

Formation of thiadiazole, thiadiazine, thiadiazepine and pyrazole derivatives in the reaction of 2,4-disubstituted thiosemicarbazides with tetracyanoethylene

Alaa A. Hassan,^{*a} Ashraf A. Aly,^a Sara M. Mostafa,^a and Dietrich Döpp^b

^a Chemistry Department, Faculty of Science, Minia University, El-Minia 61519, Egypt

^b Organische Chemie, Universität Duisburg-Essen, D-45117 Essen, Germany

Email: alaahassan2001@mu.edu.eg

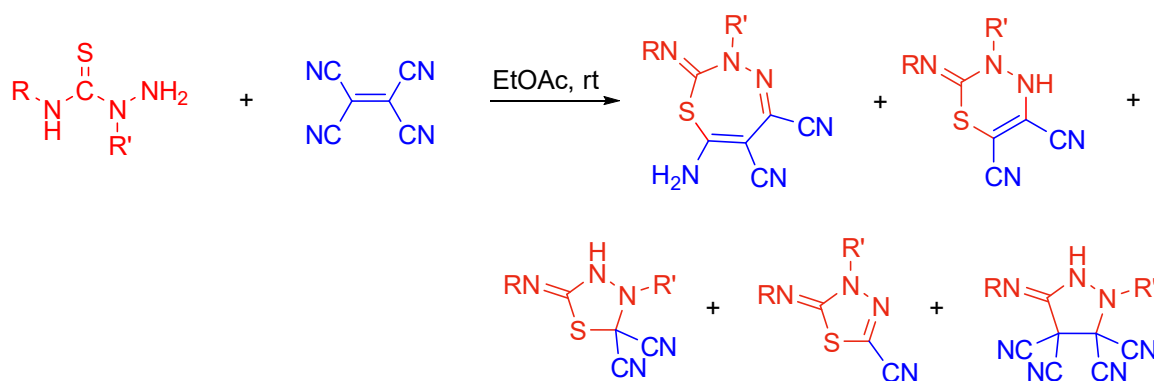
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Abstract

The reaction of 2,4-disubstituted thiosemicarbazides with tetracyanoethylene gave mixtures of 1,3,4-thiadiazole, 1,3,4-thiadiazine, 1,3,4-thiadiazepine and pyrazolidine derivatives. Rationale mechanisms for these transformations are presented.



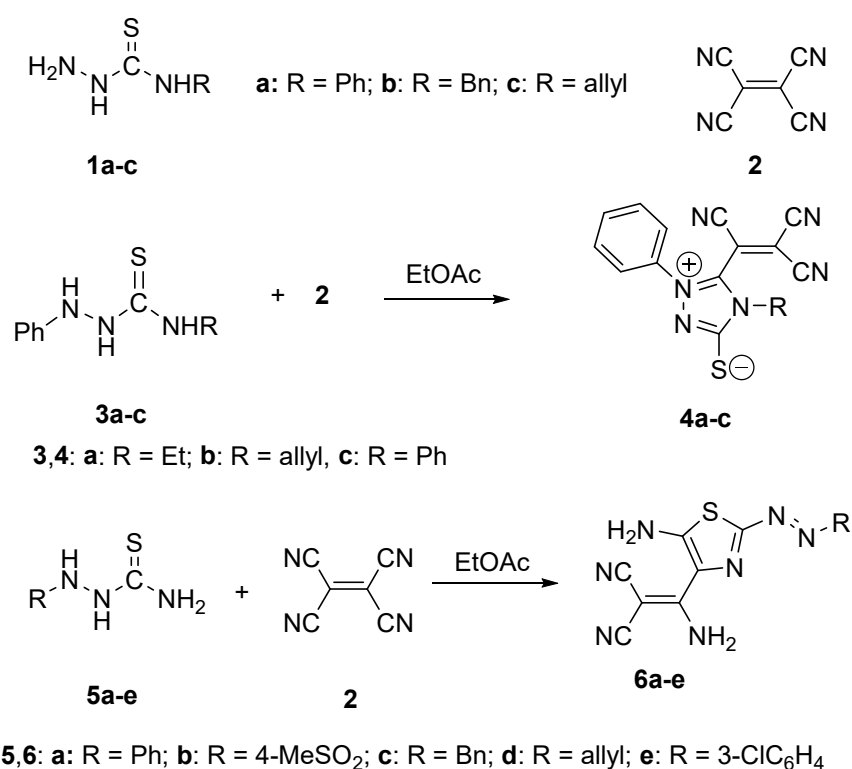
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Introduction

Carbothioamides and their analogues play a significant role among other nitrogen and sulfur containing compounds used in syntheses of different heterocycles as pyrazoles,¹ 1,2,4-triazoles,² and 1,3,4-thiadiazoles¹ due to their accessibility and ability to act as bifunctional nucleophiles.³⁻¹⁰ Metal complexes of thiosemicarbazides display biological activities.¹¹⁻¹³

Thiosemicarbazides are derivatives of carbothioamides and contain several nucleophilic centers. They are also ideal candidates and valuable building blocks for the synthesis of different families of heterocyclic compounds.¹⁴⁻¹⁷ Many diseases such as cancer may be treated by using thiosemicarbazides and thus their development is still in progress.^{18,19}

It has been reported that 4-substituted thiosemicarbazides **1a-c** (Scheme 1) reacted with tetracyanoethylene (TCNE, **2**) in ethyl acetate with admission of air to give thiadiazepine and pyrazolothiadiazole derivatives as well as 3-amino-4,5-dicyanopyrazole.²⁰

