Pergamon

Tetrahedron 58 (2002) 8113–8118

TETRAHEDRON

Diisopropylaminoisocyanide and DMAD in multiple component reactions (MCRs): novel synthesis of substituted 1-amino-3-pyrrolin-2-ones by reaction with aldehydes and dicarbonyl compounds

Vijay Nair,[a,*] Joseph Swaroop Mathen,[a] S. Viji,[a] R. Srinivas,[b] M. V. Nandakumar[a] and Luxmi Varma[a]

[a]*Organic Chemistry Division, Regional Research Laboratory (CSIR), Trivandrum 695 019, India*
[b]*Mass Spectrometry Center, Indian Institute of Chemical Technology (CSIR), Hyderabad 500 007, India*

Received 31 January 2002; revised 5 July 2002; accepted 1 August 2002

Abstract—The zwitterion generated from diisopropylaminoisocyanide and dimethyl acetylenedicarboxylate (DMAD) reacts with a variety of carbonyl and dicarbonyl compounds affording substituted 1-aminopyrrolin-2-ones. © 2002 Elsevier Science Ltd. All rights reserved.

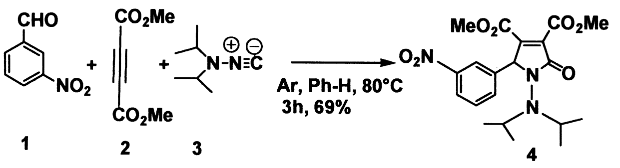
1. Introduction

Isocyanides,[1] regarded for many years as compounds with unpleasant odour and very few chemical and pharmaceutical applications, are now looked upon as useful synthons with interesting chemical properties. The change in attitude can be attributed primarily to the renaissance of the isocyanide based multicomponent reactions (MCRs)[2] viz., the Passerini three component reaction (P-3CR)[3] and more importantly the Ugi four component reaction (U-4CR),[4] with its ability to deliver enormous *sortiment*[5] of peptide analogs and heterocyclic compounds for sustaining the drug discovery programs of the pharmaceutical industry.

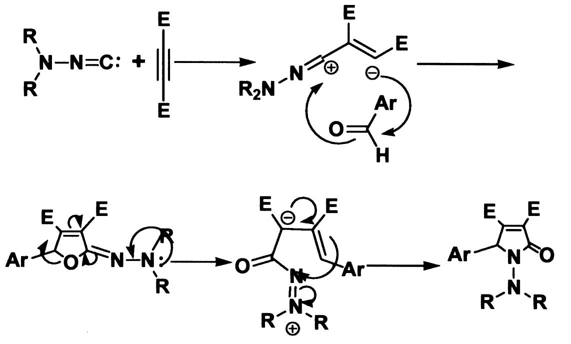
The recent interest in the chemistry of isocyanides has been mainly focused on the reactivity of *C*-isocyanides. The multiple component reactions of *N*-isocyanides are virtually unknown except for two isolated reports.[6] Against this backdrop, and in the context of our general interest in multiple component reactions,[7] we have undertaken a study of MCRs involving diisopropylaminoisocyanide and DMAD. A preliminary report on the reactivity of the resultant zwitterion with aldehydes has been published.[8] In this paper, we present the results of an extended investigation of the reactivity of the zwitterion with a variety of aldehydes and dicarbonyl compounds leading to the formation of 1-aminopyrrolin-2-one derivatives.

2. Results and discussion

Our studies were initiated by the reaction of diisopropylaminoisocyanide with DMAD and 3-nitrobenzaldehyde. A mixture of the three in benzene under an atmosphere of argon, when heated for 3 h under reflux afforded the 1-aminopyrrolin-2-one derivative **4** in 69% yield (Scheme 1). The product was characterized on the basis of spectroscopic data. The pyrrolin-2-one derivative presumably arises from a Dimroth-type rearrangement[9] of the primary adduct, the furanone hydrazone (Scheme 2). The product



Scheme 1.



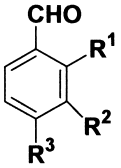
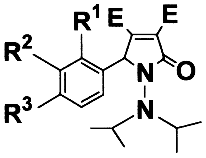
Scheme 2.

Keywords: aminoisocyanide; multiple component reactions; carbonyl compounds; 1-aminopyrrolin-2-ones.

