2-Methylthio-4-chloro-6-methyl-7-butyl-8-oxo-7,8-dihydropyrimido[5,4-d]pyrimidine (XII). A 1.2-g (3.8 mmole) sample of XI was refluxed with 20 ml of $POCl_3$, after which the resulting solution was vacuum evaporated, and the residue was treated with ice. The aqueous solution was neutralized with dry $NaHCO_3$ and extracted with chloroform. The chlorofom was vacuum evaporated, and the residue was triturated with petroleum ether to give 0.5 g of XII.

LITERATURE CITED

1. H. Spitzbarth, Arzneimittel-Forsch., 9, 59 (1959).
2. F. G. Fischer and J. Roch, Ann., 572, 217 (1951).
3. N. E. Britikova, L. A. Belova, K. A. Chkhikvadze, and O. Yu. Magidson, Khim. Geterotsikl. Soedin., No. 2, 270 (1973).
4. Masuo Murakami, Shigemi Kawahara, Sanae Ishida, Mikio Ohno, and Hiroshi Horigychi, US patent No. 3,562,265 (1971); Ref. Zh. Khim., 21N, 470 (1971).

REACTIVITIES AND TRANSFORMATIONS OF PHENAZYL RADICALS

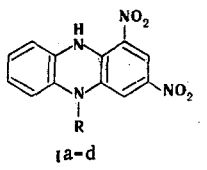
I. N. Borukhova, V. F. Gryazev, Z. V. Pushkareva, Z. V. Pushkareva, and V. I. Koryakov

UDC 547.864.3:543.422.27

The kinetics of the recombination of phenazyl radicals and their reaction with secondary amines were studied by ESR spectroscopy. A relationship between the reactivities of the radicals and the character of the substituent in the 5 position was observed. The possibility of the addition of secondary amines to the dihydrophenazine system was shown during a study of the reaction of phenazyl radicals with the former.

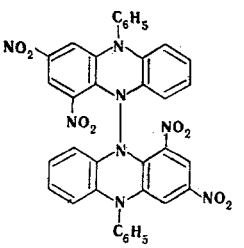
Continuing our study of the free radicals of a number of 5-substituted dihydrophenazines [1], we made a kinetic study of their recombination and reaction with secondary amines.

The radicals were generated by oxidation of dihydrophenazines Ia-d with lead dioxide in benzene, and the formation of paramagnetic particles was recorded with an RÉ-1301 radiospectrometer. The observed decrease in the intensities of the ESR signals with time (Fig. 1) provided evidence for recombination of the free radical particles and was accompanied by conversion of the green color characteristic for a solution of the free radical to violet.



Ia-d

I a R = n-C_4H_9; b R = C_6H_5; c R = 2,4-$(NO_2)_2C_6H_3$; d R = 2,4,6-$(NO_2)_3C_6H_2$



II

To study the structure of the transformation product we undertook the preparative oxidation of Ib with subsequent exhaustive recombination of the generated radical and chromatographic separation of the resulting solution on Al_2O_3.

S. M. Kirov Ural Polytechnic Institute, Sverdlovsk 620002.

Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 4, pp. 521-524, April, 1977. Original article submitted May 7, 1976.

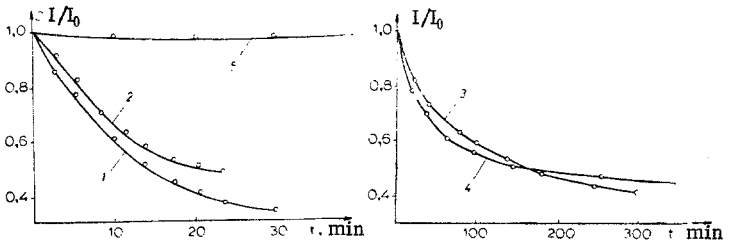


Fig. 1. Kinetic curves of the recombination of radicals of Ia-d in air: 1) Ia; 2) Ib; 3) Ic; 4) Id; 5) curve of the recombination of the radical of Ib in vacuo (I/I_0 is the intensity of the ESR signal of the radical referred to the intensity of the signal of a standard sample).

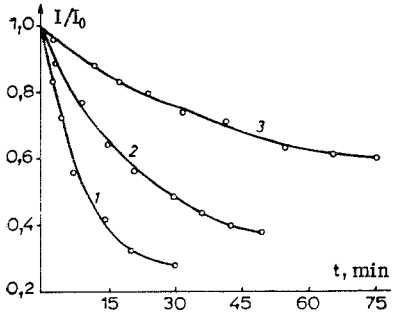


Fig. 2. Kinetic curves of the reaction of radicals of Ib-d with carbazole at 50°C in vacuo: 1) Ib; 2) Ic; 3) Id (I/I_0 is the intensity of the ESR signal of the radical referred to the intensity of the signal of a standard sample).

