# Chemical Interactions between 1,2,4-Triazole-3-thiols and π-Acceptors

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4-Amino-5-mercapto-5-substituted 4-amino-1,2,4-triazole-3-thiols **1a**, **b** reacted with tetrachloro-, tetrafluoro-*p*-benzoquinone and 2,3-dichloro-1,4-naphthoquinone as well as 2-(dicyanomethylene)-1,3-indandione via charge-transfer (CT) complex formation giving naphthotriazolothiadiazinone **2a**—**d**, bistriazolobenzobisthiadiazine **3a**—**d**, triazolobenzothiadiazinone **4a**, **b**, bistriazolonaphthobisthiadiazine **5a**, **b**, and indenatriazolothiadiazepine **7a**, **b** derivatives.

5-Substituted 4-amino-1,2,4-triazole-3-thiols **1a**, **b** have been extensively utilized for the synthesis of fused heterocycles.[1—12] There is also increasing interest in triazole-3-thiols **1** due to their bactericidal properties against staphytococcus aurens[13] as well as its activity as antisecretory agent.[14]

In the field of charge-transfer (CT) complexes it has been reported that the activity of the pharmacologically active compounds (donors) operates via association with electron acceptors.[15,16]

In continuation to our strategy which is concerned with the synthesis of heterocycles[17—20] via interactions between simple heterocyclic rings (donors) and electron acceptors, we report here in the results of our investigations on the behavior of 1,2,4-triazole-3-thiol **1**, as biologically active electron donor, towards some π-acceptors such as 2,3,5,6-tetrachloro-*p*-benzoquinone (CHL), 2,3,5,6-tetrafluoro-*p*-benzoquinone (TFQ), 2,3-dichloro-1,4-naphthoquinone (DCHNQ), 2-(dicyanomethylene)-1,3-indandione (CNIND), and tetracyanoethylene (TCNE).

It has been reported earlier[5] that, the reaction between 1,2,4-triazole-3-thiol **1** and CHL afforded 6,13-dichloro-3,10-diethylbis[1,2,4]triazole[3,4-*b*:3′,4′-*b*′]benzo[1,2-*e*:4,5-*e*′]bis[1,3,4]thiadiazine.

As shown in Table 1 the absorption maxima obtained by mixing separate solutions of the donor **1a**, **b** and acceptors (CHL or TFQ) components fall into the visible region (477—505 nm). These maxima are attributed to CT-complex formation, since neither of the components alone absorbs in this region. Moreover, these maxima were dissociate reversibly into its components on dissolution.[21] On application of Job's method of continuous variation,[22] a 1:1 stoichiometric ratio for these complexes is also a clear evidence for CT-complexation. The variation of band intensities was slow enough to allow determination of the absorbance of the initially formed CT-complexes. These CT-complexes gradually disappeared to give a reddish-brown precipitate. This behavior may be explained as an initial formation of unstable CT-complexes followed by the formation of triazolobenzothiadiazinone **2a**, **b** and bistriazolobenzobisthiadiazine **3a**, **b** derivatives (Scheme 1).

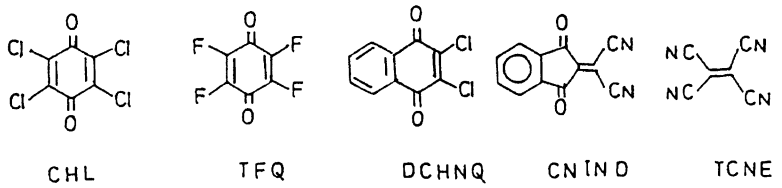
Table 1. Absorption ($\lambda_{max}$) of the CT-Complexes between 1,2,4-Triazole-3-thiol **1a**, **b** and π-Acceptors in Ethyl Acetate at Room Temperature (25 °C)

