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One-pot synthesis of novel 1, 8-dioxo-decahydroacridines containing phenol and benzamide moiety and their synthetic uses

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Abstract. An efficient synthesis of some new 1, 8-dioxo-decahydroacridines is achieved via one-pot, three-component condensation of aromatic aldehydes, cyclic diketone, and 4-amino benzamide/4-aminophenol. Reaction of these acridines with dimethylacetylene dicarboxylate and triphenylphosphine or cyclohexylisocyanide gives stable phosphorus ylides or 4H-chromene derivatives, respectively, with good yields.

Keywords. Decahydroacridine; 4-amino benzamide; 4-aminophenol; ylide; 4H-chromene.

1. Introduction

Recently, multicomponent reactions (MCRs) have been considered as a superior synthetic strategy.[1] The MCRs are very flexible, atom economic in nature, and proceed through a sequence of reaction equilibria yielding the target product.[2]

Acridine derivatives have a wide spectrum of biological activities as antibacterial, antimalarial, anticancer and mutagenic properties. Acridine systems have attracted considerable attention due to their potential pharmacological activity. There are many industrial applications for acridine and its derivatives which are a class of compounds well-known since the 19th century when they were first used as pigments and dyes.[3,4] To date, acridine derivatives have been reported with a range of chemical and physical properties. Their utility in the pharmaceutical industry has also been reported.[5] Thus, the synthesis of acridine derivatives is an important and principal task in organic chemistry.

A straightforward method for the synthesis of these compounds involves a condensation between aldehydes, dimedone and an amine that is catalysed by various compounds such as poly-phosphoric acid,[6] L-proline,[7] organic solvents,[8] ionic liquids[9] and microwave irradiation.[10] Each of these methods has limitations such as poor yield, cumbersome workup procedure and generation of by-products.

As a part of our ongoing research efforts to develop more efficient and simple methods in heterocycle synthesis,[11] herein we report for the first time a synthesis of 1, 8-dioxodecahydroacridines containing benzamide and phenol moiety (scheme 1).

2. Experimental

All chemicals were purchased from Merck chemical company and were used without further purification.

Melting points were obtained on an Electrothermal-9100 melting point apparatus and were uncorrected. IR spectra were recorded on a Brucker Tensor-27 FTIR spectrometer. NMR spectra were recorded on BRUKER DRX-500, 400, 300 and 250 AVANCE NMR spectrometer using $CDCl_3$ and DMSO-d_6 as solvent.

Mass spectra were recorded on an Agilent Technologies' MS-5973 (70 eV) mass spectrometer. Elemental analyses were performed on a Heraeus CHN-O-Rapid analyser.

2.1 *General procedure for the preparation of decahydroacridine-1, 8-diones*

A mixture of aldehyde (1 mmol), β-dicarbonyl compound (2 mmol), 4-amino benzamide (1.5 mmol) and two drops of HCl in 5 mL DMF was refluxed for 90 min. After completion of the reaction as indicated by TLC, the mixture was poured into ice cold water. The resulting precipitate was purified by recrystalization from ethanol to afford decahydroacridine-1, 8-diones **1a–h**. The same procedure was used for synthesis of compounds **1i–o**.

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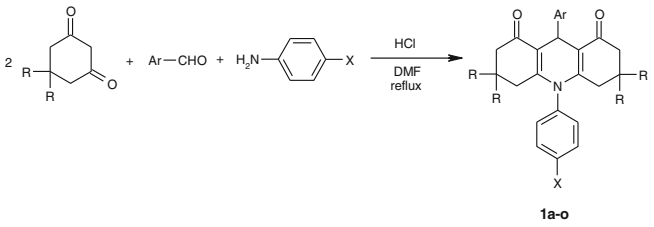


Scheme 1. Synthesis of 1, 8-dioxodecahydroacridines containing benzamide and phenol moiety.

2.2 *Preparation of phosphorus ylides 2a*

To a magnetically well-stirred solution of triphenylphosphine (1 mmol, 0.262 g) and **1 g** (1 mmol) in ethyl acetate (10 mL) was added dropwise a diluted solution of DMAD (1 mmol, 0.142 g) in ethyl acetate (1 mL) at room temperature. The reaction mixture was then stirred for 4 h. After completion of the reaction (monitored by TLC), n-hexane was added to the reaction mixture and the resulting precipitate was filtered off and recrystalized by a 1:1 mixture of hexane–ethyl acetate. This procedure was used for the synthesis of **2b–d**.

2.3 *Preparation of 4H-chromene 4a*

Cyclohexyl isocyanide (1 mmol) was added dropwise to a magnetically stirred solution of acridinone (1 mmol) and DMAD (1mmol) in 10 mL CHC_{l3}, at 0°C over 10 min. The reaction mixture was then allowed to warm up to room temperature and stand for 24 h. The solvent was removed under reduced pressure and the residue was separated by silica gel column chromatography using n-hexane–ethyl acetate as eluent. This procedure was used for the synthesis of **4b** and **c**.

2.4 *Characterization data*

2.4a *4-(1, 2, 3, 4, 5, 6, 7, 8-Octahydro-1, 8-dioxo-9-phenylacridin-10(9H)-yl) benzamide (1a)*: IR (KBr) ($\nu_{max,}$ cm^{-1}): 1604, 1636, 1678, 2951, 3058, 3265, 3317. ^{1}H NMR (300 MHz, DMSO-d_6): δ(ppm) 1.44–2.18 (12H, m), 5.11 (1H, s, CH), 7.08 (1H, t, $J = 7.2$ Hz, arom), 7.19–7.32 (4H, m, arom), 7.48 (3H, br, NH_2 and arom), 8.01 (2H, d, $J = 8.6$ Hz, arom), 8.15 (1H, s, arom). ^{13}C NMR (75 MHz, DMSO-d_6): δ(ppm) 21.1, 28.1, 31.6, 36.7, 114.3, 126.2, 127.9, 128.5, 129.3, 130.2, 135.3, 141.4, 147.1, 152.5, 167.3, 195.9. MS, *m/z*(%): 367 (M-45, 68), 295 (100), 131 (92). Anal. Calcd. for $C_{26}H_{24}N_2O_3$: C, 75.71; H, 5.86; N, 6.79. Found: C, 75.90; H, 5.50; N, 6.85.

