

RING TRANSFORMATION OF 5H-1,2-DIAZEPINONES INTO PYRAZOLES

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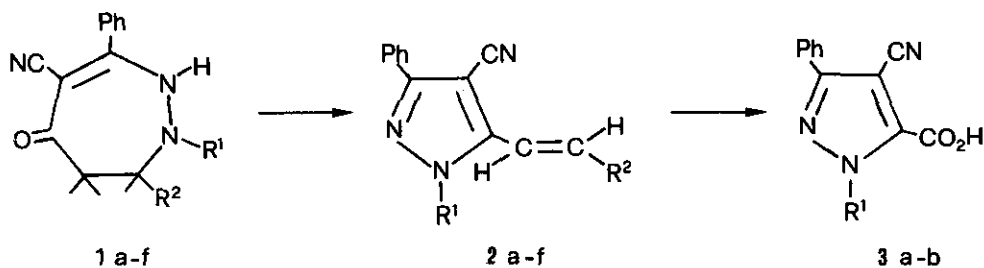
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**Abstract**-6-Cyano-2,3-disubstituted 1,2,3,4-tetrahydro-5H-1,2-diazepin-5-ones (1a-f) underwent ring transformation in acidic media to give in good yields 4-cyano-5-[2-(substituted ethenyl)]-3-phenylpyrazoles (2a-f) which can be easily oxidized to pyrazoles containing *o*-functional groups.

In the course of our studies, we have recently reported that 1,2-diazepinones (1a-f) are readily available by alkaline hydrolysis of isoxazolopyridazinones.<sup>1</sup> The present communication deals with the still unreported ring transformation of 5H-1,2-diazepin-5-ones<sup>2,3</sup> into pyrazoles containing *o*-functional groups, a promising class of compounds to obtain condensed heterocycles with potential biological activity.<sup>4,5</sup>

Conversion of compounds 1a-f into the corresponding pyrazoles 2a-f was performed in good yields (65-75%) by refluxing for 15-50 min a solution of the diazepinone in acetone with 5M hydrochloric acid.<sup>6</sup> Compounds 2a-f were obtained in very small amount (5-10%) also in the alkaline hydrolysis of isoxazolopyridazinones.

SCHEME



- a R<sup>1</sup>=H R<sup>2</sup>=C<sub>6</sub>H<sub>5</sub>
- b R<sup>1</sup>=H R<sup>2</sup>=p-ClC<sub>6</sub>H<sub>4</sub>
- c R<sup>1</sup>=H R<sup>2</sup>=2-thienyl

- d R<sup>1</sup>=CH<sub>3</sub> R<sup>2</sup>=C<sub>6</sub>H<sub>5</sub>
- e R<sup>1</sup>=CH<sub>3</sub> R<sup>2</sup>=p-ClC<sub>6</sub>H<sub>4</sub>
- f R<sup>1</sup>=CH<sub>3</sub> R<sup>2</sup>=2-thienyl

- a R<sup>1</sup>=H
- b R<sup>1</sup>=CH<sub>3</sub>

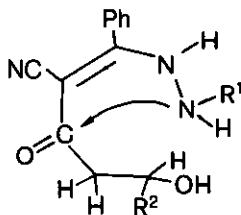
Assigned structures for the new pyrazoles 2a-f were supported by their chemical and spectroscopic properties and by elemental analysis data. In particular their  $^1\text{H}$ -nmr spectra showed signals (Table 1) attributable to the olefinic protons with coupling constants of 16 Hz, as requested for *trans*-structures. Moreover, oxidation of 2a-f with a 2.5%  $\text{KMnO}_4$  solution in acetone under a  $\text{CO}_2$  atmosphere at room temperature yielded the acids 3a-b,<sup>7</sup> potential intermediates for the synthesis of condensed pyrazole heterocycles.<sup>8</sup>

