

REACTION OF 2,6-DIPHENYL-4-PENTAFLUOROPHENYLVERDAZYL
WITH DISUBSTITUTED MONO- AND DIBROMOMETHANES

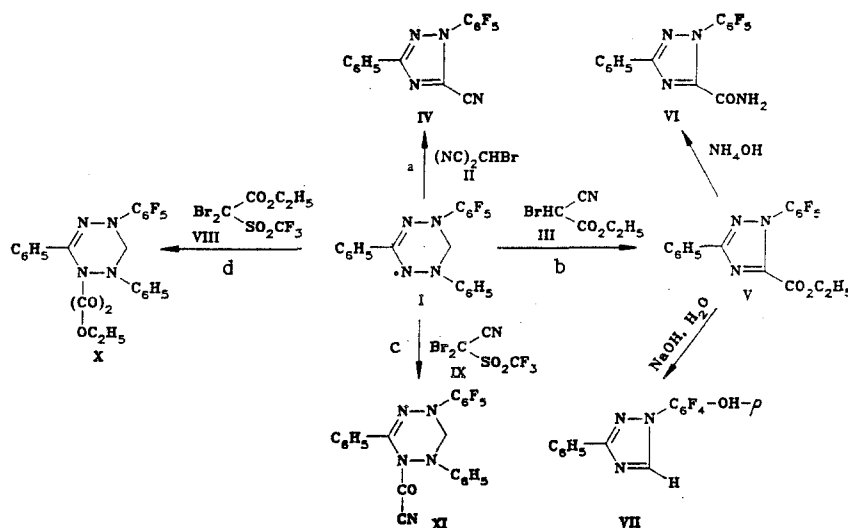
E. I. Tomilenko, P. I. Ogoiko,
and V. I. Staninets

UDC 547.461.3'792.7'883.07:541.
127'543.422.25

Dicyano- and dicyanoethoxycarbonylbromomethane cause fragmentation of 2,6-diphenyl-4-pentafluorophenylverdazyl to 1,3,5-trisubstituted 1,2,4-triazoles. Trifluoromethylsulfonylcyano- and trifluoromethylethoxycarbonyldibromomethane acylate the dazyl radical to give 1-R-2,6-diphenyl-4-pentafluorophenyl-1,2,3,4-tetrahydro-sym-tetrazines.

We have previously shown [1-3] that 2,4,6-triarylverdazyl radicals, which are strong electron donors, react with compounds containing labile "positive" halogen to give a range of products, depending on the structure of each reactant.

The purpose of the present investigation was to study further these reactions, as exemplified by 2,6-diphenyl-4-pentafluorophenylverdazyl (I). It was found that with the bromo-cyanomethanes (II) and (III) (pathways a and b), the radical (I) undergoes fragmentation to 1-pentafluorophenyl-3-phenyl-5-R-1,2,4-triazoles (IV) and (V). Also formed is the hydrobromide of the 2,4,6-triarylleuoverdazyl [2] in 50% yield. The triazole (V) is readily converted into the amide (VI) and the triazole (VII).



The brominated triflones (VIII) and (IX) (pathways c and d) acylate the radical in the 1-position to give the corresponding 1,2,3,4-tetrahydro-sym-tetrazines (X) and (XI); in this case, the amount of hydrobromide salt fell to 20-30%, and there was also obtained a difficultly identifiable mixture of salts, which according to its elemental analysis contained bromine, fluorine, and sulfur.

According to [4], the most likely reaction center in 2,6-diphenyl-4-pentafluorophenylverdazyl (I) is at N₍₁₎, the N₍₄₎-N₍₅₎ bond becoming stronger when an electron-acceptor group is present at N₍₄₎. In the present case therefore, in contrast to the findings in (2), a mixture of triazoles was not obtained even when the substituents at N₍₂₎ and N₍₄₎ were varied.

Institute of Organic Chemistry, Academy of Sciences of the Ukrainian SSR, Kiev 252660.
Translated from *Khimiya Geterotsiklicheskih Soedinenii*, No. 9, pp. 1251-1254, September, 1989.
Original article submitted December 21, 1988; revision submitted February 20, 1989.