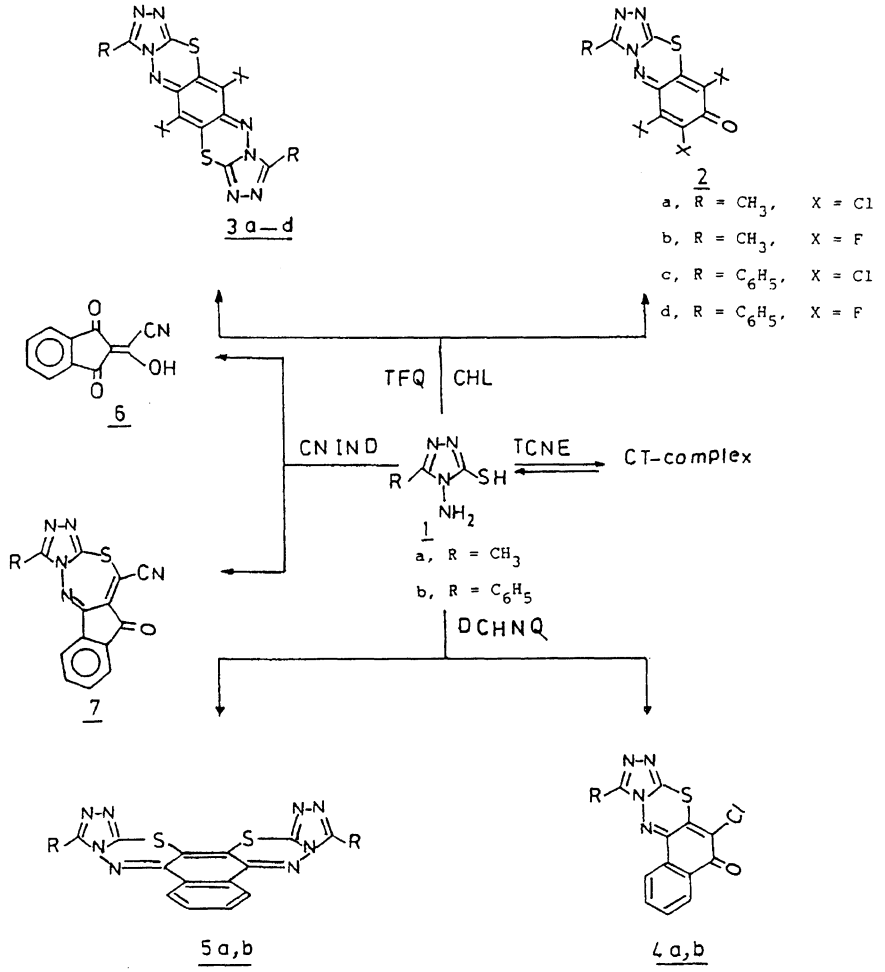
| Donor | Acceptor | $\lambda_{max}$ (nm) | Donor | Acceptor | $\lambda_{max}$ (nm) |
|---|---|---|---|---|---|
| **1a** | CHL | 505 | **1a** | DCHNQ | 476 (sh) |
| **1b** | CHL | 490 | **1b** | DCHNQ | 465 (sh) |
| **1a** | TFQ | 497 | **1a** | TCNE | 538 |
| **1b** | TFQ | 477 | **1b** | TCNE | 522 |

In a similar manner, compounds **1a**, **b** react with DCHNQ to give two products; naphthotriazolothiadiazinone **4a**, **b** and bistriazolonaphthobisthiadiazine **5a**, **b** derivatives. The mechanism of formation of the products **2**—**5** may be explained on the basis of the reactions of α-halo ketones with 1,2,4-triazole-3-thiols,[5,9—12] which accompanied with elimination of HX followed by cyclocondensation reactions.

On the other hand, **1a**, **b** did not form CT-complexes with CNIND in ethyl acetate. However, on mixing both CNIND and **1** in pyridine an initial CT-complex was formed, ($\lambda_{max}$=648—675 nm) and its absorbance increased slowly after few minutes. Moreover, it has been found that the absorbance of these CT-complexes increases with increasing temperature, which is presumably tend to accelerate the interactions between the components. This behavior indicate that an initial CT-complexes was formed and subsequent chemical reaction took place within few days at room temperature or after few hours on heating in presence of air.

2-(Cyanohydroxymethylene)-1,3-indandione (**6**) was first filtered off as a precipitate from the reaction mixture. Chromatographic purification of the filtrate gave 10*H*-indeno[1,2-*e*][1,2,4]triazolo[3,4-*b*][1,3,4]-thiadiazepine **7a**, **b** derivatives. In the light of these studies the rational formation of compounds **6** and **7** is illustrated in Scheme 2. 1,2,4-Triazole **1** and CNIND form in the initial step a CT-complex, which followed by a complete electron transfer to form a radical ion pair **8**. Proton transfer from compound **1** to pyridine (solvent) gave the radical **9**, which recombine with **10** to give the anion **11**. Elimination of a cyanide ion from **11** gave **12**. Addition of $H_2O$ to **12** form 2-(cyanohydroxymethylene)-1,3-indandione (**6**) and 1,2,4-triazole-3-thiol **1**. In the other route, **12** gave the indeno[1,2-*e*][1,2,4]triazolo [3,4-*b*][1,3,4]thiadiazepine **7a**, **b**, by an intramolecular




Scheme 1.

condensation reaction. The proposed structures for **7a, b** are confirmed by the analytical data (Table 2) as well as the IR and $^1$H NMR spectral data (Table 3).