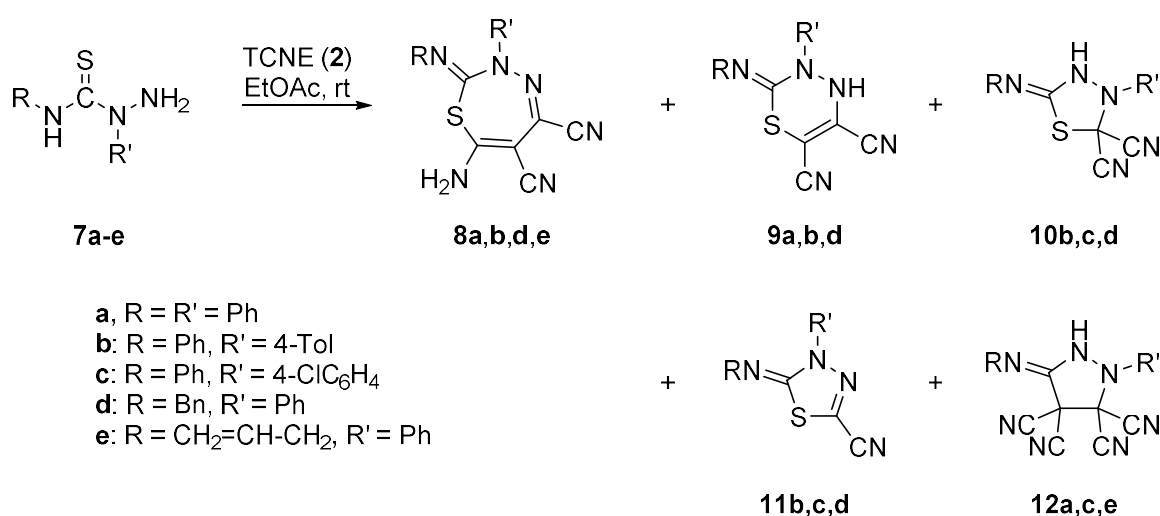


Scheme 1. Previously reported reactions of TCNE **2** with thiosemicarbazides **1**, **3** and **5**.

Upon mixing *N*-substituted-2-phenylhydrazinecarbothioamides **3a-c** with TCNE **2** mesoionic 1,2,4-triazolium-3-thiolate derivatives **4a-c** were observed (Scheme 1).²¹ The reaction of 2-substituted hydrazinecarbothioamides **5a-e** with TCNE **2** afforded 2{amino-[5-amino-2-(substituted diazenyl)thiazolyl]methylene}malonitrile **6a-e** (Scheme 1).²² This unique and variable reactivity shown in the three aforementioned examples warranted a more detailed investigation.

Results and Discussion

We investigated the behavior of other analogous 2,4-disubstituted thiosemicarbazides **7a-e** towards TCNE **2** (Scheme 2). Treatment of **7a-e** with two molar equivalents of TCNE **2** in ethyl acetate at room temperature resulted in a green coloration of the solution which later turned to dark brown. This behavior may be due to initial formation of unstable charge-transfer (CT) complexes followed by a chemical reaction. Monitoring of the reaction by visible spectroscopy failed since the reaction was fast and also at lower concentration no significant color changes were observed. Concentration of the preparative runs gave a precipitate which by washing with ethyl acetate yielded a yellowish brown solid of compounds **8**. The remaining soluble materials were subjected to preparative layer chromatography giving numerous colored zones, from which products **9-12** were isolated (Scheme 2).



Scheme 2. The products formed during the reaction of **7a-e** with TCNE **2**.

From their elemental composition and spectroscopic characteristics, these products can be regarded as resulting from 1:1 combinations of the starting materials **7a-e** and TCNE **2** with loss of one or two fragments giving rise to the gross compositions listed in Table 1 together with the eliminated fragments and the structural requirements as delineated from spectroscopic evidence.

Thiadiazepines 8a,b,d,e: The molecular ions in their EI-mass spectra support the molecular masses and the gross compositions. Further, the following common features of fragmentation patterns supported the assigned structures: Loss of C₅H₂N₄ giving intense (M⁺-118) ions, and loss of RN=C=S giving rise to the ion *m/z* 209 common in the spectra of compounds **8a,d,e**. The IR spectra show characteristic absorption for the NH₂ group in the ranges 3333 to 3170, and 2210-2220 for cyano groups and 1617-1625 cm⁻¹ for C=N. The ¹H NMR spectra show the presence of a NH₂ group by broad signals in the range 7.01-7.09 ppm for two protons, and for **8e**, the additionally expected signals for the allyl group at δ_H: 4.21-4.26, 5.07-5.16 and 5.86-5.93 ppm. ¹³C NMR spectra clearly support the absence of a C=S group in **8a,b,d,e** and the presence of an isothiourea carbon in the range from 165.81 to 166.78 ppm. In the ¹³C NMR spectrum of **8a**, thiadiazepine C-6 and C-7 resonate at δ_C = 108.12 and 158.24 ppm, respectively, in accordance with the observed trends in the δ values for C-atoms in push-pull alkenes.^{23,24}

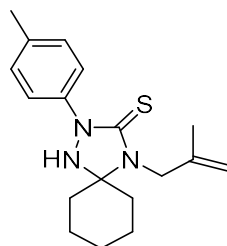
Table 1. Composition and essential features of products obtained by 1:1 combination of starting materials **7** ($RR'CH_3N_3S$) and TCNE **2** (C_6N_4) with elimination of low molecular weight fragments. For meanings of R, R' see Scheme 2

| Case | Gross composition | Fragments eliminated | Essential structural features from spectral data | Products |
|------|-------------------|----------------------------------|--|-----------------|
| A | $RR'C_6H_2N_6S$ | HCN | No C=S, two CN, no NH, one NH_2 , one C=NR | 8a,b,d,e |
| B | $RR'C_5HN_5S$ | Two HCN | No C=S, two CN, one NH, no NH_2 , one C=NR | 9a,b,d |
| C | $RR'C_4HN_5S$ | $C_3H_2N_2$ (malononitrile) | No C=S, two CN, one NH, no NH_2 , one C=NR | 10b,c,d |
| D | $RR'C_3N_4S$ | $C_4H_3N_3$ (malononitrile, HCN) | No C=S, one CN, no NH, no NH_2 , one C=NR | 11b,c,d |
| E | $RR'C_7HN_7$ | H_2S | No S, four CN, one NH, no NH_2 , one C=NR | 12a,c,e |

Dihydrothiazines 9a,b,d: Sharp IR absorptions are shown for cyano groups at 2212-2220 and a NH group at 3315-3336, a C=N group at 1626-1631 as well as for aryl ring stretchings at 1585-1592 cm^{-1} . The 1H NMR spectrum ($DMSO-d_6$) of **9d** clearly shows the presence of thiadiazine NH at δ_H 6.99 ppm and benzyl CH_2 at 4.91 ppm in addition to the phenyl protons (δ_H 7.15-7.68 ppm). In its ^{13}C NMR spectrum, thiadiazine C-2, C-5 and C-6 resonate at δ_C 164.91, 140.65 and 101.76 ppm, respectively. Further, peaks at 118.06-118.27 ppm for CN support the assigned structure. The presence of a Ph- CH_2 group is also evident from the ^{13}C DEPT-NMR spectrum exhibiting a negative signal at δ_C 53.66 ppm. The molecular formulas of compounds **9a,b,d** were supported by elemental analyses and mass spectra which showed the expected molecular ion peaks. For **9a** the EI-mass spectrum needs a brief comment: m/z 91 represent a C_4HN_3 fragment formed by release of $RN=C=S + RN$ from the molecular ion. Alternative structures could be ruled out according to the ^{13}C NMR spectra of **9a,b,d** since the thiadiazine C-5, C-6 are regularly downfield shifted [**9a** (C-5: 140.22, C-6: 101.16), **9b** (C-5: 140.56, C-6: 100.83), **9d** (C-5: 140.65, C-6: 100.76)]²⁵ compared to $=C(CN)_2$ (which would resonate in the range 61-74 ppm.

