THE VAN ALPHEN REARRANGEMENT. THERMAL, CATALYTIC, AND PHOTOLYTIC TRANSFORMATION OF 3,3,5-TRIPHENYLPYRAZOLENINE-4-CARBOXYLIC ACID ESTERS*

M. I. Komendantov and R. R. Bekmukhametov

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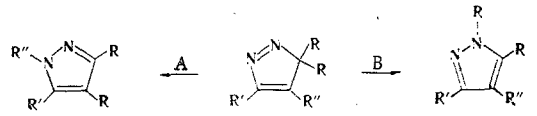
The thermal, catalytic, and acid-catalyzed transformation of 3,3,5-triphenylpyrazolenine-4-carboxylic acid esters was studied. The thermal and acid-catalyzed isomerization of the pyrazolenines leads not only to pyrazoles but also to isopyrazoles. A mechanism involving a 1,5-suprafacial sigmatropic shift is proposed for the isomerization. It is shown that the migration of substituents from the 4 position of the pyrazolenine ring, which has been previously proposed as a variant of the van Alphen rearrangement, does not occur.

One of the characteristic properties of pyrazolenine systems is their ability to undergo the van Alphen rearrangement, i.e., to undergo isomerization to the corresponding pyrazoles. This sort of isomerization may proceed via two pathways [2]:



II I III

Thus methyl 3,4,5-triphenylpyrazole-1-carboxylate (IIa, pathway A) and methyl 1,3,5-triphenylpyrazole-4-carboxylate (IIIa, pathway B) were obtained as a result of isomerization of methyl 3,3,5-triphenylpyrazolenine-4-carboxylate (Ia, R = R' = Ph, R'' = CO_2CH_3) [3, 4]. Although the isomerization of pyrazolenines via path B has been observed repeatedly and confirmed by a number of investigators [4, 5], there is no convincing proof for the formation of pyrazoles via path A.

* See [1] for a preliminary communication.

TABLE 1. UV, IR, and PMR Spectra of the Compounds Obtained

Compound	UV spectrum, λ_{max}, nm (log ε)	IR spectrum, ν, cm^{-1}	PMR spectrum, τ, ppm*
Ia	239 (4,27), 294 (3,80)	1729 (C=O)	6,51 s (OCH_3)
Ib	240 (4,31), 300 (3,65)	1728 (C=O)	5,91 q (CH_2), 9,01 s (CH_3)
IIa	269 (4,36)	1760 (C=O)	—
IIIa	239 (4,47)	1712 (C=O)	6,47 s (OCH_3)
IIIb	242 (4,41)	1710 (C=O)	6,00 q (CH_2), 9,02 s (CH_3)
IVa	292 (4,04)	1711 (C=O), 1825 (C=C)	—
IVb	292 (4,03)	1710 (C=O), 1823 (C=C)	—
V	234 (4,49)	1701 (C=O)	—
VI	246 (4,15)	3458 (N—H)	—
VIIa	325 (4,29)	1750 (C=O)	6,33 s (OCH_3)
VIIb	324 (4,25)	1748 (C=O)	—

* Abbreviations: s is singlet and q is quartet.

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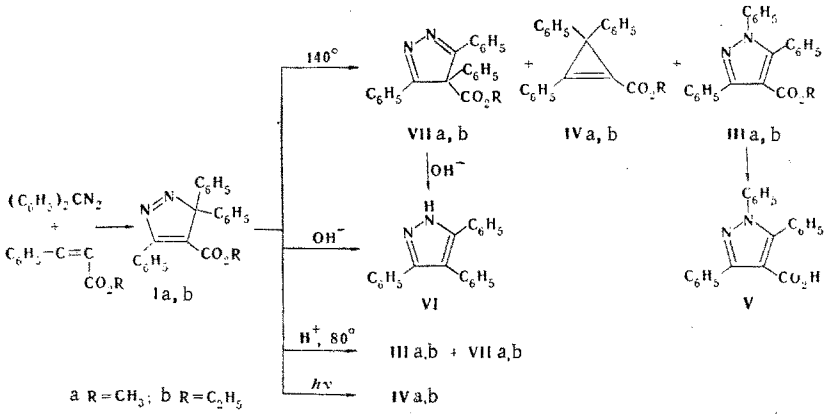
TABLE 2. Calculated Coefficients of the HOMO and LVMO of Radicals XI and Radical Cations XII

