An Efficient Multicomponent Synthesis of Polysubstituted Pyrrolidines and Tetrahydropyrimidines Starting Directly from Nitro Compounds in Water[1]

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Abstract: A distinct approach for the synthesis of 1,3,3-trisubstituted 4,5-dioxopyrrolidines and 1,3,4,5-tetrasubstituted 1,2,3,6-tetrahydropyrimidines has been discovered, in the form of a three-component reaction of nitroarenes, formaldehyde, and dialkyl acetylenedicarboxylates using indium in dilute aqueous HCl at room temperature. The molar ratios of these substrates are 1:1:4 and 2:1:4 for the preparation of dioxopyrrolidines and tetrahydropyrimidines, respectively. The reactions involve the reduction of nitro compounds to amines, which are simultaneously attacked by dialkyl acetylenedicarboxylates and formaldehyde. The products are formed in good to high yields.

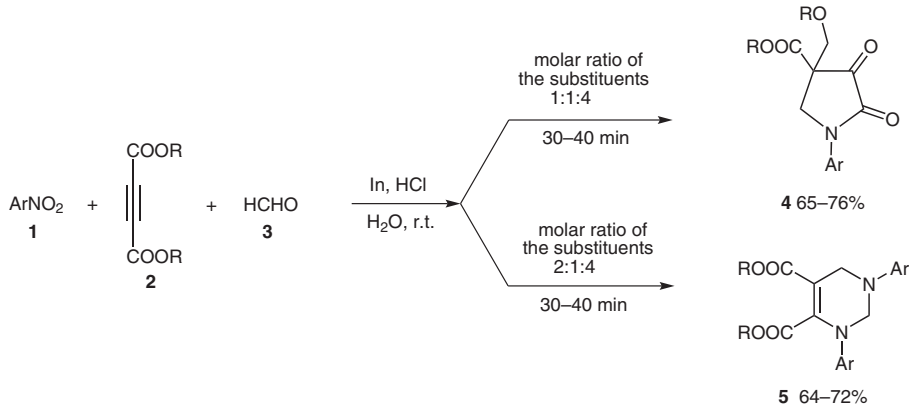
Key words: pyrrolidines, tetrahydropyrimidines, nitro compounds, multicomponent synthesis, reactions in water

Pyrrolidines and pyrimidines are considered as important biologically active heterocycles. The former exhibit anticancer, antibacterial, and antifungal properties[2] while the latter antiviral, anti-inflammatory, and muscarinic agonist activities.[3] Tetrahydropyrimidines are also responsible for salt and heat sensitivity of protein–DNA interactions.[4] Dioxopyrrolidines and tetrahydropyrimidines can be prepared by multicomponent reactions[5] of anilines, formaldehyde, and alkynoates, but the methods involving these reactions are limited.[6] Moreover, high temperature, long reaction time, and the exchange of the functional groups of the alkynoates with the solvents are the problems in different earlier methods. Another point to mention is that the 4,5-dioxopyrrolidine derivatives prepared by Cao et al. was initially considered[6a] as 3,6-dihydro-1,3-oxazines and very recently their structures have been revised[6b] through X-ray crystallographic analysis. Here, we report a distinct approach for the synthesis of 4,5-dioxopyrrolidine and tetrahydropyrimidine derivatives starting directly from the nitro compounds.

In continuation of our work[7] on the development of useful synthetic methodologies using aqueous medium, we have discovered that 1,3,3-trisubstituted 4,5-dioxopyrrolidines and 1,3,4,5-tetrasubstituted 1,2,3,6-tetrahydropyrimidines can be synthesized efficiently through the three-component reactions of nitroarenes, dialkyl acetylenedicarboxylates, and formaldehyde using indium in dilute aqueous HCl at room temperature. 4,5-Dioxopyrrolidine derivatives were formed using a molar ratio of 1:1:4 of these substrates, while tetrahydropyrimidines were produced when this ratio was 2:1:4 (Scheme 1).

Initially, nitrobenzene (1 mmol) was treated with dimethyl acetylenedicarboxylate (DMAD, 1 mmol) and formaldehyde (4 mmol) using different metals such as Sn, Zn, In, and Fe in aqueous HCl at room temperature (Table 1).