2.4b *4-(1, 2, 3, 4, 5, 6, 7, 8-Octahydro-9-(3-nitrophenyl)-1, 8-dioxoacridin-10(9H)-yl) benzamide (1b)*: IR (KBr) ($\nu_{max,}$ cm^{-1}): 1621, 1640, 1690, 2951, 3164, 3425. ^{1}H NMR (300 MHz, DMSO-d_6): δ(ppm) 1.44–2.19 (12H, m), 5.19 (1H, s, CH), 7.52–7.57 (4H, m, arom), 7.73 (1H, d, $J = 7.5$ Hz, arom), 7.98 (1H, d, $J = 7.8$ Hz, arom), 8.03 (2H, d, $J = 8.1$ Hz, arom), 8.10 (2H, arom and NH), 8.12 (1H, br, NH). ^{13}C NMR (75 MHz, DMSO-d_6): δ(ppm) 21.1, 28.1, 32.3, 36.5, 113.5, 121.4, 122.6, 129.3, 130.3, 134.6, 141.1, 148.0, 149.0, 153.3, 167.3, 196.4.
MS, *m/z* (%): 458 (M+1, 3), 91 (100). Anal. Calcd. for $C_{26}H_{23}N_3O_5$: C, 68.26; H, 5.07; N, 9.18. Found: C, 68.40; H, 5.37; N, 9.30.

2.4c *4-(1, 2, 3, 4, 5, 6, 7, 8-Octahydro-9-(4-nitrophenyl)-1, 8-dioxoacridin-10(9H)-yl) benzamide (1c)*: IR (KBr) ($\nu_{max,}$ cm^{-1}): 1604, 1633, 1680, 2949, 3200, 3373. ^{1}H NMR (300 MHz, DMSO-d_6): δ(ppm) 1.60–2.18 (12H, m), 5.19 (1H, s, CH), 7.55–7.57 (5H, m, arom, NH), 8.03 (2H, d, $J = 7.5$ Hz, arom), 8.10 (2H, d, $J = 7.5$ Hz, arom), 8.16 (1H, br, NH). ^{13}C NMR (75 MHz, DMSO-d_6): δ(ppm) 21.0, 28.2, 32.6, 39.0, 113.3, 123.8, 129.3, 130.2, 135.4, 141.1, 153.3, 154.5, 167.2, 195.9. MS, *m/z* (%): 457 (M, 2.5), 55 (100). Anal. Calcd. for $C_{26}H_{23}N_3O_5$: C, 68.26; H, 5.07; N, 9.18. Found: C, 68.33; H, 4.74; N, 8.96.

2.4d *4-(1, 2, 3, 4, 5, 6, 7, 8-Octahydro-3, 3, 6, 6-tetramethyl-1, 8-dioxo-9-phenylacridine-10(9H)-yl) benzamide (1d)*: IR (KBr) ($\nu_{max,}$ cm^{-1}): 1604, 1642, 1681, 2956, 3189, 3455. ^{1}H NMR (300 MHz, DMSO-d_6): δ(ppm) 0.68 (6H, s), 0.85 (6H, s), 1.73 (2H, d, $J = 17.4$ Hz), 1.97 (2H, d, $J = 16.0$ Hz), 2.15 (4H, dd, $J_1 = 15.9$ Hz, $J_2 = 3.6$ Hz), 5.01 (1H, s), 7.07 (1H, t, $J = 6.6$ Hz), 7.20–7.30 (4H, m), 7.47 (2H, d, $J = 6.9$ Hz), 7.58 (1H, s, br, NH), 8.04 (2H, d, $J = 7.5$ Hz), 8.17 (1H, s, br, NH).^{13}C NMR (75 MHz, DMSO-d_6): δ(ppm) 26.4, 29.6, 32.4, 41.3, 113.5, 126.2, 128.0, 128.4, 135.3, 141.3, 146.6, 150.5, 167.4, 195.6. MS, *m/z*(%): 468 (M, 10), 391 (84), 335 (49), 83 (100). Anal. Calcd. for $C_{30}H_{32}N_2O_3$: C, 76.90; H, 6.88; N, 5.98. Found: C, 77.01; H, 6.69; N, 6.17.

2.4e *4-(1, 2, 3, 4, 5, 6, 7, 8-Octahydro-3, 3, 6, 6-tetramethyl-1, 8-dioxo-9-[(3-nitrophenylacridine-10(9H)-yl)]benzamide (1e)*: IR (KBr) ($\nu_{max,}$ cm^{-1}): 1603, 1641, 1685, 2958, 3055, 3375, 3492. ^{1}H NMR (300 MHz, DMSO-d_6): δ(ppm) 0.67 (6H, s), 0.85 (6H, s), 1.76 (2H, d, $J = 17.7$ Hz), 1.99 (2H, d, $J = 15.9$ Hz), 2.17 (2H, d, $J = 3.9$ Hz), 2.23 (2H, d,

J = 6.0 Hz), 5.11 (1H, s), 7.54 (1H, br, NH), 7.56–7.60 (3H, m), 7.76 (1H, d, J = 7.5 Hz), 7.98 (1H, d, J = 8.1 Hz), 8.05–8.11 (3H, m), 8.18 (1H, br, NH).^{13}C NMR (75 MHz, DMSO-d_6): δ(ppm) 26.4, 29.6, 32.5, 41.3, 112.7, 121.5, 122.6, 129.7, 130.3, 134.8, 135.5, 141.0, 147.8, 148.6, 151.3, 167.3, 195.7. MS, *m/z*(%): 495 (M-18, 21), 391 (100), 273 (42). Anal. Calcd. for $C_{30}H_{31}N_3O_5$: C, 70.16; H, 6.08; N, 8.18. Found: C, 70.35; H, 6.22; N, 8.05.

2.4f *4-(1, 2, 3, 4, 5, 6, 7, 8-Octahydro-3, 3, 6, 6-tetramethyl-1, 8-dioxo-9-[(4-nitrophenylacridine-10(9H)-yl)]benzamide (1f)*: IR (KBr) ($\nu_{max,}$ cm^{-1}): 1603, 1640, 1681, 2958, 3193, 3330, 3460. ^{1}H NMR (300 MHz, DMSO-d_6): δ(ppm) 0.67 (6H, s), 0.85 (6H, s), 1.75 (2H, d, J = 17.4 Hz), 1.97 (2H, d, J = 15.9 Hz), 2.18 (4H, d, J = 15.9 Hz), 5.10 (1H, s), 7.56 (1H, br, NH), 7.57 (4H, d, J = 6.6 Hz), 8.06 (2H, d, J = 6.3 Hz), 8.13 (2H, d, J = 6.3 Hz), 8.19 (1H, br, NH). ^{13}C NMR (75 MHz, DMSO-d_6): δ(ppm) 26.5, 29.6, 32.5, 33.4, 41.4, 112.4, 123.8, 129.5, 130.2, 135.5, 141.1, 146.1, 151.2, 154.0, 167.4, 195.6. MS, *m/z*(%): 513 (M, 5), 391 (34), 313 (48), 262 (94), 57 (100). Anal. Calcd. for $C_{30}H_{31}N_3O_5$: C, 70.16; H, 6.08; N, 8.18. Found: C, 70.35; H, 6.22; N, 8.39.