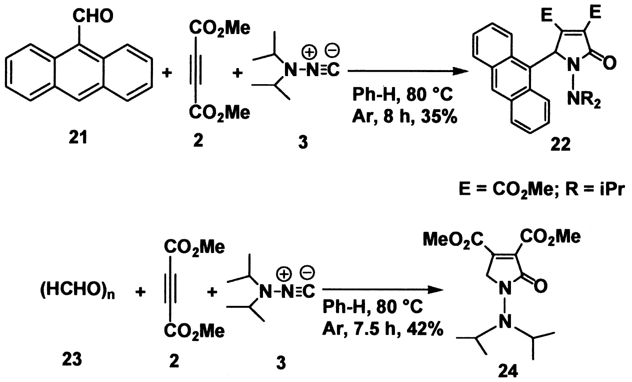
* Corresponding author. Tel.: +91-471-490406; fax: +91-471-491712/490186; e-mail: vijaynair_2001@yahoo.com

PII: S0040-4020(02)00939-0

Table 1. Reaction of *N*-isocyanide and DMAD with aldehydes

Sl. no.		Reaction time (h)		Yield (%)[a]
1	**5** R^1=R^2=H; R^3=NO_2	3	**6** R^1=R^2=H; R^3=NO_2	65
2	**7** R^1=R^2=H; R^3=Cl	2	**8** R^1=R^2=H; R^3=Cl	55
3	**9** R^2=R^3=H; R^1=Cl	2.5	**10** R^2=R^3=H; R^1=Cl	57
4	**11** R^1=R^2=H; R^3=CF_3	3.5	**12** R^1=R^2=H; R^3=CF_3	79
5	**13** R^1=R^2=H; R^3=Me	3	**14** R^1=R^2=H; R^3=Me	52
6	**15** R^2=R^3=H; R^1=Me	3	**16** R^2=R^3=H; R^1=Me	54
7	**17** R^1=R^2=H; R^3=OBn	5	**18** R^1=R^2=H; R^3=OBn	45
8	**19** R^1=R^2=R^3=H	5	**20** R^1=R^2=R^3=H	30

[a] Isolated yield, E=CO_2Me.

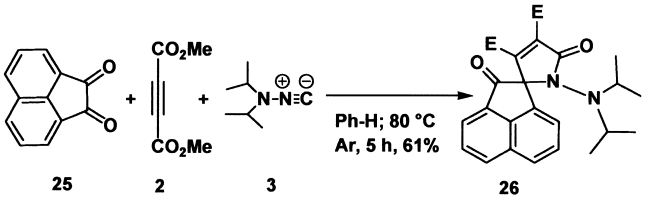


Scheme 3.

was differentiated from the primary adduct by means of spectroscopic techniques—NOESY and HMBC.[8]

The reaction has been found to be general with a number of benzaldehydes, both electron rich and electron deficient. Similar reaction was observed with 9-anthraldehyde and formaldehyde also. The results are summarized in Table 1 and Scheme 3. It may be pointed out that enolizable aldehydes failed to give the products, presumably due to the quenching of the zwitterion by the enol.

Subsequent to the above studies, we investigated the reaction of the zwitterion generated from *N*-isocyanide and DMAD with some dicarbonyl compounds. In an initial experiment, a mixture of acenaphthene quinone, DMAD and *N*-isocyanide in benzene was heated under reflux in an atmosphere of argon for 5 h affording the spirocompound **26** in 61% yield (Scheme 4). The product was characterized on the basis of spectroscopic data.



Scheme 4.

The reaction has been found to be general with a number of 1,2- and 1,4-dicarbonyl compounds and the results are summarized in Table 2.

In conclusion, we have devised a novel MCR involving an aminoisocyanide for the synthesis of substituted 1-amino-pyrrolin-2-ones.

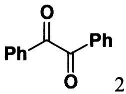
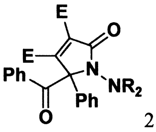
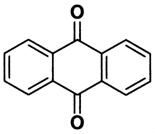
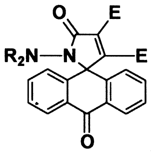
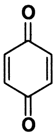
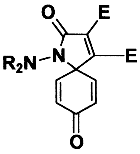
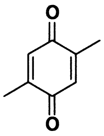
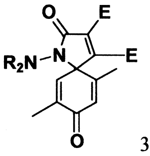
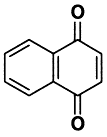
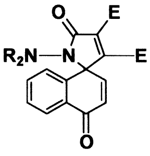
3. Experimental