TABLE 1. Physicochemical Properties of Compounds Obtained

Com- pound	Empirical formula	mp, °C (solvent for crystalliza- tion)	IR spectrum* ¹ (KBr)	UV spectrum* ² , λ max, nm (log ε)	PMR spectrum* ³ , δ, ppm	M ⁺ , m/z (%)	Yield* ⁴ , %
IV	C ₁₅ H ₅ F ₃ N ₄	138 (n-hexane)	1000, 1090 (CF), 1450, 1540, 2260 (C≡N)	242 (4,10)	7.10...7.95 (m, 5H, C ₆ H ₅)	336 (99)	20
V	C ₁₇ H ₁₀ F ₃ N ₅ O ₂	125 (abs. ethano1)	1010, 1090 (CF), 1450, 1510, 1740 C=O), 2290 (CH alk.)	241 (4,41)	1.25 (t, 3H, CH ₃); 4.35 (q, 2H, CH ₂); 7.25 (m, 5H, C ₆ H ₅)	383 (88)	34
VI	C ₁₅ H ₇ F ₃ N ₄	165 (n-hexane- benzene, 1:1)	1005, 1080 (CF), 1450, 1510, 1615, 1720 (C=O), 3470 (NH ₂)	242 (4,60)	7.46...8.09 (m, 5H, C ₆ H ₅)	—	88
VII	C ₁₄ H ₃ F ₄ N ₃ O	203 (ethano1)	990, 1100 (CF), 1240, 1340, 1370, 1450, 1520, 1550, 3130 (o-F...HO) [7]	250 (4,39)	7.41 (m, 3H, C ₆ H ₅); 8.11 (m, 2H, C ₆ H ₅); 8.73 (s, 1H, CH)	309 (72)	91
X	C ₂₃ H ₁₇ F ₃ N ₄ O ₃	115 (ethano1-n- hexane, 5:1)	770, 940, 1005 (CF), 1060 (CF), 1240, 1370, 1555, 1760...1790 (C=O twin peaks [3])	227 (4,29), 317 (4,18)	1.08 (t, 3H, CH ₃); 4.19 (q, 2H, CH ₂); 5.27, 5.76 (d, d, 2H, CH ₂ , J=13.2 Hz); 7.05...7.60 (m, 10H, 2C ₆ H ₅)	504 (12.5)	32
XI	C ₂₂ H ₁₂ F ₃ N ₅ O	188 n-hexane- benzene, 1:1)	780, 910, 975, 1030 (CF), 1125, 1160, 1315, 1480, 1580, 1705 (C=O), 2210 (C≡N)	227 (4,30), 307 (4,21)	5.80, 5.94 (d,d), 2H, CH ₂ , J= =13 Hz); 7.06...7.59 (m, 10H, 2C ₆ H ₅)	457 (12)	30

*¹The IR spectrum of the tetrazine (XI) was obtained in CCl₄ on a Specord 75 IR.

*²The UV spectra of triazoles (IV) and (V) were obtained in n-hexane, of (VI) and (VII) in acetonitrile, and of tetrazines (X) and (XI) in ethanol.

*³The PMR spectra of triazoles (IV) and (V) were obtained in CDCl₃, external standard HMDS.

*⁴Calculated on verdazyl (I) reacted for (IV), (V), (X), and (XI), and on triazole (V) for (VI) and (VII).

The triazoles obtained, (IV) and (V), carried a pentafluorophenyl substituent in the 1-position, and the sym-tetrazines (X) and (XI) were formed as a single isomer (Table 1).

It is clear that the presence of an acceptor substituent at N₄ reduces the electron donor properties of the verdazyl (I) as compared with 2,4,6-triphenylverdazyl [5]. It will be seen, therefore, that despite the characteristic coloration of the reaction mixture, we have been unable to isolate 2,6-diphenyl-4-pentafluorophenylverdazylum bromide from these reactions, as described in [2].

