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Reactions with Tetracyanoethene: Synthesis of Some New Pyrazoline, Oxadiazine, Pyrrole and Thiazolylpyrrole Derivatives

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ABSTRACT. A number of pyrazoline, oxadiazine, pyrrole and thiazolylpyrrole derivatives were synthesised *via* the reactions of tetracyanoethene with hydrazonoyl chlorides, amides and 2-cyanomethyl-2-thiazolin-4-one. The structures of the newly synthesised heterocycles were established on the basis of elemental analysis, spectroscopic data as well as synthesis via other routes.

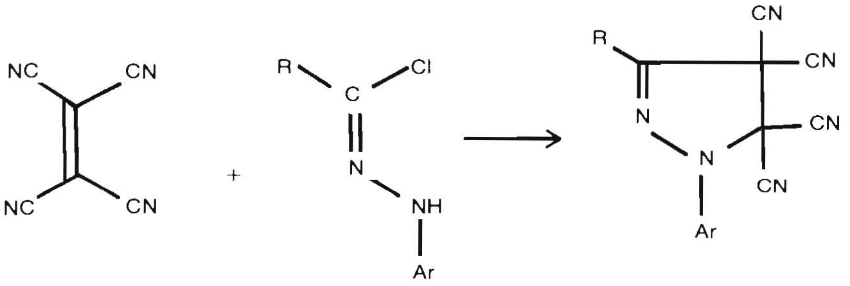
Tetracyanoethene (1) is a versatile reagent which has been extensively utilized in the synthesis of heterocyclic derivatives (Fatiadi 1983, 1986). In continuation of our program directed towards the use of activated nitriles in heterocyclic synthesis, (Abdel Galil *et al.* 1987, 1988), we report here on the reaction of tetracyanoethene with a variety of hydrazonoyl chlorides, cyanoacetamide, cyanothioacetamide, cyanoacetanilide, cyanothioacetanilide and 2-cyanomethyl-2-thiazolin-4-one. The reactions resulted in the synthesis of several pyrrole, pyrazole, oxadiazine and thiazolylpyrrole derivatives bearing latent functional substituents which appear promising for both biological activity studies as well as for further chemical transformations.

Results and Discussion

Thus, 1 reacted with N-phenylbenzhydrazonoyl chloride (2a) in benzene in the presence of triethylamine to yield the cycloadduct of molecular formula $C_{19}H_{10}N_6$ ($M^{+\cdot} = 322$). The pyrazoline structure 3a could be assigned for the reaction product based on elemental analysis and IR and ^{1}H-NMRspectral data (Table 2). Moreover, in the ^{13}C-NMR spectrum, 3a revealed three characteristic signals assignable to C-3 (δ 155.9), C-4 (δ 40.2) and C-5 (δ 61.5) respectively, as well as four signals (113.8, 114.0, 115.4, 116.1) for the CN carbons and eight signals (127.2-136.3) for the phenyl carbons, supporting the given 3-phenyl-$\triangle^2$-pyrazoline structure (Breitmaier and Voelter 1978, Johnson and Jankowsky 1972).

In a similar manner, the hydrazonoyl chlorides 2b-d reacted with 1 to give the corresponding cycloadducts 3b-d. Their structures were assigned on the same backgrounds as for 3a (cf. Experimental part). On the other hand, trials to conduct the reaction under practically the same experimental conditions utilizing the hydrazonoyl chlorides 2e,f were unsuccessful and led to the formation of the corresponding tetrazines (Shawali and Fahmi 1977, Hassaneen *et al.* 1984) as the only isolable products. This behaviour might be attributed to the strong electron-withdrawing nature of the arylsulfonyl group in 2e,f (Ito *et al.* 1976).