All reactions were carried out in oven dried glassware under an atmosphere of argon. The melting points were recorded on a Mel-Temp apparatus and are uncorrected. The IR spectra were recorded on Bomem MB series FT-IR spectrophotometer and Nicolet Impact 400D spectrophotometer, using potassium bromide pellets. NMR spectra were recorded on Bruker-300 MHz FT NMR spectrometer using $CDCl_3$–CCl_4 mixture (3:1) as the solvent. The chemical shifts are given in the δ scale with tetramethylsilane (^1H) and $CDCl_3$ (^{13}C) as the internal standards. Elemental analysis was carried out using Perkin–Elmer 2400 CHNS analyzer. Mass spectra were recorded under E1/HRMS (at 5000 resolution) using Auto Spec. M mass spectrometer. Petroleum ether refers to the fraction boiling between 60 and 80°C. Gravity column chromatography was performed using silica gel (100–200 mesh) with mixtures of petroleum ether (or hexane) and ethyl acetate as eluent. Chromatographic separations have also been carried out using Chromatotron®. Solvents used for the experiments have been dried and distilled according to the literature procedure.[10] Analytical tlc was performed on glass plates coated with silica gel containing 13% $CaSO_4$ as the binder. Diisopropylamine and formic acid (98–100%) were purchased from local chemical suppliers and used without further purification. The aldehydes, dicarbonyl compounds and DMAD were purchased from Aldrich Chemical Co., USA. The diisopropylaminoisocyanide was synthesized according to the reported procedure.[11]

3.1. General experimental procedure

To a mixture of the carbonyl compound (1 equiv.) and DMAD (1.1 equiv.) in anhydrous benzene at 80°C under an atmosphere of argon was added a solution of

Table 2. Reaction of *N*-isocyanide and DMAD with dicarbonyl compounds

Sl. no.	Dicarbonyl compound	Reaction time (h)	Product	Yield (%)[a]
1	 27	12	 28	50
2	 29	8	 30	70
3	 31	12	 32	62
4	 33	9	 34	73
5	 35	6	 36	61

[a] Isolated yield, E=CO_2Me, R=*i*Pr.

diisopropylaminoisocyanide (1.5 equiv.) in benzene. The mixture was heated under reflux for an appropriate time (as given in the details for individual experiments). On completion of the reaction, as indicated by the tlc of the reaction mixture, the solvent was evaporated off using a rotary evaporator. The crude product was subjected to chromatography using silica gel on a Chromatotron® using mixtures of petroleum ether and ethyl acetate as the eluent. The fractions were pooled together and concentrated under vacuum to afford the product.

3.1.1. Dimethyl 1-(diisopropylamino)-2-(3-nitrophenyl)-5-oxo-2,5-dihydro-1*H*-pyrrole-3,4-dicarboxylate (4).[8]

The reaction of 3-nitrobenzaldehyde (0.030 g, 0.2 mmol) and DMAD (0.031 g, 0.027 mL, 0.22 mmol) in 1 mL anhydrous benzene at 80°C with diisopropylaminoisocyanide (0.0378 g, 0.3 mmol) in 0.5 mL benzene under reflux for 3 h afforded, after work up and chromatography with 5% EtOAc–hexane mixture, 0.0579 g (69%) of the product **4** as an yellow solid; crystallized from ether–hexane mixture; yellow crystals, mp 115–117°C. IR (KBr): 1053, 1096, 1222, 1249, 1354, 1465, 1529, 1613, 1682, 1735, 2976 cm^{-1}. ^1H NMR ($CDCl_3$, δ): 1.09 (d, *J*=6.1 Hz, 12H), 3.21 (m, 2H), 3.81 (s, 3H), 3.97 (s, 3H), 7.32 (s, 1H), 7.52 (t, *J*=7.9 Hz, 1H), 7.87 (d, *J*=7.6 Hz, 1H), 8.07 (d, *J*=7.7 Hz, 1H), 8.38 (s, 1H). ^{13}C NMR ($CDCl_3$, δ): 19.00, 51.46, 52.86, 87.63, 115.72, 119.43, 121.88, 129.70, 130.06, 130.83, 138.92, 148.61, 163.93, 164.61, 165.21. Anal. calcd for $C_{20}H_{25}N_3O_7$: C, 57.28;H 5.97; N, 10.02. Found: C, 57.39;H 5.99; N, 10.10.

3.1.2. Dimethyl 1-(diisopropylamino)-2-(4-nitrophenyl)-5-oxo-2,5-dihydro-1*H*-pyrrole-3,4-dicarboxylate (6).

The reaction of 4-nitrobenzaldehyde (0.030 g, 0.2 mmol) and DMAD (0.031 g, 0.027 mL, 0.22 mmol) in 1 mL anhydrous benzene at 80°C with diisopropylaminoisocyanide (0.0378 g, 0.3 mmol) in 0.5 mL benzene at reflux for 3 h after work up and chromatography using 5% EtOAc–hexane mixture afforded 0.0544 g (65%) of the product **6** as an yellow solid; crystallized from Et_2O–petroleum ether. mp 117–118°C. IR (KBr): 1094, 1240, 1319, 1472, 1512, 1593, 1673, 1734, 2978 cm^{-1}. ^1H NMR ($CDCl_3$, δ): 1.10 (d, *J*=6.2 Hz, 12H), 3.23 (m, 2H), 3.82 (s, 3H), 3.95 (s, 3H), 7.35 (s, 1H), 7.66 (t, *J*=8.7 Hz, 2H), 8.21 (d, *J*=8.8 Hz, 2H). ^{13}C NMR ($CDCl_3$, δ): 19.90, 51.39, 52.77, 88.21, 117.20, 124.13, 124.29, 134.95, 138.56, 146.10, 164.03, 164.30, 165.05. Anal. calcd for $C_{20}H_{25}N_3O_7$: C, 57.27; H, 6.01; N, 10.02. Found: C, 57.51; H, 6.01; N, 10.07.

