*Short Communication*

# Facile Synthesis of Novel Fused 1,2,3-Triazolo[1,5-*a*]pyridines from *o*-Formyl(azido)azoles

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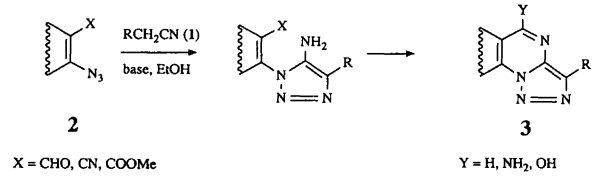
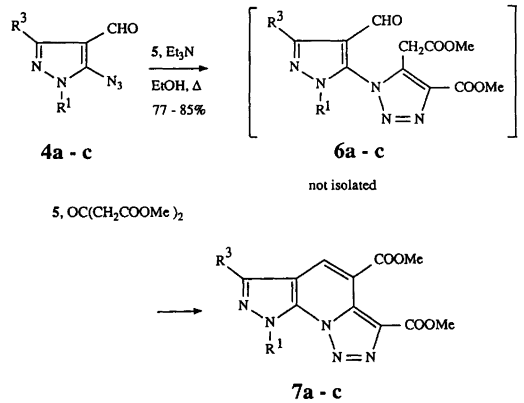
Dedicated to Professor Salo Gronowitz on the occasion of his 65th birthday.

Heterocycles bearing an azido function have found wide application in organic synthesis.[1] Active methylene nitriles **1** are known to condense with *o*-substituted aryl azides **2** in a two-step process, to yield tricyclic triazolo-pyrimidines **3**.[2,3] Carbocyclic[2] and heterocyclic[3] azides have been used (Scheme 1).



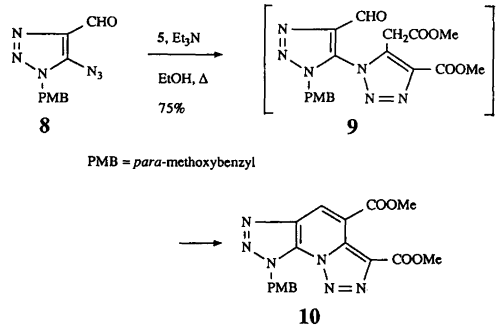

*Scheme 1.*

It was envisaged that an intramolecular nucleophilic attack by a carbanion in the second step on the formyl moiety would result in a similar condensation to triazolo-pyridines (Scheme 2). Thus, the readily available[4] 5-azido-4-formylpyrazoles **4a–c** were reacted with dimethyl 3-oxopentanedioate **5** and triethylamine. In the first step the (3-pyrazol-3-yl-1,2,3-triazol-4-yl)acetates **6a–c** were formed via a Dimroth reaction.[5] These unstable intermediates could not be isolated but readily condensed under the reaction conditions to form pyrazolo[4,3-*e*][1,2,3]triazolo[1,5-*a*]pyridines **7a–c** in high yields (Scheme 2).



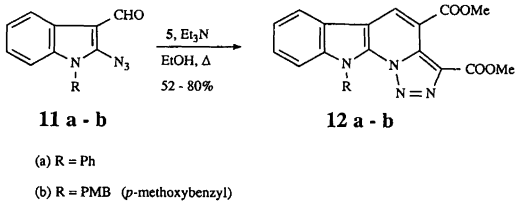

*Scheme 2.*

The azidotriazole **8**[4] condensed similarly, and in this case a 75 % yield of the pyridineditriazole **10** was obtained (Scheme 3).




*Scheme 3.*

Analogously, the tetracyclic indoles **12a,b** could be obtained in fair yields from the corresponding azides **11a,b**[6] (Scheme 4).