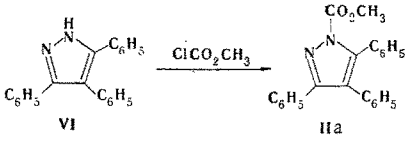
Compound	HOMO coefficients					c_ic_j		LVMO coefficients					c_ic_j	
	1	2	3	4	5	c_3c_2	c_3c_4	1	2	3	4	5	c_3c_2	c_3c_4
XIa	−0,44	0,44	0,56	0	−0,56	0,25	0	0,56	−0,56	0,44	0	−0,44	−0,25	0
XIb	0,37	−0,37	−0,35	0	0,35	0,13	0	0,14	0,14	−0,28	0,26	−0,28	−0,04	−0,07
XIIa	−0,63	0	0,59	0,44	−0,23	0	0,26	−0,56	0,39	−0,58	0,16	0,43	−0,23	−0,09
XIIb	0,57	−0,19	−0,29	−0,23	0,24	0,06	0,07	−0,20	0,25	−0,43	0,26	0	−0,11	−0,11

In order to study the direction and mechanism of the van Alphen rearrangement, we investigated the thermal, acid-catalyzed, and photolytic transformation of the methyl (Ia) and ethyl (Ib) esters of 3,3,5-triphenylpyrazolenine-4-carboxylic acid, which were obtained by reaction of diphenyldiazomethane with the appropriate phenylpropiolic acid esters.

When esters I were heated, two compounds, which were isomeric with respect to the starting pyrazolenines, were obtained in addition to cyclopropene derivatives IV.



The physical constants and spectral characteristics of one of the isomers were in agreement, respectively, with the previously described methyl (IIIa) [4] and ethyl (IIIb) [6] esters of 1,3,5-triphenylpyrazole-4-carboxylic acid, and their structures were also confirmed by hydrolysis to known acid V [7]. The melting point of the other isomer obtained by heating ester Ia coincided with the melting point of the previously described [3, 4] pyrazole IIa. However, van Alphen and Hüttel and co-workers [3, 4] cite the formation of 3,4,5-triphenylpyrazole (VI) during the hydrogenolysis of pyrazole IIa as the only evidence in favor of structure IIa. This cannot constitute proof, inasmuch as the hydrolysis of starting pyrazolenines I, just as the hydrolysis of isopyrazoles VII, leads to the same result. In fact, the structure of 3,4,5-triphenylisopyrazole-4-carboxylic acid ester (VII), with which the IR and UV spectra are in agreement, corresponds to the above-mentioned isomer. The most convincing confirmation of this is offered by the UV spectra, in which the position and intensity of the long-wave maximum (λ_{max} 325 nm, log ε 4.25) coincide with the analogous characteristics of similar isopyrazoles [8] and other model compounds [9]. The presence of this sort of long-wave maximum is by no means linked with the structure of pyrrazoles IIa, inasmuch as absorption at 240-270 nm (Table 1) is characteristic for phenyl-substituted pyrazoles. The synthesis of an authentic sample of pyrazole IIa, which we accomplished via the following scheme, became a decisive proof in favor of our reasoning:



The melting point and the spectral characteristics of the pyrazole (IIa) that we obtained were not in agreement with the analogous data for the compound previously isolated in [3, 4].

Just as in the case of thermal isomerization, pyrazoles III and isopyrazoles VII were isolated in the case of acid-catalyzed isomerization of pyrazolenines I in glacial acetic acid. However, whereas the pyrazole to isopyrazole ratio was 7:1 in the case of thermal isomerization, it was 1:1.25 in the case of

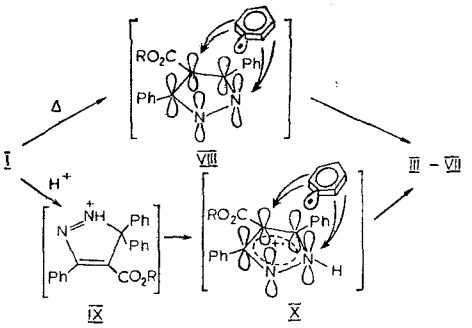
acid-catalyzed isomerization. Nitrogen cleavage products – the corresponding cyclopropene derivatives, namely, methyl (IVa) [11] and ethyl (IVb) 2,3,3-triphenylcyclopropene-1-carboxylates – were obtained in the photolytic decomposition [10] of pyrazolenines I as the only reaction products. Isomerization products were not detected in the reaction mixture.

