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A new type of cascade reaction: direct conversion of carbonyl compounds and malononitrile into substituted tetracyanocyclopropanes

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ABSTRACT

A new type of chemical cascade reaction was found: the direct formation of cyclopropanes from carbonyl compounds and C–H acid. The action of free halogen or active halogen containing compounds on a mixture of 1 equiv of carbonyl compound and 2 equiv of malononitrile in a basic alcohol solution results in the formation of substituted 1,1,2,2-tetracyanocyclopropanes in 15–80% yield. The latter are well-known precursors for the different bicyclic heterosystems, among them compounds containing a cyclopropane ring and possessing different types of pharmacological activity. Thus, the new, simple and efficient 'one-pot' way to substituted tetracyanocyclopropanes in 50–80% yield was found directly from such simple and reasonable starting compounds as aldehydes, or some cyclic ketones, or substituted cyclohexanones and malononitrile.

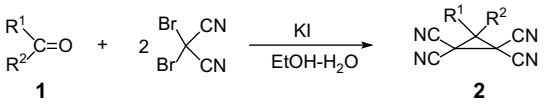
1. Introduction

The discovery of new synthetic methodologies to facilitate the preparation of organic compounds is a pivotal focal point of research activity in the field of modern organic, bioorganic and medicinal chemistry.[1]

The cyclopropyl group is a vital structural unit in many synthetic and naturally occurring compounds, exhibiting a wide spectrum of biologic properties ranging from enzyme inhibition to herbicidal, antibiotic, antitumour and antiviral activities.[2–4] Thus, the prevalence of cyclopropane containing compounds with biological activity, whether isolated from natural sources or rationally designed pharmaceutical agents, has inspired chemists to find novel and diverse approaches to their synthesis.

Though methods of cyclopropane synthesis have long been documented, so far, all of them consist of two main groups: (1) intramolecular cyclization or (2) interaction of two different molecules (addition of carbenes to olefins or Michael initiated ring closure (MIRC) are the most known examples of this type).[2,4]

Nevertheless there are some special famous methods of cyclopropane ring construction. One of them is well-known Wideqvist reaction, namely the interaction of two molecules of bromomalononitrile with carbonyl compounds **1** in the presence of a stoichiometric quantity of potassium iodide with the formation of the corresponding substituted tetracyanocyclopropanes **2** (Scheme 1).[5]



Scheme 1.

Later, in the electrochemical variant of Wideqvist reaction, bromomalononitrile was replaced by malononitrile and a catalytic amount of sodium bromide.[6,7] In the electrochemical variant for the reaction of aldehydes a low temperature (0 °C) is necessary;[7] whereas for ketones a three- to four-fold excess of ketone is needed to obtain tetracyanocyclopropanes **2** in good yields.[6,7] Additionally, in the case of cyclohexanone, the electrochemical process cannot be stopped on the formation of the corresponding tetracyanocyclopropane; co-electrolysis of cyclohexanone and malononitrile in ethanol in the presence of sodium bromide under these conditions furnishes 2-amino-1,5-dicyano-4,4-diethoxy-6,6-pentamethylene-3-azabicyclo[3.1.0]-hex-2-ene in 62% yield (Scheme 2).[6]

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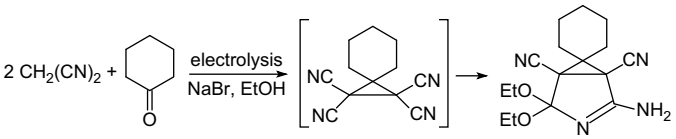
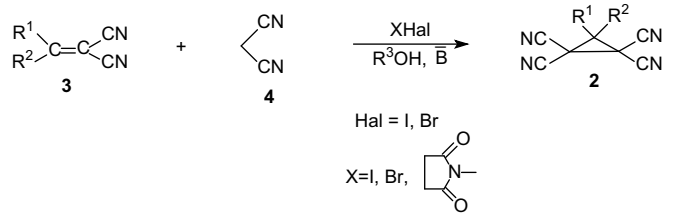


Scheme 2.

Recently we suggested a new strategy of chemical route to the cyclopropane structure: the direct transformation of benzylidenemalononitriles **3** and malononitrile **4** into 1,1,2,2-tetracyanocyclopropanes **2** (Scheme 3).[8]



Scheme 3.

