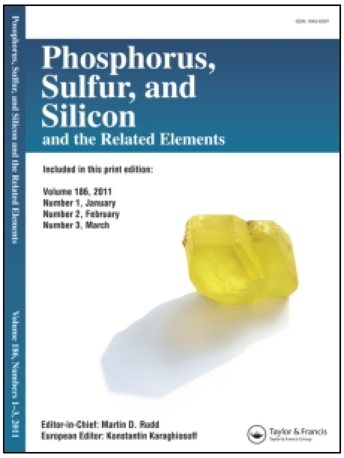

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1,5-Diphenyl-3,3-dicyano-1,5-pentanedione: A Synthon for Novel Heterocycles

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1,5-DIPHENYL-3,3-DICYANO-1,5-PENTANEDIONE: A SYNTHON FOR NOVEL HETEROCYCLES

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*1,5-Diphenyl-3,3-dicyano-1,5-pentanedione has been used to incorporate N, O, S to obtain 1,4-dihydropyridine, 4*H*-pyran, and 4*H*-thiopyran, which in turn serve as precursors for the synthesis of novel spiro heterocycles. All the compounds were characterized by IR and NMR spectral data.*

Keywords: 1,4-Dihydropyridine; 4*H*-pyran; 4*H*-thiopyran; spiro heterocycles

INTRODUCTION

At the outset we choose to study the chemistry of simple molecules for designing novel structures capable of performing a variety of functions. One such system is 1,5-diaryl-3,3-disubstituted-1,5-pentanedione which has been obtained by the reaction of phenacyl bromide with active methylene compounds such as dimethylmalnoate, ethyl cyanoacetate and malononitrile.[1] The synthetic utility and reactivity of 1,5-diaryl-3,3-dimethoxycarbonyl-3-cyano-3-ethoxycarbonyl-1,5-pentanediones has been exploited for the incorporation of N, O, S as heteroatoms to obtain 2,6-diaryl-4,4-dimethoxycarbonyl-4-cyano-4-ethoxycarbonyl-1,4-dihydropyridine,2,6-diaryl-4,4-dimethoxycarbonyl-4-cyano-4-ethoxycarbonyl-4*H*-pyran and 2,6-diaryl-4,4-dimethoxycarbonyl-4-cyano-4-ethoxycarbonyl-4*H*-thiopyran. These results led us to plan and execute the synthesis of some spiro heterocycles by exploting the *gem* diester/cyanoester functionalities of the latter compounds.[2–4] Following theses observations and being undeterred by the results,[5–10] we now report in

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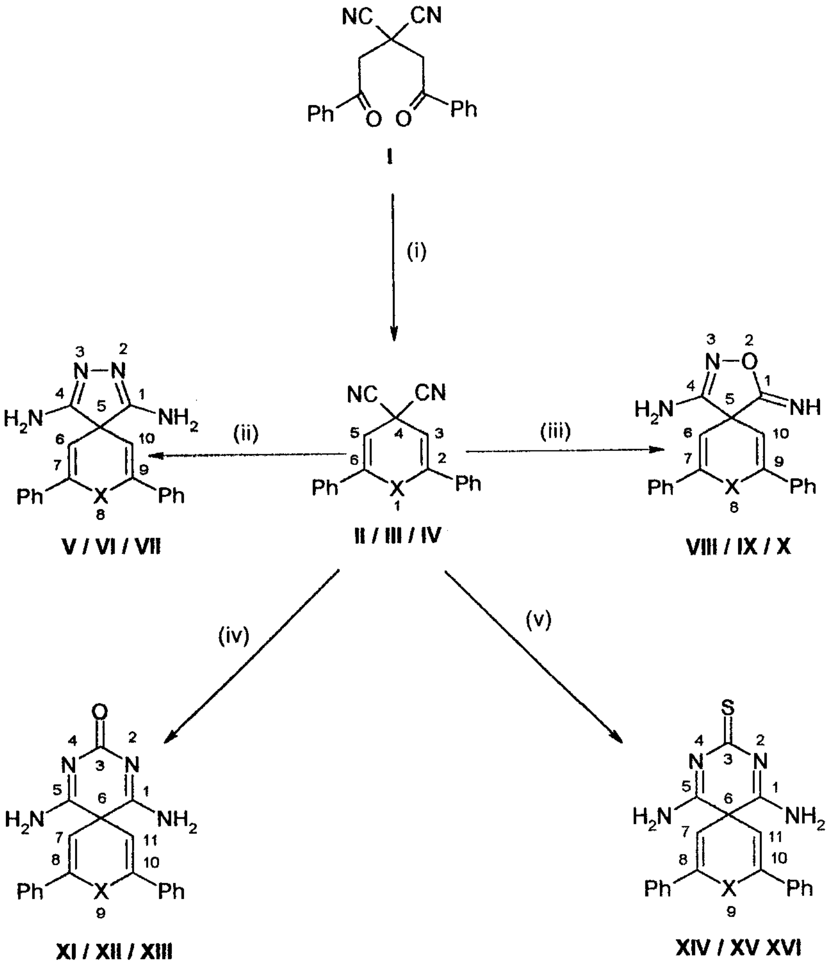
the present communication on the reactivity of 1,5-diaryl-3,3-dicyano-1,5-pentanedione.