3.1.3. Dimethyl 2-(4-chlorophenyl)-1-(diisopropylamino)-5-oxo-2,5-dihydro-1*H*-pyrrole-3,4-dicarboxylate (8).

The reaction of 4-chlorobenzaldehyde (0.028 g, 0.2 mmol) and DMAD (0.031 g, 0.027 mL, 0.22 mmol) in 1 mL anhydrous benzene at 80°C with diisopropylaminoisocyanide (0.0378 g, 0.3 mmol) in 0.5 mL benzene under reflux for 2 h after work up and chromatography using 5%

EtOAc–hexane mixture afforded 0.0449 g (55%) of the product **8** as a colourless viscous liquid. IR (CCl_4): 1097, 1226, 1251, 1364, 1487, 1620, 1683, 1740, 2938 cm^{-1}. ^{1}H NMR ($CDCl_3$, δ): 1.09 (d, J=6.2 Hz, 12H), 3.20 (m, 2H), 3.79 (s, 3H), 3.89 (s, 3H), 7.24 (s, 1H), 7.31 (d, J=8.5 Hz, 2H), 7.50 (d, J=8.5 Hz, 2H). ^{13}C NMR ($CDCl_3$, δ): 19.00, 51.27, 52.51, 52.86, 87.36, 113.67, 126.23, 127.82, 128.84, 133.53, 140.77, 163.74, 164.74, 165.47. HRMS calcd for $C_{20}H_{25}ClN_2O_5$: 408.145200. Found: 408.143458.

3.1.4. Dimethyl 2-(2-chlorophenyl)-1-(diisopropylamino)-5-oxo-2,5-dihydro-1*H*-pyrrole-3,4-dicarboxylate (10). The reaction of 2-chlorobenzaldehyde (0.028 g, 0.0224 mL, 0.2 mmol) and DMAD (0.031 g, 0.027 mL, 0.22 mmol) in 1 mL anhydrous benzene at 80°C with diisopropylaminoisocyanide (0.0378 g, 0.3 mmol) in 0.5 mL benzene under reflux conditions for 2.5 h after work up and chromatography using 5% EtOAc–hexane mixture afforded 0.0465 g (57%) of the product **10** as a semi-solid; crystallized from Et_2O–petroleum ether to afford colourless crystals. mp 81–82°C. IR (KBr): 1100, 1243, 1366, 1475, 1610, 1683, 1741, 2983 cm^{-1}. ^{1}H NMR ($CDCl_3$, δ): 1.08 (d, J=6.2 Hz, 12H), 3.18 (m, 2H), 3.73 (s, 3H), 3.81 (s, 3H), 7.28 (m, 2H), 7.43 (m, 3H). ^{13}C NMR ($CDCl_3$, δ): 18.97, 51.12, 51.93, 52.73, 86.08, 116.25, 126.34, 129.93, 130.05, 131.82, 133.95, 141.59, 164.06, 164.47, 165.14. Anal. calcd for $C_{20}H_{25}ClN_2O_5$: C, 58.75; H, 6.16; N, 6.93. Found: C, 58.94; H, 6.31; N, 6.89.

3.1.5. Dimethyl 1-(diisopropylamino)-2-oxo-5-[4-(trifluoromethyl)phenyl]-2,5-dihydro-1*H*-pyrrole-3,4-dicarboxylate (12). The reaction of 4-trifluoromethylbenzaldehyde (0.034 g, 0.0273 mL, 0.2 mmol) and DMAD (0.031 g, 0.027 mL, 0.22 mmol) in 1 mL anhydrous benzene at 80°C with diisopropylaminoisocyanide (0.0378 g, 0.3 mmol) in 0.5 mL benzene at reflux for 3.5 h after work up and chromatography using 5% EtOAc–hexane mixture afforded 0.0698 g (79%) of the product **12** as a pale yellow semi-solid. IR (CCl_4): 845, 1126, 1228, 1252, 1378, 1485, 1625, 1687, 1740, 2983 cm^{-1}.^{1}H NMR ($CDCl_3$, δ): 1.09 (d, J=6.2 Hz, 12H), 3.22 (m, 2H), 3.80 (s, 3H), 3.92 (s, 3H), 7.29 (s, 1H), 7.63 (m, 4H). ^{13}C NMR ($CDCl_3$, δ): 19.00, 51.28, 52.60, 52.78, 87.61, 115.25, 122.21, 124.60, 125.56, 125.81, 128.88, 129.31, 132.50, 139.72, 163.85, 164.56, 165.33. HRMS calcd for $C_{21}H_{25}F_3N_2O_5$: 442.17156. Found: 443.178362 (MH^+).