Considering the reaction time and yield, indium[8] was found to be most effective to carry out this conversion. Subsequently indium/aqueous HCl system was used to prepare a series of 1,3,3-trisubstituted 4,5-dioxopyrrolidines (Table 2) following the above method (Scheme 1).



Scheme 1 Synthesis of polysubstituted 4,5-dioxopyrrolidines and tetrahydropyrimidines starting directly from nitro compounds

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Table 1 Synthesis of Polysubstituted 4,5-Dioxopyrrolidine **4a** Using Different Metals[a]

Entry	Metal	Time	Yield (%)[b]
1	Sn	10 h	30
2	Zn	7 h	32
3	In	30–40 min	65
4	Fe	14 h	10

[a] Reaction conditions: nitrobenzene (1.0 mmol), DMAD (1.0 mmol), formaldehyde (4.0 mmol), metal (2.0 mmol), and aq 1 M HCl at r.t.
[b] Isolated yields of pure compounds after column chromatography.

Table 2 Synthesis of 1,3,3-Trisubstituted 4,5-Dioxopyrrolidines[a]

Entry	Ar	R	Product[b]	Time (min)	Yield (%)[c]
1	Ph	Me	**4a**	35	65
2	4-MeC_6H_4	Me	**4b**	35	66
3	4-$MeOC_6H_4$	Me	**4c**	40	69
4	4-FC_6H_4	Me	**4d**	30	75
5	4-ClC_6H_4	Me	**4e**	35	73
6	4-BrC_6H_4	Me	**4f**	35	73
7	3-ClC_6H_4	Me	**4g**	40	76
8	4-HOC_6H_4	Me	**4h**	40	76
9	3-MeC_6H_4	Me	**4i**	35	68
10	4-$F_3CC_6H_4$	Me	**4j**	40	70
11	Ph	Et	**4k**	40	70
12	3-MeC_6H_4	Et	**4l**	40	67
13	3-ClC_6H_4	Et	**4m**	40	70
14	4-FC_6H_4	Et	**4n**	30	75
15	4-$MeOC_6H_4$	Et	**4o**	40	67

[a] Reaction conditions: nitroarene (1.0 mmol), alkynoate (1.0 mmol), formaldehyde (4.0 mmol), In metal (2.0 mmol), and aq 1 M HCl at r.t.
[b] All products were fully characterized by usual spectroscopic techniques.
[c] Yields of pure isolated products after column chromatography.

Various nitroarenes were used to prepare these compounds. Both dimethyl and diethyl acetylenedicarboxylates afforded the desired products smoothly. The 4,5-dioxopyrrolidine derivatives were formed in good to high yields (65–76%) within 30–40 minutes. The reaction conditions were mild and various functionalities such as hydroxy, ether, and halogen remained intact.

When the reaction of nitroarenes (2 mmol), dialkyl acetylenedicarboxylates (1 mmol) and formaldehyde (4 mmol) was conducted under similar conditions as applied for the preparation of pyrrolidine derivatives (Scheme 1), 1,3,4,5-tetrasubstituted 1,2,3,6-tetrahydropyrimidines were obtained within 30–40 minutes (Table 3).

Table 3 Synthesis of Tetrasubstituted Tetrahydropyrimidines[a]

Entry	Ar	R	Product[b]	Time (min)	Yield (%)[c]
1	Ph	Me	**5a**	40	64
2	4-FC_6H_4	Me	**5b**	30	72
3	4-ClC_6H_4	Me	**5c**	40	67
4	4-BrC_6H_4	Me	**5d**	30	72
5	4-MeC_6H_4	Me	**5e**	35	65
6	4-$MeOC_6H_4$	Me	**5f**	40	67
7	4-$F_3CC_6H_4$	Me	**5g**	40	68
8	Ph	Et	**5h**	35	67
9	4-$F_3CC_6H_4$	Et	**5i**	40	67
10	4-FC_6H_4	Et	**5j**	35	67