2.4g *4-(1, 2, 3, 4, 5, 6, 7, 8-Octahydro-3, 3, 6, 6-tetramethyl-1, 8-dioxo-9-[(4-chlorophenylacridine-10(9H)-yl)]benzamide (1 g)*: IR (KBr) ($\nu_{max,}$ cm^{-1}): 1602, 1642, 1689, 2959, 3200, 3356. ^{1}H NMR (300 MHz, DMSO-d_6): δ(ppm) 0.67 (6H, s), 0.84 (6H, s), 1.72 (2H, d, J = 17.4 Hz), 1.97 (2H, d, J = 16.5 Hz), 2.17 (4H, d, J = 16.8 Hz), 4.98 (1H, s), 7.28 (4H, m), 7.50 (2H, d, J = 6.3 Hz), 7.59 (1H, br, NH), 8.40 (2H, d, J = 6.3 Hz), 8.18 (1H, br, NH). ^{13}C NMR (75 MHz, DMSO-d_6): δ(ppm) 26.5, 29.6, 32.2, 32.4, 41.4, 113.1, 128.4, 129.6, 129.9, 130.7, 135.4, 141.2, 145.6, 150.7, 167.4, 195.6. MS, *m/z* (%): 502 (M, 5), 391 (45), 57 (100). Anal. Calcd. for $C_{30}H_{31}ClN_2O_3$: C, 71.63; H, 6.21; N, 5.57. Found: C, 71.85; H, 6.36; N, 5.85.

2.4h *4-(1, 2, 3, 4, 5, 6, 7, 8-Octahydro-3, 3, 6, 6-tetramethyl-1, 8-dioxo-9-[(4-bromophenylacridine-10(9H)-yl)]benzamide (1 h)*: IR (KBr) ($\nu_{max,}$ cm^{-1}): 1602, 1642, 1687, 2871, 2958, 3197, 3353. ^{1}H NMR (300 MHz, DMSO-d_6): δ(ppm) 0.68 (6H, s), 0.84 (6H, s), 1.72 (2H, d, J = 17.1 Hz), 1.98 (2H, d, J = 15.9 Hz), 2.17 (4H, d, J = 17.4 Hz), 4.96 (1H, s), 7.24 (2H, d, J = 6.6 Hz), 7.41 (2H, d, J = 7.8 Hz), 7.50 (2H, d, J = 6.9 Hz), 7.6 (1H, s), 8.04 (2H, d, J = 7.2 Hz), 8.18 (1H, NH). ^{13}C NMR (75 MHz, DMSO-d_6): δ(ppm) 26.5, 29.6, 32.3, 32.5, 41.4, 113.0, 119.3, 129.6, 130.4, 131.3, 135.3, 141.2, 145.9, 150.7, 167.3, 195.6. MS, *m/z*(%): 548 (M+1, 4), 391 (100), 55 (81). Anal. Calcd. for $C_{30}H_{31}BrN_2O_3$: C, 65.81; H, 5.71; N, 5.12. Found: C, 65.98 H, 5.79; N, 4.89.

2.4i *9-(4-Chloro-phenyl)-10-(4-hydroxy-phenyl)-3, 4, 6, 7, 9, 10-hexahydro-2H, 5H-acridine-1, 8-dione (1i)*: IR (KBr) ($\nu_{max,}$ cm^{-1}): 1612, 1639, 3162.^{1}H NMR (500 MHz, DMSO-d_6): δ(ppm) 1.59-2.28 (12H, m), 5.10 (1H, s, CH), 6.89 (2H, d, J = 10.0 Hz, arom), 7.11 (1H, d, J = 7.8 Hz, arom), 7.28 (5H, m, arom), 9.97 (1H, br, OH). ^{13}C NMR (125 MHz, DMSO-d_6): δ(ppm) 20.6, 27.6, 30.8, 36.1, 113.2, 115.8, 116.1, 127.9, 129.2, 129.9, 130.9, 145.6, 153.2, 157.7, 195.4. MS, *m/z* (%): 419 (M, 1.5), 364 (44), 217 (100). Anal. Calcd. for $C_{25}H_{22}ClNO_3$: C, 71.51; H, 5.28; N, 3.34. Found: C, 71.62; H, 5.45; N, 3.57.

2.4j *9-(4-Bromo-phenyl)-10-(4-hydroxy-phenyl)-3, 4, 6, 7, 9, 10-hexahydro-2H, 5H-acridine-1, 8-dione (1j)*: IR (KBr) ($\nu_{max,}$ cm^{-1}): 1612, 1636, 3157. ^{1}H NMR (500 MHz, DMSO-d_6): δ(ppm) 1.59–2.24 (12H, m), 5.09 (1H, s, CH), 6.89 (2H, d, J = 11.0 Hz, arom), 7.22 (2H, d, J = 9.5 Hz, arom), 7.28 (1H, d, J = 9.5 Hz, arom), 7.42 (2H, d, J = 10.0 Hz, arom), 10.05 (1H, br, OH). ^{13}C NMR (125 MHz, DMSO-d_6): δ(ppm) 20.6, 27.6, 30.9, 36.1, 113.2, 115.8, 116.1, 129.6, 129.9, 130.8, 146.1, 153.3, 157.7, 195.4. MS, *m/z*(%): 464 (M+1, 0.5), 372 (50), 293 (87), 217 (100). Anal. Calcd. for $C_{25}H_{22}BrNO_3$: C, 64.66; H, 4.78; N, 3.02. Found: C, 64.87; H, 4.95; N, 3.25.

2.4k *10-(4-Hydroxy-phenyl)-9-(4-nitro-phenyl)-3, 4, 6, 7, 9, 10-hexahydro-2H, 5H-acridine-1,8-dione (1 k)*: IR (KBr) ($\nu_{max,}$ cm^{-1}): 1610, 1638, 3171.^{1}H NMR (500 MHz, DMSO-d_6): δ(ppm) 1.60–2.50 (12H, m), 5.22 (1H, s, CH), 6.90 (2H, d, J = 11.0 Hz, arom), 7.20 (1H, d, J = 8.0 Hz, arom), 7.30 (1H, d, J = 8.5 Hz, arom), 7.55 (2H, d, J = 11.0 Hz, arom), 8.12 (2H, d, J = 11.0 Hz, arom), 9.99 (1H, br, OH). ^{13}C NMR (125 MHz, DMSO-d_6): δ(ppm) 20.6, 27.6, 32.0, 36.1, 112.6, 115.8, 123.4, 128.6, 129.2, 130.1, 130.9, 145.6, 153.8, 154.1, 195.3. MS, *m/z* (%): 364 (100), 77(49). Anal. Calcd. for $C_{25}H_{22}N_2O_5$: C, 69.76; H, 5.15; N, 6.51. Found: C, 70.01; H, 5.33; N, 6.84.