The isomerization of pyrazolenines to pyrazoles and isopyrazoles under both thermal and acid-catalyzed conditions can be represented as a 1,5-sigmatropic shift [1, 12], the only difference being that migration of the phenyl group in the pyrazolenine to give a phenyl radical (radical VIII) in an intermediate step occurs during thermal isomerization, whereas in acid catalysis migration occurs in cation IX to give a phenyl radical–radical cation pair (X).

XIa, b XIIa, b

$R' = CO_2CH_3$; a R = H; b $R = CH_2=CH$

Quantum-chemical calculations make it possible to explain the observed direction of isomerization during thermal and acid-catalyzed processes, as well as the absence of isomerization products during photolytic decomposition of pyrazolenines. The results of calculations made for model radicals XI and radical cations XII of the compounds are presented in Table 2 (calculations could not be made for VIII and X because of the limited possibilities of the computer used).



Only the higher occupied molecular orbitals (HOMO) will participate in the isomerization process, inasmuch as the coefficients of the lower vacant molecular orbitals (LVMO) in the adjacent atoms between which migration of the phenyl group occurs have different signs. Inasmuch as the photolytic decomposition of pyrazolenines predetermined participation of the LVMO in the process, the absence of isomerization products during photolysis becomes understandable. On the other hand, a comparison of the HOMO coefficients obtained for the corresponding radicals and radical cations makes it possible to explain the predominant formation of pyrazole III during thermal isomerization and the ratio of the pyrazoles (III) and isopyrazoles (VII) formed under the conditions of the acid-catalyzed process. The probability of isomerization will be determined by the product of the coefficients ($c_i c_j$) of the HOMO of the atoms between which migration occurs [13]. Thus isomerization with migration of a phenyl group to the N_2 atom should be expected when the pyrazolenines are heated, inasmuch as $c_2 > c_4$ (Table 2). Migration to the C_4 atom is preferable in the acid-catalyzed isomerization. The results of calculations of model radicals XIb and radical cation XIIb, which are apparently closer to investigated systems VIII and X, correlate most satisfactorily with the experimental data. Thus the isomerization of pyrazolenines proceeds via a mechanism involving a 1,5-suprafacial sigmatropic shift: a 1,5-sigmatropic shift to the nitrogen atom leads to the formation of a pyrazole, whereas a shift to the carbon atom leads to an isopyrazole.

EXPERIMENTAL

The PMR spectra of $CHCl_3$ solutions of the compounds were recorded with a Varian HA-100 spectrometer with hexamethyldisiloxane as the internal standard. The UV spectra of methanol solutions were obtained with a Perkin–Elmer M-402 spectrophotometer. The IR spectra of chloroform solutions were recorded with a UR-10 spectrometer (Table 1). The quantum-chemical calculations were made by the Hückel MO method with the following parameters: $h_{\dot{N}} = 0.5$, $h_N = 2$, $k_{C=N} = 1$, $h_{\dot{O}} = 1.5$, $k_{C=O} = 1.4$ [14], $h_{\ddot{O}} = 2$, and $k_{C-O} = 0.8$ [15]. The course of the reactions and the separation of the reaction mixtures were moni-

TABLE 3. Physical Constants and Results of Elementary Analysis of III, IV, and VII

Compound	mp, °C	Found, %			Empirical formula	Calculated, %			Yield, % (synthetic method)*
		C	H	N		C	H	N	
IIIa	140	77,8	5,3	7,7	$C_{25}H_{18}N_2O_2$	78,0	5,1	7,9	75 (B); 40 (C)
IIIb	146	78,1	5,4	7,7	$C_{24}H_{20}N_2O_2$	78,2	5,5	7,6	70 (B); 40 (C)
IVa	128	84,6	5,4	—	$C_{23}H_{18}O_2$	84,6	5,6	—	60 (A); 8 (B)
IVb	95	84,4	6,0	—	$C_{24}H_{20}O_2$	84,7	5,9	—	55 (A); 8 (B)
VIIa	198	77,9	5,2	7,9	$C_{25}H_{18}N_2O_2$	78,0	5,1	7,9	10 (B); 50 (C)
VIIb	143—144	78,0	5,4	7,6	$C_{24}H_{20}N_2O_2$	78,2	5,5	7,6	10 (B); 50 (C)

* Symbols: A indicates photolytic decomposition, B indicates thermal isomerization, and C indicates acid-catalyzed isomerization of the pyrazolenines.

tored by means of thin-layer chromatography (TLC) and column chromatography, respectively, with activity II aluminum oxide and elution with hexane–diethyl ether (7:3). The physical constants and results of elementary analysis of III, IV, and VII are presented in Table 3.

