Electronically Modified Amine Substituted Alkynols for Regio-selective Synthesis of Dihydrofuran Derivatives

Vijay V, a Manjusha V. Karkhelikar, b B. Sridhar, c Nedaossadat Mirzadeh, d Pravin R. Likhar a,b,* plikhar@iict.res.in

Contents

1) General Techniques S2
2) $^1$H NMR, $^{13}$C NMR Spectral Data of 4a-4l S3-S14
3) $^1$H NMR, $^{13}$C NMR Spectral Data of 5a-5k S15-S23
4) $^1$H NMR, $^{13}$C NMR Spectral Data of 6d, 7b, 8a and 9d S24-S27
5) X-ray Crystallographic Study of 5e and 8a S28-S30
General Techniques:

NMR spectra were recorded in Fourier transform mode. The $^1$H NMR and $^{13}$C NMR spectra were recorded on a 300 MHz, 400 MHz, and 500 MHz spectrophotometer using CDCl$_3$ and TMS as the internal standard. Multiplicities in the $^1$H NMR spectra are described as: s = singlet, d = doublet, t = triplet, q = quartet, qt = quintet, m = multiplet, bs = broad singlet; coupling constants are reported in Hz. Low (MS) and high (HRMS) resolution mass spectra were recorded by ion trap method and mass/charge (m/z) ratios are reported as values in atomic mass units. All the melting point is uncorrected.
$^{1}H$ NMR and $^{13}C$ NMR of 4a
$^{1}H$ NMR and $^{13}C$ NMR of 4b
$^1$H NMR and $^{13}$C NMR of 4c
$^{1}H$ NMR and $^{13}C$ NMR of 4d
$\text{H NMR and C NMR of 4e}$
$^{1}H$ NMR and $^{13}C$ NMR of 4f
$^{1}H$ NMR and $^{13}C$ NMR of 4g
$^1$H NMR and $^{13}$C NMR of 4h
$^{1}$H NMR and $^{13}$C NMR of 4i
\textbf{\textsuperscript{1}H NMR and \textsuperscript{13}C NMR of 4j}
$^1$H NMR and $^{13}$C NMR of 4k
1H NMR and 13C NMR of 4l
$^1$H NMR and $^{13}$C NMR of 5a
$^1$H NMR and $^{13}$C NMR of 5b
$^{1}H$ NMR and $^{13}C$ NMR of 5d
$^1$H NMR and $^{13}$C NMR of 5e
$^1$H NMR and $^{13}$C NMR of 5f
$^1$H NMR and $^{13}$C NMR of 5g

520
$^{1}H$ NMR and $^{13}C$ NMR of 5h
$^1$H NMR and $^{13}$C NMR of 5i
$^{1}H$ NMR and $^{13}C$ NMR of 5k
$^1$H NMR and $^{13}$C NMR of 6d
$^1$H NMR and $^{13}$C NMR of 7b
$^1$H NMR and $^{13}$C NMR of 8a
$^1$H NMR and $^{13}$C NMR of 9d
X-ray Crystallographic Study:

**Compound 5e:**

The molecular structure of 5e, with the atom-numbering scheme. Displacement ellipsoids are drawn at the 30% probability level. Dashes line indicate a hydrogen bond.

X-ray data of compound 5e was collected at room temperature using a Bruker Smart Apex CCD diffractometer with graphite monochromated MoKα radiation (\(\lambda=0.71073\text{Å}\)) with ω-scan method.\(^1\) Preliminary lattice parameters and orientation matrices were obtained from four sets of frames. Integration and scaling of intensity data were accomplished using SAINT program.\(^1\) The structures were solved by Direct Methods using SHELXS\(^2\) and refinement was carried out by full-matrix least-squares technique using SHELXL.\(^2\) Anisotropic displacement parameters were included for all non-hydrogen atoms. The hydrogen atom attached to nitrogen atom was located in a difference density map and refined isotropically. All other H atoms were

---

\(^1\) Preliminary lattice parameters and orientation matrices were obtained from four sets of frames.