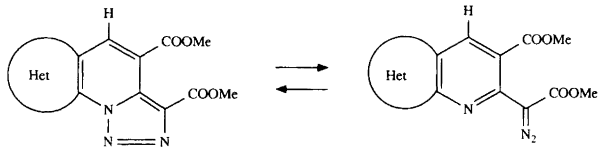



*Scheme 4.*

Fused 1,2,3-triazoles undergo ring-chain tautomerism and are in equilibrium with open-chain diazo imines.[7] This equilibrium is reported to be shifted entirely to the closed form in the triazolopyridine series[8] although in this case, the intermediate diazopyridine could be trapped as the perchlorate salt.[8a]

For the fused systems **7a–c**, **10** and **12a,b** the open diazo form **13** is present in significant amounts as can be seen from the IR spectra (2110 $cm^{-1}$). In the mass spectra an abundant $M^{+\cdot} - 28$ ion is seen, and the strongly broadened NMR spectra indicate a fast equilibrium. The

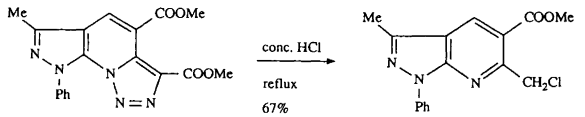
effect is more pronounced in the pyrazole series and for *N*-aryl substituted heterocycles (Scheme 5).



**7a - c, 10, 12a - b** **13**

*Scheme 5.*

It has been reported[2] that hydrolysis and decarboxylation precedes triazole-ring scission. Thus, tricycle **7a** was smoothly converted into the functionalized pyrazolopyridine **14** with concentrated hydrochloric acid (Scheme 6).



**7a** **14**

*Scheme 6.*

During this work our attention was drawn to a recent paper,[9] in which similar condensations of *ortho*-functionalized aryl azides with dimethyl 3-oxopentanedioate under the influence of strong bases (NaOEt or Amberlite

*Table 1.* Spectral data of compounds **7a–c**, **10** and **12a,b**.

| Product | Yield (%) | M.p./°C | Molecular formula[e] | IR(KBr) $\nu$/cm$^{-1}$ [f] | $^1$H NMR ($CDCl_3$, TMS)[g] $\delta$ ($J$/Hz)[h] | MS (70 eV) $m/z$ (%)[i] |
|---|---|---|---|---|---|---|
| **7a** | 85 | 154–155[b] | $C_{18}H_{15}N_5O_4$ (365.3) | 2212 (C=$N_2$) 1724 (C=O) | 2.75 (s, 3 H, $CH_3$), 3.80–3.95 (br, 6 H, $CH_3O$), 7.55–7.85 (m, 5 H, Ph), 8.55 (br s, 1 H, pyridine) | 365 ($M^+$, 4), 337 ($M^+ - 28$, 100), 294 ($M^+ - N_2 - CO - Me$, 91), 266 (294 – CO, 91), 77 (88) |
| **7b** | 77 | 178–180[c] | $C_{18}H_{14}N_5O_4$ (365.3) | 2110 (C=$N_2$) 1736 (C=O) | 3.95 (s, 3 H, $CH_3O$), 4.05 (s, 3 H, $CH_3O$), 4.75 (s, 3 H, $CH_3N$), 7.55 (m, 3 H, Ph), 7.85 (m, 2 H, Ph), 8.45 (s, 1 H, pyridine) | 365 ($M^+$, 16), 337 ($M^+ - N_2$, 100), 294 (337 – CO – Me, 80), 266 (294 – CO, 69), 77 (13) |
| **7c** | 84 | 164–165[c] | $C_{23}H_{17}N_5O_4$ (427.3) | 2214 (C=$N_2$) 1719 (C=O) | 3.84 (s, 3 H, $CH_3O$), 3.92 (s, 3 H, $CH_3O$), 7.30–7.60 (m, 7 H, Ph), 8.02 (m, 2 H, Ph), 8.30 (m, 1 H, Ph), 8.73 (s, 1 H, pyridine) | 427 ($M^+$, 9), 399 ($M^+ - N_2$, 99), 356 (79), 328 (65), 77 (100) |
| **10** | 75[a] | 147–148[b] | $C_{18}H_{16}N_6O_5$ (396.3) | 2116 (C=$N_2$) 1740 (C=O) | 3.80 (s, 3 H, $CH_3O$), 4.05 (s, 6 H, $CH_3O$), 6.25 (s, 2 H, $CH_2N$), 6.80 and 7.55 (m, 2 H, aryl), 8.45 (s, 1 H, pyridine) | 396 ($M^+$, not detected), 368 ($M^+ - N_2$, 20), 121 ($CH_3OC_7H_7^+$, 100) |
| **12a** | 80 | 153–155[d] | $C_{22}H_{16}N_4O_4$ (400.4) | 2107 (C=$N_2$) 1719 (C=O) | 3.80 (br s, 3 H, $CH_3O$), 3.95 (br s, 3 H, $CH_3O$), 7.32–7.65 (m, 8 H, Ph and indole), 8.10 (m, 1 H, indole), 8.80 (br s, 1 H, pyridine) | 400 ($M^+$, 14), 372 ($M^+ - N_2$, 82), 329 (100), 301 (66), 77 (20) |
| **12b** | 52 | 153–154[b] | $C_{24}H_{20}N_4O_5$ (444.4) | 2105 (C=$N_2$) 1724 (C=O) | 3.70 (s, 3 H, $CH_3O$), 3.95 (s, 3 H, $CH_3O$), 6.30 (s, 2 H, $CH_2N$), 6.70 and 7.18 (m, 2 H, aryl), 7.15 (m, 3 H, indole), 8.00 (m, 1 H, indole), 8.55 (s, 1 H, pyridine) | 444 ($M^+$, 3), 416 ($M^+ - N_2$, 33), 121 ($CH_3OC_7H_7^+$, 100) |