Cascade reactions have been utilized as powerful method to construct molecular complexity from readily available starting materials by combining two or more reactions into a single transformation.[9] As such, cascade reactions are of increasing importance in modern organic chemistry. This is not only due to the need for the more efficient and less labour-intense methodologies for the synthesis of organic compounds, but also a consequence of the increasing importance of the environmental considerations in chemistry. Thus, cascade reactions have significant economical and ecological benefits when one performs several synthetic steps in one operation without isolating the reaction intermediates. From this point of view the best route to the substituted 1,1,2,2-tetracyanocyclopropanes **2** could be the 'one-pot' chemical cascade process starting directly from carbonyl compounds and malononitrile.

2. Results and discussion

In the present study we report our results on the direct 'one-pot' cascade transformation of carbonyl compounds and malononitrile into the substituted 1,1,2,2-tetracyanocyclopropanes **2** (Scheme 4).

First, to evaluate the synthetic potential of the proposed procedure and to optimize the general conditions, the cascade transformation of benzaldehyde **1a**, and malononitrile **4** into the corresponding 3-phenyl-1,1,2,2-tetracyanocyclopropanes **2a** was studied (Table 1).

Excellent conversions of starting compounds were obtained under all conditions studied. The best yield of cyclopropane **2a** (75%) was achieved when the reaction was carried out in ethanol by the action of bromine in the presence of 1 equiv of EtONa (entry 10, Table 1). The second step was devoted to the careful evaluation of EtONa quantity needed for the reaction (Table 2).

The best yield of cyclopropane **2a** (83%) was obtained when 1.2 equiv of EtONa was used (entry 3, Table 2). The increase of EtONa quantity beyond 1.2 equiv (entries 4 and 5, Table 2) resulted in a sufficient decrease of the reaction yield, that may be connected with the activation of undesired base induced oligomerization processes of malononitrile.[10]

Under the optimal conditions thus found, i.e., bromine as active halogen compound, 1.2 equiv of EtONa as base, and ethanol as solvent, the substituted carbonyl compounds **1a–o** and malononitrile **4** were transformed into corresponding substituted 1,1,2,2-tetracyanocyclopropanes **2a–o** in 61–83% yields (Table 3).

In the case of aldehydes **1d** and **1i** (entries 4 and 9, Table 3) the quantity of EtOH was increased up to 40 mL because of the lower

Table 1
Cascade transformation of benzaldehyde **1a** and malononitrile **4** into 3-phenyl-1,1,2,2-tetracyanocyclopropane **2a**[a]

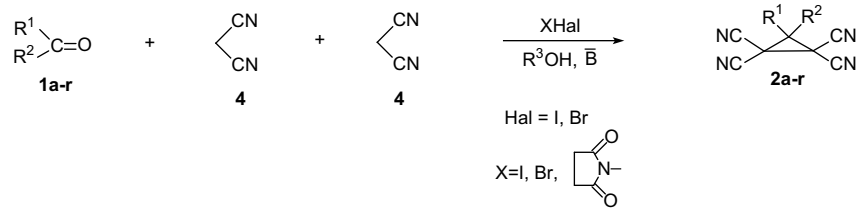
Entry	Alcohol	XHal	Base	Yield of **2a**[b] (%)
1	MeOH	I_2	NaOH	25
2	MeOH	I_2	KOH	31
3	EtOH	I_2	KOH	38
4	EtOH	I_2	NaOEt	45
5	MeOH	NBS	KOH	32
6	EtOH	NBS	KOH	43
7	EtOH	NBS	NaOEt	56
8	MeOH	Br_2	KOH	39
9	EtOH	Br_2	KOH	62
10	EtOH	Br_2	EtONa	75

[a] Benzaldehyde **1a** (10 mmol), 20 mmol of malononitrile **4**, 10 mmol of halogen or NBS, 10 mmol of base, 20 mL of alcohol, time of the reaction—3 h.
[b] Isolated yield (isolated by filtration of the reaction mixture).

Table 2
Influence of EtONa quantity on the 3-phenyl-1,1,2,2-tetracyanocyclopropane **2a** yield[a]

Entry	Quantity of EtONa (equiv)	Yield of **2a**[b] (%)
1	0.5	55
2	1.0	75
3	1.2	83
4	1.5	57
5	2.0	32

[a] Benzaldehyde **1a** (10 mmol), 20 mmol of malononitrile **4**, 10 mmol of bromine, 20 mL of alcohol, time of the reaction—3 h.
[b] Isolated yield (isolated by filtration of the reaction mixture).