The compound isolated in this manner did not display absorption in the region of the frequencies of the stretching vibration of the N–H bond, but its elementary composition corresponded to the starting 1,3-dinitro-5-phenyldihydrophenazine (Ib). An ESR signal was not observed when the recombination product was heated for a long time in solution in the presence of α,α-diphenyl-β-picrylhydrazine, selected as a paramagnetic particle "trap." This fact constitutes evidence that a stable substance that is not inclined to undergo thermal dissociation is formed as a result of the recombination. A 10,10'-bis(1,3-dinitro-5-phenylphenazyl) structure (II) can therefore, be assumed for the product. The possibility of the formation of this sort of dimer was demonstrated in [2]

To obtain a comparative evaluation of the rates of recombination of the investigated radicals we studied the kinetics of this process by means of ESR spectroscopy in the presence of air oxygen and in vacuo. The kinetic curves obtained are presented in Fig. 1, and the rate constants calculated from a second-order equation [3] are presented in Table 1.

As seen from Table 1, recombination in vacuo is slowed down markedly; this is in good agreement with the literature data on the effect of dissolved oxygen on the stabilities of free radicals [4, 5].

The increase in the stabilities in the series of radicals can be explained, on the one hand, by an increase in the degree of delocalization of the unpaired electron as the electron-acceptor properties of the substituent in the 5 position increases and, on the other, by the increase in the degree of solvation of the molecules of the radicals as their polarities change. However, a study of the electronic spectra of the phenazyl radicals in a number of solvent with different dielectric constants [benzene, dioxane, acetone, acetonitrile, and dimethylformamide (DMF)] showed that the visible portion of the spectrum characteristic for these systems [1] retains its configuration. The solvation effect in this case can therefore, be disregarded, and the change in the stabilities of the investigated radicals can be explained by the effect of the substituent in the 5 position.

TABLE 1. Rate Constants of Recombination of the Radicals of Ia-d

Radical	K, liter·mole^{-1}·min^{-1}	
	in the presence of air, $K \cdot 10^3$	in vacuo, $K \cdot 10^4$
Ia	67,3	21,8
Ib	52,6	11,1
Ic	7,21	7,57
Id	3,99	4,12

TABLE 2. Rate Constants and Activation Energies (E_A) for the Reaction of Phenazyl Radicals with Carbazole at 50°C

Radical	$K \cdot 10^2$, min^{-1}	E_A, kcal/mole
Iб	6,38	10,90
Iв	2,81	11,20
Iг	1,03	10,10

To obtain more detailed information regarding the reactivities of the phenazyl radicals we undertook a study of the kinetics of their reaction with secondary aromatic amines [6].

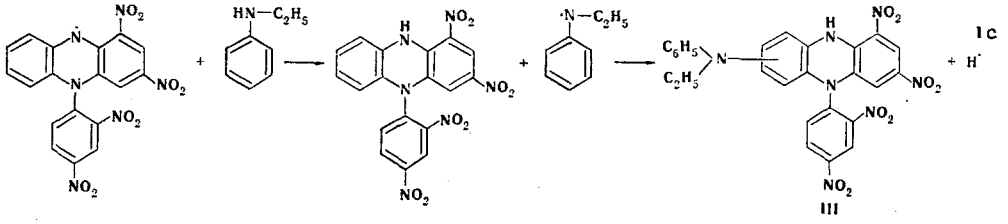
The kinetics of this process were studied by means of ESR spectroscopy of benzene solutions under vacuum conditions. The kinetic curves are presented in Fig. 2, and the rate constants for the reaction of the phenazyl radicals with carbazole at 50°, calculated from a first-order equation [3] (in the case of excess secondary amine), and the activation energies are given in Table 2.

The rate of reaction of the radical of Ia with carbazole was found to be comparable to the rate of recombination of this radical.

As a result of a study of the kinetics of both processes it can be concluded that, despite the noncoplanarity of the molecules of the investigated compounds [7], the substituent in the 5 position has a sufficiently strong effect on the reactivity of the dihydrophenazine system.

A comparison of the E_A values (Table 2) in the phenazyl radical series shows that their reactions with secondary amines are characterized by approximately the same activation barriers that correspond to processes with the participation of free radicals [6, 8].