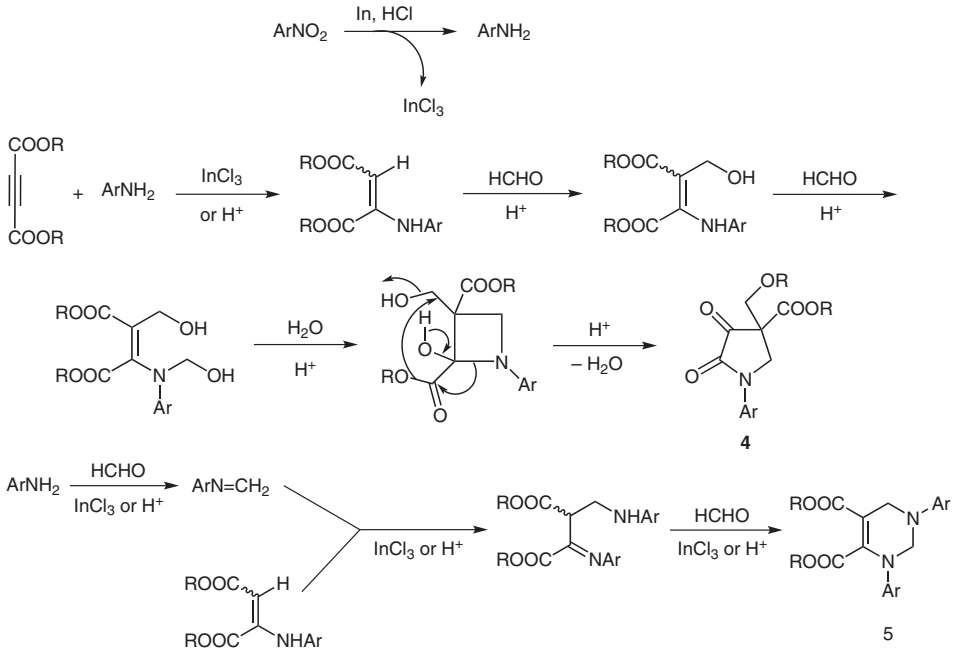
[a] Reaction conditions: nitroarene (2.0 mmol), alkynoate (1.0 mmol), formaldehyde (4.0 mmol), In metal (4.0 mmol), and aq 1 M HCl at r.t.
[b] All products were fully characterized by usual spectroscopic techniques.
[c] Yields of pure isolated products after column chromatography.

In this case also various nitrobenzenes having different functionalities and both dimethyl and diethyl acetylenecarboxylates were used. The yields of the products were good to high (64–72%). The structures of dioxopyrrolidines and tetrahydropyrimidines were settled from their spectral (IR, ^1H and ^{13}C NMR, ESIMS and HRESIMS) data.

In the present conversions, nitro compounds were initially reduced to amines,[9] which then reacted with dialkyl acetylenedicarboxylates and formaldehyde to form the desired heterocycles (Scheme 2).

In conclusion, we have developed a novel efficient method for the synthesis of polysubstituted 4,5- dioxopyrrolidines and tetrahydropyrimidine derivatives through a distinct approach involving the multicomponent reaction of nitro compounds, dialkyl acetylenedicarboxylates, and formaldehyde using indium in dilute aqueous HCl at room temperature. The direct application of nitro compounds, conversion in water, and mild reaction conditions are the advantages of the present method.

The silica gel F_{254} plates were used for TLC in which the spots were examined under UV light and then developed by I_2 vapor. Column chromatography was performed with silica gel (BDH 100–200 mesh). Solvents were purified according to standard procedures. The spectra were recorded with the following instruments; IR: Perkin-Elmer RX1 FT-IR spectrophotometer; NMR: Varian Gemini 200 MHz (^1H) and 50 MHz (^{13}C) spectrometer; ESIMS: VG-Autospec micromass and HRMS: QSTAR XL, Hybrid MS system (Applied Biosystems).