Moreover it has been found that 1reacted with N-benzoylphenylhydrazine (4) in ethanol in the presence of a catalytic amount of triethylamine to yield a product which could be formulated as the 5-imino-1,3,4-oxadiazine derivative 6 ($M^{+\cdot} = 313$) (cf. chart 2). The structure 6 was established using elemental and spectral studies. The reaction leading to 6 is assumed to proceed via the formation of the intermediate acyclic tricyanovinyl derivative 5 which subsequently cyclizes via HCN elimination under the applied reaction conditions to yield the final isolable product 6. The conversion of 6 into the corresponding 1,3,4-oxadiazin-5-one derivative 7 was achieved by boiling its ethanolic solution with hydrochloric acid (cf. chart 2).



1

3a-d

2a , R = C_6H_5, Ar = C_6H_5
b , R = C_2H_5OOC, Ar = C_6H_5
c , R = C_2H_5OOC, Ar = $C_6H_4-CH_3-P$
d , R = CH_3CO, Ar = $C_6H_4-CH_3-P$
e , R = C_6H_5, Ar = $SO_2-C_6H_5$
g , R = C_6H_5, Ar = $SO_2-C_{10}H_7$

Chart 1

The study was also extended to investigate the behaviour of 1 towards the action of some amide, anilide and thiazolinone derivatives. Thus, 1 reacted with cyanoacetamide (8a) in ethanol in the presence of triethylamine to afford a product of molecular formula $C_6H_2N_4O$ ($M^{+\cdot} = 146$) resulting from the addition of one mole of 8a to one mole of 1 to yield the acyclic Michael adduct 9a followed by the loss of one mole of malononitrile to yield 10 which cyclized under the applied reaction conditions to give the final reaction product which could be formulated as the pyrrole derivative 11a based on elemental and spectral data (cf. chart 3).

Similar to its behaviour towards 8a, compound 1 reacted with cyanothioacetamide 8b to afford the pyrrolethione derivative 11b (cf. chart 3). On the other hand, non-identifiable products could be isolated by treating 1 with cyanoacetanilide or cyanothioacetanilide. In addition, compound 1 reacted with 2-cyanomethyl-2-thiazolin-4-one (12) in ethanol in the presence of triethylamine to yield a product of molecular formula $C_{11}H_4N_6OS$ ($M^{+\cdot} = 268$). Three possible isomeric structures (13–15) could be considered for the reaction product (cf. chart 4). Structure 13 was readily ruled out based on the fact that the reaction product exhibit NH_2 absorption peaks in its IR spectrum. The thiazolylpyrrole structure 15 was considered for the reaction product based on identity of the reaction product with compound 15 prepared by the reaction of 12 and the pyrrole derivative 11 in ethanol in the presence of triethylamine (cf. chart 4).

Experimental

All m.p.'s are uncorrected. The IR spectra (KBr) were recorded on a Pye Unicam SP-1000 spectrophotometer. ^1H NMR spectra were obtained in $(CD_3)_2SO$ with a Bruker WM 300 spectrometer with $SiMe_4$ as internal standard and chemical shifts expressed as δ values. Mass spectra were recorded on MS 30 and MS 9 (AEI) spectrometers 70 eV. ^{13}C NMR spectra were recorded at the Institut für Organische Chemie und Biochemie, Universität Bonn, West Germany. Microanalytical data were performed by the Microanalytical Centre at Cairo University.

General procedure for the reaction of 1 with 2a-f

A suspension of 1 (0.01 mole) in dry benzene (50 ml) was treated with an equimolar amount of the appropriate hydrazonoyl chlorides and then triethylamine (1 ml) was added. The reaction mixture was refluxed for 1 h, and the triethylamine hydrochloride was filtered. Removal of the solvent followed by the addition of absolute ethanol (10 ml) gave solids which crystallized from ethanol (cf. Table 1).