3.1.6. Dimethyl 1-(diisopropylamino)-2-(4-methylphenyl)-5-oxo-2,5-dihydro-1*H*-pyrrole-3,4-dicarboxylate (14). The reaction of 4-methylbenzaldehyde (0.024 g, 0.021 mL, 0.2 mmol) and DMAD (0.031 g, 0.027 mL, 0.22 mmol) in 1 mL anhydrous benzene at 80°C with diisopropylaminoisocyanide (0.0378 g, 0.3 mmol) in 0.5 mL benzene under reflux continued for 3 h. The solvent was evaporated off and the crude reaction mixture was subjected to chromatography on silica gel and elution with 5% EtOAc–hexane mixture afforded 0.0403 g (52%) of the product **14** as a pale yellow viscous liquid. IR (CCl_4): 740, 1101, 1225, 1266, 1366, 1473, 1617, 1681, 1739, 2984 cm^{-1}.^{1}H NMR ($CDCl_3$, δ): 1.09 (d, J=6.3 Hz, 12H), 2.35 (s, 3H), 3.19 (m, 2H), 3.78 (s, 3H), 3.88 (s, 3H), 7.148 (d, J=7.9 Hz, 2H), 7.21 (s, 1H), 7.44 (d, J=8.1 Hz, 2H). ^{13}C NMR ($CDCl_3$, δ): 19.44, 21.37, 51.16, 52.35, 52.85, 87.17, 104.83, 112.37, 125.13, 126.63, 129.26, 137.62, 142.30, 163.68, 164.92, 165.73. HRMS calcd for $C_{21}H_{28}N_2O_5$: 388.199822. Found: 388.198982.

3.1.7. Dimethyl 1-(diisopropylamino)-2-(2-methylphenyl)-5-oxo-2,5-dihydro-1*H*-pyrrole-3,4-dicarboxylate (16). The reaction of 2-methylbenzaldehyde (0.024 g, 0.023 mL, 0.2 mmol) and DMAD (0.031 g, 0.027 mL, 0.22 mmol) in 1 mL anhydrous benzene at 80°C with diisopropylaminoisocyanide (0.0378 g, 0.3 mmol) in 0.5 mL benzene under reflux for 3 h after work up and chromatography using 5% EtOAc–hexane mixture afforded 0.0419 g (54%) of the product **16** as an yellow semi-solid, crystallized from Et_2O–petroleum ether. mp 60–61°C. IR (KBr): 1060, 1098, 1246, 1366, 1471, 1615, 1679, 1740, 2982 cm^{-1}. ^{1}H NMR ($CDCl_3$, δ): 1.06 (d, J=6.2 Hz, 12H), 2.35 (s, 3H), 3.17 (m, 2H), 3.73 (s, 3H), 3.80 (s, 3H), 7.25 (m, 5H). ^{13}C NMR ($CDCl_3$, δ): 19.00, 20.69, 51.14, 52.02, 52.74, 86.07, 114.86, 125.46, 128.77, 129.10, 130.25, 130.48, 137.76, 144.42, 164.29, 164.73, 165.16. Anal. calcd for $C_{21}H_{28}N_2O_5$: C, 64.93; H, 7.27; N, 7.21. Found: C, 64.34; H, 7.65; N, 7.21.

3.1.8. Dimethyl 2-[4-(benzyloxy)phenyl]-1-(diisopropylamino)-5-oxo-2,5-dihydro-1*H*-pyrrole-3,4-dicarboxylate (18). The reaction of 4-benzyloxybenzaldehyde (0.0424 g, 0.2 mmol) and DMAD (0.031 g, 0.027 mL, 0.22 mmol) in 1 mL anhydrous benzene at 80°C with diisopropylaminoisocyanide (0.0378 g, 0.3 mmol) in 0.5 mL benzene under reflux for 5 h after work up and chromatography using 5% EtOAc–hexane mixture afforded 0.0432 g (45%) of the product **18** as a colourless viscous liquid. IR (CCl_4): 1100, 1179, 1251, 1467, 1610, 1681, 1738, 2983 cm^{-1}. ^{1}H NMR ($CDCl_3$, δ): 1.08 (d, J=6.2 Hz, 12H), 3.19 (m, 2H), 3.78 (s, 3H), 3.87 (s, 3H), 5.08 (s, 2H), 6.94 (d, J=8.7 Hz, 2H), 7.20 (s, 1H), 7.36 (m, 7H). ^{13}C NMR ($CDCl_3$, δ): 19.89, 51.17, 52.34, 52.85, 70.02, 88.75, 115.01, 122.43, 126.89, 127.39, 128.03, 136.83, 158.59, 163.62, 164.98, 165.78. HRMS calcd for $C_{27}H_{32}N_2O_6$: 480.226037. Found: 480.227617.

