FLOW-VACUUM PYROLYSIS OF POLYCYCLIC COMPOUNDS. 23

PYROLYSIS OF t-BUTYL-TETRAZOLO[1,5-a]DIBENZO[c,g]AZOCINES AS SYNTHESIS METHOD OF SUBSTITUTED 5H- AND 6H-INDOLO[2,3-b]QUINOLINES

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The flow-vacuum pyrolysis (FVP) of 2-t-butyl-tetrazolo[1,5-a]dibenzo[c,g]azocine (5) and 10-t-butyl-tetrazolo[1,5-a]dibenzo[c,g]azocine (6) in quartz tube, inert atmosphere (argon, flow rate 4mL/min) between 475-500°C at 1mmHg was investigated using GC/MS. The stable reaction products, 2-t-butyl-6H-indolo[2,3-b]quinoline (3) and 2-t-butyl-5H-indolo[2,3-b]quinoline (4) were separated and characterized by IR, 1H-, 13C-NMR and mass spectroscopy. A radical mechanism explaining the formation of above mentioned reaction products is suggested.

Cryptolepis genus derived compounds are commonly used in therapeutical and industrial purposes. Cryptolepis roots extracts have been used to treat a variety of diseases as malaria, infections of the respiratory, urogenital tracts and arthritis. Moreover, the same extracts have been utilized for dyeing leather and textiles. Cryptolepis sanguinolenta roots contain alkaloids with indoloquinoline skeletons. Specific compounds (as cryptolepine and neocryptolepine) were isolated from the biologically active plant extracts and their structures were determined. Many groups focused on the organic synthesis and testing of the derivatives of parent active structures (exempl: methyl-substituted indolo[2,3-b]quinolines as novel cytotoxic, DNA topoisomerase II inhibitors).

In 1999, we obtained 6H-indolo[2,3-b]quinoline (2a) (norcryptotackiene) by flow-vacuum pyrolysis of tetrazolo[1,5-a]dibenzo[c,g]azocine (1). (Scheme 1).

[Diagram of scheme 1]

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Herein, we aimed to synthesize $t$-butyl-indolo[2,3-b]quinolines (3,4) by flow vacuum pyrolysis of corresponding tetrazoles ($t$-butyl-tetrazolo[1,5-a]dibenzo[c,g]azocines, 5, 6) in the same reaction conditions as for thermal decomposition of other polycyclic compounds$^{11-13}$.

\[ \text{RESULTS} \]

t-Butyl-tetrazolo[1,5-a]dibenzo[c,g]azocines 5 and 6 were initially obtained in 1998$^{14}$ by reaction of 2-$t$-butyl-dibenzosuberenone (7) with triazidochlorosilane generated in situ from silicon tetrachloride and sodium azide, at 25-35°C in anhydrous acetonitrile (Scheme 2).

The mixture of 5 and 6 (white crystals, m.p. = 201-203°C after recrystallization from methanol) could not be preparative separated by thin liquid chromatography (TLC).

Thus, their spectral characterization was performed using enriched TLC fractions.

$IR$ spectrum$^1$ (CH$_2$Cl$_2$, cm$^{-1}$) mixture: 836 m, 1000 w, 1101 m, 1365 w, 1380 m, 1470 m, 1500 s, 1598 m, 2870 m, 2905 m, 2968 s, 3070 w.

$^1$IR spectrum was registered on a C. Zeiss Jena UR-20 double beam spectrometer.
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3H-NMR spectrum(2) (CDCl₃, δ, ppm, J Hz, TMS internal standard): For compound 5: 1.32 (s; 9H; 3CH₃); 6.71 (d; 12.2; 1H); 6.83 (d; 12.2; 1H¹); 7.20-7.61 (m; 7H; H 3, 4, 8, 9, 11, 12). For compound 6: 1.31 (s; 9H; 3CH₃); 6.70 (d; 12.2; 1H¹); 6.85 (d; 12.2; 1H¹); 7.20-7.61 (m; 7H; H 3, 4, 8, 9, 11, 12).