a R^1 = H, R^2 = Ph; **b** R^1 = H, R^2 = 4-MeC_6H_4; **c** R^1 = H, R^2 = 4-$MeOC_6H_4$; **d** R^1 = H, R^2 = 2-$MeOC_6H_4$;

e R^1 = H, R^2 = 4-FC_6H_4; **f** R^1 = H, R^2 = 2-ClC_6H_4; **g** R^1 = H, R^2 = 3-ClC_6H_4; **h** R^1 = H, R^2 = 4-ClC_6H_4;

i R^1 = H, R^2 = 2,4-$Cl_2C_6H_3$; **j** R^1 = H, R^2 = 3-BrC_6H_4; **k** R^1 = H, R^2 = 3-$NO_2C_6H_4$; **l** R^1 = H, R^2 = 4-$NO_2C_6H_4$;

m R^1 = H, R^2 = naphth-1-yl; **n** R^1 = H, R^2 = Et; **o** R^1 = H, R^2 = *n*-Pr; **p** R^1 = Me, R^2 = Me; **q** R^1 = Me, R^2 = Et;

r R^1 = Et, R^2 = Et

Scheme 4.

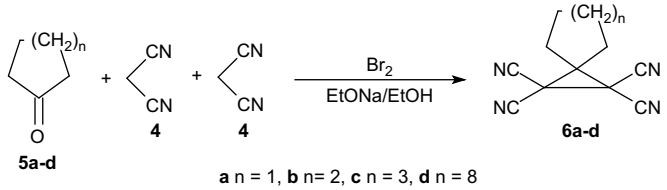
Table 3
Cascade transformation of carbonyl compounds **1a–r** and malononitrile **4** into 3-substituted-1,1,2,2-tetracyanocyclopropanes **2a–r**[a]

Entry	Carbonyl compound	R^1	R^2	Cyclopropane, yield[b] (%)
1	**1a**	H	C_6H_5	**2a**, 83
2	**1b**	H	4-MeC_6H_4	**2b**, 72
3	**1c**	H	4-$MeOC_6H_4$	**2c**, 77
4[c]	**1d**	H	2-$MeOC_6H_4$	**2d**, 63
5	**1e**	H	4-FC_6H_4	**2e**, 75
6	**1f**	H	2-ClC_6H_4	**2f**, 71
7	**1g**	H	3-ClC_6H_4	**2g**, 65
8	**1h**	H	4-ClC_6H_4	**2h**, 82
9[c]	**1i**	H	2,4-$Cl_2C_6H_4$	**2i**, 63
10	**1j**	H	3-BrC_6H_4	**2j**, 61
11	**1k**	H	3-$NO_2C_6H_4$	**2k**, 78
12	**1l**	H	4-$NO_2C_6H_4$	**2l**, 62
13	**1m**	H	Naphth-1-yl	**2m**, 76
14	**1n**	H	Et	**2n**, 65
15	**1o**	H	*n*-Pr	**2o**, 73
16	**1p**	Me	Me	**2p**, 43
17	**1q**	Me	Et	**2q**, 33
18	**1r**	Et	Et	**2r**, 15

[a] Carbonyl compounds **1a–r** (10 mmol), 20 mmol of malononitrile **4**, 10 mmol of bromine, 12 mmol of EtONa, 20 mL of EtOH, time of the reaction—3 h.
[b] Isolated yield (isolated by filtration of the reaction mixture).
[c] EtOH (40 mL).

solubility of the corresponding intermediate benzylidenemalononitriles in EtOH. When 20 mL of ethanol was used in the cases of aldehydes **1d** and **1i** the corresponding 4-methoxybenzylidenemalononitrile and 2,4-dichlorobenzylidenemalononitrile were obtained in 42% and 47% yields, accompanied by cyclopropanes **2d** and **2i**, 28% and 25% yields according to the data of NMR spectroscopy. Thus, under conditions used from the aliphatic and aromatic aldehydes **1a–o** the substituted 1,1,2,2-tetracyanocyclopropanes **2a–o** were obtained in 61–83% yields. This cascade process is not very good in the case of linear ketones; the yields of 3,3-disubstituted 1,1,2,2-tetracyanocyclopropanes **2p–r** were only in the range 15–43%. The next part of the investigation was concerned with cyclic ketones (Scheme 5, Table 4).

Among the cyclic ketones the best result was found in the case of cyclohexanone; spirobicyclic tetracyanocyclopropane **6b** was obtained in 75% yield. Sufficiently good results were achieved also in the cases of cyclopentanone and cycloheptanone, the yields of corresponding spirobicyclic tetracyanocyclopropanes **6a** and **6c** were 52% and 63% correspondingly (Table 4).



a n = 1, **b** n= 2, **c** n = 3, **d** n = 8

Scheme 5.