2.4l *9-(4-Chloro-phenyl)-10-(4-hydroxy-phenyl)-3, 3, 6, 6-tetramethyl-3, 4, 6, 7, 9, 10-hexahydro-2H, 5H-acridine-1,8-dione (1 l)*: IR (KBr) ($\nu_{max,}$ cm^{-1}): 1620, 1642, 3259.^{1}H NMR (500 MHz, DMSO-d_6): δ(ppm)

0.72 (6H, s), 0.89 (6H, s), 1.83 (2H, d, $J = 22.0$ Hz), 2.00 (2H, d, $J = 20.0$ Hz), 2.17 (2H, d, $J = 5.5$ Hz), 2.21 (2H, d, $J = 7.5$ Hz), 5.00 (1H, s), 6.93 (2H, t, $J = 8.0$ Hz, arom), 7.15 (1H, d, $J = 8.5$ Hz, arom), 7.22 (1H, d, $J = 9.5$ Hz, arom), 7.29 (4H, m, arom), 10.02 (1H, br, OH). ^{13}C NMR (125 MHz, DMSO-d_6): 26.1, 29.2, 31.6, 31.8, 40.8, 49.4, 112.3, 116.0, 127.8, 129.3, 129.9, 130.1, 131.0, 145.2, 151.2, 157.7, 195.0. MS, *m/z* (%): 475 (M, 47), 390 (13), 364 (100). Anal. Calcd. for $C_{29}H_{30}ClNO_3$: C, 73.17; H, 6.35; N, 2.94. Found: C, 73.33; H, 6.48; N, 3.18.

2.4m *10-(4-Hydroxy-phenyl)-3, 3, 6, 6-tetramethyl-9-(3-nitro-phenyl)-3, 4, 6, 7, 9, 10-hexahydro-2H, 5H-acridine-1, 8-dione (1 m)*: IR (KBr) ($\nu_{max,}$ cm^{-1}): 1610, 1642, 3164.^{1}H NMR (500 MHz, DMSO-d$_6$): δ(ppm) 0.70 (6H, s), 0.90 (6H, s), 1.86 (2H, d, $J = 22.0$ Hz), 2.01 (2H, d, $J = 20.0$ Hz), 2.02 (2H, d, $J = 11.0$ Hz), 2.24 (2H, d, $J = 13.0$ Hz), 5.13 (1H, s), 6.95 (2H, t, $J = 10.0$ Hz, arom), 7.15 (1H, d, $J = 8.5$ Hz, arom), 7.25 (1H, d, $J = 10.0$ Hz, arom), 7.58 (1H, t, $J = 9.5$ Hz, arom), 7.75 (1H, d, $J = 10.0$ Hz, arom), 8.01 (1H, dd, $^1J = 10.5$ Hz, $^2J = 3.0$ Hz, arom), 8.12 (1H, d, $J = 2.5$ Hz, arom), 10.05 (1H, br, OH). ^{13}C NMR (125 MHz, DMSO-d_6): δ(ppm) 25.9, 29.2, 31.9, 32.3, 40.8, 49.3, 111.9, 116.1, 120.9, 121.9, 129.1, 129.6, 131.0, 134.2, 147.3, 148.3, 151.8, 157.8, 195.1. MS, *m/z*(%): 486 (M, 16), 469 (29), 364 (100). Anal. Calcd. for $C_{29}H_{30}N_2O_5$: C, 71.59; H, 6.21; N, 5.76. Found: C, 71.78; H, 6.45; N, 6.03.

2.4n *9-(4-Bromo-phenyl)-10-(4-hydroxy-phenyl)-3, 3, 6, 6-tetramethyl-3, 4, 6, 7, 9, 10 -hexahydro-2H, 5H-acridine-1, 8-dione (1n): IR (KBr) ($\nu_{max,}$ cm^{-1})*: 1620, 1641, 3256.^{1}H NMR (500 MHz, DMSO-d$_6$): δ(ppm) 0.71 (6H, s), 0.89 (6H, s), 1.82 (2H, d, $J = 22.0$ Hz), 1.99 (2H, d, $J = 20.0$ Hz), 2.17 (2H, d, $J = 5.0$ Hz), 2.21 (2H, d, $J = 7.5$ Hz), 4.98 (1H, s), 6.93 (2H, t, $J = 8.5$ Hz, arom), 7.14 (1H, d, $J = 9.0$ Hz, arom), 7.24 (3H, d, $J = 10.5$ Hz, arom), 7.43 (2H, d, $J = 10.5$ Hz, arom), 10.02 (1H, br, OH). ^{13}C NMR (125 MHz, DMSO-d_6): δ(ppm) 26.1, 29.2, 31.7, 31.8, 40.8, 49.4, 112.3, 116.0, 116.4, 118.6, 129.2, 129.7, 130.7, 145.6, 151.2, 157.7, 195.0. MS, *m/z* (%): 520 (M+1, 6), 519 (13), 364 (100). Anal. Calcd. for $C_{29}H_{30}BrNO_3$: C, 66.92; H, 5.81; N, 2.69. Found: C, 67.13; H, 5.98; N, 2.96.

2.4o *10-(4-Hydroxy-phenyl)-3, 3, 6, 6-tetramethyl-9-phenyl-3, 4, 6, 7, 9, 10-hexahydro-2H, 5H-acridine-1, 8-dione (1o)*: IR (KBr) ($\nu_{max,}$ cm^{-1}): 1636, 3169.^{1}H NMR (500 MHz, DMSO-d$_6$): δ(ppm) 0.71 (6H, s), 0.89 (6H, s), 1.82 (2H, d, $J = 21.5$ Hz), 1.99 (2H, d, $J = 20.0$ Hz), 2.17 (2H, d, $J = 10.0$ Hz), 2.21 (2H, d, $J = 12.0$ Hz), 5.03 (1H, s), 6.93 (2H, t, $J = 8.5$ Hz, arom), 7.09 (2H, t, $J = 9.0$ Hz, arom), 7.23 (3H, d, $J = 10.0$ Hz, arom), 7.29 (2H, d, $J = 8.5$ Hz, arom), 10.02 (1H, br, OH). ^{13}C NMR (125 MHz, DMSO-d_6): δ(ppm) 26.0, 29.3, 31.7, 31.8, 40.8, 49.5, 112.7, 116.5, 125.7, 127.4, 127.8, 129.4, 131.1, 146.3, 151.0, 157.6, 195.0. MS, *m/z* (%): 441 (M, 9), 364 (94), 77 (100). Anal. Calcd. for $C_{29}H_{31}NO_3$: C, 78.88; H, 7.08; N, 3.17. Found: C, 79.01; H, 7.41; N, 3.48.