Although the electron affinity of TCNE is higher than that of CNIND, CHL, and TFQ,[21] the interaction between TCNE and 1,2,4-triazole-3-thiol **1** results only in formation of stable CT-complexes in ethyl acetate or pyridine (Table 1). This behavior can be attributed to the presence of carbonyl groups in CNIND or 1,4-benzoquinones which allowed the formation of stable fused heterocyclic systems.

## Experimental

Melting points: Uncorrected. UV-vis spectra: Perkin–Elmer Lambda 2 spectrophotometer; 1.0 cm stoppered silica cells. IR spectra: Shimadzu 470 and Nicolet 320 FT-IR spectrophotometers (KBr). $^1$H NMR spectra: Bruker WM 400 (400.1 MHz); chemical shifts in $\delta$ (ppm), TMS as internal standard. MS: Finnigan MAT 8430; 70 eV. Elemental analyses: Microanalytical unit at Cairo University.

**Materials:** 5-Substituted 4-amino-1,2,4-triazole-3-thiols **1a, b** were prepared according to the literature.[23] 2,3,5,6-Tetrachloro-*p*-benzoquinone (CHL, Aldrich) was recrystallized several times from benzene before use; 2,3,5,6-tetrafluoro-*p*-benzoquinone (TFQ, Janssen) was used without further purifications; tetracyanoethylene (TCNE, Janssen) was recrystallized from chlorobenzene; 2-(dicyanomethylene)indan-1,3-dione (CNIND) was prepared according to the procedure described by Chatterijee,[24] and 2,3-dichloro-1,4-