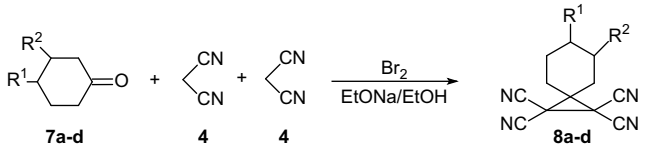
Table 4
Cascade transformation of cyclic ketones **5a–d** and malononitrile **4** into spirobicyclic tetracyanocyclopropanes **6a–d**[a]

Entry	Cyclic ketone	*n*	Cyclopropane, yield[b] (%)
1	**5a**	1	**6a**, 52
2	**5b**	2	**6b**, 75
3	**5c**	3	**6c**, 63
4	**5d**	8	**6d**, 25

[a] Cyclic ketones **5a–d** (10 mmol), 20 mmol of malononitrile **4**, 10 mmol of bromine, 12 mmol of EtONa, 20 mL of EtOH, time of the reaction—3 h.
[b] Isolated yield (isolated by filtration of the reaction mixture).

This new cascade process is also useful for substituted cyclohexanones (Scheme 6, Table 5).

Hence this cascade method is useful for the direct 'one-pot' synthesis of tetracyanocyclopropanes from aldehydes, acetone, some cyclic ketones, substituted cyclohexanones and malononitrile.



a R^1 = Me, R^2 = H;**b** R^1 = *t*-Bu, R^2 = H; **c** R^1 = Ph, R^2 = H; **d** R^1 = H, R^2 = Me;

Scheme 6.

Table 5
Cascade transformation of substituted cyclohexanones **7a–d** and malononitrile **4** into spirobicyclic tetracyanocyclopropanes **8a–d**[a]

Entry	Cyclic ketone	R^1	R^2	Cyclopropane, yield[b] (%)
1	**7a**	Me	H	**8a**, 63
2	**7b**	*t*-Bu	H	**8b**, 76
3	**7c**	Ph	H	**8c**, 70
4	**7d**	H	Me	**8d**, 61

[a] Cyclic ketones **7a–d** (10 mmol), 20 mmol of malononitrile **4**, 10 mmol of bromine, 12 mmol of EtONa, 20 mL of EtOH, time of the reaction—3 h.
[b] Isolated yield (isolated by filtration of the reaction mixture).

Taking into consideration the data obtained, the following reaction scheme was proposed for the direct cascade transformation of carbonyl compounds and malononitrile into substituted tetracyanocyclopropanes (Scheme 7).

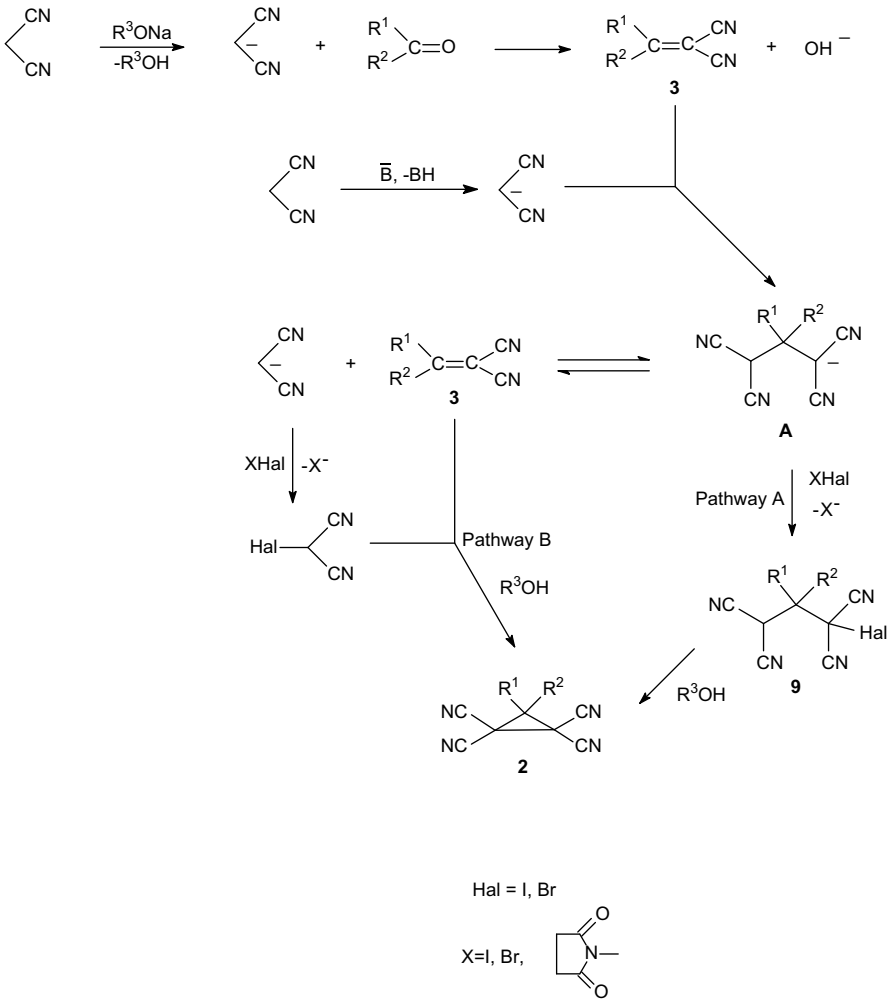
First, by the action of base, the anions of malononitrile arise in the solution, then by the usual way Knoevenagel condensation of carbonyl compound with anion of malonitrile takes place with the formation of alkylidenemalononitrile **3**.[11] Addition of the second anion of malononitrile to alkylidenemalononitrile **3** leads to anion **A**, which exist in alcohol solution in the equilibrium with alkylidenemalononitrile **3** and the anion of malononitrile.[12] Then halogenation of anion **A** results in 1-halogeno-1,1,3,3-tetracyanopropane **9** formation, which is cyclized into tetracyanocyclopropane **2** (pathway A). Alternative malononitrile anion halogenation, and addition of halogenomalononitrile anion to alkylidenemalononitrile **3** leads also to tetracyanocyclopropane **2** (pathway B). Concerted realization of two last reaction pathways A and B ensures for the most part of carbonyl compounds studied 50–80% yield of the substituted tetracyanocyclopropanes **2**.