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1,3,4-Thiadiazolidines 10b,c,d: These compounds show a characteristically yellow color. The molecular structure of **10b** was supported by the following findings: The gross formula $C_{17}H_{13}N_5S$ represented a product from one molecule of thiosemicarbazide and one molecule of TCNE **2** with loss one molecule of malononitrile $CH_2(CN)_2$. The presence of two cyano groups at δ_C 117.92 and 118.48 ppm is documented, and a signal for thiadiazolidine C-5 at δ_C 162.92 as well as the absence of C=S favor structure **10b**. The 1H NMR spectrum of **10b** showed the presence of thiadiazolidine NH (δ_H 10.81 ppm) being due to conjugation with a π system or adjacent to a C=N double bond, whereas an isolated NH in a five membered ring like **18** has been reported to resonate at 4.5 pm.³⁰



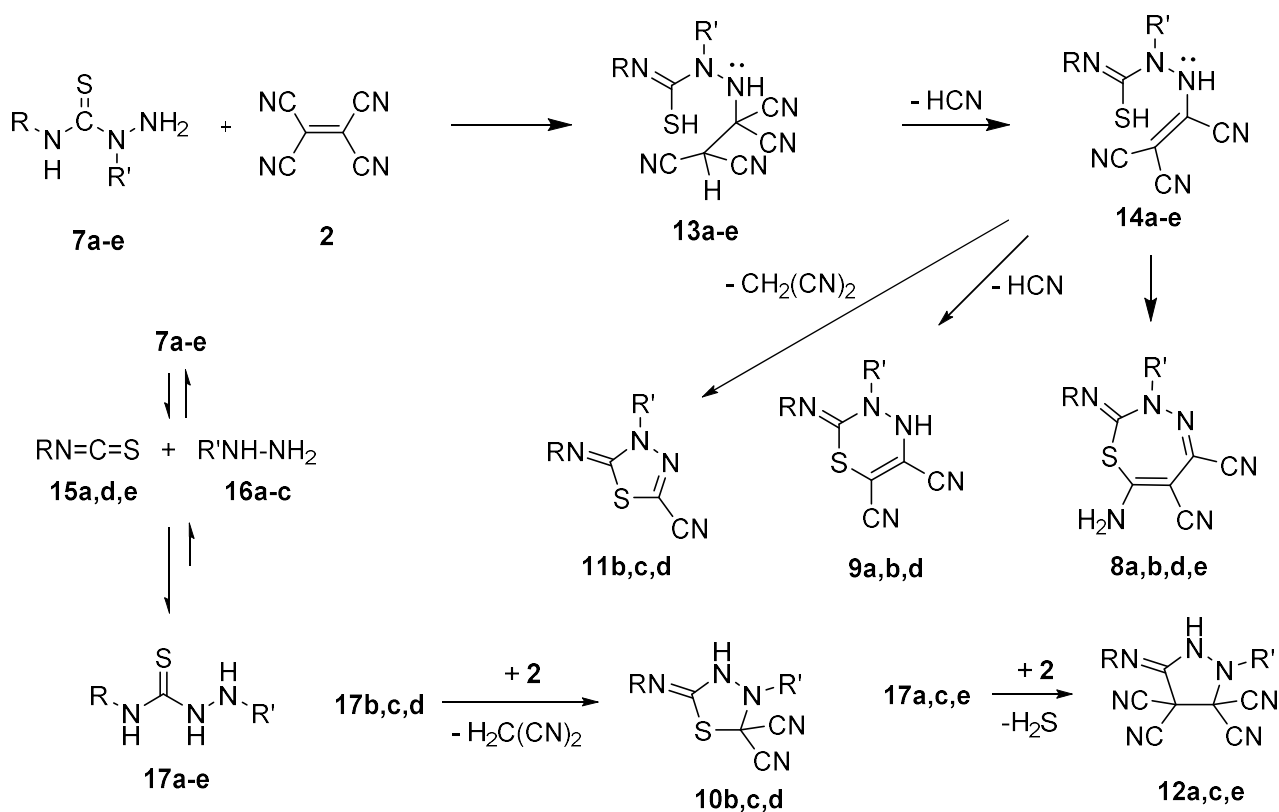
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In the ^{13}C NMR spectrum of **10b** the thiadiazolidine C-2 bearing two carbonitrile groups was observed at δ_c 66.17 ppm. The mass spectra of **10b,d** show a fragment at m/z 292 (representing the release of HCN from the molecular ions) whereas loss of $\text{RN}=\text{C}=\text{S}$ gives rise to fragments with m/z 157. Furthermore, treatment of **10b,c,d** with diluted alcoholic KOH followed by neutralization did not change the compounds to **11b,c,d** (see below) as expected. Therefore compounds **10** carry the R'-group at N-3 and not at N-4. This can be explained in the following way: 2,4-diarylthiosemicarbazides are known for their thermal instability relative to their constitutionally isomeric 1,4-diarylthiosemicarbazides³¹ and therefore it is likely that products **10** result from the latter rearranged starting materials. In addition, the rearrangement of **7** may be facilitated in the radical cationic stage of **7** inside the initial charge transfer complexes formed upon mixing the reactants **7** and TCNE **2** (see Scheme 3).