Ethyl 3,3,5-Triphenylpyrazolenine-4-carboxylate (Ib). A solution of 4 g (23 mmole) of ethyl phenylpropiolate [16] and 6 g (31 mmole) of diphenyldiazomethane [17] in 20 ml of hexane was refluxed on a water bath for 4 h. After the starting ester had disappeared in the reaction mixture (according to TLC), the hexane was vacuum evaporated, and the residue was chromatographed with a column filled with Al_2O_3 to give 4.7 g (55%) of ester Ib with mp 96° and R_f 0.4. Found: C 78.3; H 5.7; N 7.5%. $C_{24}H_{20}N_2O_2$. Calculated: C 78.2; H 5.5; N 7.6%.

Methyl 3,3,5-Triphenylpyrazolenine-4-carboxylate (Ia). As in the preceding experiment, ester Ia, with mp 102° [4], was obtained from methyl phenylpropiolate in 65% yield.

Photolytic Decomposition of Pyrazolenines Ia, b. A solution of 2 g of pyrazolenine I in 250 ml of hexane was iradiated for 2 h with an immersible high-pressure UV lamp of the Hanau S-81 type (70 W). A total of 100 ml (80%) of nitrogen was evolved. The hexane was vacuum evaporated, and the residue was subjected to column chromatography to give esters IV in 55-60% yields.

Thermal Isomerization of Pyrazolenines Ia,b. A solution of 2 g of pyrazolenine I and 0.01 g of hydroquinone (used as a stabilizer) in 10 ml of o-xylene was refluxed on an oil bath (140-150°) for 40 min. A total of 10 ml (8%) of nitrogen was evolved. When the mixture was cooled, 1.2 g of crystalline ester III precipitated. The crystals were removed by filtration and washed with 3 ml of benzene. The solvent was removed by vacuum evaporation, and the residue was subjected to column chromatography. The following three substances were isolated: 0.15 g (8%) of cyclopropene IV with R_f 0.6, 0.3 g of pyrazole III in an overall yield of 1.5 g (70-75%) with R_f 0.35, and 0.2 g (10%) of ester VII with R_f 0.2.

Acid Isomerization of Pyrazolenines Ia,b. A solution of 1 g of pyrazolenine I in 10 ml of glacial acetic acid was heated on a water bath (80-90°) for 3 h, after which it was cooled and diluted with water. The resulting precipitate was removed by filtration, washed with water, dried, and dissolved in 3 ml of benzene. The solution was subjected to column chromatography to give 0.4 g (40%) of pyrazole III and 0.5 g (50%) of isopyrazole VII.

Hydrolysis of Pyrazolenines Ia,b and Isopyrazoles VIIa,b. A solution of 0.5 g of pyrazolenine I (or isopyrazole VII) in 5 ml of a 10% solution of sodium hydroxide in methanol was refluxed for 2 h on a water bath. The mixture was diluted with water, and the resulting precipitate was removed by filtration and washed with water. The yield of 3,4,5-triphenylpyrazole (VI) with mp 261° (from benzene) [18] was 0.4 g (95%).

Hydrolysis of Pyrazoles III. A solution of 1 g of pyrazole III in 10 ml of a 10% solution of sodium hydroxide in methanol was refluxed on a water bath for 4 h. It was then diluted with 40 ml of water, and the alcohol was evaporated completely. The residual mixture was cooled and acidified with 10% sulfuric acid. The resulting precipitate was removed by filtration and washed with water to give 0.9 g (95%) of 1,3,5-triphenylpyrazole-4-carboxylic acid (V) with mp 239° (from benzene) [17].

Methyl 3,4,5-Triphenylpyrazole-1-carboxylate (IIa). A 0.5-g (5 mmole) sample of methyl chlorocarbonate was added with cooling to 0.25 g (0.8 mmole) of pyrazole VI in 10 ml of pyridine. The pyridine

was evaporated, and the residue was washed with water, dried, and recrystallized from pentane to give 0.2 g (60%) of pyrazole IIa with mp 168-169°. Found: C 77.9; H 5.4; N 7.8%. $C_{23}H_{18}N_2O_2$. Calculated: C 78.0; H 5.1; N 7.9%.

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