The pathway A correlates with the earlier known method of the synthesis of tetracyanosubstituted cyclopropanes suggested by Mariella and Roth.[13] This method includes bromination of 2-alkylsubstituted 1,1,3,3-tetracyanopropanes in aqueous ethanol with instant formation of 3-alkyl substituted 1,1,2,2-tetracyanosubstituted cyclopropanes.

The pathway B is similar to the earlier known method for the synthesis of tetracyanosubstituted cyclopropanes as the reaction of alkylidene- or benzylidenemalononitriles and bromomalononitrile[14–18] in aqueous ethanol without use of base as bromomalononitrile is a reasonably strong acid, which can furnish a sufficient concentration of bromodicyanocarbanion for the reaction.[19]

3. Conclusion

In conclusion, a new cascade 'one-pot' reaction was found, namely the direct formation of cyclopropane structures from



Scheme 7.

carbonyl compounds and malononitrile. The action of free halogen or active halogen containing compounds on the 1 equiv of carbonyl compound and 2 equiv of malononitrile in basic alcohol solution results in the formation of substituted-1,1,2,2-tetracyanocyclopropanes in 15–80% yields. The latter are well-known precursors for different bicyclic heterosystems, among them compounds containing a cyclopropane ring[7,20] and possessing different types of pharmacological activity.[2,21] Thus, a new simple and efficient way to 3-substituted tetracyanocyclopropanes in 60–80% yields was found starting from such simple and reasonable compounds as aldehydes, some cyclic ketones or substituted cyclohexanones and malononitrile. The procedure utilizes inexpensive reagents, it is easily carried out and the work up is not complicated. 3-Substituted-1,1,2,2-tetracyanocyclopropanes are crystallized directly from the reaction mixture, consequently, the isolation includes only filtration and washing with warm water.

4. Experimental section

4.1. General remarks

Chemicals were purchased from Aldrich® and Acros®. All melting points were measured with a Gallenkamp melting point apparatus and are uncorrected. ^{1}H and ^{13}C NMR spectra were recorded with a Bruker WM-250, Bruker AM-300 and Bruker Avance II 300 spectrometers at ambient temperature. Chemical shifts (δ) are given in parts per million relative to Me_4Si for DMSO-d_6 and $CDCl_3$ solutions. IR spectra were registered with a SPECORD M82 spectrometer in KBr pellets. Mass spectra (EI, 70 eV) were obtained directly using Finningan MAT INCOS 50 spectrometer.

4.2. Typical procedure

To a 10 mL ethanolic solution of carbonyl compound (10 mmol) and malononitrile **4** (1.32 g, 20 mmol) in a 50 mL beaker, 0.82 g (12 mmol) of sodium ethoxide in 10 mL of ethanol was added during 1 min. Then 10 mmol (0.51 mL) of bromine was added for 1 min without external cooling. The mixture was magnetically stirred at room temperature for 3 h. Then solid phase was filtered off, washed with warm water and dried in a desiccator over P_2O_5 to isolate pure product.

All compounds gave expected NMR spectra. For new compounds, satisfactory elemental analyses, mass and IR spectroscopy data were obtained.