1,3,4-Thiadiazoles 11b,c,d: The ^1H NMR spectrum of **11b** clearly does not show any thiadiazole NH (neither isolated nor in conjugation with a $\text{C}=\text{N}$ bond). The ^{13}C NMR gave signals at 153.38 and 165.11 assigned to thiadiazole C-2 and C-5, respectively. The mass spectrum of compound **11b** exhibits a molecular ion peak at m/z 292 (28%). Analogous data was found for **11c,d**. There was no ^{13}C signal to indicate a $\text{C}=\text{S}$ bond.

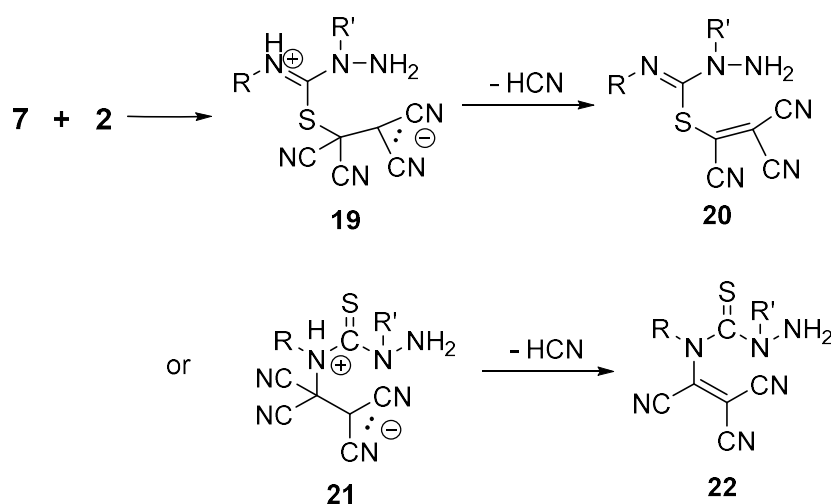
Pyrazolidines 12a,c,e: These compounds do not contain sulfur but each one contains seven N atoms, thus the molecular mass of **12e** represents a gross composition ($\text{C}_{16}\text{H}_{11}\text{N}_7$) reached from the rearranged 1,4-disubstituted isomer **17e** (see Scheme 3) and **2** after loss of H_2S . This was confirmed by the mass spectrometry (m/z 301, 100%, M^+). The IR spectrum showed bands at 2212 and 2215 cm^{-1} due to cyano groups, 3336 (NH) as well as 1627 ($\text{C}=\text{N}$). The ^1H NMR spectrum indicated the presence of broad band at (δ_{H} 11.32 ppm) due to the pyrazolidine NH conjugated to a $\text{C}=\text{N}$ bond. The ^1H NMR showed also the presence of an allyl group which gave rise to three multiplets centered at 4.25, 5.22–5.35 and 5.92–5.97 ppm due to allyl CH_2N , allyl $\text{CH}_2=$ and allyl $-\text{CH}=$, respectively. The presence of allyl group was also evident from the ^{13}C DEPT NMR spectrum exhibiting a positive signal at δ_c 135.13 (allyl $\text{CH}=$) and negative signals at 43.08 and 115.37 ppm due to allyl CH_2N and allyl $\text{CH}_2=$, respectively, further peaks at 116.85, 116.96, 117.08, 117.33 [$\text{C}(\text{CN})_2$].³²⁻³⁴ For data of the analogous compounds **12a,c** see the Experimental part.

Overview of product formation: A rationale for the formation of products **8-12** is presented in Scheme 3. Disubstituted thiosemicarbazides **7a-e** and TCNE **2** give the neutral adduct **13**. Elimination of a molecule of HCN from the adduct **13** generates the tricyanovinyl intermediate **14** which cyclizes to thiadiazepine derivatives **8**. Also the products **9** and **11** require the intermediate formation of **14**. Elimination of another molecule of HCN from the latter affords the thiadiazine derivatives **9**, whereas elimination of malononitrile from **14** gives rise to thiadiazole derivatives **11**.



Scheme 3. Rationale for formation of products **8-12**. For meanings of R and R' see Scheme 2.

In principle, one can discuss initial tricyanovinylolation products **20** and **22** originating from the primary adducts **19** and **21** from thiosemicarbazide **7** and TCNE **2** (Scheme 4) since products **11** may also be formed from **20** with loss of malononitrile, and adducts of **2** to N-4 of 1,4-disubstituted thiosemicarbazides have been discussed before.²¹



Scheme 4. Conceivable alternative adducts from the reaction of thiosemicarbazides **7a-e** with TCNE **2**. For meanings of R and R' see Scheme 2.

It has also been reported earlier in an investigation of the interaction of TCNE **2** with two 4-substituted thiosemicarbazides that the –SH group is the reactive center,³⁵ but the formation of the products **8,9** and **11** supported our rationalization via the involvement of the tricyanovinyl product **14** for at least these three compounds (Scheme 3).

As outlined there, the NH₂ group first attacks the double bond of **2** forming the products. Since, the reaction required multiple steps and by necessity moderate yields (see Table 2) have to be accepted and it will not be possible to clarify every detail. This needs to be taken into account when determining and evaluating yields (see Table 2).

Table 2. Yields of products formed according to Scheme 3

| | Starting materials | | Products and yields (%) | | | | | Total yield (%) |
|-----------|-------------------------------------|-----------------------------------|-------------------------|----------------|-----------------|-----------------|-----------------|-----------------|
| | R | R' | 8 | 9 | 10 | 11 | 12 | |
| 7a | Ph | Ph | 8a : 45 | 9a : 21 | | | 12a : 22 | 88 |
| 7b | Ph | 4-Tol | 8b : 39 | 9b : 22 | 10b : 14 | 11b : 16 | | 91 |
| 7c | Ph | 4-ClC ₆ H ₄ | | | 10c : 38 | 11c : 20 | 12c : 24 | 82 |
| 7d | Bn | Ph | 8d : 41 | 9d : 21 | 10d : 16 | 11d : 15 | | 93 |
| 7e | H ₂ C=CH-CH ₂ | Ph | 8e : 51 | | | | 12e : 28 | 79 |

Conclusions

The reactions and products presented provide insight into the spontaneous reactions between the electron-donating 2,4-disubstituted thiosemicarbazides **7a-e** and TCNE **2**. In fairly complex and multistep processes five types of heterocyclic products **8-12** are formed from **7a-e** and TCNE **2**. Consequently, TCNE **2** acts as a building block in heterocyclization of 2,4-disubstituted thiosemicarbazides.