Table 1. Physical and spectroscopic data of the new pyrazoles<sup>9</sup>

Comp.	Yield %	mp (°C)	Cryst. solvent	IR $\nu_{\text{max}}$ ( $\text{cm}^{-1}$ ) nujol	$^1\text{H}$ -nmr ( $\delta$ :ppm)
2a	65	188	benzene	3190(NH), 2220(C=N), 960(-CH=CH-)	7.15 and 7.90(AB, 2H, <i>trans</i> -CH=CH-), 7.32-8.10(m, 10H, 2xArH <sub>5</sub> ), 14.18(exch. br s, 1H, NH)
2b	68	245	EtOH	3190(NH), 2220(C=N), 960(-CH=CH-)	7.13 and 7.85(AB, 2H, <i>trans</i> -CH=CH-), 7.40-7.95(m, 9H, ArH <sub>5</sub> and ArH <sub>4</sub> ), 14.12 (exch. br s, 1H, NH)
2c	67	200	$\text{CHCl}_3$	3180(NH), 2220(C=N), 960(-CH=CH-)	6.85 and 7.95(AB, 2H, <i>trans</i> -CH=CH-), 7.10-7.99(m, 8H, ArH <sub>5</sub> and thienyl protons), 14.00(exch. br s, 1H, NH)
2d	69	117	EtOH	2200(C=N), 960 (-CH=CH-)	4.00(s, 3H, N-CH <sub>3</sub> ), 6.85 and 7.70(AB, 2H, <i>trans</i> -CH=CH-), 7.26-8.15(m, 10H, 2xArH <sub>5</sub> )
2e	74	130	EtOH	2200(C=N), 960 (-CH=CH-)	4.00(s, 3H, N-CH <sub>3</sub> ), 6.83 and 7.79(AB, 2H, <i>trans</i> -CH=CH-), 7.35-8.15(m, 9H, ArH <sub>5</sub> and ArH <sub>4</sub> )
2f	70	122	EtOH	2200(C=N), 950 (-CH=CH-)	4.00(s, 3H, N-CH <sub>3</sub> ), 6.70 and 7.58(AB, 2H, <i>trans</i> -CH=CH-), 6.90-8.15(m, 8H, ArH <sub>5</sub> and thienyl protons)
3a	51 (dec)	260	$\text{H}_2\text{O}$	3400-2500br(OH), 3150(NH), 2180(C=N), 1700(C=O)	5.35(exch. br, 2H, NH and OH), 7.40-7.79 (m, 3H, ArH <sub>3</sub> , m/p), 7.83-8.00(m, 2H, ArH <sub>2</sub> , o)
3b	49 (dec)	220	$\text{H}_2\text{O}$	3500-2400br(OH), 2200(C=N), 1720(C=O)	4.30(s, 3H, N-CH <sub>3</sub> ), 7.00(exch. br s, 1H, OH) 7.35-7.70(m, 3H, ArH <sub>3</sub> , m/p), 7.90-8.10(m, 2H, ArH <sub>2</sub> , o)

solvent: (2a-c), 3a and 3b  $\text{DMSO-d}_6$ ; (2d-f)  $\text{CDCl}_3$

The pyrazoles 2a-f are thought to arise from an initial protonation at the N-1 of the diazepines, opening of the ring and nucleophilic addition of water to give 4.



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These intermediates eventually give the compounds 2a-f by attack of the 1-NH group on the carbonyl carbon and subsequent elimination of water from the newly formed side chain.

#### ACKNOWLEDGEMENT

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6. Treatment of compound 1c with 5M hydrochloric acid was carried out at room temperature for 24 h.
7.  $^{13}\text{C}$ -nmr data (DMSO- $d_6$ ) for compound 3b: 158.4 (CO), 151.1 (C-3), 138.7 (C-5), 129.9 (C-ipso), 129.5 (C-para), 128.95 (C-o/m), 126.3 (C-m/o), 113.8 (CN), 92.0 (C-4) and 40.35 (N-Me).
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9. All new compounds gave satisfactory elemental analysis data (C, H, and N). Melting points are uncorrected.

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