*4.2.1. 3-Phenyl-1,1,2,2-tetracyanocyclopropane (**2a**)*

White solid. Yield 1.81 g (83%); mp 229–230 °C (lit. mp[15] 227–230 °C); ^{1}H NMR δ_H (250 MHz, DMSO-d_6) 5.27 (s, 1H, CH), 7.44–7.52 (m, 3H, Ar), 7.74–7.82 (m, 2H, Ar).

*4.2.2. 3-(4-Methylphenyl)-1,1,2,2-tetracyanocyclopropane (**2b**)*

White solid. Yield 1.67 g (72%); mp 226–229 °C (lit. mp[15] 227–230 °C); ^{1}H NMR δ_H (300 MHz, DMSO-d_6) 2.33 (s, 3H,

CH_3), 5.23 (s, 1H, CH), 7.30 (d, *J* 7.8 Hz, 2H, Ar), 7.68 (d, *J* 7.8 Hz, 2H, Ar).

*4.2.3. 3-(4-Methoxyphenyl)-1,1,2,2-tetracyanocyclopropane (**2c**)*

Yellow solid. Yield 1.91 g (77%); mp 208–210 °C (lit. mp[15] 209–210 °C); ^{1}H NMR δ_H (300 MHz, DMSO-d_6) 3.79 (s, 3H, OCH_3), 5.15 (s, 1H, CH), 7.04 (d, *J* 8.4 Hz, 2H, Ar), 7.73 (d, 8.4 Hz, 2H, Ar).

*4.2.4. 3-(2-Methoxyphenyl)-1,1,2,2-tetracyanocyclopropane (**2d**)*

Yellow solid. Yield 1.56 g (63%); mp 240–241 °C (lit. mp[8] 240–241 °C); ^{1}H NMR δ_H (250 MHz, DMSO-d_6) 3.89 (s, 3H, OCH_3), 5.04 (s, 1H, CH), 7.05 (t, *J* 7.6 Hz, 1H, Ar), 7.19 (d, *J* 8.6 Hz, 1H, Ar), 7.48 (t, *J* 7.6 Hz, 1H, Ar), 7.76 (d, *J* 7.3 Hz, 1H, Ar).

*4.2.5. 3-(4-Fluorophenyl)-1,1,2,2-tetracyanocyclopropane (**2e**)*

White solid. Yield 1.77 g (75%); mp 216–217 °C (lit. mp[8] 216–217 °C); ^{1}H NMR δ_H (300 MHz, DMSO-d_6) 5.25 (s, 1H, CH), 7.34 (t, *J* 8.5 Hz, 2H, Ar), 7.86–8.00 (m, 2H, Ar).

*4.2.6. 3-(2-Chlorophenyl)-1,1,2,2-tetracyanocyclopropane (**2f**)*

White solid. Yield 1.79 g (71%); mp 245–247 °C (lit. mp[15] 246–248 °C); ^{1}H NMR δ_H (300 MHz, DMSO-d_6) 5.48 (s, 1H, CH), 7.48–7.62 (m, 2H, Ar), 7.68–7.74 (m, 1H, Ar), 8.03–8.09 (m, 1H, Ar).

*4.2.7. 3-(3-Chlorophenyl)-1,1,2,2-tetracyanocyclopropane (**2g**)*

White solid. Yield 1.65 g (65%); mp 187–189 °C (lit. mp[15] 183–185 °C); ^{1}H NMR δ_H (300 MHz, DMSO-d_6) 5.35 (s, 1H, CH), 7.51–7.59 (m, 2H, Ar), 7.77–7.85 (m, 1H, Ar), 8.08 (s, 1H, Ar).

*4.2.8. 3-(4-Chlorophenyl)-1,1,2,2-tetracyanocyclopropane (**2h**)*

White solid. Yield 2.07 g (82%); mp 250–251 °C (lit. mp[15] 248–250 °C); ^{1}H NMR δ_H (300 MHz, DMSO-d_6) 5.28 (s, 1H, CH), 7.59 (d, *J* 8.5 Hz, 2H, Ar), 7.88 (d, *J* 8.5 Hz, 2H, Ar).

*4.2.9. 3-(2,4-Dichlorophenyl)-1,1,2,2-tetracyanocyclopropane (**2i**)*

White solid. Yield 1.81 g (63%); mp 226–228 °C (lit. mp[15] 225–228 °C); ^{1}H NMR δ_H (250 MHz, DMSO-d_6) 5.48 (s, 1H, CH), 7.66 (dd, J_1 8.5 Hz, J_2 1.9 Hz, 1H, Ar), 7.93 (d, *J* 1.9 Hz, 1H, Ar), 8.10 (d, *J* 8.5 Hz, 1H, Ar).