Experimental Section

General. Melting points were determined using open glass capillaries on a Gallenkamp melting point apparatus and are uncorrected. The IR spectra were recorded with a Shimadzu 408 or a Bruker Vector 22 spectrometer using KBr pellets. ¹H 300 MHz and ¹³C NMR 75 MHz spectra, all in DMSO-*d*₆, have been registered using a Bruker WM 300 instrument, 500 MHz ¹H and 125 MHz ¹³C NMR spectra on a Bruker DRX 500 spectrometer. Chemical shifts are expressed as δ [ppm] with reference to tetramethylsilane as an internal standard, s = singlet, d = doublet, m = multiplet, br = broad, ¹³C assignments were made with the aid of DEPT 135/90 spectra. Mass spectra were obtained with an AMD 604 doubly focusing instrument using electron-impact ionization (70 eV). Elemental analyses were run by the microanalytical center, Cairo university. Preparative layer chromatography (plc) was made on 1.0 mm thick air-dried layers of slurry applied silica gel Merck PF₂₅₄ on 48 cm wide and 20 cm high glass plates, zones were detected by their color and indicator fluorescence quenching upon exposure to 254 nm light and extracted with acetone. Starting materials: 2,4-disubstituted thiosemicarbazides **7a-e** were prepared according to the literature³⁶ adapting Noto's procedure.³¹

Reaction of 2,4-disubstituted thiosemicarbazides 7a-e with 2. General procedure. A solution of 2,4-disubstituted thiosemicarbazide **7a-e** (1.0 mmol) in dry ethyl acetate (30 mL) was added dropwise with stirring at room temperature to a solution of **2** (2.0 mmol) in ethyl acetate (20 mL). The color changed gradually from green to brown. Stirring was continued for 48 h with admission of air to complete the reaction. The reaction mixture was filtered and the precipitate was washed several times with cold ethyl acetate until the washing remained colorless. The precipitate was dried and recrystallized from ethanol to give thiadiazepine derivatives **8a,b,d,e**. The filtrate was concentrated to dryness and the residue was kept at 80 °C under vacuum to sublime off all unreacted TCNE **2**. The residue was then separated by plc (100 mg per plate) using a suitable solvent mixture as eluent (c-hexane/ethyl acetate 5:1 for the reactions of **2** with **7a**, **7c** and **7e**, c-hexane/ethyl acetate 3:1 for the reactions of **2** with **7b** and **7d**) to give numerous colored zones, the intense of which were removed and extracted. The fastest migrating zone contained the thiadiazoles **11b,c,d**, the second zone contained the thiadiazolidines **10b,c,d**, the third characteristically yellow zone contained the thiadiazine derivatives **9a,b,d**, and finally the slowest migrating zone contained the pyrazolidine derivatives **12a,c,e**. Extraction of zones with acetone gave residues, which were rechromatographed to separate the pure compounds.

7-Amino-3-phenyl-2-(phenylimino)-2,3-dihydro-1,3,4-thiadiazepine-5,6-dicarbonitrile (8a). Yellow crystals (310 mg, 45%), mp 274-276 °C (EtOH). IR ($\tilde{\nu}/\text{cm}^{-1}$): 3310-3170 (NH_2), 2215 ($\text{C}\equiv\text{N}$), 1617 ($\text{C}=\text{N}$), 1590 (phenyl ring stretching). ^1H NMR (300 MHz): δ_{H} 7.05 (2H, br, NH_2), 7.12-7.68 (10H, m, 2Ph). ^{13}C NMR (75 MHz): δ_{C} 108.12 (thiadiazepine C_6), 116.69, 117.22 ($\text{C}\equiv\text{N}$), 127, 37, 128.12, 128.62, 129.00, 129.48 (Ar CH), 138.16, 144.55 (Ar C), 151.52 (C-5), 158.29 (C-7), 166.78 (C-2). MS: m/z (%) 344 (M^+ , 100), 209 ($\text{M}^+ - \text{PhN}=\text{C}=\text{S}$, 16), 118 (34), 91 (26), 77 (47), 66 (21). Anal. calcd for $\text{C}_{18}\text{H}_{12}\text{N}_6\text{S}$ (344.39): C, 62.77; H, 3.51; N, 24.40; S, 9.31. Found: C, 62.59; H, 3.67; N, 24.33; S, 9.19.

7-Amino-2-(phenylimino)-3-*p*-tolyl-2,3-dihydro-1,3,4-thiadiazepine-5,6-dicarbonitrile (8b). Yellow crystals (280 mg, 39%), mp 282-284 °C (MeCN). IR ($\tilde{\nu}/\text{cm}^{-1}$): 3333-3185 (NH_2), 2220 ($\text{C}\equiv\text{N}$), 1622 ($\text{C}=\text{N}$), 1605 (phenyl ring stretching). ^1H NMR (500 MHz): δ_{H} 2.27 (s, 3 H, CH_3), 7.01 (2H, br, NH_2), 7.22-7.76 (9H, m, Ar CH). ^{13}C NMR (125 MHz): δ_{C} 22.41 (CH_3), 106.94 (thiadiazepine C_6), 117.18, 117.39 ($\text{C}\equiv\text{N}$), 126.83, 127.57, 127.88, 128.82, 129.65 (Ar CH), 137.25, 146.22 (Ar C), 150.96 (C-5), 159.12 (C-7), 166.66 (C-2). MS: m/z (%) 358 (M^+ , 100), 223 (24), 118 (29), 91 (37), 77 (32), 66(41). Anal. calcd for $\text{C}_{19}\text{H}_{14}\text{N}_6\text{S}$ (358.42): C, 63.67; H, 3.94; N, 23.45; S, 8.95. Found: C, 63.79; H, 4.12; N, 23.28; S, 9.14.