In order to assess the reactivity of 2,6-diphenyl-4-pentafluorophenylverdazyl, reactions a and b have been examined kinetically. In benzene at 25°C, the radical (I) in concentrations of $(20-50) \cdot 10^{-2}$ mmole/liter reacts with dicyanobromomethane (30-67 mmole/liter) (path a) considerably more slowly ($k_2 = (16 \pm 1) \cdot 10^{-3}$ liter/mole·sec) than 2,4,6-triphenylverdazyl [6]. The reaction is also slow in acetonitrile ($k_2 = 19 \pm 1) \cdot 10^{-2}$ liter/mole·sec), and no reaction takes place with cyanoethoxycarbonylbromomethane in benzene.

EXPERIMENTAL

IR spectra were obtained on a UR-20, and UV spectra on a Specord UV-vis, PMR spectra were recorded on a Bruker WP-200 spectrometer (200 MHz) in acetone-D₆ (internal standard HMDS), and mass spectra on an MS-1302, ionizing voltage 70-100 eV, temperature 150-170°C. Column and thin layer chromatography were carried out with silica gel grade L 100/160 and Silufol UV-254, eluent benzene. Reaction rates were determined spectrophotometrically by the change in optical density of solutions of 2,6-diphenyl-4-pentafluorophenylverdazyl [4] at λ_{\max} in the visible region of the spectrum. The elemental analyses for C, H, N, and F were in agreement with the calculated values.

1-Pentafluorophenyl-3-phenyl-5-cyano-1,2,4-triazole (IV) was obtained as in [2], from 1.5 mmole of the verdazyl (I) [4] and 1 mmole of dicyanobromomethane (II) in benzene.

1-Pentafluorophenyl-3-phenyl-5-ethoxycarbonyl-1,2,4-triazole (V) was obtained similarly, from (I) and cyanoethoxycarbonylmethyl bromide (III) in benzene-acetonitrile, 1:1. After one hour, the precipitated 2,6-diphenyl-4-pentafluorophenylleucoverdazyl hydrobromide was filtered off, the filtrate evaporated under reduced pressure, and the residue extracted repeatedly with n-hexane or ether to remove the triazole. The extracts were evaporated, and the products crystallized.

1-Pentafluorophenyl-3-phenyl-5-carboxamido-1,2,4-triazole (VI). A mixture of 0.97 g (2.5 mmole) of the triazole (V) in 10 ml of 25% ammonia was stirred for five days at room temperature, using a magnetic stirrer. The product was filtered off and dried in a vacuum desiccator over P₂O₅ to give 0.79 g of colorless crystals.

1-(4'-Hydroxytetrafluorophenyl)-3-phenyl-1,2,4-triazole (VII). A mixture of 0.4 g (1.1 mmole) of (V) and 5 ml of 2 M sodium hydroxide was boiled for ten minutes under reflux. During this time, the solid dissolved, and the turbid solution was then filtered. The filtrate was acidified with conc. hydrochloric acid with ice-cooling, and the colorless solid which separated was filtered off, washed with cold water, and dried in a vacuum desiccator over P₂O₅ to give 0.31 g of colorless crystals.

1-Ethoxyalyl-2,6-diphenyl-4-pentafluorophenyl-1,2,3,4-tetrahydro-sym-tetrazine (X). A mixture of 1.8 g (4.4 mmole) of (I) and 0.58 g (1.5 mmole) of trifluoromethylsulfonylethoxycarbonyldibromomethane (VIII) [3] in 45 ml of a mixture of acetonitrile and benzene (1:8) was kept for one day at room temperature. The precipitated 2,6-diphenyl-4-pentafluorophenylleucoverdazyl hydrobromide (0.42 g) was filtered off, and the filtrate evaporated to dryness. The residue was extracted with n-hexane or ether, and the extract evaporated to give 0.7 g of the tetrazine (X). The residue consisted of a difficultly identifiable mixture of salts (0.6 g) of a blue color. The tetrazine (X) (yellow crystals) was purified either by repeated crystallization, or by column chromatography (R_f 0.35-0.40).

1-Cyanofornyl-2,6-diphenyl-4-pentafluorophenyl-1,2,3,4-tetrahydro-sym-tetrazine (XI). The verdazyl (I) (0.6 g, 1.5 mmole) was mixed with 0.17 g (0.5 mmole) of trifluoromethylsulfonyldibromomethane (IX) [8] in 35 ml of benzene at room temperature. After one day, the leucoverdazyl hydrobromide (0.24 g) was filtered off. The filtrate was evaporated to dryness, and the tetrazine (XI) isolated by TLC (R_f 0.4).