RESULTS AND DISCUSSION

The key precursors 2,6-diphenyl-4,4-dicyanodihydropyridine (**II**), 2,6-diphenyl-4,4-dicyano-4*H*-pyran (**III**), and 2,6-diphenyl-4,4-dicyano-4*H*-thiopyran (**IV**) were prepared by treatment of 1,5-diaryl-3,3-dicyano-1,5-pentanedione (**I**) with ammonium acetate in acetic acid,[11] P_2O_5 in dry benzene,[12] and P_2S_5 in xylene[13] respectively. The absence of carbonyl absorption around 1690 in their IR spectra indicated the formation of **II–IV**. Further, the presence of a band around 3300 (NH) indicates he formation of **II**. The ^{1}H NMR spectra of **II–IV** showed a singlet in the region 5.08–5.98 ppm which account for (C_3-H and C_5-H) protons. The ^{13}C NMR spectra exhibited resonance signals for ring carbons of **II–IV** at 106.25–121.62 (C_3 and C_5), 142.13–149.44 (C_2 and C_6) and 42.41–44.53 (C_4). The cyclocondensation of **II–IV** with hydrazine hydrate and hydroxylamine hydrochloride in the presence of NaOMe furnished, 7,9-diphenyl-2,3,8-triaza-spiro[4.5] deca-1,3,6,9-tetraene-1,4-diamine (**V**)/7,9-diphenyl-8-oxa-2,3-diaza-spiro[4.5]deca-1,3,6,9-tetraene-1,4-diamine (**VI**)/7,9-diphenyl-8-thia-2,3-diaza-spiro [4.5]deca-1,3,6,9-tetraene-1,4-diamine (**VII**), 1-imino-7,9-diphenyl-2-oxa-3,8-diaza-spiro[4.5]deca-3,6,9-trien-4-ylamine (**VIII**)/1-imino-7,9-diphenyl-2,8-dioxa-3-aza-spiro[4.5]deca-3,6,9-trien-4-ylamine (**IX**)/1-imino-7,9-diphenyl-2-oxa-8-thia-3-aza-spiro[4.5]deca-3,6,9-trien-4-ylamine (**X**) respectively. A similar reaction of **II–IV** with urea and thiourea in presence of NaOMe, MeOH gave 1,5-diamino-8,10-diphenyl-2,4,9-triaza-spiro[5.5]undeca-1,4,7,10-tetraen-3-one (**XI**)/1,5-diamino-8,10-diphenyl-9-oxa-2,4-diaza-spiro[5.5]undeca-1,4,7,10-tetraen-3-one (**XII**)/1,5-diamino-8,10-diphenyl-9-thia-2,4-diaza-spiro[5.5]undeca-1,4,7,10-tetraen-3-one (**XIII**), and 1,5-diamino-8,10-diphenyl-2,4,9-triaza-spiro[5.5]undeca-1,4,7,10-tetraene-3-thione (**XIV**)/1,5-diamino-8,10-diphenyl-9-oxa-2,4-diaza-spiro[5.5]undeca-1,4,7,10-tetraene-3-thione (**XV**)/1,5-diamino-8,10-diphenyl-9-thia-2,4-diaza-spiro[5.5]undeca-1,4,7,10-tetraene-3-thione (**XVI**) respectively (Scheme 1 and Table I). The IR spectra of **V–XVI** exhibited absorption bands in the region 1650–1690 ($\underline{CO}$NH and NH$\underline{CO}$NH) and 3200–3300 (NH_2, NH). Apart from this **XVI** showed a absorption at 1521 (C=S). The methine protons of **V–XVI** showed a singlet almost in the same region as in **II–IV**, apart from this another singlet was observed for NH_2 and NH in the region 6.41–9.94 ppm. The δ_C values obtained for **V–XVI** further supports their structures (Table II).