7-Amino-2-(benzylimino)-3-phenyl-2,3-dihydro-1,3,4-thiadiazepine-5,6-dicarbonitrile (8d). Dark yellow crystals (294 mg, 41%), mp 227-229 °C (MeCN). IR ($\tilde{\nu}/\text{cm}^{-1}$): 3325-3210 (NH_2), 2210 ($\text{C}\equiv\text{N}$), 1625 ($\text{C}=\text{N}$), 1590 (phenyl ring stretching). ^1H NMR (300 MHz): δ_{H} 4.92 (2H, s, CH_2), 7.09 (2H, br, NH_2), 7.17-7.58 (5H, m, Ar H). ^{13}C NMR (75 MHz): δ_{C} 51.12 (CH_2), 107.86 (C-6), 116.84, 117.05 ($\text{C}\equiv\text{N}$), 127.17, 127.63, 128.12, 129.22, 129.76 (Ar CH), 134.12, 139.16 (Ar C), 152.11 (C-5), 158.73 (C-7), 165.94 (C-2). MS: m/z (%) 358 (M^+ , 64), 209 (22), 118 (15), 91 (100), 77 (57), 66 (51). Anal. calcd for $\text{C}_{19}\text{H}_{14}\text{N}_6\text{S}$ (358.42): C, 63.67; H, 3.94; N, 23.45; S, 8.95. Found: C, 63.51; H, 3.86; N, 23.62; S, 8.77.

2-(Allylimino)-7-amino-3-phenyl-2,3-dihydro-1,3,4-thiadiazepine-5,6-dicarbonitrile (8e). Pale yellow crystals (314 mg, 51%). mp 174-176 °C (EtOH). IR ($\tilde{\nu}/\text{cm}^{-1}$): 3310-3240 (NH_2), 2215 ($\text{C}\equiv\text{N}$), 1620 ($\text{C}=\text{N}$), 1585 (phenyl ring stretching). ^1H NMR (300 MHz): δ_{H} 4.21-4.26 (2H, br, allyl CH_2N), 5.07-5.16 (2H, m, allyl $\text{CH}_2=$), 5.86-5.93 (1H, m, allyl $\text{CH}=\text{}$), 7.05 (2H, br, NH_2), 7.32-7.51 (m, SH, Ar H). ^{13}C NMR (75 MHz): δ_{C} 44.17 (allyl CH_2N), 108.12 (C-6), 115.76 (allyl $\text{CH}_2=$), 116.91, 117.53 ($\text{C}\equiv\text{N}$), 127.63, 128.56, 129.16 (Ar CH), 135.26 (allyl $\text{CH}=\text{}$), 137.65 (Ar C), 151.82 (C-2), 159.12 (C-7), 165.81 (C-2). MS: m/z (%) 308 (M^+ , 57), 209 (29), 118 (36), 91 (74), 77 (100), 66 (46). Anal. calcd for $\text{C}_{15}\text{H}_{12}\text{N}_6\text{S}$ (308.36): C, 58.43; H, 3.92; N, 27.25; S, 10.40. Found: C, 58.61; H, 4.09; N, 27.11; S, 10.23.

3-Phenyl-2-(phenylimino)-3,4-dihydro-2H-1,3,4-thiadiazine-5,6-dicarbonitrile (9a). Orange crystals (133 mg, 21%), mp 210-212 °C (MeCN). IR ($\tilde{\nu}/\text{cm}^{-1}$): 3326 (NH), 2216, 2220 ($\text{C}\equiv\text{N}$), 1625 ($\text{C}=\text{N}$), 1585 (phenyl ring stretching). ^1H NMR (300 MHz): δ_{H} 6.98 (1H, br, NH), 7.26-7.82 (10H, m, Ar H). ^{13}C NMR (75 MHz): δ_{C} 101.16 (C-6), 118.12, 118.43 ($\text{C}\equiv\text{N}$), 127.51, 127.82, 128.11, 129.37, 129.75, 129.94 (Ar CH), 134.89, 147.88 (Ar C), 140.22 (C-5), 165.33 (C-2). MS: m/z (%) 317 (M^+ , 18), 226 (11), 211 (83), 182 (67), 135 (35), 105 (41), 77 (100), 76 (71), 65 (31). Anal. calcd for $\text{C}_{17}\text{H}_{11}\text{N}_5\text{S}$ (317.37): C, 64.34; H, 3.49; N, 22.07; S, 10.10. Found: C, 64.16; H, 3.64; N, 21.93; S, 9.94.

2-(Phenylimino)-3-*p*-tolyl-3,4-dihydro-2H-1,3,4-thiadiazine-5,6-dicarbonitrile (9b). Reddish orange crystals (139 mg, 22%), mp 235-237 °C (MeCN). IR ($\tilde{\nu}/\text{cm}^{-1}$): 3315 (NH), 2218 ($\text{C}\equiv\text{N}$), 1631 ($\text{C}=\text{N}$), 1592 (phenyl ring stretching). ^1H NMR (300 MHz): δ_{H} 2.31 (3H, s, CH_3), 7.0 (1H, br, NH), 7.22-7.75 (9H, m, Ar H). ^{13}C NMR (75 MHz): δ_{C} 20.75 (CH_3), 100.83 (C-6), 117.97, 118.73 ($\text{C}\equiv\text{N}$), 127.36, 128.21, 129.64, 129.97, 130.12 (Ar CH), 134.2, 135.27, 147.67 (Ar C), 140.56 (C-5), 165.11 (C-2). MS: m/z (%) 331 (M^+ , 12), 226 (26), 196 (57), 135 (46), 119 (64), 91 (100), 77 (72), 76 (65). Anal. calcd for $\text{C}_{18}\text{H}_{13}\text{N}_5\text{S}$ (331.39): C, 65.24; H, 3.95; N, 21.13; S, 9.68. Found: C, 65.24; H, 4.11; N, 20.95; S, 9.84.

2-(Benzylimino)-3-phenyl-3,4-dihydro-2H-1,3,4-thiadiazine-5,6-dicarbonitrile (9d). Pale orange crystals (140 mg, 21%), mp 201-202 °C (MeCN). IR ($\tilde{\nu}/\text{cm}^{-1}$): 3336 (NH), 2212 ($\text{C}\equiv\text{N}$), 1628 ($\text{C}=\text{N}$), 1590 (phenyl ring stretching). ^1H NMR (300 MHz): δ_{H} 4.91 (2H, s, CH_2), 6.99 (1H, br, NH), 7.15-7.68 (5H, m, Ar H). ^{13}C NMR (75 MHz): δ_{C} 53.66 (CH_2), 100.76 (C-6), 118.06, 118.27 ($\text{C}\equiv\text{N}$), 127.43, 127.77, 128.06, 128.84, 129.25, 129.82 (Ar CH), 135.71, 137.77 (Ar C), 140.65 (C-5), 164.91 (C-2). MS: m/z (%) 331 (M^+ , 29), 226 (17), 182 (41), 149 (66), 91 (100), 77 (75), 76 (84). Anal. calcd for $\text{C}_{18}\text{H}_{13}\text{N}_5\text{S}$ (331.39): C, 65.24; H, 3.95; N, 21.13; S, 9.68. Found: C, 65.39; H, 4.09; N, 21.28; S, 9.52.