Scheme 2 Proposed pathway for the synthesis of polysubstituted pyrrolidines and tetrahydropyrimidines starting directly from nitro compounds

1,3,3-Trisubstituted 4,5-Dioxopyrrolidines 4; General Procedure

To a mixture of nitro compound **1** (1.0 mmol) and In (325 mesh, 2.0 mmol) were added aq 1 M HCl (1 mL) and H_2O (2 mL). The mixture was stirred at r.t. for 10 min followed by addition of alkynoate **2** (1 mmol). After 10 min, formaldehyde (**3**; 4.0 mmol) was added and the stirring was continued. The reaction was monitored by TLC. After completion, the mixture was washed with sat. aq $NaHCO_3$ (3 × 5 mL) and H_2O (3 × 5 mL), and extracted with EtOAc (3 × 5 mL). The combined extracts were concentrated and the residue was subjected to column chromatography (silica gel, hexanes–EtOAc) to obtain pure 4,5-dioxopyrrolidine derivative (Table 2).

Tetrasubstituted Tetrahydropyrimidines 5; General Procedure

For the preparation of tetrahydropyrimidines, the similar experimental procedure as above for the 1,3,3-trisubstituted 4,5-dioxopyrrolidines was followed using nitro compound **1** (2.0 mmol), alkynoate **2** (1.0 mmol), and formaldehyde (**3**; 4.0 mmol), along with In (325 mesh, 4.0 mmol), aq 1 M HCl (2 mL), and H_2O (3 mL) (Table 3).

The spectral (IR, ^1H and ^{13}C NMR, and MS) and analytical data of the unknown products are given below.

Methyl 1-(4-Hydroxyphenyl)-3-methoxymethyl-4,5-dioxopyrrolidine-3-carboxylate (4h)

Yield: 76%.

IR (KBr): 3388, 1772, 1699, 1515, 1458 cm^{-1}.

^1H NMR (200 MHz, $CDCl_3$): δ = 7.65 (2 H, d, *J* = 8.0 Hz), 6.93 (2 H, d, *J* = 8.0 Hz), 4.51 (1 H, d, *J* = 12.0 Hz), 4.22 (1 H, d, *J* = 12.0 Hz), 4.00 (1 H, d, *J* = 10.0 Hz), 3.90 (1 H, d, *J* = 10.0 Hz), 3.80 (3 H, s), 3.31 (3 H, s).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 194.2, 166.2, 156.0, 155.6, 130.2, 120.8, 115.7, 72.6, 59.9, 55.1, 53.0, 49.9.

ESIMS: *m*/*z* = 294 $[M + H]^+$.

HRMS (ESI): *m*/*z* calcd for $C_{14}H_{16}NO_6$ $[M + H]^+$: 294.0977; found: 294.0978.

Methyl 3-Methoxymethyl-1-(3-methylphenyl)-4,5-dioxopyrrolidine-3-carboxylate (4i)

Yield: 68%.

IR (KBr): 1771, 1702, 1512, 1252 cm^{-1}.

^1H NMR (200 MHz, $CDCl_3$): δ = 7.69 (1 H, d, *J* = 2.0 Hz), 7.62 (1 H, dd, *J* = 8.0 Hz), 7.31 (1 H, t, *J* = 8.0 Hz), 7.09 (1 H, dd, *J* = 8.0, 2.0 Hz), 4.49 (1 H, d, *J* = 12.0 Hz), 4.20 (1 H, d, *J* = 12.0 Hz), 3.93 (1 H, d, *J* = 10.0 Hz), 3.88 (1 H, d, *J* = 10.0 Hz), 3.76 (3 H, s), 3.22 (3 H, s), 2.43 (3 H, s).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 192.9, 166.2, 156.1, 139.6, 139.0, 129.9, 129.2, 128.1, 120.0, 116.3, 72.8, 59.5, 55.1, 53.8, 49.0, 21.4.

ESIMS: *m*/*z* = 292 $[M + H]^+$.

HRMS (ESI): *m*/*z* calcd for $C_{15}H_{18}NO_5$ $[M + H]^+$: 292.1179; found: 292.1192.

Methyl 1-(4-Trifluoromethylphenyl)-3-methoxymethyl-4,5-dioxopyrrolidine-3-carboxylate (4j)

Yield: 70%.

IR (KBr): 1777, 1737, 1613, 1462 cm^{-1}.

^1H NMR (200 MHz, $CDCl_3$): δ = 8.02 (2 H, d, *J* = 8.0 Hz), 7.72 (2 H, d, *J* = 8.0 Hz), 4.54 (1 H, d, *J* = 12.0 Hz), 4.22 (1 H, d, *J* = 12.0 Hz), 3.99 (1 H, d, *J* = 10.0 Hz), 3.89 (1 H, d, *J* = 10.0 Hz), 3.80 (3 H, s), 3.34 (3 H, s).