II, V, VIII, XI, XIV X = NH; III, VI, IX, XII, XV X = O
IV, VII, X, XIII, XVI X = S

(i) NH_4OAc in AcOH / P_2O_5 in dry Benzene / P_2S_5 in Xylene

(ii) $NH_2.NH_2.H_20$ / NaOMe in MeOH; (iii) $NH_2OH.HCl$ / NaOMe in MeOH

(iv) NH_2CONH_2 / NaOMe in MeOH; (v) NH_2CSNH_2 / NaOMe in MeOH

SCHEME 1

TABLE I Physical and Analytical Data of Compounds **II–XVI**

Compd. no.	m.p. (°C)	Yield (%)	Mol. formula (mol. wt.)	Found (calcd.) % C	H	N
II	176–178	65	$C_{19}H_{13}N_3$ (283.34)	80.70 (80.54)	4.55 (4.62)	15.05 (14.83)
III	141–142	55	$C_{19}H_{12}N_2O$ (284.32)	80.34 (80.27)	4.33 (4.25)	10.01 (9.85)
IV	182–183	51	$C_{19}H_{12}N_2S$ (300.38)	75.89 (75.97)	4.09 (4.03)	9.48 (9.33)
V	273–275	57	$C_{19}H_{17}N_5$ (315.38)	72.52 (72.36)	5.50 (5.43)	22.32 (22.21)
VI	249–251	59	$C_{19}H_{16}N_4O$ (316.37)	72.02 (72.14)	5.14 (5.10)	17.56 (17.71)
VII	263–265	54	$C_{19}H_{16}N_4S$ (332.43)	68.50 (68.65)	4.96 (4.85)	16.70 (16.85)
VIII	233–234	61	$C_{19}H_{16}N_4O$ (316.37)	72.35 (72.14)	5.04 (5.10)	17.85 (17.71)
IX	205–206	58	$C_{19}H_{15}N_3O_2$ (317.35)	71.80 (71.91)	4.82 (4.76)	13.32 (13.24)
X	211–212	63	$C_{19}H_{15}N_3OS$ (333.41)	68.28 (68.45)	4.46 (4.53)	12.76 (12.60)
XI	277–279	57	$C_{20}H_{17}N_5O$ (343.39)	70.14 (69.96)	5.11 (4.99)	20.23 (20.39)
XII	289–291	60	$C_{20}H_{16}N_4O_2$ (344.38)	69.92 (69.76)	4.77 (4.68)	16.38 (16.27)
XIII	268–270	57	$C_{20}H_{16}N_4OS$ (360.44)	66.75 (66.65)	4.40 (4.47)	15.71 (15.54)
XIV	295–297	63	$C_{20}H_{17}N_5S$ (359.46)	66.70 (66.83)	4.72 (4.77)	19.60 (19.48)
XV	282–284	65	$C_{20}H_{16}N_4OS$ (360.44)	66.50 (66.65)	4.57 (4.47)	15.45 (15.54)
XVI	286–288	59	$C_{20}H_{16}N_4S_2$ (376.51)	63.98 (63.80)	4.20 (4.28)	15.01 (14.88)

Conclusion

The versatality of carbonyl and dicyano functions have been made use as tools for the synthesis of novel spiro heterocycles by a facile synthetic strategy.

EXPERIMENTAL

Melting points were determined on Mel-Temp apparatus and were uncorrected. The IR spectra were recorded on Perkin-Elmer 1600 series FT-IR spectrometer using KBr pellets. The wave numbers were given