Table 2. Analytical and Physical Data of Compounds **2**—**7**

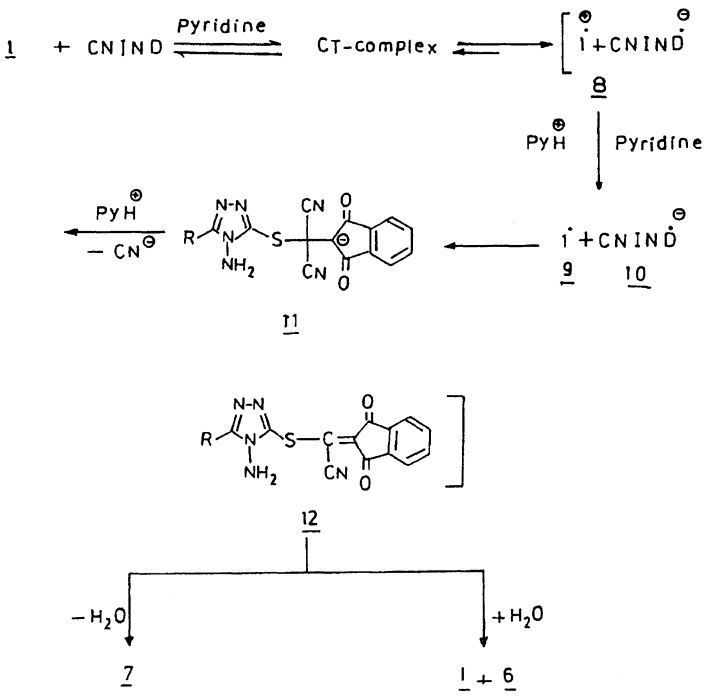
| Compound[a] | Yield % | Mp °C | Color of crystal | Solvent of recrystallization | Mol. formula (M. wt) | Analyses(%) Found (Calcd) C | H | N | Cl |
|---|---|---|---|---|---|---|---|---|---|
| **2a** | 22 | 196—197 | Orange | Ethanol | $C_9H_3N_4Cl_3SO$ (321.49) | 33.48 (33.60 | 1.03 0.93 | 17.55 17.43 | 32.91 33.08) |
| **2b** | 19 | 227—229 | Reddish-brown | Ethanol | $C_9H_3N_4F_3SO$ (272.12) | 39.77 (39.69 | 1.19 1.11 | 20.44 20.59) | — |
| **2c** | 24 | 238—240 | Orange | Ethanol | $C_{14}H_5N_4Cl_3SO$ (383.65) | 43.96 (43.83 | 1.19 1.31 | 14.46 14.60 | 27.86 27.72) |
| **2d** | 21 | 181—182 | Reddish-brown | Ethanol | $C_{14}H_5N_4F_3SO$ (334.28) | 50.42 (50.30 | 1.66 1.51 | 16.81 16.76) | |
| **3a** | 74 | 261—263 | Orange | Acetonitrile | $C_{12}H_6N_8Cl_2S_2$ (397.27) | 36.31 (36.28 | 1.49 1.52 | 28.18 28.21 | 17.92 17.84) |
| **3b** | 68 | 296—298 | Reddish-brown | Ethyl acetate | $C_{12}H_6N_8F_2S_2$ (364.36) | 39.39 (39.55 | 1.54 1.66 | 30.89 30.75) | — |
| **3c** | 71 | 188—190 | Reddish-brown | Acetonitrile | $C_{22}H_{10}N_8Cl_2S_2$ (521.42) | 50.51 (50.68 | 2.07 1.93 | 21.63 21.49 | 13.72 13.60) |
| **3d** | 66 | 265—267 | Brown | Acetonitrile | $C_{22}H_{10}N_8F_2S_2$ (488.51) | 53.97 (54.09 | 2.18 2.06 | 23.11 22.94) | — |
| **4a** | 31 | 244—245 | Pale-yellow | Benzene | $C_{13}H_7N_4ClSO$ (302.74) | 51.73 (51.58 | 2.28 2.33 | 18.64 18.51 | 11.88 11.71) |
| **4b** | 28 | 231—233 | Yellow | Benzene | $C_{18}H_9N_4ClSO$ (364.82) | 59.41 (59.26 | 2.58 2.49 | 15.23 15.36 | 9.55 9.72) |
| **5a** | 62 | 289—291 | Orange | Acetonitrile | $C_{16}H_{10}N_8S_2$ (378.44) | 50.91 (50.78 | 2.48 2.66 | 29.77 29.61) | |
| **5b** | 68 | 276—278 | Orange | Acetonitrile | $C_{26}H_{14}N_8S_2$ (502.58) | 61.97 (62.14 | 2.93 2.81 | 22.21 22.30) | |
| **6** | 79 | 209—211 | Brown | Ethanol | $C_{11}H_5NO_3$ (199.16) | 66.51 (66.34 | 2.66 2.53 | 6.88 7.03) | |
| **7a** | 19 | >300 | Yellow | Ethanol | $C_{14}H_7N_5SO$ (293.30) | 57.43 (57.33 | 2.23 2.41 | 24.06 23.88) | |
| **7b** | 16 | 175—177 | Yellow | Ethanol | $C_{19}H_9N_5SO$ (355.38) | 64.38 (64.22 | 2.69 2.55 | 19.52 19.71) | |

a) The nomenclature of some of these compounds as follows: **2c**: 6,7,9-Trichloro-3-phenyl-8*H*-1,2,4-triazolo[3,4-*b*][4,1,2]-benzothiadiazin-8-one. **3c**: 6,13-Dichloro-3,10-diphenylbis[1,2,4]triazolo[3,4-*b*:3′,4′-*b*′]benzo[1,2-*e*:4,5-*e*′]bis[1,3,4]thiadiazine. **4b**: 6-Chloro-10-phenyl-5*H*-naphtho[1,2-*a*][1,2,4]triazolo[3,4-*b*][1,3,4]thiadiazin-5-one. **5b**: 3,12-Diphenylbis[1,2,4]triazolo[3,4-*b*:3′, 4′,-*b*′]naphtho[1,2-*e*:4,3-*e*′]bis[1,3,4]thiadiazine. **7b**: 10-Oxo-3-phenyl-10*H*-indeno[1,2-*e*][1,2,4]triazolo[3,4-*b*][1,3,4]thiadiazepine-11-carbonitrile.