3.1.9. Dimethyl 1-(diisopropylamino)-2-phenyl-5-oxo-2,5-dihydro-1*H*-pyrrole-3,4-dicarboxylate (20). The reaction of benzaldehyde (0.028 g, 0.020 mL, 0.2 mmol) and DMAD (0.031 g, 0.027 mL, 0.22 mmol) in 1 mL anhydrous benzene at 80°C with diisopropylaminoisocyanide (0.0378 g, 0.3 mmol) in 0.5 mL benzene under reflux for 5 h after work up and using 5% EtOAc–hexane mixture afforded 0.0224 g (30%) of the product **20** as an yellow viscous liquid. IR (CCl_4): 1100, 1224, 1251, 1363, 1479, 1615, 1680, 1742, 2981 cm^{-1}. ^{1}H NMR ($CDCl_3$, δ): 1.08 (d, J=6.2 Hz, 12H), 3.20 (m, 2H), 3.79 (s, 3H), 3.89 (s, 3H), 7.23 (s, 1H), 7.25 (d, J=4.5 Hz, 2H), 7.33 (m, 2H), 7.55 (m, 2H). ^{13}C NMR ($CDCl_3$, δ): 18.75, 19.36, 51.19, 52.44, 52.81, 87.25, 124.94, 127.69, 128.57, 129.30, 141.71, 163.72, 164.84, 165.71. HRMS calcd for $C_{20}H_{26}N_2O_5$: 374.184172. Found: 374.183233.

3.1.10. Dimethyl 2-(9-anthryl)-1-(diisopropylamino)-5-oxo-2,5-dihydro-1*H*-pyrrole-3,4-dicarboxylate (22). The reaction of 9-anthraldehyde (0.042 g, 0.2 mmol) and DMAD (0.031 g, 0.027 mL, 0.22 mmol) in 1 mL anhydrous benzene at 80°C with diisopropylaminoisocyanide (0.0378 g, 0.3 mmol) in 0.5 mL benzene under reflux for

8 h after work up and chromatography using 5% EtOAc–hexane mixture afforded 0.034 g (35%) of the product **22** as an yellow semi-solid; crystallized from Et_2O–petroleum ether. mp 195–196°C. IR (KBr): 1096, 1221, 1376, 1448, 1480, 1609, 1675, 1735, 2979 cm^{-1}. ^1H NMR ($CDCl_3$, δ): 1.063 (d, J=6.2 Hz, 12H), 3.14 (m, 2H), 3.32 (s, 3H), 3.87 (s, 3H), 7.42 (t, J=3.8 Hz, 4H), 7.49 (s, 1H), 7.80 (m, 2H), 7.98 (m, 2H), 8.50 (s, 1H). ^{13}C NMR ($CDCl_3$, δ): 19.00, 51.20, 51.68, 52.77, 85.45, 123.14, 125.25, 125.95, 126.32, 128.41, 129.37, 131.16, 132.29, 142.07, 163.80, 165.26, 165.47. Anal. calcd for $C_{28}H_{30}N_2O_5$: C, 70.87; H, 6.37; N, 5.90. Found: C, 71.09; H, 6.53; N, 6.30.

3.1.11. Dimethyl 1-(diisopropylamino)-2-oxo-2,5-dihydro-1*H*-pyrrole-3,4-dicarboxylate (24). The reaction of DMAD (0.0284 g, 0.025 mL, 0.2 mmol) and paraformaldehyde (0.018 g, 0.6 mmol) in 1 mL anhydrous benzene at 80°C with diisopropylaminoisocyanide (0.0378 g, 3 mmol) in 0.5 mL benzene under reflux for 7.5 h after work up and chromatography on silica gel. Elution with 3% EtOAc–hexane mixture afforded 0.025 g (42%) of **24** as an yellow viscous liquid. IR (CCl_4): 784, 1081, 1202, 1344, 1485, 1607, 1674, 1748, 2975 cm^{-1}. ^1H NMR ($CDCl_3$, δ): 1.06 (d, J=6.3 Hz, 12H), 3.19 (m, 2H), 3.23 (s, 3H), 3.25 (s, 3H), 7.29 (s, 1H), 7.43 (s,1H).^{13}C NMR ($CDCl_3$, δ): 19.00, 51.11, 51.61, 52.67, 84.42, 117.89, 137.84, 162.55, 165.51, 65.72. HRMS (FAB) calcd for $C_{14}H_{22}N_2O_5$: 298.15287. Found: 299.161912 (MH^+).