TABLE II NMR Spectral Data of Compounds **II–XVI**

Compd. no.	^{1}H NMR (δ, ppm)	^{13}C NMR (δ, ppm)
II	5.08 (s, 2H, C_3 and C_5-H), 7.25–7.80 (m, 10H, ArH), 8.71 (s, 1H, NH)	42.41 (C_4), 107.69 (C_3 and C_5), 113.98 (CN), 142.13 (C_2 and C_6)
III	5.79 (s, 2H, C_3 and C_5-H), 7.26–7.78 (m, 10H, ArH)	43.01 (C_4), 106.25 (C_3 and C_5), 114.26 (CN), 149.15 (C_2 and C_6)
IV	5.98 (s, 2H, C_3 and C_5-H), 7.25–7.81 (m, 10H, ArH)	44.53 (C_4), 121.62 (C_3 and C_5), 113.54 (CN), 142.44 (C_2 and C_6)
V	4.84 (s, 2H, C_6 and C_{10}-H), 7.23–7.89 (m, 10H, ArH), 9.25 (bs, 5H, NH_2 and NH)	48.46 (C_5), 112.67 (C_6 and C_{10}), 139.25 (C_7 and C_9), 174.12 (C_1 and C_4)
VI	4.87 (s, 2H, C_6 and C_{10}-H), 7.24–7.80 (m, 10H, ArH), 9.17 (bs, 4H, NH_2)	41.24 (C_5), 109.41 (C_6 and C_{10}), 146.69 (C_7 and C_9), 173.85 (C_1 and C_4)
VII	5.74 (s, 2H, C_6 and C_{10}-H), 7.24–7.79 (m, 10H, ArH), 9.67 (bs, 4H, NH_2)	50.49 (C_5), 126.23 (C_6 and C_{10}), 142.58 (C_7 and C_9), 176.94 (C_1 and C_4)
VIII	4.82 (s, 2H, C_6 and C_{10}-H), 6.42–6.44 (bs, 4H, NH_2, NH), 7.20–7.78 (m, 10H, ArH)	47.92 (C_5), 111.29 (C_6 and C_{10}), 141.49 (C_7 and C_9), 172.21, 178.49 (C_1 and C_4)
IX	4.96 (s, 2H, C_6 and C_{10}-H), 6.49–6.52 (bs, 3H, NH_2, NH), 7.22–7.79 (m, 10H, ArH)	50.74 (C_5), 107.46 (C_6 and C_{10}), 149.42 (C_7 and C_9), 172.47, 178.79 (C_1 and C_4)
X	5.88 (s, 2H, C_6 and C_{10}-H), 6.45–6.47 (bs, 3H, NH_2, NH), 7.24–7.80 (m, 10H, ArH)	49.23 (C_5), 125.26 (C_6 and C_{10}), 142.96 (C_7 and C_9), 174. 23, 180.12 (C_1 and C_4)
XI	4.79 (s, 2H, C_7 and C_{11}-H), 6.41–6.42 (bs, 5H, NH_2, NH), 7.23–7.78 (m, 10H, ArH)	45.64 (C_6), 112.91 (C_7 and C_{11}), 140.19 (C_8 and C_{10}), 159.82 (C_3), 168.01 (C_1 and C_5)
XII	4.90 (s, 2H, C_7 and C_{11}-H), 6.41 (bs, 4H, NH_2), 7.24–7.80 (m, 10H, ArH)	50.68 (C_6), 107.68 (C_7 and C_{11}), 148.98 (C_8 and C_{10}), 159.68 (C_3), 168.29 (C_1 and C_5)
XIII	5.87 (s, 2H, C_7 and C_{11}-H), 6.44 (bs, 4H, NH_2), 7.20–7.78 (m, 10H, ArH)	49.49 (C_6), 128.34 (C_7 and C_{11}), 142.12 (C_8 and C_{10}), 159.59 (C_3), 168.42 (C_1 and C_5)
XIV	4.74 (s, 2H, C_7 and C_{11}-H), 7.25–7.79 (m, 10H, ArH), 9.94 (bs, 5H, NH_2 and NH)	48.89 (C_6), 113.24 (C_7 and C_{11}), 140.09 (C_8 and C_{10}), 161.24 (C_1 and C_5), 172.48 (C_3)
XV	4.92 (s, 2H, C_7 and C_{11}-H), 7.23–780 (m, 10H, ArH), 9.94 (bs, 4H, NH_2)	51.62 (C_6), 107.56 (C_7 and C_{11}), 149.24 (C_8 and C_{10}), 161.43 (C_1 and C_5), 172.26 (C_3)
XVI	5.90 (s, 2H, C_7 and C_{11}-H), 7.24–7.79 (m, 10H, ArH), 9.93 (bs, 4H, NH_2)	52.46 (C_6), 128.29 (C_7 and C_{11}), 142.86 (C_8 and C_{10}), 167.99 (C_1 and C_5), 172.08 (C_3)

in cm^{-1}. NMR spectra were recorded on a Bruker spectrospin 300 MHz spectrometer with TMS as an internal standard using $CDCl_3$/DMSO-d_6 as solvent. The chemical shifts were measured in ppm. The elemental analyses were obtained from Micro analytical laboratory, University of Pune, Pune, India. Purity of the compounds were checked by TLC using silica gel 'G' (BDH) and hexane-ethyl acetate (3:1) as eluents.