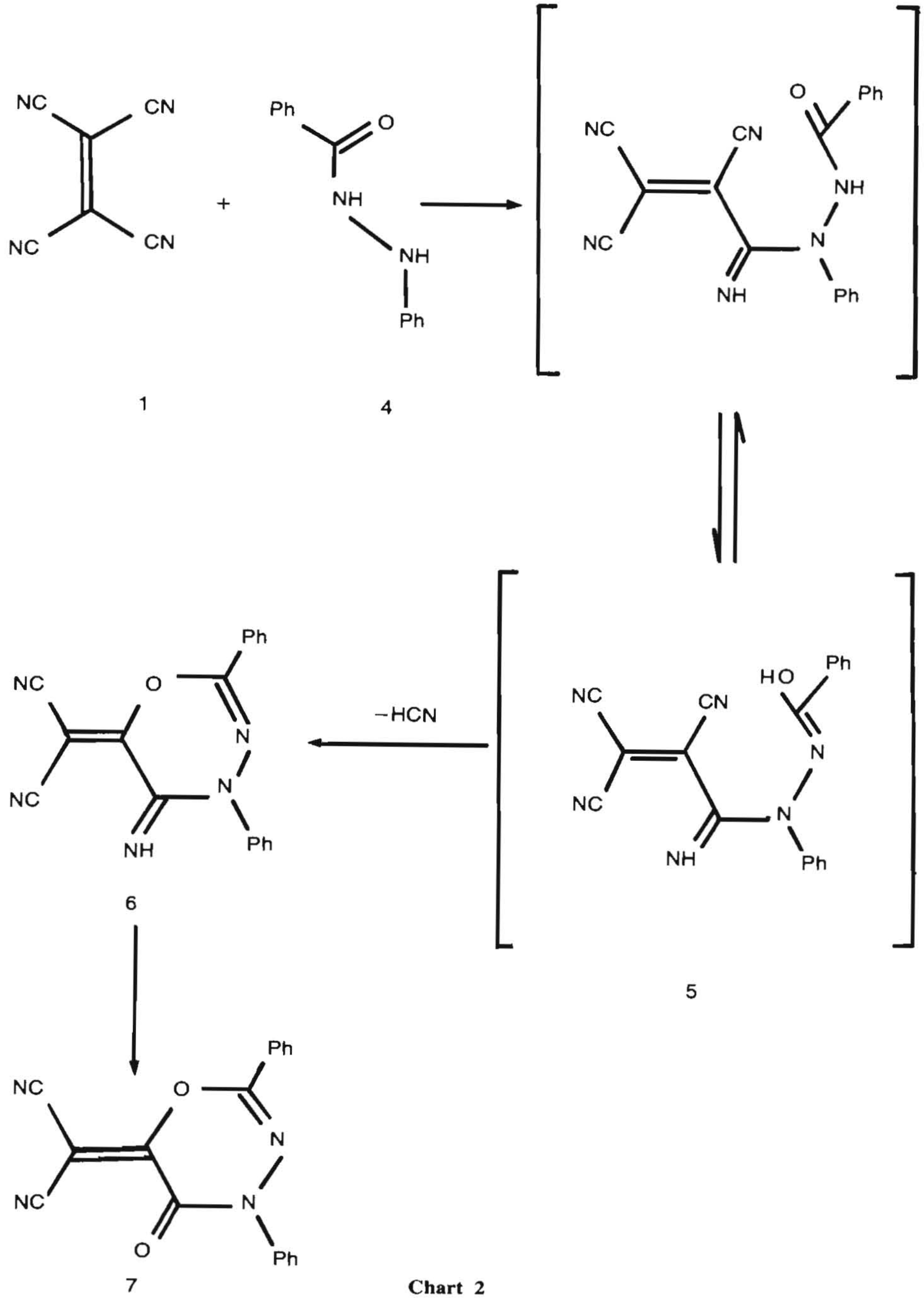


Chart 2

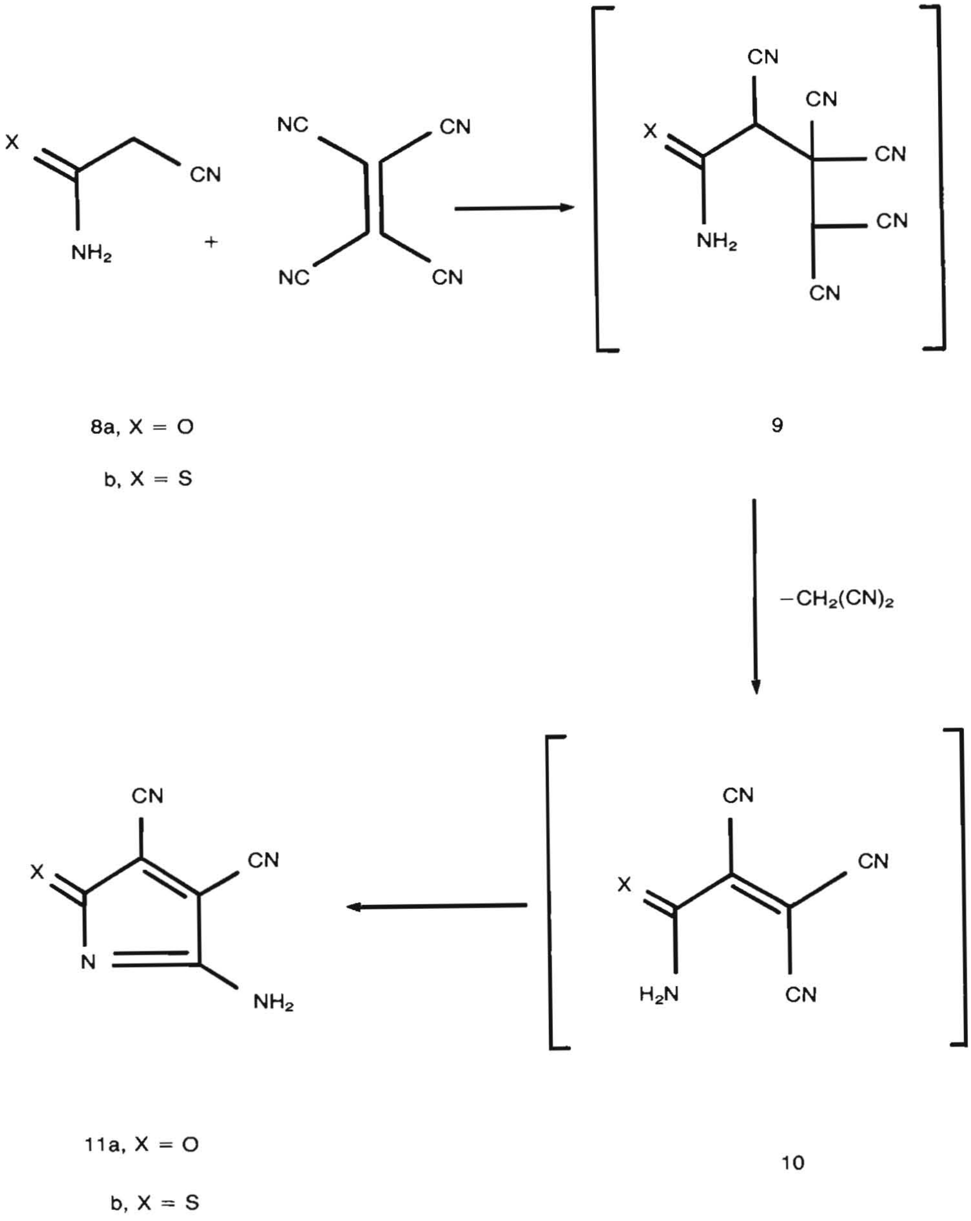

X
CN
NH₂
+
NC
CN
NC
CN
X
CN
CN
CN
CN
NH₂
CN
8a, X = O
b, X = S
9
−CH₂(CN)₂
CN
X
CN
NH₂
N
CN
X
CN
H₂N
CN
11a, X = O
b, X = S
10

