

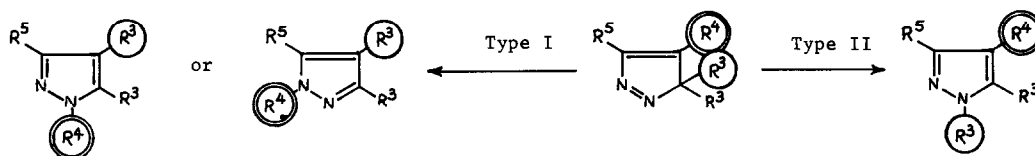
ON THE VAN ALPHEN-HUTTEL REARRANGEMENT ACID-CATALYSED REARRANGEMENT OF PYRAZOLENINES INTO ISOPYRAZOLES.

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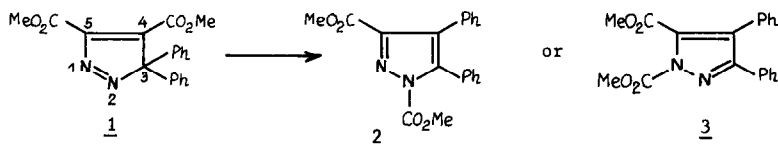
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The rearrangement of 3,3-disubstituted pyrazolenines was first investigated by Van Alphen in 1943,¹ then by Hüttl in 1960.² Both proposed two types of rearrangements which can be summarized as follows



The Van Alphen-Hüttl rearrangement of type I has been observed if R⁴ is a hydrogen or an ester group and that of type II if R³ is an aryl group.

We have reinvestigated in acetic acid the 3,3-diphenyl 4,5-dicarbomethoxy pyrazolenine 1 rearrangement, according to Van Alphen,¹ it would give the pyrazole 2 or 3, F = 150°, through a mechanism of type I.



After refluxing for two hours in acetic acid, a compound with the same melting point was effectively obtained with a 70 % yield, which was given the 3,4-diphenyl 4,5-dicarbomethoxyisopyrazole structure 4 from the following data

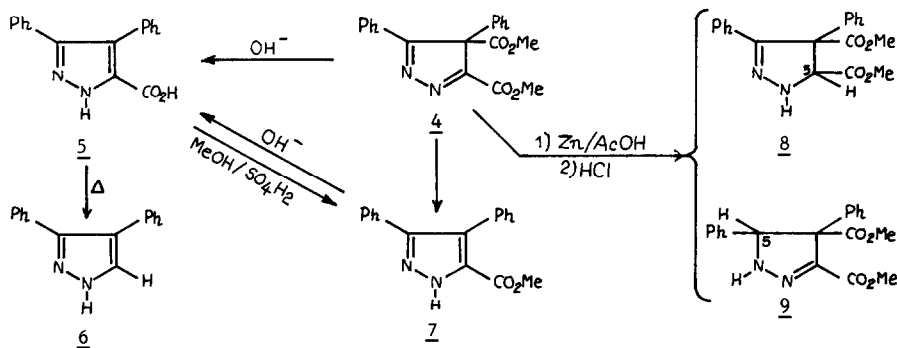
- NMR spectrum in CDCl₃ 3.70 and 3.90 (CO₂Me), 7.1 to 7.55 (m) (8H) and 7.8 to 8.15 (m) (2H) (Ph).

- When 4 is saponified, the acid 5 is obtained which in turn, after heating, gives the 3(5),4-diphenyl pyrazole 6.³ This shows that the pyrazolenine 1 does not undergo a rearrangement of type II, which would have led to the 1,5-diphenyl 3,4-dicarbomethoxy pyrazole (this compound has already been described F = 97°⁴).

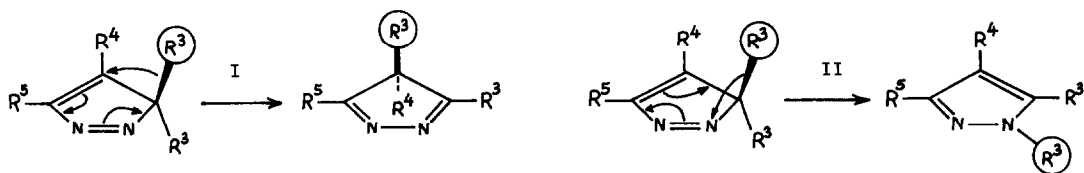
- After refluxing 48 hours with acetic acid compound 4 yields the 3(5),4-diphenyl 5(3)-carbomethoxy pyrazole 7¹.

- After compound 4 has been reduced with zinc dust and acetic acid and the N-COME group hydrolysed with hydrochloric acid,^{5,6} a mixture of two 2-pyrazolines, 8 (F = 149-150°) and 9 (F = 170-171°) is obtained or a mixture of two diastereoisomers of the same 2-pyrazoline, the

NMR spectra of both compounds in DMSO- d_6 exhibit a signal due to the proton H_5 , which appears as a doublet ($J = 2.5$ Hz) by coupling with NH 4.60 and 5.25 ppm respectively. As the isopyrazole 4 is the only structure which could give a 4,4-disubstituted 2-pyrazoline, we can rule out the alternative ones 2 or 3.



Therefore we propose the following formal representation for the Van Alphen-Hüttel rearrangements ⁷



Some differences may occur in the rearrangement of type I depending on the nature of the substituents bound to the sp^3 carbon of isopyrazole if they are alkyl or aryl groups the compound is stable⁵, if $R^4 = H$, it is isomerised into a NH-pyrazole, finally, if R^4 is an ester group and under drastic conditions of heating or acidity, the isopyrazole loses this substituent from the 4 position affording the NH-pyrazole.

REFERENCES

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3. W. Wislicenus and A. Ruthing, *Annalen*, 1911, 379, 256.
4. K. von Auwers and H. Mauss, *Ber.*, 1926, 59, 611.
5. R. Baumes, J. Elguero, R. Jacquier and G. Tarrago, unpublished results.
6. As a matter of fact, the corresponding N-acetylated pyrazolines are isolated in a first step.
7. These rearrangements can be carried out on simple heating in this case they could be described as a sigmatropic change of order [1,5] (supra-supra, i.e. with retention of configuration of the migrating group) which are thermally allowed.