General Procedure for the Preparation of 2,6-Diphenyl-4,4-dicyano-1,4-dihydropyridine (II)

A mixture of **I** (10 mmol), ammonium acetate (1.5 g) and acetic acid (20 ml) was refluxed for 3 h. The reaction mixture was cooled and poured onto crushed ice. The product obtained was recrystallized from methanol to get **II**.

General Preparation for the Preparation of 2,6-Diphenyl-4,4-dicyano-4H-pyran (III)

The compound **I** (10 mmol) was dissolved in dry benzene (30 ml). To this phosphorus pentoxide (2 g) was added and refluxed for 6–10 h using Dean-Stark apparatus. The reaction mixture was filtered, washed with water and brine, and dried (an. Na_2SO_4). Evaporation of the solvent under vacuo resulted a residue which on recrystallization from methanol furnished **III**.

General Procedure for the Preparation of 2,6-Diphenyl-4,4-dicyano-4H-thiopyran (IV)

To a solution **I** (10 mmol) in xylene (25 ml), phosphorus pentasulfide (15 mmol) was added and refluxed for 12 h at 130–140°C. The reaction mixture was cooled and filtered to remove excess phosphorus pentasulfide. The solvent was removed under reduced pressure. The residue was recrystallized from methanol to afford **IV**.

General Procedure for the Preparation of 7,9-Diphenyl-2,3,8-triaza-spiro[4.5]deca-1,3,6,9-tetraene-1,4-diamine (V)/7,9-Diphenyl-8-oxa-2,3-diaza-spiro[4.5]deca-1,3,6,9-tetraene-1,4-diamine (VI)/7,9-Diphenyl-8-thia-2,3-diaza-spiro[4.5]deca-1,3,6,9-tetraene-1,4-diamine (VII)

The compound **II**/**III**/**IV** (10 mmol), 80% hydrazine hydrate (15 mmol) in methanol (25 ml) was taken. To this 10% NaOMe (5 ml) was added and refluxed for 5–6 h. The contents were cooled and poured onto crushed ice containing AcOH. The product obtained was recrystallized from methanol to get **V/VI/VII**.

General Procedure for the Preparation of 1-Imino-7,9-diphenyl-2-oxa-3,8-diaza-spiro[4.5]deca-3,6,9-trien-4-ylamine (VIII)/1-Imino-7,9-diphenyl-2,8-dioxa-3-aza-spiro[4.5]deca-3,6,9-trien-4-ylamine (IX)/1-Imino-7,9-diphenyl-2-oxa-8-thia-3-aza-spiro [4.5]deca-3,6,9-trien-4-Ylamine (X)

To an equimolar (10 mmol) mixture of **II/III/IV** and hydroxylamine hydrochloride, 10% NaOMe (5 ml) was added and refluxed for 5 h. The reaction mixture was cooled, poured onto crushed ice, and acidified with AcOH. The crude product separated was filtered and recystallized from methanol to afford **VIII/IX/X**.

General Procedure for the Preparation of 1,5-Diamino-8,10-diphenyl-2,4,9-triaza-spiro[5.5]undeca-1,4,7,10-tetraen-3-one (XI)/1,5-Diamino-8,10-diphenyl-9-oxa-2,4-diaza-spiro[5.5]undeca-1,4,7,10-tetraen-3-one (XII)/1,5-Diamino-8,10-diphenyl-9-thia-2,4-diaza-spiro [5.5]undeca-1,4,7,10-tetraen-3-one (XIII)

A mixture of **II/III/IV** (5 mmol), urea (5 mmol), methanol (20 ml), and 10% NaOMe (3 ml) was refluxed for 8–10 h. The solution was cooled and poured onto crushed ice containing AcOH. The solid obtained was separated and recystallized from methanol to furnish **XI/XII/XIII**.

General Procedure for the Preparation of 1,5-Diamino-8,10-diphenyl-2,4,9-triaza-spiro[5.5]undeca-1,4,7,10-tetraene-3-thione (XIV)/1,5-Diamino-8,10-diphenyl-9-oxa-2,4-diaza-spiro[5.5]undeca-1,4,7,10-tetraene-3-thione (XV)/1,5-Diamino-8,10-diphenyl-9-thia-2,4-diaza-spiro[5.5]undeca-1,4,7,10-tetraene-3-thione (XVI)

To an equimolar solution (10 mmol) of **II/III/IV** and thiourea, 10% NaOMe (5 ml) was added and refluxed for 9–10 h. The reaction mixture was cooled, poured onto crushed ice and acidified with AcOH. The resultant solid was separated and recrystallized from methanol to get **XIV/XV/XVI**.

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