3.1.12. Spirocompound 26. The reaction of acenaphthenequinone (0.0364 g, 0.2 mmol) and DMAD (0.031 g, 0.027 mL, 0.22 mmol) in 1 mL anhydrous benzene at 80°C with diisopropylaminoisocyanide (0.0378 g, 0.3 mmol) in 0.5 mL benzene under reflux for 5 h after work up and chromatography using 5% EtOAc–hexane mixture afforded 0.055 g (61%) of the product **26** as an yellow semi-solid. IR (CCl_4): 776, 1441, 1474, 1652, 1685, 1708, 1738, 2979 cm^{-1}. ^1H NMR ($CDCl_3$, δ): 0.39 (d, J=6.5 Hz, 3H), 0.57 (d, J=6.7 Hz, 3H), 0.89 (d, J=6.7 Hz, 3H), 1.03 (d, J=6.4 Hz, 3H), 3.10 (m, 1H), 3.38 (m, 1H), 3.46 (s, 3H), 3.96 (s, 3H), 7.43–8.18 (m, 6H). ^{13}C NMR ($CDCl_3$, δ): 21.71, 22.69, 22.87, 23.03, 52.67, 52.95, 53.37, 55.12, 77.63, 121.79, 122.51, 126.57, 128.17, 128.44, 130.98, 131.89, 133.28, 133.54, 138.27, 141.27, 141.87, 144.10, 160.18, 162.01, 166.50, 195.71. HRMS calcd for $C_{25}H_{26}N_2O_6$: 450.179087. Found: 450.179934.

3.1.13. Dimethyl 2-benzoyl-1-(diisopropylamino)-5-oxo-2-phenyl-2,5-dihydro-1*H*-pyrrole-3,4-dicarboxylate (28). The reaction of benzil (0.042 g, 0.2 mmol) and DMAD (0.031 g, 0.027 mL, 0.22 mmol) in 1 mL anhydrous benzene at 80°C with diisopropylaminoisocyanide (0.0378 g, 0.3 mmol) in 0.5 mL benzene under reflux for 12 h after work up and chromatography using 5% EtOAc–hexane mixture afforded 0.048 g (50%) of the product **28** as an yellow viscous liquid. IR (CCl_4): 787, 912, 1027, 1059, 1098, 1250, 1365, 1446, 1485, 1610, 1677, 1737, 2975 cm^{-1}.^1H NMR ($CDCl_3$, δ): 1.08 (d, J=6.1 Hz), 3.18 (m, 2H), 3.68 (s, 3H), 3.73 (s, 3H), 7.39 (m, 9H), 8.07 (d, J=7.1 Hz, 1H). HRMS calcd for $C_{27}H_{30}N_2O_6$: 478.210387. Found: 478.210246.

3.1.14. Spirocompound 30. The reaction of 9,10-anthraquinone (0.0416 g, 0.2 mmol) and DMAD (0.031 g, 0.027 mL, 0.22 mmol) in 1 mL anhydrous benzene at 80°C with diisopropylaminoisocyanide (0.0378 g, 0.3 mmol) in 0.5 mL benzene under reflux for 8 h. After work up and chromatography using 10% EtOAc–hexane mixture afforded 0.066 g (70%) of the product **30** as an yellow semi-solid. IR (CCl_4): 727, 791, 913, 1023, 1098, 1267, 1437, 1456, 1601, 1672, 1710, 1735, 1751, 2955, 2971 cm^{-1}. ^1H NMR ($CDCl_3$, δ): 0.39 (d, 6H), 0.59 (d, 6H), 2.74 (m, 2H), 3.48 (s, 3H), 4.01 (s, 3H), 7.32 (m, 2H), 7.56 (m, 4H), 8.33 (m, 2H). ^{13}C NMR ($CDCl_3$, δ): 22.31, 22.63, 52.78, 53.13, 54.87, 68.68, 98.27, 126.59, 128.14, 129.47, 133.35, 133.71, 137.04, 145.17, 160.04, 162.37, 165.87, 182.72. HRMS calcd for $C_{27}H_{28}N_2O_6$: 476.194737. Found: 476.194004.