13C-NMR spectrum(2) (CDCl₃, δ, ppm): 31.08 (CH₃ from 6); 31.15 (CH₃ from 5); 34.90 (C¹⁴ from 5); 34.93 (C¹⁴ from 6); 120.05 (Cq); 123.24 (Cq); 125.64 (CH); 126.32 (CH); 126.41 (CH); 126.85 (CH); 126.92 (CH); 128.17 (CH); 128.73 (CH); 128.76 (CH); 129.50 (CH); 129.63 (CH); 129.89 (CH); 130.19 (CH); 130.82 (CH); 131.16 (CH); 131.16 (CH); 132.38 (Cq); 132.66 (Cq); 133.21 (CH); 134.12 (CH); 136.61 (Cq); 137.25 (Cq); 154.72 (C¹⁵ from 6); 156.18 (C¹⁵ from 5).

The flow-vacuum pyrolysis of 5 and 6 was performed with the same devices and reaction conditions as for 1: the quartz tube (60 cm length, 10 mm internal diameter, filled with quartz chips on 30 cm length); temperature (475-500°C) and pressure (1 mmHg) were monitored by a thermocouple and a McLeod manometer under inert atmosphere (argon, flow rate: 4 mL/min), respectively. The reaction products were dissolved in methylene chloride, the solvent was evaporated in vacuo and the residue was analyzed by a gas chromatograph coupled with a mass spectrometer (GC/MS) (Scheme 3).

![Scheme 3](image)

The 2-t-butyl-6H-indolo[2,3-b]quinoline (3) and 2-t-butyl-5H-indolo[2,3-b]quinoline (4) could not be separated by thin liquid chromatography and the full characterisation by 1H- and 13C-NMR was realized using enriched TLC fractions (3/4: 66.4% / 33.6%).

IR spectrum(i) (KBr, cm⁻¹): 726 vs, 824 vs, 911 m, 1263 m, 1361 s, 1408 s, 1464 vs, 1611 vs, 2861 m, 2956 vs, 3117 m.

1H-NMR spectrum(3) (CDCl₃, δ, ppm, J Hz) for 3: 1.46 (9H, s); 7.30 (1H, ddd, 7.2, 7.6, 1.0); 7.54 (1H, ddd, 7.2, 8.0, 1.0); 7.59 (1H, d, 8.0); 7.89 (1H, dd, 8.9, 2.2); 7.99 (1H, d, 2.2); 8.12 (1H, d, 8.9); 8.18 (1H, d, 7.6); 8.79 (1H, s); 10.83 (1H, NH, bs).

3H-NMR and 13C-NMR spectra were registered on a VARIAN GEMINI spectrometer at 300 MHz for 1H and 75 MHz for 13C using TMS as internal standard.

3H-NMR spectra were registered on a Bruker AVANCE DRX 500 spectrometer at 500.132 MHz using TMS as internal standard. The instrument was equipped with a 5-mm multinuclear, inverse-detection probe with a z-gradient. The three-bond 1H, 13C correlation experiment was acquired using the gradient COSY cosygqf pulse program with 2K data points and 2 transients in t₂ per 512 increments in t₁. The one-bond 1H, 13C correlation experiments were acquired using the gradient HMQC inv4gqf pulse program with an evolution delay of 3.45 ms for an average J(1H, 13C) of 160 Hz. The experiments resulted in a 1K data points and 4 transients in t₂ per 256 increments in t₁. The long-range 1H, 13C correlation experiments were recorded using the gradient HMBC inv4gplnqf pulse program with 1K data points and 2 transients in t₂ per 512 increments in t₁.
1H-NMR shifts for compound 4: 1.49 (9H, s); 7.50 (1H, ddd, 8.0, 6.8, 1.0); 7.52 (1H, d, 8.4); 7.63 (1H, dd, 8.4, 1.8); 7.76 (1H, ddd, 8.2, 6.8, 1.4); 8.07 (1H, d, 8.0); 8.15 (1H, d, 8.2); 8.22 (1H, d, 1.8); 8.82 (1H, s); 10.66 (1H, NH, bs). (Fig. 1).