*4.2.10. 3-(3-Bromophenyl)-1,1,2,2-tetracyanocyclopropane (**2j**)*

White solid. Yield 1.81 g (61%); mp 186–187 °C (lit. mp[8] 186–187 °C); ^{1}H NMR δ_H (250 MHz, DMSO-d_6) 5.32 (s, 1H, CH), 7.45 (t, *J* 8.5 Hz, 1H, Ar), 7.69 (d, *J* 8.5 Hz, 1H, Ar), 7.88 (d, *J* 8.5 Hz, 1H, Ar), 8.23 (s, 1H, Ar).

*4.2.11. 3-(3-Nitrophenyl)-1,1,2,2-tetracyanocyclopropane (**2k**)*

White solid. Yield 2.05 g (78%); mp 244–245 °C (lit. mp[15] 246–247 °C); ^{1}H NMR δ_H (300 MHz, DMSO-d_6) 5.46 (s, 1H, CH), 7.82 (t, *J* 8.0 Hz, 1H, Ar), 8.28–8.41 (m, 2H, Ar), 9.01 (s, 1H, Ar).

*4.2.12. 3-(4-Nitrophenyl)-1,1,2,2-tetracyanocyclopropane (**3l**)*

White solid. Yield 1.63 g (62%); mp 232–234 °C (lit. mp[15] 232–235 °C); ^{1}H NMR δ_H (300 MHz, DMSO-d_6) 5.50 (s, 1H, CH), 8.20 (d, *J* 8.8 Hz, 2H, Ar), 8.36 (d, *J* 8.8 Hz, 2H, Ar).

*4.2.13. 3-(1-Naphthyl)-1,1,2,2-tetracyanocyclopropane (**2m**)*

White solid. Yield 2.04 g (76%); mp 257–259 °C (lit. mp[15] 249–252 °C); ^{1}H NMR δ_H (300 MHz, DMSO-d_6) 5.85 (s, 1H, CH), 7.59–7.72 (m, 2H, Ar), 7.77–7.92 (m, 2H, Ar), 8.06–8.16 (m, 3H, Ar).

*4.2.14. 3-Ethyl-1,1,2,2-tetracyanocyclopropane (**2n**)*

White solid. Yield 1.11 g (65%); mp 194–196 °C (lit. mp[22] 197 °C); ^{1}H NMR δ_H (300 MHz, DMSO-d_6) 1.14 (t, *J* 7.4 Hz, 3H, CH_3), 1.70–1.82 (m, 2H, CH_2), 3.81 (t, *J* 7.4 Hz, 3H, CH).

*4.2.15. 3-n-Propyl-1,1,2,2-tetracyanocyclopropane (**2o**)*

White solid. Yield 1.34 g (73%); mp 136–138 °C (lit. mp[7] 136–138 °C); ^{1}H NMR δ_H (250 MHz, DMSO-d_6) 0.96 (t, *J* 7.3 Hz, 3H, CH_3), 1.51–1.65 (m, 2H, CH_2), 1.69–1.77 (m, 2H, CH_2) 3.87 (t, *J* 7.3 Hz, 1H, CH).

*4.2.16. 3,3-Dimethyl-1,1,2,2-tetracyanocyclopropane (**2p**)*

White solid. Yield 0.73 g (43%); mp 208–210 °C (lit. mp[14] 209.5–210 °C); ^{1}H NMR δ_H (300 MHz, DMSO-d_6): 1.58 (s, 6H, CH_3).

*4.2.17. 3-Ethyl-3-methyl-1,1,2,2-tetracyanocyclopropane (**2q**)*

White solid. Yield 0.61 g (33%); mp 207–208 °C (lit. mp[7] 208–209 °C); ^{1}H NMR δ_H (300 MHz, DMSO-d_6) 1.33 (t, *J* 7.4 Hz, 3H, CH_3), 1.75 (s, 3H, CH_3), 2.16 (q, *J* 7.4 Hz, 2H, CH_2).

*4.2.18. 3,3-Diethyl-1,1,2,2-tetracyanocyclopropane (**2r**)*

White solid. Yield 0.30 g (15%); mp 165–166 °C (lit. mp[22] 167–168 °C); ^{1}H NMR δ_H (300 MHz, DMSO-d_6) 1.29 (t, *J* 7.4 Hz, 6H, CH_3), 2.05 (q, *J* 7.4 Hz, 4H, CH_2).