^{13}C NMR (50 MHz, $CDCl_3$): δ 193.1, 166.1, 155.9, 141.0, 135.0, 125.8 (br), 124.9, 119.4, 74.2, 60.0, 55.1, 53.8, 49.2.

ESIMS: *m*/*z* = 346 $[M + H]^+$.

HRMS (ESI): *m*/*z* calcd for $C_{15}H_{14}F_3NO_5$ + Na $[M + Na]^+$: 368.0721; found: 368.0726.

Ethyl 3-Ethoxymethyl-1-phenyl-4,5-dioxopyrrolidine-3-carboxylate (4k)

Yield: 67%.

IR (KBr): 1769, 1696, 1513, 1459 cm^{-1}.

^{1}H NMR (200 MHz, $CDCl_3$): δ = 7.81 (1 H, d, *J* = 2.0 Hz), 7.78 (1 H, dd, *J* = 8.0, 2.0 Hz), 7.42 (1 H, t, *J* = 8.0 Hz), 7.16 (1 H, dd, *J* = 8.0, 2.0 Hz), 4.50 (1 H, d, *J* = 12.0 Hz), 4.28–4.18 (3 H, m), 3.99 (1 H, d, *J* = 10.0 Hz), 3.90 (1 H, d, *J* = 10.0 Hz), 3.48 (2 H, q, *J* = 7.0 Hz), 2.43 (3 H, s), 1.27 (3 H, t, *J* = 7.0 Hz) 1.10 (3 H, t, *J* = 7.0 Hz).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 193.3, 166.2, 156.1, 139.4, 139.2, 135.0, 130.0, 128.2, 120.4, 116.0, 70.5, 67.5, 61.5, 55.6, 49.8, 23.4, 15.0, 14.3.

ESIMS: *m*/*z* = 320 $[M + H]^+$.

HRMS (ESI): *m*/*z* calcd for $C_{17}H_{22}NO_5$ $[M + H]^+$: 320.1497; found: 320.1488.

Ethyl 3-Ethoxymethyl-1-(3-methylphenyl)-4,5-dioxopyrrolidine-3-carboxylate (4l)
Yield: 70%.

IR (KBr): 1775, 1720, 1593, 1481 cm^{-1}.

^{1}H NMR (200 MHz, $CDCl_3$): δ = 7.82 (1 H, dd, *J* = 8.0, 2.0 Hz), 7.80 (1 H, d, *J* = 2.0 Hz), 7.36 (1 H, t, *J* = 8.0 Hz), 7.21 (1 H, dd, *J* = 8.0, 2.0 Hz), 4.43 (1 H, d, *J* = 12.0 Hz), 4.28–4.16 (3 H, m), 3.95 (1 H, d, *J* = 10.0 Hz), 3.88 (1 H, d, *J* = 10.0 Hz), 3.45 (2 H, q, *J* = 7.0 Hz), 1.23 (3 H, t, *J* = 7.0 Hz) 1.08 (3 H, t, *J* = 7.0 Hz).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 192.3, 165.5, 156.2, 140.0, 135.12, 130.0, 126.6, 124.8, 119.1, 117.3, 70.3, 67.5, 62.7, 55.2, 49.0, 15.1, 14.3.

ESIMS: *m*/*z* = 340, 342 $[M + H]^+$.

HRMS (ESI): *m*/*z* calcd for $C_{16}H_{19}ClNO_5$ $[M + H]^+$: 340.0951; found: 340.0963.

Dimethyl 1,3-Di(*p*-tolyl)-1,2,3,6-tetrahydropyrimidine-4,5-dicarboxylate (5e)
Yield: 65%.

IR (KBr): 1743, 1698, 1578, 1514, 1436, 1260 cm^{-1}.

^{1}H NMR ($CDCl_3$, 200 MHz): δ = 7.04 (2 H, d, *J* = 8.0 Hz), 6.99 (2 H, d, *J* = 8.0 Hz), 6.82 (2 H, d, *J* = 8.0 Hz), 6.79 (2 H, d, *J* = 8.0 Hz), 4.81 (2 H, s), 4.12 (2 H, s), 3.71 (3 H, s), 3.53 (3 H, s), 2.32 (3 H, s), 2.23 (3 H, s).