Chart 3

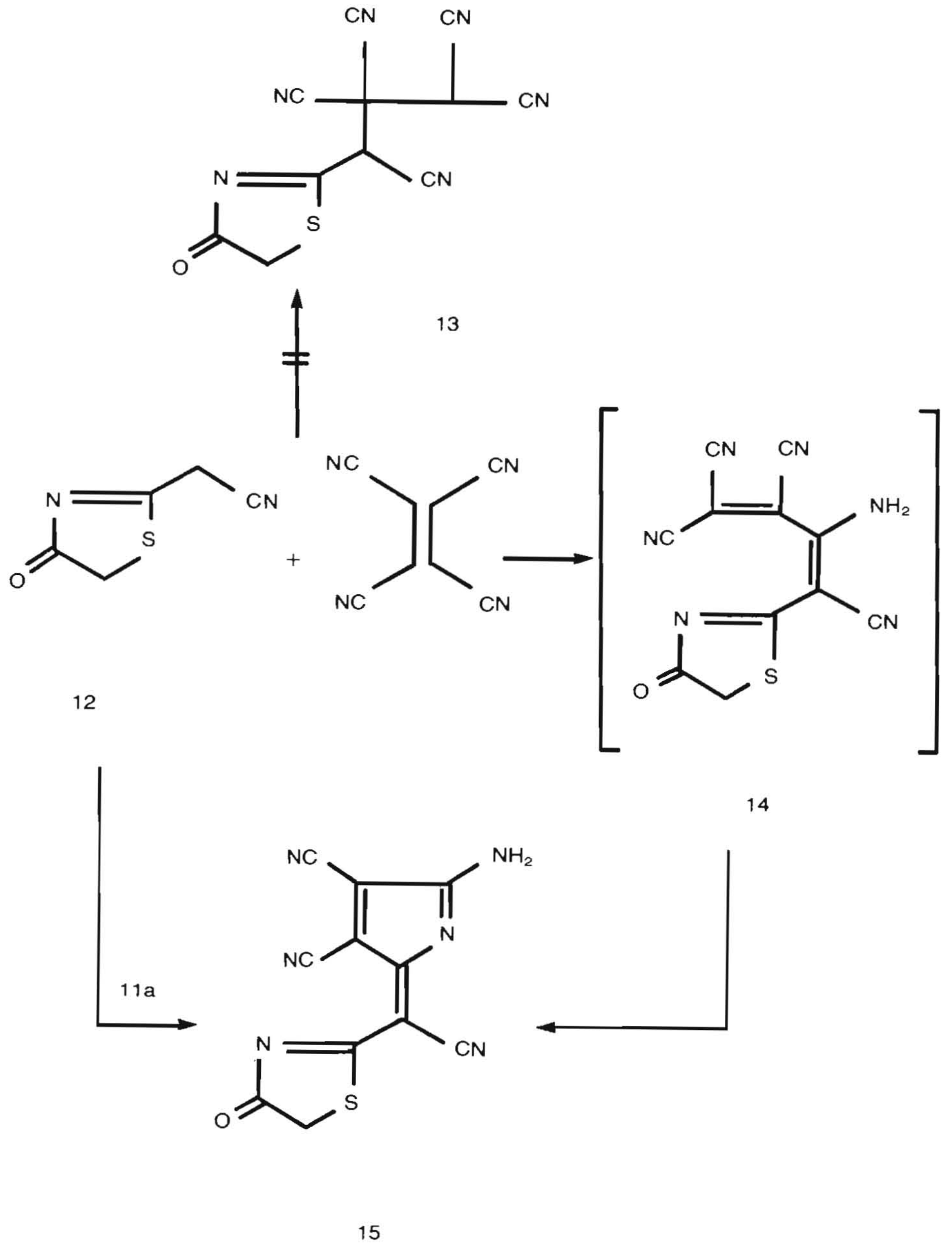


Chart 4

General procedure for the reaction of 1 with 4, 8a,b and 12

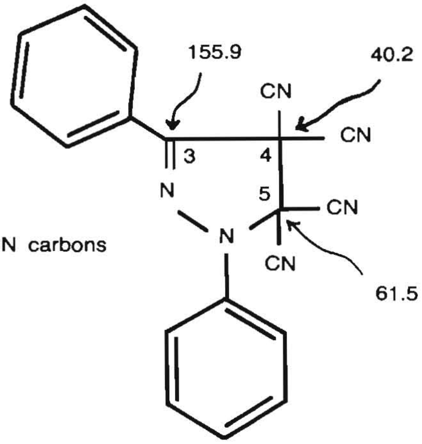
A suspension of 1 (0.01 mole) and an equimolar amount of 4, 8a,b or 12 in ethanol (50 ml) was refluxed with triethylamine (1 ml) for 2-3 h (TLC control) and then evaporated to dryness under reduced pressure. The residue was filtered off and crystallized from ethanol (cf. Table 1).

Conversion of 6 into 7

A solution of 6 (1 g) in ethanol (25 ml) was treated with conc. hydrochloric acid (5 ml) and heated under reflux for 2 h. The reaction mixture was then poured onto ice-cold water and the resulting solid product was filtered off, washed with water and crystallized from ethanol to give 7 (cf. Table 1).

Table 1. List of the newly synthesized compounds

Comp.	MP. °C	Yield %	Mol. Formula (M. Wt.)	% Analysis Calcd./Found			
				C	H	N	S
3a	206	47	$C_{19}H_{10}N_6$ (322)	70.81 70.90	3.11 3.30	26.09 26.20	– –
3b	214-216	51	$C_{16}H_{10}N_6O_2$ (318)	60.38 60.10	3.17 3.20	26.40 26.60	– –
3c	192	63	$C_{17}H_{12}N_6O_2$ (332)	61.44 61.50	3.64 3.70	25.29 25.40	– –
3d	149	43	$C_{16}H_{10}N_6O$ (302)	63.57 63.70	3.33 3.20	27.80 28.00	– –
6	>260	69	$C_{18}H_{11}N_5O$ (313)	69.00 68.60	3.54 3.70	22.35 22.20	– –
7	179	82	$C_{18}H_{10}N_4O$ (314)	68.79 68.60	3.21 3.10	17.83 17.70	– –
11a	143	71	$C_6H_2N_4O$ (146)	49.32 49.10	1.38 1.50	38.35 38.50	– –