LITERATURE CITED

1. E. I. Tomilenko and V. I. Staninets, *Ukr. Khim. Zh.*, **53**, 533 (1987).
2. E. I. Tomilenko, A. M. Nesterenko, V. N. Kalinin, and V. I. Staninets, *Khim. Geterotsikl. Soedin.*, No. 7, 981 (1987).
3. E. I. Tomilenko, P. I. Ogoiko, and V. I. Staninets, No. 11, 1532 (1987).
4. I. G. Ryabokon', V. N. Kalinin, O. M. Polumbrik, and L. N. Markovskii, *Khim. Geterotsikl. Soedin.*, No. 10, 1425 (1985).
5. O. M. Polumbrik, *The Chemistry of Verdazyl Radicals* [in Russian], Naukova Dumka, Kiev (1984), p. 97.
6. E. I. Tomilenko, V. I. Staninets, V. P. Kukhar', and I. P. Beletskaya, *Dokl. Akad. Nauk SSSR*, **252**, 129 (1980).
7. D. G. Holland, N. T. McDevitt, J. V. Pustinger, Jr., and J. E. Strobel, *J. Org. Chem.*, **32**, 3671 (1967).
8. P. I. Ogoiko, A. Ya. Nazaretyan, A. Ya. Il'chenko, and L. M. Yagupol'skii, *Zh. Org. Khim.*, **16**, 1397 (1980).

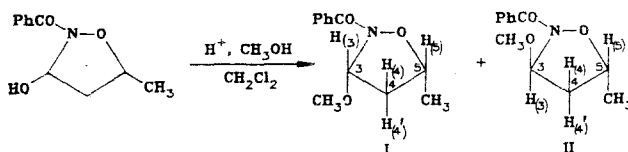
SPATIAL STRUCTURE OF 2-BENZOYL-3-METHOXY-5-METHYLISOXAZOLIDINE

I. F. Leshcheva, D. S. Yufit,
L. A. Sviridova, I. A. Motorina,
G. A. Golubeva, K. N. Zelenin,
Yu. T. Struchkov, and Yu. G. Bundel'

UDC 548.737+547.786.1:541.1
623:543.422.25

The nuclear Overhauser effect and x-ray diffraction analysis have been employed to determine the spatial structure of the diastereoisomeric 2-benzoyl-3-methoxy-5-methylisoxazolidines. It has been found that the predominant isomer in the reaction mixture has the cis-configuration.

We have previously shown that substituted hydroxamic acids react with crotonaldehyde to give a mixture of the two diastereoisomeric pairs of 3-hydroxyisoxazolidines, in a ratio of 1:1 [1], although in solution this ratio may vary, since these compounds undergo ring-chain tautomerism. In order to exclude the influence of this factor and also of intermolecular hydrogen bonding, the stereochemistry of the functionally substituted isoxazolidines obtained was examined in the case of 2-benzoyl-3-methoxy-5-methylisoxazolidine, obtained as in [2]. This compound consists of a mixture of the diastereoisomeric pairs (I) and (II) in a ratio of 2:1, this ratio being constant under the reaction conditions, probably as a result of the differing stabilities of the isomers.



Quantitative separation of the mixture into its diastereoisomers was carried out by high performance flash chromatography (see Experimental), to give enriched mixtures with (I):(II) ratios of 20:1 and 1:6. For the spectral studies, mixtures with (I):(II) 20:1 and 1:1 were used.

To determine the configurations of the diastereoisomers (I) and (II), we measured the stationary proton-proton nuclear Overhauser effect (NOE) by difference spectroscopy [3]. The NOE was expressed as a percentage from the expression:

M. V. Lomonosov Moscow State University, Moscow 119899. A. N. Nesmeyenov Institute of Heteroorganic Compounds, Moscow 117813. S. M. Kirov Military Medical Academy, Leningrad 194175. Translated from *Khimiya Geterotsiklicheskikh Soedinenii*, No. 9, pp. 1255-1260, September 1989. Original article submitted April 15, 1988.