^{13}C NMR ($CDCl_3$, 50 MHz): δ = 166.2, 164.6, 146.0, 140.8, 136.8, 130.7, 130.6, 129.8, 129.7, 125.2, 118.3, 118.1, 69.2, 52.5, 51.4, 47.6, 21.0, 20.5.

ESI-MS: *m*/*z* = 381 $[M + H]^+$

HRMS (ESI): *m*/*z* calcd for $C_{22}H_{24}N_2O_4$ + Na $[M + Na]^+$: 403.1633; found: 403.1647.

Dimethyl 1,3-Bis(4-methoxyphenyl)-1,2,3,6-tetrahydropyrimidine-4,5-dicarboxylate (5f)
Yield: 68%.

IR (KBr): 1742, 1695, 1582, 1438, 1249 cm^{-1}.

^{1}H NMR ($CDCl_3$, 200 MHz): δ = 6.90 (2 H, d, *J* = 8.0 Hz), 6.81 (2 H, d, *J* = 8.0 Hz), 6.74 (2 H, d, *J* = 8.0 Hz), 6.70 (2 H, d, *J* = 8.0 Hz), 4.72 (2 H, s), 4.11 (2 H, s), 3.72 (6 H, s), 3.70 (3 H, s), 3.53 (3 H, s).

^{13}C NMR ($CDCl_3$, 50 MHz): δ = 166.2, 164.1, 158.0, 154.2, 147.5, 142.1, 135.3, 127.1, 120.0, 114.6, 114.1, 96.9, 70.2, 55.2, 55.0, 51.9, 51.0, 47.4.

ESI-MS: *m*/*z* = 435 $[M + Na]^+$.

HRMS (ESI): *m*/*z* calcd for $C_{22}H_{24}N_2O_6$ + Na $[M + Na]^+$: 435.1532; found: 435.1516.

Dimethyl 1,3-Bis[4-(trifluoromethyl)phenyl]-1,2,3,6-tetrahydropyrimidine-4,5-dicarboxylate (5g)
Yield: 67%.

IR (KBr): 1742, 1706, 1610, 1437 cm^{-1}.

^{1}H NMR (200 MHz, $CDCl_3$): δ = 7.58 (2 H, d, *J* = 8.0 Hz), 7.41 (2 H, d, *J* = 8.0 Hz), 7.11 (2 H, d, *J* = 8.0 Hz), 6.82 (2 H, d, *J* = 8.0 Hz), 5.00 (2 H, s), 4.31 (2 H, s), 3.75 (3 H, s), 3.62 (3 H, s).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 165.8, 164.0, 150.2, 147.0, 145.2, 127.1 (br), 124.0, 119.5, 118.2, 116.0, 105.0, 67.2, 52.6, 52.0, 47.2.

ESIMS: *m*/*z* = 489 $[M + H]^+$.

HRMS (ESI): *m*/*z* calcd for $C_{22}H_{18}F_6N_2O_4$ + Na $[M + Na]^+$: 511.1068; found: 511.1060.

Diethyl 1,3-Bis[4-(trifluoromethyl)phenyl]-1,2,3,6-tetrahydropyrimidine-4,5-dicarboxylate (5i)
Yield: 67%.

IR (KBr): 1738, 1700, 1612, 1327 cm^{-1}.

^{1}H NMR (200 MHz, $CDCl_3$): δ = 7.54 (2 H, d, *J* = 8.0 Hz), 7.41 (2 H, d, *J* = 8.0 Hz), 7.12 (2 H, d, *J* = 8.0 Hz), 6.83 (2 H, d, *J* = 8.0 Hz), 4.99 (2 H, s), 4.31 (2 H, s), 4.21 (2 H, q, *J* = 7.0 Hz), 4.03 (2 H, q, *J* = 7.0 Hz), 1.31 (3 H, q, *J* = 7.0 Hz), 1.03 (3 H, q, *J* = 7.0 Hz).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 166.0, 163.4, 150.2, 146.7, 144.9, 126.9 (br), 123.7, 119.5, 118.2, 116.7, 114.2, 105.0, 67.0, 62.1, 61.0, 47.3, 14.2, 13.6.