3.1.15. Dimethyl 1-(diisopropylamino)-2,8-dioxo-1-azaspiro[4.5]deca-3,6,9-triene-3,4-dicarboxylate (32). The reaction of 1,4-benzoquinone (0.0216 g, 0.2 mmol) and DMAD (0.031 g, 0.027 mL, 0.22 mmol) in 1 mL anhydrous benzene at 80°C with diisopropylaminoisocyanide (0.0378 g, 0.3 mmol) in 0.5 mL benzene under reflux for 12 h after work up and chromatography using 10% EtOAc–hexane mixture afforded 0.047 g (62%) of the product **32** as an yellow semi-solid. IR (CCl_4): 790, 915, 1045, 1065, 1102, 1276, 1347, 1456, 1632, 1674, 1705, 1732, 2974 cm^{-1}. ^1H NMR ($CDCl_3$, δ): 0.99 (d, J=6.6 Hz, 6H), 1.14 (d, J=6.4 Hz, 6H), 3.40 (m, 2H), 3.69 (s, 3H), 3.86 (s, 3H), 6.45 (m, 4H). ^{13}C NMR ($CDCl_3$, δ): 23.17, 23.39, 52.87, 52.95, 55.12, 66.20, 132.91, 137.14, 142.32, 143.42, 159.99, 161.42, 164.52, 183.95. HRMS calcd for $C_{19}H_{24}N_2O_6$: 376.16344. Found: 377.172810.

3.1.16. Dimethyl 1-(diisopropylamino)-6,9-dimethyl-2,8-dioxo-1-azaspiro[4.5]deca-3,6,9-triene-3,4-dicarboxylate (34). The reaction of 2,5-dimethyl-1,4-benzoquinone (0.0272 g, 0.2 mmol) and DMAD (0.031 g, 0.027 mL, 0.22 mmol) in 1 mL anhydrous benzene at 80°C with diisopropylaminoisocyanide (0.0378 g, 0.3 mmol) in 0.5 mL benzene under reflux for 9 h after work up and chromatography using 10% EtOAc–hexane mixture afforded 0.059 g (73%) of the product **34** as a semi-solid; crystallized from Et_2O–petroleum ether. mp 138–140°C. IR (KBr): 737, 1028, 1201, 1278, 1360, 1437, 1644, 1682, 1709, 1731, 1753 cm^{-1}. ^1H NMR ($CDCl_3$, δ): 0.96–1.18 (m, 12H), 1.83 (S, 3H), 1.96 (s, 3H), 3.14 (m, 1H), 3.36 (m, 1H), 3.76 (s, 3H), 3.91 (s, 3H), 6.21 (s, 1H), 6.36 (s, 1H). ^{13}C NMR ($CDCl_3$, δ): 15.68, 18.77, 3.25, 23.43, 53.08, 53.10, 54.30, 55.33, 77.43, 131.96, 137.01, 139.83, 145.59, 149.97, 160.55, 161.00, 165.95, 185.72. Anal. calcd for $C_{21}H_{28}N_2O_6$: C, 62.36; H, 6.98; N, 6.93. Found: C, 62.04; H, 6.93; N, 7.31.

3.1.17. Spirocompound 36. The reaction of 1,4-naphthoquinone (0.0316 g, 0.2 mmol) and DMAD (0.031 g, 0.027 mL, 0.22 mmol) in 1 mL anhydrous benzene at 80°C with diisopropylaminoisocyanide (0.0378 g, 0.3 mmol) in 0.5 mL benzene under reflux for 6 h after work up and chromatography using 10% EtOAc–hexane mixture afforded 0.052 g (61%) of the product **36** as an yellow viscous liquid, which solidified on standing; crystallized from ether–hexane, mp 182–183°C. IR (KBr): 767, 909, 1153, 1285, 1364, 1385, 1455, 1667, 1699, 1732, 2973 cm^{-1}. ^{1}H NMR (CDCl$_3$, δ): 0.53 (d, J=6.4 Hz, 3H), 0.61 (d, J=6.3 Hz, 3H), 1.01 (d, J=6.2 Hz, 3H), 1.17 (d, J=5.8 Hz, 3H), 2.91 (m, 1H), 3.41 (m, 1H), 3.62 (s, 3H), 3.98 (s, 3H), 6.63 (d, J=10.0 Hz, 1H), 6.72 (d, J=10.0 Hz, 1H), 7.22 (d, J=7.3 Hz, 1H), 7.55 (m, 2H), 8.17 (m, 1H). ^{13}C NMR (CDCl$_3$, δ): 22.19, 22.39, 23.33, 23.61, 52.82, 53.05, 54.85, 55.14, 67.27, 126.53, 127.45, 129.44, 132.69, 132.99, 133.24, 136.36, 137.58, 142.37, 144.85, 160.04, 161.89, 165.46, 183.42. Anal. calcd for $C_{23}H_{26}N_2O_6$: C, 64.54; H, 6.18, N, 6.53. Found: C, 64.78; H, 6.15, N, 6.57.

Acknowledgements

J. S. M. thanks Council of Scientific and Industrial Research, Government of India, New Delhi for research fellowship.

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