2.4p *Dimethyl-2-(4-[3, 3, 6, 6-tetramethyl-1, 8-dioxo-9-phenyl-2, 3, 4, 5, 6, 7, 8, 9-octahydro-10(1H)-acridinyl]benzoylamino)-3-(1, 1, 1-triphenyl-λ^5-phosphanylidene)succinate(2a)*: Yellow powder. M.p. 189–190°C. IR (KBr) ($\nu_{max,}$ cm^{-1}): 1650, 1740, 2960, 3063, 3450. ^{1}H NMR (500 MHz, $CDCl_3$): δ(ppm) 0.81 (6H, s, 2CH$_3$), 0.97 (6H, s, 2CH$_3$), 1.80–2.23 (8H, m, 4CH$_2$), 3.19 (3H, s, OCH$_3$), 3.74 (3H, s, OCH$_3$), 4.77 (1H, d, $^3J_{PH} = 18.5$ Hz, $^3J_{HH} = 11.0$ Hz, P=C-CH), 5.28 (1H, s, CH), 7.09–8.06 (25H, m, arom and NH). ^{13}C NMR: 26.7, 29.7, 32.5, 41.9, 42.7 (d, $^1J_{PC} = 115.7$ Hz, P=C), 49.2 (OCH$_3$), 50.2, 52.2 (d, $^2J_{PC} = 22.6$ Hz, P=C-CH), 52.5 (OCH$_3$), 114.7, 126.0, 126.2 (d, $^1J_{PC} = 114.2$ Hz, C^{ipso}), 127.8, 128.1, 128.7 (d, $^3J_{PC} = 15.2$ Hz, C^{meta}), 132.3 (d, $^4J_{PC} = 3.0$ Hz, C^{para}), 133.0 (d, $^2J_{PC} = 12.1$ Hz, C^{ortho}), 136.4, 141.4, 146.0, 149.3, 165.4, 170.8, 173.5, 195.9. Anal. Calcd. for $C_{54}H_{53}N_2O_7P$: C, 74.30; H, 6.12; N, 3.21. Found: C, 74.48; H, 6.25; N, 3.46.

2.4q *Dimethyl-2-(4-[3, 3, 6, 6-tetramethyl-1, 8-dioxo-9-(4-chlorophenyl)-2, 3, 4, 5, 6, 7, 8, 9-octahydro- 10 (1H)-acridinyl]benzoylamino)-3-(1, 1, 1-triphenyl-λ^5-phosphanylidene)succinate (2b)*: White powder. M.p. 178–179°C. IR (KBr) ($\nu_{max,}$ cm^{-1}): 1640, 1738, 2954, 3058, 3439.^{1}H NMR (500 MHz, $CDCl_3$): δ(ppm) 0.81 (6H, s, 2CH$_3$), 0.96 (6H, s, 2CH$_3$), 1.80–2.23 (8H, m, 4CH$_2$), 3.19 (3H, s, OCH$_3$), 3.74 (3H, s, OCH$_3$), 4.77 (1H, d, $^3J_{PH} = 18.5$ Hz, $^3J_{HH} = 11.0$ Hz, P=C-CH), 5.23 (1H, s, CH), 7.21–8.59 (24H, m, arom and NH). ^{13}C NMR (125 MHz, $CDCl_3$): 26.8, 29.7, 32.7, 41.9, 42.9 (d, $^1J_{PC} = 158.7$ Hz, P=C), 49.2, 50.2 (d, $^2J_{PC} = 22.0$ Hz, P=C-CH), 52.5, 114.4, 126.2 (d, $^1J_{PC} = 114.8$ Hz, C^{ipso}), 128.2, 128.7 (d, $^3J_{PC} = 15.4$ Hz, C^{meta}), 129.3, 131.6, 132.4, (d, $^4J_{PC} = 3.0$ Hz, C^{para}), 133.8 (d, $^2J_{PC} = 12.1$ Hz, C^{ortho}), 136.5, 141.2, 144.6, 149.5, 165.4 (C=O amide), 170.7 (d, $^2J_{PC} = 16.2$ Hz, C=O ester), 173.4 (d, $^3J_{PC} = 8.1$ Hz, C=O ester), 195.8. Anal. Calcd. for $C_{54}H_{52}ClN_2O_7P$: C, 71.48; H, 5.78; N, 3.09. Found: C, 71.65; H, 5.70; N, 3.26.

2.4r *Dimethyl-2-(4-[3, 3, 6, 6-tetramethyl-1, 8-dioxo-9-(4-bromophenyl)-2, 3, 4, 5, 6, 7, 8, 9-octahydro-10 (1H)-acridinyl]benzoylamino)-3-(1, 1, 1-triphenyl-λ^5-phosphanylidene)succinate (2c)*: White powder. M.p. 170–173°C. IR (KBr) ($\nu_{max,}$ cm^{-1}): 1645, 1740, 2950, 3050, 3441. ^{1}H NMR (250 MHz, $CDCl_3$): δ(ppm) 0.80 (6H, s, 2CH_3), 0.95 (6H, s, 2CH_3), 1.71–2.23 (8H, m, 4CH_2), 3.18 (3H, s, OCH_3), 3.72 (3H, s, OCH_3), 4.77 (1H, d, $^3J_{PH}$ = 7.5 Hz, $^3J_{HH}$ = 1.5 Hz, P=C-CH), 5.21 (1H, s, CH), 7.25–8.54 (24H, m, arom and NH). ^{13}C NMR (62.5 MHz, $CDCl_3$): δ(ppm) 26.7, 29.7, 32.5, 41.9, 43.0 (d, $^1J_{PC}$ = 131.18 Hz, P=C), 49.0, 50.1, 50.4, 52.4, 114.4, 119.8, 126.3 (d, $^1J_{PC}$ = 93.7 Hz, C^{ipso}), 127.0, 128.7 (d, $^3J_{PC}$ = 12.3 Hz, C^{meta}), 129.7, 131.1, 132.3 (C^{para}), 133.8 (d, $^2J_{PC}$ = 9.8 Hz, C^{ortho}), 136.5, 141.2, 145.1, 149.4, 165.3 (C=O amide), 170.8 (d, $^2J_{PC}$ = 4.1 Hz, C=O ester), 173.5 (d, $^3J_{PC}$ = 1.7 Hz, C=O ester), 195.8. Anal. Calcd. for $C_{54}H_{52}BrN_2O_7P$: C, 68.14; H, 5.51; N, 2.94. Found: C, 68.34; H, 5.67; N, 3.22.