13C-NMR spectrum (CDCl3, δ, ppm) for compound 3: 31.54 (C19); 35.08 (Cq18); 111.30 (C10); 119.03 (Cq15); 120.46 (C12); 121.55 (Cq14); 121.89 (C13); 124.11 (C1); 124.35 (Cq14); 126.64 (C4); 128.17 (C16); 128.51 (C3,11); 141.63 (Cq9); 145.33 (Cq5); 146.3 (Cq2); 153.81 (Cq7). For compound 4: 32.05 (C19); 35.07 (Cq18); 110.82 (C4); 118.4 (C1); 119.56 (Cq16); 121.12 (Cq17); 123.38 (C12); 124.66 (Cq14); 126.56 (C3); 127.81 (C15); 129.09 (C11); 129.25 (C13); 139.62 (Cq5); 143.87 (Cq2); 146.80 (Cq9); 153.78 (Cq7). (Fig. 2).

Mass spectrum (m/z, relative abundance %): For compound 3: 51 (2); 63 (2); 75 (2); 89 (2); 102 (4); 115 (46); 129 (9); 137 (4); 190 (4); 218 (20); 231 (11); 243 (11); 259 (B.P., 100); 274 (M, 30).
For compound 4: 51 (2); 63 (2); 75 (2); 89 (3); 102 (11); 115 (37); 129 (7); 190 (4); 218 (17); 231 (9); 243 (15); 259 (B.P., 100); 274 (M, 33).

The component X, formed with 34% yield, could not be preparative separated by TLC as pure compound due to its instability. Its mass spectrum indicated a molecular mass of 262.

Mass spectrum (m/z, relative abundance %) for compound X: 63(1); 89 (1); 102 (1); 115 (1); 126 (1); 139 (1); 150 (1); 165 (2); 178 (5); 190 (9); 203 (10); 218 (17); 219 (17); 249 (3); 262 (B.P., M, 100,); 263 (M+1, 59).

413C-NMR spectra were registered on a Bruker AVANCE DRX 500 spectrometer at 125.758 MHz. See n. 3.
5VARIAN 3400 gas-chromatograph with split/splitless injector coupled with a VARIAN SATURN II mass spectrometer provided with ion trap. Analysis conditions: capillary DB-5 column (30 m length; 0.25 mm internal diameter); injector temperature: 250°C; split rate: 1:5; temperature program: 60-280°C at 10°C/min; carrier gas: helium (flow-rate 1mL/min); temperature of transfer line: 250°C; electron ionization: 70 eV.
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The formation of carbodiimides in pyrolyses of tetrazoles is proved by isolation of such intermediates and their dimmers at low temperatures. Transformation of \textit{t}-butyl-carbodiimide \textit{8} in the stable reaction products \textit{3} and \textit{4} is explained by a sequence of thermally allowed concerted processes: [2+2+2] electrocyclization\textsuperscript{10} [routes \textit{a}) and \textit{b})] followed by successive [1.5H] migrations, \textit{t}-butyl being used as marker group. The route \textit{a}) is preferred because 2-\textit{t}-butyl-6H-indolo[2,3-\textit{b}]quinoline (3) is more stable than its isomer \textit{4} as proven by energy calculation (0.5 Kcal/mol difference).
In conclusion, in this work we have presented the similar thermal behavior in flow-vacuum pyrolysis conditions of \( t \)-butyl-tetrazolo[1,5-\( a \)]dibenzo[c,g]azocines 5 and 6 with unsubstituted derivative 1.

The synthesis of 2-\( t \)-butyl-6H-indolo[2,3-b]quinoline and 2-\( t \)-butyl-5H-indolo[2,3-b]quinoline certifies flow vacuum pyrolysis as a fast procedure obtaining substituted quinolines with potential biological activity.

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**REFERENCES**