5-(Phenylimino)-4-*p*-tolyl-1,3,4-thiadiazolidine-2,2-dicarbonitrile (10b). Yellow crystals (89 mg, 14%), mp 177-178 °C (MeOH). IR ($\tilde{\nu}/\text{cm}^{-1}$): 3423 (NH), 2210 ($\text{C}\equiv\text{N}$), 1625 ($\text{C}=\text{N}$), 1580 (phenyl ring stretching). ^1H NMR (500 MHz): δ_{H} 2.28 (3H, s, CH_3), 6.95-7.63 (9H, m, Ar H), 10.81 (1H, br, thiadiazolidine NH). ^{13}C NMR (125 MHz): δ_{C} 21.46 (CH_3), 66.17 (C-2), 117.92, 118.48 ($\text{C}\equiv\text{N}$), 127.86, 128.21, 128.65, 129.43, 130.12 (Ar CH), 136.02, 138.12, 148.50 (Ar C), 162.92 (C-5). MS: m/z (%) 319 (M^+ , 17), 292 (61), 184 (42), 157 (38), 135 (39), 105 (100), 77 (83), 66 (69). Anal. calcd for $\text{C}_{17}\text{H}_{13}\text{N}_5\text{S}$ (319.38): C, 63.93; H, 4.10; N, 21.93; S, 10.04.

Found: C, 64.14; H, 3.96; N, 22.12; S, 9.89.

4-(4-Chlorophenyl)-5-(phenylimino)-1,3,4-thiadiazolidine-2,2-dicarbonitrile (10c). Pale yellow crystals (264 mg, 38%), mp 185-186 °C (MeCN). IR ($\tilde{\nu}/\text{cm}^{-1}$): 3394 (NH), 2216 ($\text{C}\equiv\text{N}$), 1615 ($\text{C}=\text{N}$), 1588 (phenyl ring stretching). ^1H NMR (300 MHz): δ_{H} 7.06-7.65 (9H, m, Ar H), 10.85 (1H, br, thiadiazolidine NH). ^{13}C NMR (75 MHz): δ_{C} 65.64 (C-2), 117.84, 118.26 ($\text{C}\equiv\text{N}$), 127.79, 128.06, 128.45, 129.48, 129.93 (Ar CH), 134.86, 137.92, 148.38 (Ar C), 163.12 (C-5). MS: m/z (%) 339/341 (M^+ , 51), 312 (36), 204 (16), 177 (21), 135 (56), 112 (38), 77 (100). Anal. calcd for $\text{C}_{16}\text{H}_{10}\text{ClN}_5\text{S}$ (339.80): C, 56.55; H, 2.97; Cl, 10.43; N, 20.6; S, 9.44. Found: C, 56.73; H, 3.12; Cl, 10.26; N, 20.78; S, 9.61.

5-(Benzylimino)-4-phenyl-1,3,4-thiadiazolidine-2,2-dicarbonitrile (10d). Yellow crystals (102 mg, 16%), mp 160-161 °C (MeCN). IR ($\tilde{\nu}/\text{cm}^{-1}$): 3418 (NH), 2210 ($\text{C}\equiv\text{N}$), 1625 ($\text{C}=\text{N}$), 1595 (phenyl ring stretching). ^1H NMR (300 MHz): δ_{H} 4.95 (2H, s, CH_2), 6.98-7.61 (10H, m, Ar H), 10.90 (1H, br, thiadiazolidine NH). ^{13}C NMR (75 MHz): δ_{C} 54.83 (CH_2), 66.14 (C-2), 117.92, 118.37 ($\text{C}\equiv\text{N}$), 127.86, 128.12, 128.53, 129.51, 130.07 (Ar CH), 135.12, 138.11, 148.26 (Ar C), 162.95 (C-5). MS: m/z (%) 319 (M^+ , 46), 292 (23), 157 (31), 170 (36), 149 (44), 91 (100), 77(81), 66 (46). Anal. calcd for $\text{C}_{17}\text{H}_{13}\text{N}_5\text{S}$ (319.38): C, 63.93; H, 4.10; N, 21.93; S, 10.04. Found: C, 64.14; H, 3.97; N, 22.14; S, 9.89.

5-(Phenylimino)-4-*p*-tolyl-4,5-dihydro-1,3,4-thiadiazole-2-carbonitrile (11b). Yellowish orange crystals (93 mg, 16%), mp 155-156 °C (MeCN). IR ($\tilde{\nu}/\text{cm}^{-1}$): 3095 (Ar CH), 2925 (aliph CH), 2215 ($\text{C}\equiv\text{N}$), 1630 ($\text{C}=\text{N}$), 1590 (phenyl

ring stretching). ^1H NMR (300 MHz): δ_{H} 2.28 (3H, s, CH_3), 7.35-7.95 (9H, m, Ar H). ^{13}C NMR (75 MHz): δ_{C} 21.23 (CH_3), 117.87 ($\text{C}\equiv\text{N}$), 127.12, 128.36, 128.57, 129.00, 129.98 (Ar CH), 136.17, 147.77 (Ar C), 153.38 (C-2), 165.11 (C-5). MS: m/z (%) 292 (M^+ , 28), 240 (10), 105 (27), 91 (100), 77 (38), 65 (41), 52 (16). Anal. calcd for $\text{C}_{16}\text{H}_{12}\text{N}_4\text{S}$ (292.36): C, 65.73; H, 4.14; N, 19.16; S, 10.97. Found C, 65.57, H, 4.03, N, 18.98; S, 11.11.