\(^2\) Anisotropic displacement parameters were included for all non-hydrogen atoms.
positioned geometrically and treated as riding on their parent C atoms [C-H = 0.93-0.97 Å and U_{iso}(H) = 1.5U_{eq}(C) for methyl H or 1.2U_{eq}(C) for other H atoms]. The methyl groups were allowed to rotate but not to tip.

**Crystal Data for 5e:** C_{17}H_{14}INO_{2} (M = 391.19): orthorhombic, space group Pbcn (no. 61), \(a = 13.7811(12)\) Å, \(b = 13.3475(11)\) Å, \(c = 16.9711(15)\) Å, \(V = 3121.7(5)\) Å\(^3\), \(Z = 8\), \(T = 294(2)\) K, \(\mu(MoK\alpha) = 2.055\) mm\(^{-1}\), \(D_{calc} = 1.665\) g/mm\(^3\), 33971 reflections measured (4.8 \(\leq\) 2\(\Theta\) \(\leq\) 56.7), 3837 unique \((R_{int} = 0.0346)\) which were used in all calculations. The final \(R_1\) was 0.0462 (>2\(\sigma(I)\)) and \(wR_2\) was 0.1179 (all data). CCDC 1405059 contains supplementary Crystallographic data for the structure. These data can be obtained free of charge at www.ccdc.cam.ac.uk/conts/retrieving.html [or from the Cambridge Crystallographic Data Centre (CCDC), 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44(0) 1223 336 033; email: deposit@ccdc.cam.ac.uk].

**Compound 8a:**

The molecular structure of 8a, with the atom-numbering scheme. Displacement ellipsoids are drawn at the 30% probability level. Dashes line indicate a hydrogen bond.

X-ray data of compound 8a was collected at room temperature using a Bruker Smart Apex CCD diffractometer with graphite monochromated MoK\(\alpha\) radiation (\(\lambda = 0.71073\)Å) with \(\omega\)-
scan method. Preliminary lattice parameters and orientation matrices were obtained from
four sets of frames.
Integration and scaling of intensity data were accomplished using SAINT program. The
structures were solved by Direct Methods using SHELXS and refinement was carried out by
full-matrix least-squares technique using SHELXL. Anisotropic displacement parameters
were included for all non-hydrogen atoms. The hydrogen atom attached to nitrogen atom was
located in a difference density map and refined isotropically. All other H atoms were
positioned geometrically and treated as riding on their parent C atoms [C-H = 0.93-0.97 Å
and U\text{iso}(H) = 1.5U\text{eq}(C) for methyl H or 1.2U\text{eq}(c) for other H atoms]. The methyl groups
were allowed to rotate but not to tip.

Crystal data for 8a: C_{17}H_{19}NO_5, M = 317.33, 0.18 x 0.16 x 0.09 mm^3, monoclinic, space
group P2_1/n (No. 14), a = 13.6571(12), b = 7.7611(7), c = 14.9680(14) Å, \beta = 91.630(2)°,
V = 1585.9(2) Å^3, Z = 4, D_c = 1.329 g/cm^3, F_{000} = 672, MoK\alpha radiation, \lambda = 0.71073 Å, T
= 294(2)K, 2\theta_{\text{max}} = 50.0º, 14739 reflections collected, 2794 unique (R_{\text{int}} = 0.0706). Final
GooF = 1.242, R1 = 0.0975, wR2 = 0.1684, R indices based on 2100 reflections with I > 2\sigma(I)
(refinement on F^2), 214 parameters, 0 restraints. \mu = 0.098 mm\(^{-1}\).CCDC 1051824 contains
supplementary Crystallographic data for the structure. These data can be obtained free of
charge at www.ccdc.cam.ac.uk/conts/retrieving.html [or from the Cambridge
Crystallographic Data Centre (CCDC), 12 Union Road, Cambridge CB2 1EZ, UK; fax:
+44(0) 1223 336 033; email: deposit@ccdc.cam.ac.uk].

Reference:
1. SMART & SAINT. Software Reference manuals. Versions 6.28a & 5.625, Bruker