11b	161	79	$C_6H_2N_4S$ (162)	44.44 44.30	1.24 1.40	34.55 34.70	19.77 19.60
15	181	68	$C_{11}H_4N_6OS$ (268)	49.25 49.30	1.50 1.60	31.33 31.50	11.95 11.80



4 signals 113.8, 114, 115.4 and 116,1 four CN carbons
8 signals (127.2 - 136.3), phenyl carbons

Fig. 1. ^{13}C data of compound 3a

Table 2. IR and ^1H NMR data of compounds 3a-b, 6, 7, 11a,b and 15

Compd.	IR [cm^{-1}] selected bands	^1H NMR (δ ppm) [DMSO-d_6]
3a	2260, 2240, 2190 (CN); 1620 (C=N)	6.8-8.1 (m, 10H, aromatic H).
3b	2250, 2240, 2180 (CN); 1760 (ester CO); 1620 (C=N)	1.3 (t, J = 7Hz, 3H, ester CH_3); 4.2 (q, J = 7Hz, 2H, ester CH_2); 7.5-7.7 (m, 5H, C_6H_5).
3c	2250, 2220, 2200 (CN); 1750 (ester CO); 1615 (C=N)	1.1 (t, J = 7Hz, 3H, ester CH_3); 2.4 (s, 3H, CH_3); 4.1 (q, J = 7Hz, 2H, ester CH_2); 7.2-7.6 (m, 4H, C_6H_4).
3d	2260, 2230, 2200 (CN); 1720 (CO); 1625 (C=N)	2.4 (s, 3H, CH_3); 2.5 (s, 3H, CH_3); 7.1-7.5 (m, 4H, C_6H_4).
6	3350 (NH); 2235, 2220 (CN); 1620 (C=N), 1600 (C=C)	3.4 (s, 1H, NH); 6.9-7.8 (m, 10H, aromatic H).
7	2240, 2220, (CN); 1680 (ring CO); 1625 (C=N); 1610 (C=C)	6.8-7.9 (m, 10H, aromatic H).
11a	3400-3250, (NH_2); 2225, 2210 (CN); 1700 (ring CO); 1620 (C=N); 1610 (C=C)	7.6 (s, 2H, NH_2).
11b	3390-3330, (NH_2); 2240, 2220 (CN); 1625 (C=N); 1600 (C=C)	4.9 (s, 2H, NH_2).
15	3395, 3360, (NH_2); 2235, 2215, 2190 (CN); 1690 (ring CO); 1620 (C=N); 1610 (C=C)	6.5 (s, 2H, NH_2); 3.7 (s, 2H, CH_2).