4-(4-Chlorophenyl)-5-(phenylimino)-4,5-dihydro-1,3,4-thiadiazole-2-carbonitrile (11c). Yellowish brown crystals (125 mg, 20%), mp 162-163 °C (EtOH). IR ($\tilde{\nu}/\text{cm}^{-1}$): 3105 (Ar CH), 2220 ($\text{C}\equiv\text{N}$), 1620 ($\text{C}=\text{N}$), 1593 (phenyl ring stretching). ^1H NMR (300 MHz): δ_{H} 7.45-8.10 (9H, m, Ar CH). ^{13}C NMR (75 MHz): δ_{C} 118.11 ($\text{C}\equiv\text{N}$), 126.94, 127.67, 128.42, 128.96, 129.66 (Ar CH), 136.89, 148.12 (Ar-Cl), 153.56 (C-2), 164.82 (C-5). MS: m/z (%) 314/312 (M^+ , 100), 260 (9), 125 (34), 91 (18), 77 (28), 51 (19). Anal. calcd for $\text{C}_{15}\text{H}_9\text{ClN}_4\text{S}$ (312.78): C, 57.60; H, 2.90; Cl, 11.33; N, 17.91; S, 10.25. Found C, 57.42; H, 3.06; Cl, 11.49; N, 18.10; S, 10.12.

5-(Benzylimino)-4-phenyl-4,5-dihydro-1,3,4-thiadiazol-2-carbonitrile (11d). Yellowish brown crystals (88 mg, 15%), mp 144-145 °C (EtOH). IR ($\tilde{\nu}/\text{cm}^{-1}$): 3125 (Ar CH), 2218 ($\text{C}\equiv\text{N}$), 1633 ($\text{C}=\text{N}$), 1587 (phenyl ring stretching). ^1H NMR (300 MHz): δ_{H} 4.95 (2H, s, CH_2), 7.25-8.0 (10H, m, Ar H). ^{13}C NMR (75 MHz): δ_{C} 53.69 (CH_2), 118.24 ($\text{C}\equiv\text{N}$), 127.13, 127.81, 128.36, 128.86, 129.46, 129.73 (Ar CH), 136.66, 138.84 (Ar C), 153.39 (C-2), 155.36 (C-5). MS: m/z (%) 292 (M^+ , 29), 240 (8), 115 (24), 91 (83), 77 (100), 65 (41), 52 (27). Anal. calcd for $\text{C}_{16}\text{H}_{12}\text{N}_4\text{S}$ (292.36): C, 65.73; H, 4.14; N, 19.16; S, 10.97. Found: C, 65.88; H, 4.04; N, 18.97; S, 11.14.

1-Phenyl-5-(phenylimino) pyrazolidine-3,3,4,4-tetracarbonitrile (12a). Pale brown crystals (148 mg, 22%), mp 294-296 °C (MeOH). IR ($\tilde{\nu}/\text{cm}^{-1}$): 3311 (NH), 2218 ($\text{C}\equiv\text{N}$), 1615 ($\text{C}=\text{N}$), 1590 (phenyl ring stretching). ^1H NMR (300 MHz): δ_{H} 7.22-7.83 (10H, m, Ar H), 11-12 (1H, br, pyrazolidine NH). ^{13}C NMR (75 MHz): δ_{C} 31.41 (C-4), 55.12 (C-3), 116.81, 116.94, 117.12, 117.39 ($\text{C}\equiv\text{N}$), 126.93, 128.18, 128.34, 129.21, 129.54, 129.91 (Ar CH), 137.14, 149.12 (Ar C), 161.16 (C-5). MS: m/z (%) 337 (M^+ , 41), 285 (100), 258 (24), 232 (8), 91 (74), 77 (85), 52 (43). Anal. calcd for $\text{C}_{19}\text{H}_{11}\text{N}_7$ (337.34): C, 67.65; H, 3.29; N, 29.06. Found, C, 67.86; H, 3.14; N, 28.89.

1-(4-Chlorophenyl)-5-(phenylimino)pyrazolidine-3,3,4,4-tetracarbonitrile (12c). Yellowish brown crystals (178 mg, 24%), mp 314-316 °C (MeCN). IR ($\tilde{\nu}/\text{cm}^{-1}$): 3325 (NH), 2220 ($\text{C}\equiv\text{N}$), 1620 ($\text{C}=\text{N}$), 1588 (phenyl ring stretching). ^1H NMR (500 MHz): δ_{H} 7.19-7.72 (9H, m, 9 H, Ar H), 11.37 (1H, br, pyrazolidine NH). ^{13}C NMR (125 MHz): δ_{C} 31.56 (C-4), 54.87 (C-3), 116.87, 116.97, 117.09, 117.28 ($\text{C}\equiv\text{N}$), 126.88, 127.91, 128.42, 129.18, 129.86 (Ar CH), 130.12, 135.16, 149.22 (Ar C), 161.55 (C-5). MS: m/z (%) 371/373 (M^+ , 26), 319 (47), 292 (17), 266 (6), 91 (100), 77 (87), 65 (63). Anal. calcd for $\text{C}_{19}\text{H}_{10}\text{ClN}_7$ (371.78): C, 61.38; H, 2.71; Cl, 9.54; N, 26.37. Found C, 61.55; H, 2.63; Cl, 9.41; N, 26.54.

5-(Allylimino)-1-phenylpyrazolidine-3,3,4,4-tetracarbonitrile (12e). Yellowish brown crystals (169 mg, 28%), mp 281-283 °C (EtOH). IR ($\tilde{\nu}/\text{cm}^{-1}$): 3336 (NH), 3086 (Ar CH), 2985 (aliph. CH), 2212, 2215 ($\text{C}\equiv\text{N}$), 1677 ($\text{C}=\text{N}$), 1580 (phenyl ring stretching). ^1H NMR (500 MHz): δ_{H} 4.28 (2H, br, allyl CH_2N), 5.22-5.35 (2H, m, allyl $\text{CH}_2=$), 5.92-5.97 (1H, m, allyl $\text{CH}=\text{}$), 7.21-7.82 (5H, m, Ar H), 11.32 (1H, br, pyrazolidine NH). ^{13}C NMR (125 MHz): δ_{C} 31.58 (C-4), 43.08 (allyl CH_2N), 54-75 (C-3), 115.37 (allyl $\text{CH}_2=$), 116.85, 116.96, 117.08, 117.33 ($\text{C}\equiv\text{N}$), 127.16, 127.96, 129.57 (Ar CH), 135.13 (allyl $\text{CH}=\text{}$), 135.98 (Ar C), 161.63 (C-5). MS: m/z (%) 301 (M^+ , 100), 249 (97), 158 (31), 77 (36), 41 (90). Anal. calcd for $\text{C}_{16}\text{H}_{11}\text{N}_7$ (301.31): C, 63.78; H, 3.66; N, 32.54. Found C, 63.92; H, 3.53; N, 32.42.

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