*4.2.19. 1,1,2,2-Tetracyanospiro[2.4]heptane (**6a**)*

White solid. Yield 1.02 g (52%); mp 250–251 °C (lit. mp[7] 250–251 °C); ^{1}H NMR (300 MHz, DMSO-d_6) 1.86–1.49 (m, 4H, CH_2), 2.01–2.07 (m, 4H, CH_2).

*4.2.20. 1,1,2,2-Tetracyanospiro[2.5]octane (**6b**)*

White solid. Yield 1.57 g (75%); mp 178–180 °C (lit. mp[14] 177–179 °C); ^{1}H NMR δ_H (300 MHz, DMSO-d_6) 1.46–1.56 (m, 2H, CH_2), 1.61–1.73 (m, 4H, CH_2), 1.80–1.90 (m, 4H, CH_2).

*4.2.21. 1,1,2,2-Tetracyanospiro[2.6]nonane (**6c**)*

White solid. Yield 1.41 g (63%); mp 169–170 °C (lit. mp[8] 170–171 °C); ^{1}H NMR δ_H (300 MHz, $CDCl_3$) 1.70–1.79 (m, 4H, CH_2), 1.80–1.92 (m, 4H, CH_2), 2.08–2.16 (m, 4H, CH_2).

*4.2.22. 1,1,2,2-Tetracyanospiro[2.10]tetradecane (**6d**)*

White solid. Yield 0.73 g (25%); mp 198–200 °C (lit. mp[14] 197–200 °C); ^{1}H NMR δ_H (300 MHz, DMSO-d_6) 1.26–1.46 (m, 14H, CH_2), 1.55–1.69 (m, 4H, CH_2), 1.80–1.92 (m, 4H, CH_2).

*4.2.23. 1,1,2,2-Tetracyano-6-methylspiro[2.5]octane (**8a**)*

White solid. Yield 1.41 g (63%); mp 165–166 °C (lit. mp[23] 166–167 °C); ^{1}H NMR δ_H (300 MHz, DMSO-d_6) 0.97 (d, *J* 6.5 Hz, 3H, CH_3), 1.12–1.32 (m, 2H, CH_2), 1.45–1.67 (m, 3H, CH, CH_2), 1.78–1.90 (m, 2H, CH_2), 2.12–2.28 (m, 2H, CH_2).

*4.2.24. 6-tert-Butyl 1,1,2,2-tetracyanospiro[2.5]octane (**8b**)*

White solid. Yield 2.02 g (76%); mp 176–178 °C (lit. mp[23] 177–179 °C); ^{1}H NMR δ_H (300 MHz, DMSO-d_6) 0.88 (s, 9H, CH_3), 1.08–1.30 (m, 3H, CH, CH_2), 1.56–1.66 (m, 2H, CH_2), 1.90–2.00 (m, 2H, CH_2), 2.15–2.30 (m, 2H, CH_2).

*4.2.25. 1,1,2,2-Tetracyano-6-phenylspiro[2.5]octane (**8c**)*

White solid. Yield 2.00 g (70%); mp 170–171 °C (lit. mp[23] 171–173 °C); ^{1}H NMR δ_H (300 MHz, $CDCl_3$) 1.75–1.85 (m, 2H, CH_2), 2.07–2.19 (m, 2H, CH_2), 2.35–2.47 (m, 4H, CH_2), 2.76–2.94 (m, 1H, CH), 7.25–7.52 (m, 5H, Ph).

*4.2.26. 1,1,2,2-Tetracyano-5-methylspiro[2.5]octane (**8d**)*

White solid. Yield 1.37 g (61%); mp 165–166 °C; ^{1}H NMR δ_H (300 MHz, DMSO-d_6) 1.10 (d, *J* 5.6 Hz, 3H, CH_3), 1.48–1.62 (m, 1H, CH), 1.70–1.86 (m, 4H, CH_2), 1.78–1.90 (m, 2H, CH_2), 2.12–2.28 (m, 2H, CH_2); ^{13}C NMR δ_c (75 MHz, DMSO-d_6) 21.6, 23.6, 24.5, 25.9, 29.6, 31.4, 32.6, 37.4, 46.1, 107.5, 107.9; MS (70 eV) *m*/*z* (relative intensity %): 224 (2) $[M]^+$, 209 (3), 196 (4), 96 (52), 95 (54), 81 (93), 67 (79), 55 (77), 41 (95), 39 (100); IR (KBr): ν=2956, 2932, 2904, 2856, 2264, 2256, 1452, 1376, 1284, 1132 cm^{-1}. Anal. Calcd

(%) for $C_{13}H_{12}N_4$: C 69.62, H 5.39, N 24.98. Found (%): C 69.41, H 5.53, N 24.87.

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