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تفاعلات مع رباعي سيانو الايثيلين : تكوين بعض مشتقات البيرازولين والاوكساديازين والبيرول والثيازوليل بيرول الجديدة

بهية يحيى رياض و عبده عثمان عبدالحميد و فتحي محمد عبدالجليل

قسم الكيمياء - كلية العلوم - جامعة القاهرة - الجيزة - مصر

تم في هذا البحث تكوين العديد من مشتقات البيرازولين والاوكساديازين والبيرول والثيازوليل بيرول الجديدة من خلال تفاعل رباعي سيانو الايثيلين مع العديد من مركبات كلوريدات الهيدرازويل وبعض الأميدات وسيانوأيثيل الثيازولينون.

وقد تم اثبات التراكيب البنائية للمشتقات غير متجانسة الحلقة المُكونَّة (المركَّبة) في هذا البحث بطرق التحليل العنصري ودراسة أطيافها للأشعة تحت الحمراء والرنين النووي المغناطيسي من نوعي البروتون ونظير الكربون - ١٣.

عند تفاعل رباعي سيانو الايثيلين في وجود ثلاثي ايثيل أمين مع مركبات كلوريدات الهيدرازويل نتج العديد من مركبات الاضافة الحلقية وقد تم التعرف على تركيبها الكيميائي بواسطة التحاليل الدقيقة للعناصر المكونة لها وكذلك باستخدام أجهزة الطيف المختلفة مثل الأشعة تحت الحمراء والرنين النووي المغناطيسي للبروتونات والرنين النووي المغناطيسي لعنصر الكربون (١٣). وقد تم اثبات أن هذه الحلقة غير المتجانسة عبارة عن مشتقات البيرازولين المختلفة.

كذلك تم تفاعل رباعي سيانو الايثيلين مع بنزويل فينيل الهيدرازين في وجود ثلاثي ايثيل أمين لتعطي مركبات الأوكساديازين من خلال تكوين مركب وسيط غير حلقي هو ثلاثي سيانو فينيل الذي تحول إلى المركب الحلقي النهائي بفقد جزيء من سيانيد الهيدروجين.

كما اشتمل البحث أيضاً على دراسة تأثير رباعي سيانو الايثيلين على مشتقات بعض الأميدات والأنيليدات والثيازولينون. فمثلاً وجد أن رباعي سيانو الايثيلين عند تفاعله مع سيانو أسيتاميد يعطي مشتقات البيرول الحلقية بينما عند تفاعله مع سيانو ثيو أسيتاميد يعطي مشتقات البيرولثيون المقابلة. وقد أمكن اثبات التراكيب البنائية أيضاً بتكوينها بطرق أخرى بديلة.

وتحتوي المركبات غير متجانسة الحلقة الجديدة على العديد من المجموعات الدالة الفعالة مما يجعلها ذات نفع عظيم سواء في اجراء التحويلات الكيميائية الأخرى للحصول على حلقيات غير متجانسة جديدة أو لاجراء المسح الشامل لخواصها البيولوجية حيث قد ثبت أن لبعض قرائنها المكونة سابقاً بعض الخواص البيولوجية كمضادات فعالة للبكتريا والفطريات.