azomethine-CH), 9.30 (s, br, 1 H, NH), 11.40 (s, br, 1 H, thiazine ring NH). IR (KBr): ν = 3420–3300 ((NH₂), 3120 (Ar-CH), 2950–2900 (Al-CH), 2210 (CN), 1635, 1600 (Ar-C=C) cm⁻¹. MS (70 eV) m/z (%) = 310 (8) [M⁺], 206 (30), 205 (100), 133 (28), 119 (15). UV (methanol): λ_{\max} = 525 nm.

C₁₄H₁₀N₆SO (310.339) Calcd. C 54.18; H 3.25; N 27.08; S 10.33.

Found C 54.45; H 3.11; N 26.91; S 10.51.

3d: Yield (89 mg) 41%, mp > 360°C, red crystals (ethanol). ¹H NMR (DMSO-*d*₆): δ 7.55–8.00 (m, 5 H, Ar-H and azomethine-CH), 9.25 (s, br, 1 H, NH), 11.35 (s, br, 1 H, thiazine ring NH). IR (KBr): 3390, 3300 (NH₂), 3120 (Ar-CH), 2940–2900 (Al-CH), 2210 (CN), 1645, 1620 (Ar-C=C) cm⁻¹. MS (70 eV) m/z (%) = 314/316 (22) [M⁺], 287 (9), 260 (11), 139 (100), 119 (66), 77 (57). UV (methanol): λ_{\max} = 510 nm.

C₁₃H₇N₆ClS (314.757) Calcd. C 49.61; H 2.24; N 26.70; S 10.19; Cl 11.26.

Found C 49.83; H 2.47; N 26.51; S 9.97; Cl 11.39.

3e: Yield (122 mg) 55%, mp > 360°C, red crystals (ethanol). ¹H NMR (DMSO-*d*₆): δ 4.20 (s, 2 H,

CH₂), 7.40–7.95 (m, 4 H, Ar-H and azomethine-CH), 9.30 (s, br, 1 H, NH), 11.36 (s, br, 1 H, thiazine ring NH). IR (KBr): ν = 3410–3330 (NH₂), 3120 (Ar-CH), 2930–2900 (Ali-CH), 2210 (CN), 1630, 1610 (Ar-C≡C) cm⁻¹. UV (methanol): λ_{\max} = 522 nm.

C₁₄H₈N₆SO₂ (324.322) Calcd. C 51.85; H 2.49; N 25.91; S 9.89.

Found C 52.17; H 2.26; N 25.67; S 10.11.

4a: Yield (54 mg) 22%, mp 240–42°C, orange crystals (ethanol). ¹H NMR (DMSO-*d*₆): δ 7.40–8.20 (m, 6 H, Ar-H and azomethine-CH), 8.80 (s, br, 2 H, NH₂). IR (KBr): ν = 3448–3310 (NH₂), 3067 (Ar-CH), 2921 (Ali-CH), 2208 (CN), 1644, 1621, 1603 (Ar-C≡C) cm⁻¹. UV (methanol): λ_{\max} = sh (480) nm.

C₁₆H₈N₈S (344.359) Calcd. C 55.81; H 2.34; N 32.54; S 9.31.

Found C 55.66; H 2.47; N 32.39; S 9.19.

4b: Yield (70 mg) 28%, mp 272–77°C, orange crystals (ethanol). ¹H NMR (DMSO-*d*₆): δ 2.33 (s, 3 H, CH₃), 7.32–8.15 (m, 5 H, Ar-H and azomethine-CH), 8.85 (s, br, 2 H, NH₂). IR (KBr): ν = 3440–3249 (NH₂), 3130 (Ar-CH), 2925 (Ali-CH), 2212 (CN), 1654, 1620, 1609 (Ar-C≡C) cm⁻¹. MS (70 eV) *m/z* (%) = 358 (60) [M⁺], 310 (11), 241 (44), 118 (100), 91 (66). UV (methanol): λ_{\max} = 485 nm.

C₁₇H₁₀N₈S (358.386) Calcd. C 56.97; H 2.81; N 31.27; S 8.95.

Found C 57.14; H 2.69; N 31.43; S 9.12.

4c: Yield (67 mg) 26%, mp 264–66°C, orange crystals (acetonitrile). ¹H NMR (DMSO-*d*₆): δ 3.80 (s, 3 H, OCH₃), 7.35–8.05 (m, 5 H, Ar-H and azomethine-CH), 8.77 (s, br, 2 H, NH₂). IR (KBr): ν = 3421–3301 (NH₂), 3012 (Ar-CH), 2957–2842 (Ali-CH), 2217–2207 (CN), 1648, 1608 (Ar-C≡C) cm⁻¹. MS (70 eV) *m/z* (%) = 374 (28) [M⁺], 241 (15), 134 (100), 133 (33), 107 (16), 92 (13), 77 (17). UV (methanol): λ_{\max} = 490 nm.

C₁₇H₁₀N₈SO (374.385) Calcd. C 54.54; H 2.69; N 29.93; S 8.56.

Found C 54.68; H 2.52; N 30.12; S 8.74.