2.4s *Dimethyl-2-(4-[3, 3, 6, 6-tetramethyl-1, 8-dioxo-9-(3-nitro phenyl)-2, 3, 4, 5, 6, 7, 8, 9-octahydro-10 (1H)-acridinyl]benzoylamino)-3-(1, 1, 1-triphenyl-λ^5-phosphanylidene)succinate (2d)*: White powder. M.p. 202–205°C. IR (KBr) ($\nu_{max,}$ cm^{-1}): 1642, 1735, 2955, 3060, 3435. ^{1}H NMR (250 MHz, $CDCl_3$): δ(ppm) 0.79 (6H, s, 2CH_3), 0.97 (6H, s, 2CH_3), 1.82-2.26 (8H, m, 4CH_2), 3.19 (3H, s, OCH_3), 3.73 (3H, s, OCH_3), 4.75 (1H, d, $^3J_{PH}$ = 14.5 Hz, $^3J_{HH}$ = 8.5 Hz, P=C-CH), 5.35 (1H, s, CH), 7.39–8.49 (24H, m, arom and NH). ^{13}C NMR: (62.5 MHz, $CDCl_3$): δ(ppm) 26.6, 29.7, 32.5, 32.8, 41.8, 44.1 (d, $^1J_{PC}$ = 144.4 Hz, P=C), 49.2, 50.1, 51.1, 52.4, 114.0, 121.2, 121.8, 126.3 (d, $^1J_{PC}$ = 88.9 Hz, C^{ipso}), 127.0, 128.8 (d, $^3J_{PC}$ = 12.2 Hz, C^{meta}), 132.3 (C^{para}), 133.8 (d, $^2J_{PC}$ = 9.9 Hz, C^{ortho}), 135.3, 136.7, 140.9, 148.1, 148.4, 150.1, 165.4 (C=O amide), 170.6 (C=O ester), 173.4 (C=O ester), 195.7. Anal. Calcd. for $C_{54}H_{52}N_3O_9P$: C, 70.65; H, 5.71; N, 4.58. Found: C, 70.84; H, 5.93; N, 5.90.

2.4t *Dimethyl-2-(cyclohexylamino)-6-[1, 8-dioxo-9-(4-chloro phenyl)-2, 3, 4, 5, 6, 7, 8, 9-octahydro-10(1H)-acridinyl]-4H-chromene-3, 4-dicarboxylate (4a)*: IR (KBr) ($\nu_{max,}$ cm^{-1}): 1636, 1732, 2854, 2929, 3270. ^{1}H NMR (500 MHz, DMSO-d_6): δ(ppm) 1.22–2.36 (22H, m), 3.74 (1H, m, CHN), 3.85 and 3.93 (6H, s, 2OCH_3), 5.34 (1H, s, CH), 5.35 (1H, s, CH), 7.13–7.37 (7H, m, arom), 7.48 (1H, br, NH). ^{13}C NMR (125 MHz, DMSO-d_6): δ(ppm) 23.8, 25.6, 27.1, 28.3, 31.7, 33.3, 36.7, 36.9, 52.5, 53.3, 58.4, 115.2, 122.9, 123.5, 128.2, 129.1, 129.8, 131.5, 134.6, 137.0, 145.1, 150.4, 152.0, 153.6, 163.4, 163.9, 164.1, 196.1. MS, *m/z* (%): 670 (M, 0.8), 611 (3), 419 (11), 308 (93), 111 (52), 55 (100). Anal. Calcd. for $C_{38}H_{39}ClN_2O_7$: C, 68.00; H, 5.86; N, 4.17. Found: C, 68.23; H, 6.06; N, 4.48.

2.4u *Dimethyl-2-(cyclohexylamino)-6-[1, 8-dioxo-9-(4-bromo phenyl)-2, 3, 4, 5, 6, 7, 8, 9-octahydro-10 (1H)-acridinyl]-4H-chromene-3, 4-dicarboxylate (4b)*: IR (KBr) ($\nu_{max,}$ cm^{-1}): 1636, 1732, 2854, 2929, 3270. ^{1}H NMR (400 MHz, DMSO-d_6): δ(ppm) 1.21–2.41 (22H, m), 3.75 (1H, m, CHN), 3.85 and 3.94 (6H, s, 2OCH_3), 5.34 (1H, s, CH), 5.35 (1H, s, CH), 7.28-7.39 (7H, m, arom), 7.48 (1H, br, NH). ^{13}C NMR (100 MHz, DMSO-d_6): δ(ppm) 23.8, 25.6, 28.3, 29.7, 31.8, 33.4, 36.6, 36.7, 52.5, 53.3, 58.4, 115.1, 119.8, 122.9, 123.5, 129.6, 130.1, 131.2, 131.5, 134.6, 137.0, 145.6, 150.3, 151.9, 153.6, 163.4, 163.9, 196.0. MS, *m/z* (%): 657 (M-58, 4), 559 (4), 465 (26), 308 (100). Anal. Calcd. for $C_{38}H_{39}BrN_2O_7$: C, 63.78; H, 5.49; N, 3.91. Found: C, 64.02; H, 5.71; N, 4.18.

2.4v *Dimethyl-2-(cyclohexylamino)-6-[3, 3, 6, 6-tetramethyl-1, 8-dioxo-9-phenyl-2, 3, 4, 5, 6, 7, 8, 9-octahydro-10(1H)-acridinyl]-4H-chromene-3, 4-dicarboxylate (4c)*: IR (KBr) ($\nu_{max,}$ cm^{-1}): 1648, 1739, 2854, 2931, 3331. ^{1}H NMR (500 MHz, DMSO-d_6): δ(ppm) 0.81 (6H, s), 0.95 (6H, s), 1.24–1.26 (10 H, m), 1.82–2.23 (8H, m), 3.72 (1H, m, CHN), 3.85 and 3.93 (6H, s, 2OCH_3), 5.27 (1H, s, CH), 5.28 (1H, s, CH), 7.08–7.44 (8H, m, arom), 7.48 (1H, br, NH). ^{13}C NMR (125 MHz, DMSO-d_6): δ(ppm) 23.6, 24.4, 25.7, 26.7, 29.7, 32.3, 32.6, 33.3, 41.7, 50.2, 52.5, 53.3, 57.9, 114.6, 125.9, 127.8, 128.0, 131.5, 146.1, 150.0, 150.4, 153.5, 163.4, 163.9, 195.0. MS, *m/z* (%): 692 (M, 0.2), 419 (11), 391 (16), 308 (90), 192 (81), 83 (72), 55 (100). Anal. Calcd. for $C_{42}H_{48}N_2O_7$: C, 72.81; H, 6.98; N, 4.04. Found: C, 73.08; H, 7.12; N, 4.30.

3. Results and Discussion

We report here, a simple and expeditious synthesis of highly substituted dioxodecahydroacridines containing benzamide and phenol moiety in excellent yields.