Table 3. The IR, $^1$H NMR, and MS Spectral Data of Compounds **2**—**7**

| Compound | IR (KBr, $cm^{-1}$) | $^1$H NMR ($\delta$, TMS)[a] | MS $m/z$ (rel intensity %) |
|---|---|---|---|
| **2a** | 1710 (CO), 1635 (Ar-C=C) | 2.63 (s, 3H, $CH_3$) | 323/321 ($M^+$; 53), 286 (61), 251 (41), 222 (16), 127 (100), 77 (26) |
| **2b** | 1690 (CO), 1630 (Ar-C=C) | 2.58 (s, 3H, $CH_3$) | 272 ($M^+$; 100), 252 (36), 224 (61), 204 (18) |
| **2c** | 1720 (CO), 1630 (Ar-C=C) | 7.65—8.45 (m, 5H, Ar-H) | 384/382 ($M^+$; 71), 347 (24), 319 (35), 189 (100), 77 (18) |
| **2d** | 1680 (CO), 1620 (Ar-C=C) | 7.73—8.32 (m, 5H, Ar-H) | 334 ($M^+$; 100), 314 (24), 286 (39), 174 (21), 146 (52), 71 (18) |
| **3a** | 2960—2940 (Ali-CH), 1630 (Ar-C=C) | 2.61 (s, 6H, $CH_3$) | 398/396 ($M^+$; 100), 363 (47), 328 (33), 77 (56) |
| **3b** | 2870—2960 (Ali-CH), 1620 (Ar-C=C) | 2.58 (s, 6H, $CH_3$) | 364 ($M^+$; 100), 326 (28), 182 (54), 71 (22) |
| **3c** | 3080—3130 (Ar-CH), 1635 (Ar-C=C) | 7.68—8.25 (m, 10H, Ar-H) | 522/520 ($M^+$; 100), 487 (19), 354 (11), 260 (14), 223 (75) |
| **3d** | 3100—3160 (Ar-CH), 1630 (Ar-C=C) | 7.73—8.46 (m, 10H, Ar-H) | 488 ($M^+$; 100), 357 (14), 182 (33) |
| **4a** | 1685 (CO), 1610 (Ar-C=C) | 2.58 (s, 3H, $CH_3$), 7.71—8.52 (m, 4H, Ar-H) | 303/302 ($M^+$; 100), 268 (61), 240 (26), 128 (39) |
| **4b** | 1680 (CO), 1630 (Ar-C=C) | 7.22—8.51 (m, 9H, Ar-H) | 365/364 ($M^+$; 100), 330 (18), 302 (49), 77 (91) |
| **5a** | 2960—2990 (Ali-CH), 1630 (Ar-C=C) | 2.59 (s, 6H, $CH_3$), 7.72—8.31 (m, 4H, Ar-H) | 378 ($M^+$; 100), 282 (39), 196 (42), 127 (48) |
| **5b** | 3090—3130 (Ar-CH), 1635 (Ar-C=C) | 7.30—8.48 (m, 4H, Ar-H) | 502 ($M^+$; 100), 425 (41), 348 (16), 190 (28) |
| **6** | 3480—3450 (OH), 2220 (CN), 1690 (CO), 1620 (Ar-C=C) | 4.60 (s, br, 1H, OH), 7.60—8.60 (m, 4H, Ar-H) | 199 ($M^+$; 100), 172 (13), 171 (62), 143 (19), 77 (38) |
| **7a** | 2210 (CN), 1710 (CO), 1620 (Ar-C=C) | 2.61 (s, 3H, $CH_3$), 7.65—8.45 (m, 4H, Ar-H) | 293 ($M^+$; 64), 267 (100), 252 (41), 224 (18), 166 (56), 77 (66) |
| **7b** | 2220 (CN), 1705 (CO), 1610 (Ar-C=C) | 7.55—8.40 (m, 9H, Ar-H) | 355 ($M^+$; 100), 329 (29), 301 (68), 224 (48), 166 (71) |

a) The solvent of $^1$H NMR is DMSO-$d_6$ except **3b** and **4b** ($CDCl_3$).



Scheme 2.

naphthoquinone (DCHNQ, Aldrich).

**The Reaction of 1,2,4-Triazole-3-thiol 1a, b with CHL, TFQ, and DCHNQ. General Procedure:** To a solution of benzoquinone or naphthoquinone (0.002 mol) in 20 ml of dry ethyl acetate, the 1,2,4-triazole-3-thiol **1a, b** (0.001 mol) in 10 ml ethyl acetate was added dropwise with stirring at room temperature. Thereafter, the mixture was stirred for 24 h, filtered and the precipitate was washed with cold ethyl acetate several times until the mother liquor become clear. The filtrate was concentrated and the residue was then chromatographed on thin-layer plates using toluene as eluent to give a characteristic colored zone. Extraction of this zone with acetone, and recrystallization from appropriate solvent afforded the pure crystalline reaction products **2a—d** and **4a, b**. Recrystallization of the precipitate from suitable solvent afforded the pure compounds **3a—d** and **5a, b**.