[a] The reaction was refluxed overnight. [b] Recrystallized from chloroform–diethyl ether. [c] Recrystallized from ethanol. [d] Recrystallized from methanol. [e] Satisfactory C, H, N microanalysis was obtained except for **12b**: Found C 64.40; H 4.92; N 11.79. Calc. for $C_{24}H_{20}N_4O_5$: C 64.86; H 4.54; N 12.61. [f] Recorded on a Perkin–Elmer 580 infrared spectrometer. [g] Except **7a** which was recorded in DMSO-$d_6$. [h] Recorded on a Bruker AC 250 or a Jeol FX-60Q NMR spectrometer. [i] Recorded on a Varian Mat 311A mass spectrometer.

IRA-400) were described. In the present investigation we used a weaker base ($Et_3N$) and heterocyclic *o*-azido aldehydes, conditions which probably led to higher yields. Moreover, the method described above[9] failed when heterocyclic azides were used as substrates.

## Experimental

Heterocyclic azides **4a–c**, **8** and **11a**, **b** were prepared from the corresponding chlorides, as described previously.[4,6]

*[1,2,3]Triazolo[1,5-a]pyridines* **7a–c**, **10** *and* **12a–c**: *general procedure.* A solution of 2 mmol azido aldehyde **4a–c**, **8**, or **11a**, **b**, 2 mmol **5** and 2 mmol triethylamine in 20 ml ethanol was refluxed for 5 min and the mixture was left to stand overnight. The solid was collected and recrystallized from the appropriate solvent (see Table 1).

*6-Chloromethyl-5-methoxycarbonyl-3-methyl-1-phenyl-1H-pyrazolo[3,4-b]pyridine* **14**. A suspension of 100 mg (0.27 mmol) **7a** in 5 ml concentrated HCl was heated with stirring for 2 h. The mixture was added to 50 ml saturated $NAHCO_3$ solution. Extraction with dichloromethane (3 × 20 ml), drying ($MgSO_4$) and chromatography of the residue over $SiO_2$ with dichloromethane ($R_f = 0.65$) gave **14** as a white solid, yield 60 mg (67%); m.p. 154–155°C (chloroform–ether). Anal. $C_{16}H_{14}ClN_3O_2$: C, H, N. MS [*E* 70 eV; *m/z* (% rel. int.)] 315 (100, $M^+$ 284 (26, $M^+ - CH_3O$). IR (KBr): 1723 (C=O), 1256 $cm^{-1}$. $^1H$ NMR ($CDCl_3$): δ = 2.65 (s, 3 H, $CH_3$), 4.00 (s, 3 H, $CH_3O$), 5.25 (s, 2 H, $CH_2Cl$), 7.30 (m, 1 H, phenyl), 7.55 (m, 2 H, phenyl), 8.30 (m, 2 H, phenyl), 8.75 (s, 1 H, CH pyridine). $^{13}C$ NMR ($CDCl_3$) δ = 12.48 ($CH_3$), 46.74 ($CH_2Cl$), 52.58 ($CH_3O$), 116.17, 118.55, 120.76, 126.09, 129.08, 134.24, 139.00, 144.00, 150.12, 157.01, 165.98 (C=O).

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## References

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