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

Giovanna Ciciani and Vittorio Dal Piaz

Dipartimento di Scienze Farmaceutiche dell'Università di Firenze, Via Gino Capponi 9, 50121 Firenze, Italy

Stefano Chimichi

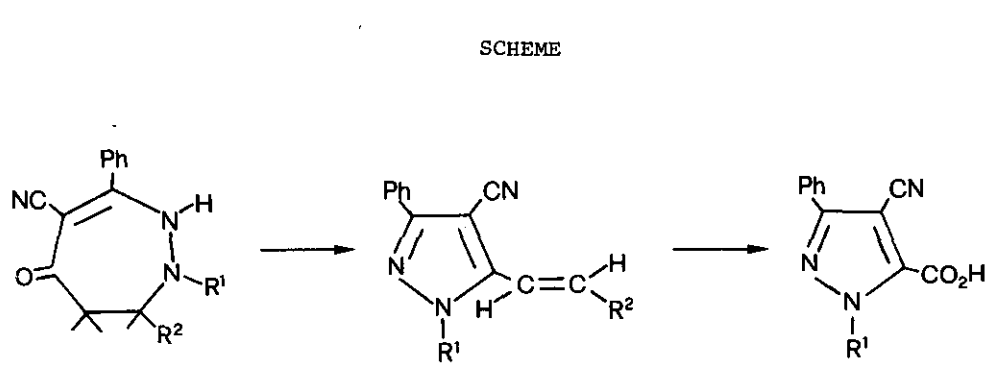
Centro di Studio del CNR sulla Chimica e la Struttura dei Composti Eterociclici e loro Applicazioni, presso l'Istituto di Chimica Organica dell'Università, Via Gino Capponi 9, 50121 Firenze, Italy

Abstract-6-Cyano-2,3-disubstituted 1,2,3,4-tetrahydro-5*H*-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.[1] The present communication deals with the still unreported ring transformation of 5*H*-1,2-diazepin-5-ones[2,3] into pyrazoles containing *o*-functional groups, a promising class of compounds to obtain condensed heterocycles with potential biological activity.[4,5]

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.[6] Compounds 2a-f were obtained in very small amount (5-10%) also in the alkaline hydrolysis of isoxazolopyridazinones.

SCHEME



1 a-f 2 a-f 3 a-b

a R^1=H R^2=C_6H_5
b R^1=H R^2=p-ClC_6H_4
c R^1=H R^2=2-thienyl
d R^1=CH_3 R^2=C_6H_5
e R^1=CH_3 R^2=p-ClC_6H_4
f R^1=CH_3 R^2=2-thienyl

a R^1=H
b R^1=CH_3

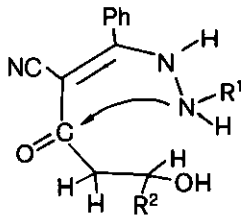
Assigned structures for the new pyrazoles 2a-f were supported by their chemical and spectroscopic properties and by elemental analysis data. In particular their ^{1}H-nmr spectra showed signals (Table 1) attributable to the olefinic protons with coupling constants of 16 Hz, as requested for *trans*-structures. Moreover, oxidation of 2a-f with a 2.5% $KMnO_4$ solution in acetone under a CO_2 atmosphere at room temperature yielded the acids 3a-b,[7] potential intermediates for the synthesis of condensed pyrazole heterocycles.[8]

Table 1. Physical and spectroscopic data of the new pyrazoles[9]

Comp.	Yield %	mp (°C)	Cryst. solvent	IR ν_{max} (cm^{-1}) nujol	^{1}H-nmr (δ:ppm)
2a	65	188	benzene	3190(NH), 2220(C≡N), 960(-CH=CH-)	7.15 and 7.90(AB, 2H, trans-CH=CH-), 7.32-8.10(m, 10H, 2xArH_5), 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, trans-CH=CH-), 7.40-7.95(m, 9H, ArH_5 and ArH_4), 14.12 (exch. br s, 1H, NH)
2c	67	200	$CHCl_3$	3180(NH), 2220(C≡N), 960(-CH=CH-)	6.85 and 7.95(AB, 2H, trans-CH=CH-), 7.10-7.99(m, 8H, ArH_5 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_3), 6.85 and 7.70(AB, 2H, trans-CH=CH-), 7.26-8.15(m, 10H, 2xArH_5)
2e	74	130	EtOH	2200(C≡N), 960 (-CH=CH-)	4.00(s, 3H, N-CH_3), 6.83 and 7.79(AB, 2H, trans-CH=CH-), 7.35-8.15(m, 9H, ArH_5 and ArH_4)
2f	70	122	EtOH	2200(C≡N), 950 (-CH=CH-)	4.00(s, 3H, N-CH_3), 6.70 and 7.58(AB, 2H, trans-CH=CH-), 6.90-8.15(m, 8H, ArH_5 and thienyl protons)
3a	51	260 (dec)	H_2O	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_3, m/p), 7.83-8.00(m, 2H, ArH_2, o)
3b	49	220 (dec)	H_2O	3500-2400br(OH), 2200(C≡N), 1720(C=O)	4.30(s, 3H, N-CH_3), 7.00(exch. br s, 1H, OH) 7.35-7.70(m, 3H, ArH_3, m/p), 7.90-8.10(m, 2H, ArH_2, o)

solvent: (2a-c), 3a and 3b DMSO-d_6 ; (2d-f) $CDCl_3$

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.

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REFERENCES AND NOTES

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6. Treatment of compound 1c with 5M hydrochloric acid was carried out at room temperature for 24 h.
7. ^{13}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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