**The Reaction of CNIND with 1,2,4-Triazole-3-thiol 1a, b.** To a solution of CNIND (416 mg, 0.002 mol) in 15 ml of dry pyridine, 1,2,4-triazole-3-thiol **1a, b** (0.001 mol) in 10 ml dry pyridine was added dropwise at room temperature with stirring. The mixture was then heated gently without increasing the temperature above 100 °C for 5 h. The solvent was removed by concentration and the residue was washed several times with ethanol to remove residual pyridine. The residue was heated in ethanol and filtered. The precipitate was washed several times with hot ethanol. The filtrate was concentrated and the residue was dissolved in acetone and then chramatographed on thin-layer plates using toluene/ethyl acetate (5:1) as eluent to give a yellow zone. Extraction of this zone with acetone and recrystallization from the appropriate solvent afforded the pure crystalline reaction products **7a, b**. The precipitate was recrystallized from acetonitrile to give 2-(cyanohydroxymethylene)-1,3-indandione (**6**) as brown crystals.

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## References

1) T. Sasaki, E. Ito, and I. Shimizu; *J. Org. Chem.*, **47**, 2757 (1982).
2) K. S. Dhada, J. Mohan, V. K. Chadha, and H. K. Pujari, *Indian J. Chem.*, **12**, 287 (1974).
3) R. G. Dickinson and N. W. Jacobsen, *J. Chem. Soc., Perkin Trans. 1*, **10**, 975 (1975).
4) W. L. Albrecht, W. D. Jones, and F. W. Sweet, *J. Heterocycl. Chem.*, **15**, 209 (1978).
5) V. K. Chadha and G. R. Sharma, *J. Indian Chem. Soc.*, **57**, 1112 (1980).
6) N. D. Heindel and J. R. Ried, *J. Heterocycl. Chem.*, **17**, 1087 (1980).
7) P. Molina and A. Tarraga, *Synthesis*, **5**, 411 (1983).
8) N. F. Eweiss, A. A. Bahajaj, and E. A. El-Sherbini, *J. Heterocycl. Chem.*, **23**, 145 (1986).
9) N. F. Eweiss and A. A. Bahajaj, *J. Heterocycl. Chem.*, **24**, 1173 (1987).
10) J. Mohan, *Indian J. Chem., Sect. B*, **22B**, 270 (1983).
11) A. K. El-Shafei, A. B. A. G. Chattas, A. Sultan, H. S. El-Kashef, and G. Vernin, *Gazz, Chim. Ital.*, **112**, 345 (1982).

12) P. Molina and M. J. Vilaplana, *J. Chem. Res.* (*S*), **1986**, 70; *Chem. Abstr.*, **105**, 6495y (1986).
13) S. A. Patil, B. M. Badiger, S. M. Kudari, and V. H. Kulkarn, *J. Indian Chem. Soc.*, **61**, 713 (1984).
14) W. L. Albrecht and W. D. Jones., U.S. Patents 4230715 (1980); *Chem. Abstr.*, **94**, 121552f (1981).
15) B. Pullman and A. Pullman, *Proc. Natl. Acad. Sci. U.S.A.*, **44**, 1197 (1958).
16) A. Szent-Györgi, "Introduction to a Submolecular Biology," Academic Press, New York (1960).
17) A. A. Hassan, Y. R. Ibrahim, N. K. Mohamed, and A. E. Mourad, *J. Prakt. Chem.*, **332**, 1049 (1990).
18) A. A. Hassan, Y. R. Ibrahim, N. K. Mohamed, and A. E. Mourad, *Liebigs Ann. Chem.*, **1991**, 71.
19) Y. R. Ibrahim, A. A. Hassan, N. K. Mohamed, and A. E. Mourad, *Arch. Pharm.* (*Weinheim, Ger.*), **325**, 389 (1992).
20) N. K. Mohamed, A. A. Hassan, Y. R. Ibrahim, and A. E. Mourad, *Pharmazie*, **47**, 592 (1992).
21) R. Foster, "Organic Charge-Transfer Complexes", Academic Press, London and New York (1969).
22) P. Job, *Ann. Chim.*, **6**, 97 (1935).
23) J. R. Reid and N. D. Heindel, *J. Heterocycl. Chem.*, **13**, 925 (1976).
24) S. Chatterijee, *J. Chem. Soc. B*, **1969**, 725.