ESIMS: *m*/*z* = 517 $[M + H]^+$.

HRMS (ESI): *m*/*z* calcd for $C_{24}H_{22}F_6N_2O_4$ + Na $[M + Na]^+$: 539.1376068; found: 539.1395.

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References

(1) Part 202 in the series: 'Studies on Novel Synthetic Methodologies'.
(2) (a) Janecki, T.; Blaszczyk, E.; Studzian, K.; Janecka, A.; Krajenska, U.; Rozalski, M. *J. Med. Chem.* **2005**, *48*, 3516. (b) Hong, C. Y.; Kim, Y. K.; Chang, J. H.; Kim, S. H.; Choi, H.; Nam, D. H.; Kim, Y. Z.; Kwak, J. H. *J. Med. Chem.* **1997**, *40*, 3584. (c) Raj, A. A.; Raghunathan, R.; Sridevi Kumari, M. R.; Raman, N. *Bioorg. Med. Chem.* **2003**, *11*, 407.
(3) (a) Nair, V.; Chi, G.; Ptak, R.; Neamati, N. *J. Med. Chem.* **2006**, *49*, 445. (b) Pattarimi, P.; Smeyne, R. J.; Morgan, J. I. *Neuroscience* **2007**, *145*, 654. (c) Messer, W. S. Jr.; Abuh, Y. F.; Paryasamy, S.; Ngur, D. O.; Edger, M. A. N.; Eissadi, A. A.; Sheih, S.; Dunbar, P. G.; Roknich, S.; Rho, T.; Fang, Z.; Ojo, B.; Zhang, H.; Huzl, J. J.; Nagy, P. I. *J. Med. Chem.* **1997**, *40*, 1230.
(4) Tozkoparan, B.; Yarim, M.; Sarac, S.; Ertan, M.; Kelicun, P.; Altinoc, G.; Demirdamar, R. *Arch. Pharm. Pharm. Med. Chem.* **2000**, *333*, 415.
(5) For recent examples of multicomponent reactions, see: (a) Ohno, H.; Ohta, Y.; Oishi, S.; Fujii, N. *Angew. Chem. Int. Ed.* **2007**, *46*, 2295. (b) Komagawa, S.; Saito, S. *Angew. Chem. Int. Ed.* **2006**, *45*, 2446. (c) Yoshida, H.; Fukushima, H.; Ohshita, J.; Kunai, A. *J. Am. Chem. Soc.* **2006**, *128*, 11040. (d) Dondas, H.; Fishwick, C. W. G.; Gai, X.; Grigg, R.; Kilner, C.; Dumrongchai, N.; Kongkathip, B.;

Kongkathip, N.; Polysuk, C.; Sridharan, V. *Angew. Chem. Int. Ed.* **2005**, *44*, 7570. (e) Pache, S.; Lautens, M. *Org. Lett.* **2003**, *5*, 4827.

(6) (a) Cao, H.; Jiang, H.-F.; Qi, C.-R.; Yao, W.-J.; Chem, H.-J. *Tetrahedron Lett.* **2009**, *50*, 1209. (b) Srikrishna A., Sridharan M., Prasad K. R.; *Tetrahedron*; **2010**, *66*: in press; DOI: 10.1016/ j.tet.2010.03.084

(7) (a) Das, B.; Banerjee, J.; Mahender, G.; Majhi, A. *Org. Lett.* **2004**, *6*, 3349. (b) Das, B.; Holla, H.; Venkateswalu, K.; Majhi, A. *Tetrahedron Lett.* **2005**, *46*, 8895. (c) Das, B.; Satyalakshmi, G.; Suneel, K.; Shashikanth, B. *Tetrahedron Lett.* **2008**, *49*, 7209.

(8) Ranu, B. C. *Eur. J. Org. Chem.* **2000**, 2347.

(9) Lee, J. C.; Choi, K. I. I.; Koh, H. Y.; Kang, Y.; Kuin, Y.; Kang, Y.; Cho, Y. S. *Synthesis* **2001**, 81.