One of the problems faced during this study was the development of a single stage method for obtaining the target decahydroacridine-1, 8-diones. Based on general and systematized data,[12–14] we propose a single stage method for the synthesis of substituted decahydroacridinediones.

Owing to activity of 4-amino benzamide, the reaction in low boiling solvents such as ethanol and acetonitrile leads to a heavy contamination of the target compounds **1a–h** by the related xanthenediones. The use of high boiling and polar DMF as solvent appears optimal and gives acridines **1a–h** without forming of xanthenediones. We used two drops of HCl as catalyst. The same conditions were used for the synthesis of **1i–o.** A reasonable mechanism for the formation of decahydroacridine-1, 8-diones is shown in scheme 2.

To determine the scope of the designed protocol, a number of commercially available aldehydes were condensed with cyclic diketones and 4-amino benzamide/4-aminophenol under optimized reaction conditions, and the results are summarized in table 1.

The reaction profile is very clean and no side products are formed. All the synthesized decahydroacridine-1, 8-diones have been characterized on the basis of elemental and spectral studies.

The IR spectrum of **1c** showed characteristic absorptions at 3200, 3373 cm^{-1} for the NH_2 group. The carbonyl groups were observed at 1633, 1680 cm^{-1}.

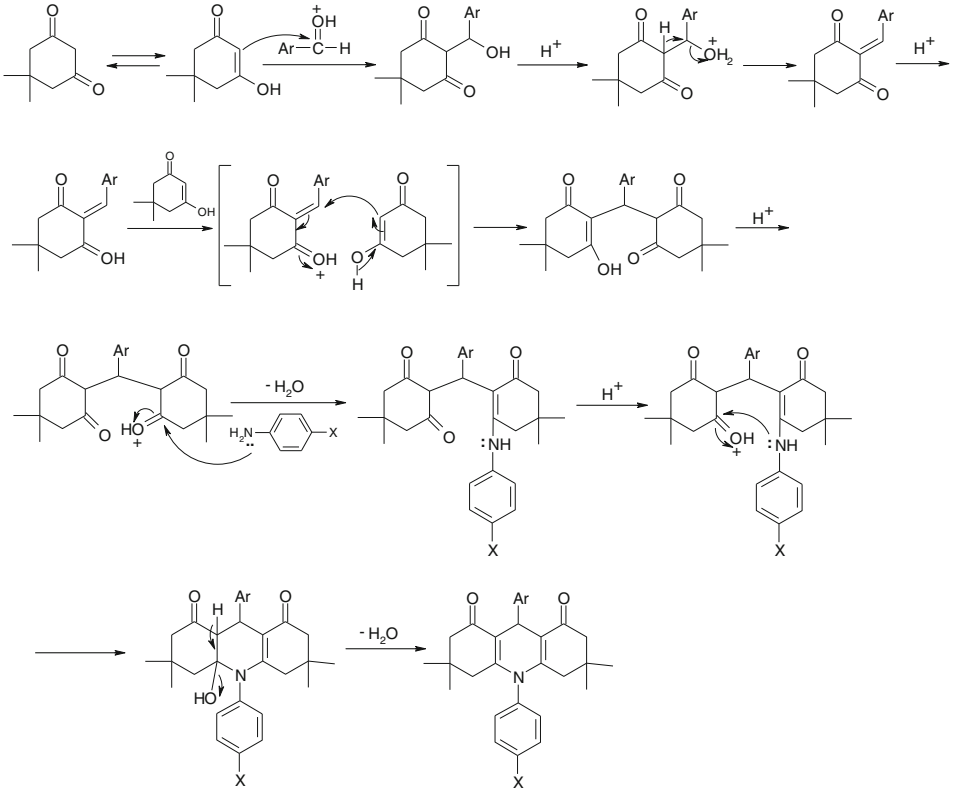
^1H NMR spectrum of **1c** remarked a singlet at 5.19 ppm for aliphatic CH while amide NH_2 group was observed at chemical shifts of 7.57 and 8.16 ppm. Aromatic signals were observed at 6.8–7.6 ppm. Signals between 1.60 and 2.18 were assigned for CH_2 protons.

^{13}CNMR of this compound showed two characteristic peaks at 167.2 and 195.9 ppm for carbonyl groups.

After successfully synthesizing a series of acridines, we turned our attention towards the synthesis of stable phosphorus ylides from these compounds. Some of these aridines were selected for this reaction. The reaction of acridines **1d–h** (scheme 3) with dimethyl acetylene dicarboxylate (DMAD) in the presence of triphenylphosphine proceeded spontaneously at room temperature in ethyl acetate, and finished within 3 h. All our attempts to obtain ylides from **1l** and **1o** were unsuccessful.

^1H and ^{13}C NMR spectra of the crude product clearly indicated the formation of phosphoranes **2a–d**. Any product other than **2a–d** could not be detected by NMR spectroscopy. Although presence of the ^{31}P nucleus complicates both the ^1H and ^{13}C NMR spectra of these compounds, it does help us obtain some valuable information by long-range spin–spin coupling constants ^{31}P with ^1H and ^{13}C nuclei.

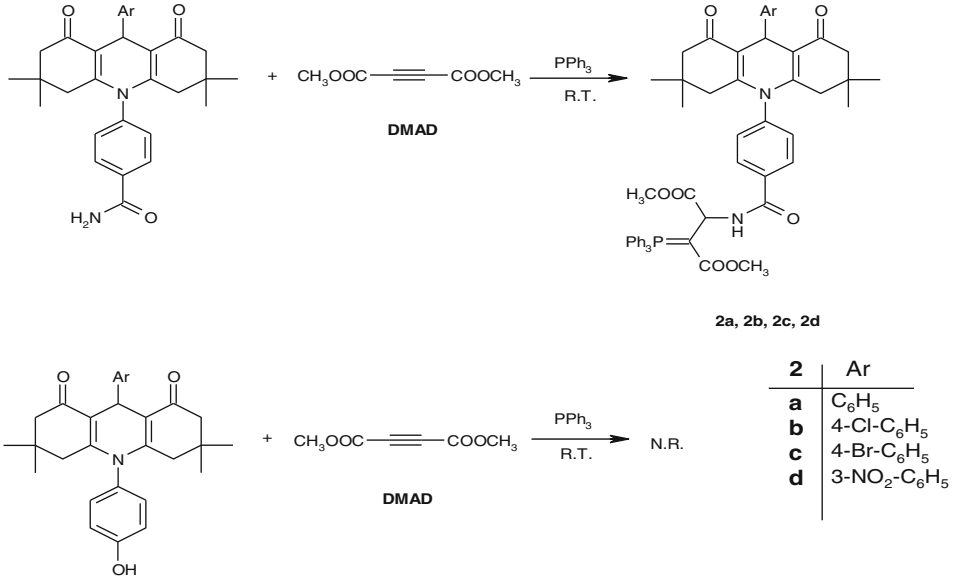
Compounds **2a–d** were apparently obtained from initial addition of triphenylphosphine as a good nucleophile to DMAD as a Michael acceptor and concomitant protonation of the intermediate **3** by the NH_2. Then, the positively charged ion is attacked by the nitrogen of