4d: Yield (55 mg) 21%, mp 228–30°C, orange crystals (acetonitrile). ¹H NMR (DMSO-*d*₆): δ 7.40–8.20 (m, 5 H, Ar-H and azomethine-CH), 8.87 (s, br, 2 H, NH₂). IR (KBr): ν = 3444–3316 (NH₂), 3099 (Ar-CH), 2959–2926 (Ali-CH), 2217, 2220 (CN), 1648, 1591 (Ar-C≡C) cm⁻¹. UV (methanol): λ_{\max} = 482 nm.

C₁₈H₇N₈ClS (378.804) Calcd. C 50.73; H 1.86; N 29.58; S 8.47; Cl 9.36.

Found C 50.81; H 1.97; N 29.42; S 8.66; Cl 9.19.

4e: Yield (66 mg) 25%, mp > 360°C, orange crystals (ethanol). ¹H NMR (DMSO-*d*₆): δ 4.20 (s, 2 H, CH₂), 7.40–8.00 (m, 4 H, Ar-H and azomethine-CH), 8.75 (s, br, 2 H, NH₂). IR (KBr): ν = 3430–3310 (NH₂), 3130 (Ar-CH), 2960–2925 (Ali-CH), 2210 (CN), 1635, 1610 (Ar-C≡C) cm⁻¹. MS (70 eV) *m/z* (%) = 388 (26) [M⁺], 241 (17), 148 (100), 147 (66), 146 (53), 121 (48). UV (methanol): λ_{\max} = 487 nm.

C₁₇H₈N₈SO₂ (388.369) Calcd. C 52.58; H 2.08; N 28.85; S 8.26.

Found C 52.31; H 1.85; N 29.11 S 8.37.

5: Yield (412 mg) 79%, mp 235–37°C, orange crystals (ethanol). ¹H NMR (DMSO-*d*₆): δ 7.88 (s, br, 2 H, NH₂), 10.60 (s, br, 1 H, NH pyridazine ring). IR (KBr): ν = 3430–3200 (NH, NH₂), 2210 (CN), 1640, 1610 (Ar-C≡C) cm⁻¹. MS (70 eV) *m/z* (%) = 261 (50) [M⁺], 205 (100), 161 (28), 146 (14), 119 (16), 56 (48). UV (methanol): λ_{\max} = 460 nm.

C₁₁H₃N₉ (261.205) Calcd. C 50.58; H 1.16; N 48.26.

Found C 50.64; H 1.23; N 48.15.

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REFERENCES

1. A. Szent Györgi, "Introduction to a Submolecular Biology," Academic Press, N.Y., 1960.
2. A. Baklien, A. Serban, R. B. Warner and K. T. Alcock, *Can.*, **1**, 064, 823, 23 Oct., 1979, *C.A.*, **92**, 71048g (1980).
3. G. M. Andrei, O. I. Pieroni, H. S. Gatica and C. E. Coto., *Drugs Exp. Clin. Res.*, **11**, 869 (1985); *C.A.*, **104**, 141731s (1986).
4. A. A. Hassan, Y. R. Ibrahim, N. K. Mohamed and A. E. Mourad, *J. Prakt. Chem.*, **332**, 1049 (1990).
5. A. A. Hassan, Y. R. Ibrahim, N. K. Mohamed and A. E. Mourad, *Justus Liebigs Ann. Chem.*, **71** (1991).
6. Y. R. Ibrahim, A. A. Hassan, N. K. Mohamed and A. E. Mourad, *Arch. Pharm. (Weinheim)*, **325**, 389 (1992).
7. N. K. Mohamed, Y. R. Ibrahim, A. A. Hassan and A. E. Mourad, *Arch. Pharm. (Weinheim)*, **326**, 245 (1993).
8. A. A. Hassan, N. K. Mohamed, Y. R. Ibrahim, and A. E. Mourad, *Justus Liebigs Ann. Chem.*, **695** (1993).
9. A. A. Hassan, N. K. Mohamed, Y. R. Ibrahim, K. U. Sadek and A. E. Mourad, *Bull. Chem. Soc. Jpn.*, **66**, 2612 (1993).
10. R. Foster, "Organic Charge-Transfer Complexes," Academic Press, London and New York, 1969.
11. L. A. Singer and D. J. Cram, *J. Am. Chem. Soc.*, **81**, 5971 (1959).
12. H. A. Benesi and J. H. Hildebrand, *J. Am. Chem. Soc.*, **71**, 2703 (1949).
13. A. E. Mourad and A. M. Tawfik, *Bull. Pol. Acad. Sci. Chem.*, **35**, 53 (1987).
14. S. Chatterjee, *J. Chem. Soc. B*, 725 (1969).
15. K. Mukherjee and L. A. Levasseur, *J. Org. Chem.*, **30**, 466 (1965).
16. K. Miyatake, *J. Pharm. Soc. Jpn.*, **72**, 1162 (1952).
17. A. I. Vogel, "A Textbook of Practical Organic Chemistry," 3rd Ed., Longman, London, 1957.