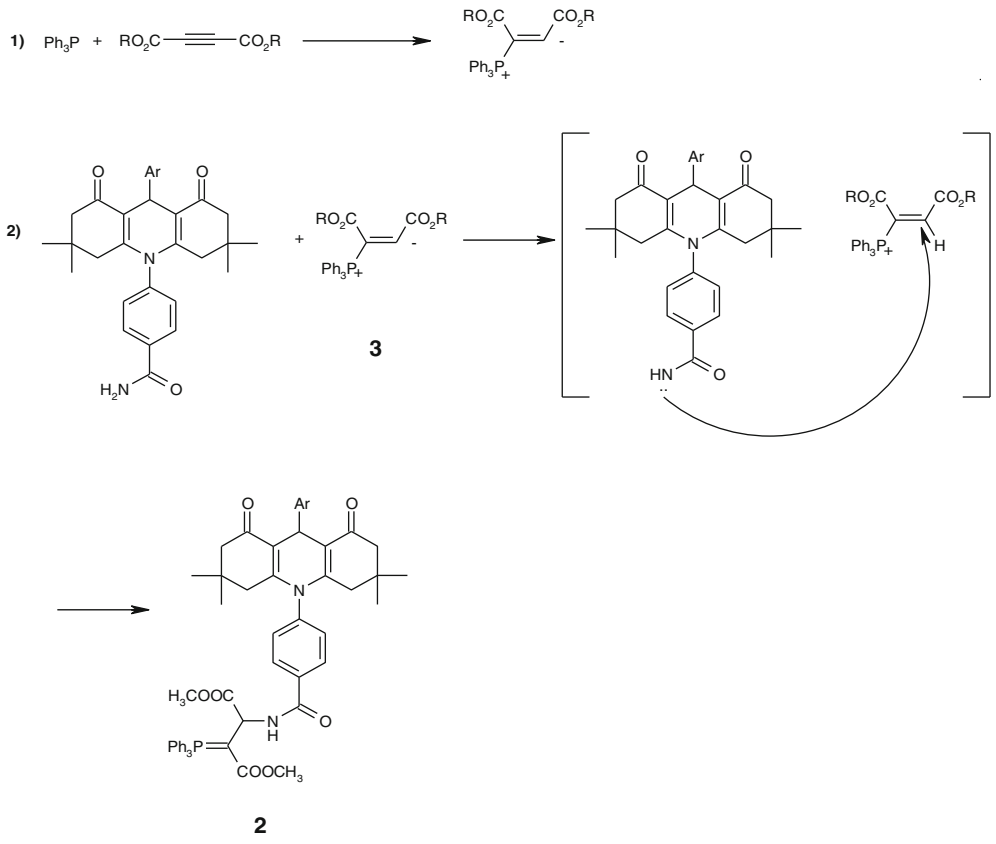
Scheme 2. Reasonable mechanism for the formation of decahydroacridine-1, 8-diones.

Table 1. One-pot synthesis of 1, 8-dioxodecahydroacridines **1a–h**.

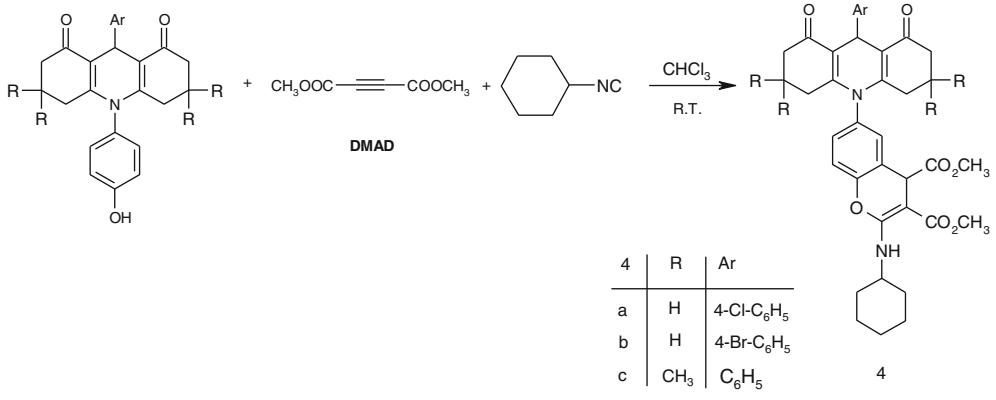
Product	R	X	Ar	M.p. (°C)	Yield (%)
1a	H	—C(=O)—NH_2	C_6H_5	312–314	97
1b	H	—C(=O)—NH_2	3-NO_2-C_6H_4	276–278	90
1c	H	—C(=O)—NH_2	4-NO_2-C_6H_4	292–294	97
1d	CH_3	—C(=O)—NH_2	C_6H_5	318–320	86
1e	CH_3	—C(=O)—NH_2	3-NO_2-C_6H_4	296–298	92
1f	CH_3	—C(=O)—NH_2	4-NO_2-C_6H_4	324–326	95
1g	CH_3	—C(=O)—NH_2	4-Cl-C_6H_4	302–304	85
1h	CH_3	—C(=O)—NH_2	4-Br-C_6H_4	305–307	93
1i	H	OH	4-Cl-C_6H_4	360–362	95
1j	H	OH	4-Br-C_6H_4	356–358	96
1k	H	OH	4-NO_2-C_6H_4	350–352	93
1l	CH_3	OH	4-Cl-C_6H_4	334–336	90
1m	CH_3	OH	3-NO_2-C_6H_4	304–306	86
1n	CH_3	OH	4-Br-C_6H_4	333–335	96
1o	CH_3	OH	C_6H_5	306–308	90



Scheme 3. Reaction of acridines with DMAD and triphenylphosphine.



Scheme 4. Plausible mechanism for the formation of phosphorus ylides from decahydroacridine-1, 8-diones.



4	R	Ar
a	H	4-Cl-C_6H_5
b	H	4-Br-C_6H_5
c	CH_3	C_6H_5

Scheme 5. Synthesis of 4H-chromene derivatives.

the conjugated base of the NH_2 to form phosphoranes **2** (scheme 4).

Finally, treatment of hydroxyl substituted acridinones with DMAD and isocyanide resulted in the formation of 4H-chromene derivatives **4** in chloroform as solvent at ambient temperature (scheme 5).

4. Conclusion

We have new acridine derivatives from simple common chemicals by using three-component condensation reactions to give the products in good to excellent isolated yields.

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