In a study of the structures of the products of the reaction of the phenazyl radicals with amines we observed that the process does not stop at first step – the formation of the corresponding dihydrophenazines Ia-d. Thus III, the elementary composition of which corresponds to the addition of the resulting aminyl radical to this dihydrophenazine, was isolated along with the easily identifiable dihydrophenazine Ic by chromatographic separation of the products of the reaction of the radical of Ic and monoethylaniline. Compound III is characterized by the presence in its mass spectrum of the corresponding molecular ion (m/e 557) and displays a band of the stretching vibration of the N–H bond (3300 cm^{-1}) peculiar to dihydrophenazines Ia-d in its IR spectrum. We were unable to establish the exact site of attack, but it can be assumed that the aminyl radical attacks the unsubstituted phenylene ring of the phenazine system, i.e., the reaction proceeds via the scheme



EXPERIMENTAL

Generation of Phenazyl Radicals and Kinetics of Their Recombination. A solution of dihydrophenazine Ia-d in dry benzene (10^{-3} M) and a 20-fold excess of powdered lead dioxide were placed in a special cuvette. After evacuation of the air to $P_{res} \simeq 10^{-4}$ mm of Hg, the powdered lead dioxide and solution were mixed and shaken for 5-60 min. The green solution of the radical was decanted into a capillary, which was placed in the thermostatted resonator of an RÉ-1301 spectrometer. The ESR signal of the radical was recorded at 20° relative to the signal of a standard sample up to a degree of conversion of ~70%.

Kinetics of the Reaction of the Phenazyl Radicals with Carbazole. Equal volumes of solutions of dihydrophenazine Ia-d (10^{-3} M) and carbazole (10^{-2} M) in benzene and powdered lead dioxide were placed in separate compartments of a cuvette. After evacuation and generation of the radical, its solution was mixed with the carbazole solution, the mixture was stirred rapidly, and the ESR signal was recorded at 20-50° as in the case of the recombination process.

Preparation of III. A 20-g sample of lead dioxide was added to 2 g (4.5 mmole) of dihydrophenazine Ia in 4.5 liters of dry benzene, and the mixture was stirred at room temperature for 1.5 h, after which 1.1 g (9 mmole) of freshly distilled monoethylaniline was added to a thoroughly filtered (to remove the oxidizing agent) solution of the radical, and the solution was stirred for 30 min. It was then chromatographed with a column filled with Al_2O_3. The eluate of the first zone contained 1.3 g of dihydrophenazine Ie, and the eluate of the second zone contained 0.5 g of III. Recrystallization of III from acetone gave violet crystals with mp 276° in 20% yield. Found: N 17.9%. $C_{26}H_{19}N_7O_8$. Calculated: N 17.6%.

LITERATURE CITED

1. Z. V. Pushkareva, I. N. Noskova, and V. F. Grayzev, Khim. Geterotsikl. Soedin., No. 10, 1428 (1970).
2. H. Leemann and E. Grandmougin, Ber., 41, 1295 (1908).
3. K. B. Yatsimirskii, Kinetic Methods of Analysis [in Russian], Khimiya, Moscow (1967), p. 18.
4. K. H. Hausser, Z. Naturwissensch., 47, 251 (1960).
5. A. A. Revina and N. A. Bakh, Dokl. Akad. Nauk SSSR, 141, No. 2, 409 (1961).
6. J. E. Hazell and K. E. Russel, Can J. Chem. 36, 1729 (1958).
7. I. G. M. Campbell, C. G. le Fevre, R. J. W. le Fevre, and E. E. Turner, J. Chem. Soc., 404 (1938).
8. E. N. Eremin, Fundamentals of Chemical Kinetics [in Russian], Moscow (1976), p. 83.

SYNTHESIS AND NITRATION OF 4-PHENYL-2,3-DIHYDRO-1H-1,5-BENZODIAZEPIN-2-ONE

T. S. Chmilenko, Z. F. Solomko, and A. N. Kost

UDC 547.892.07:542.958.1

Analysis of the UV spectra of the reaction products shows that in the nitration of 4-phenyl-2,3-dihydro-1H-1,5-benzodiazepin-2-one the nitro group is directed to the benzodiazepine ring rather than to the phenyl ring to give a 7-nitro derivative.

It has been shown that the nitration of 4-methyl-2,3-dihydro-1H-1,5-benzodiazepin-2-one leads to the formation of a 7-nitro derivative [1], i.e., substitution takes place in the para position relative to the amide group rather than para to the ketimine group. The introduction of a phenyl group in the 4 position could, in view of the conjugation of the π electrons of the substituent with the carbon–nitrogen double bond [2], create, on the one hand, conditions for coplanarity of the rings and, on the other, substantially raise the electron density on the $C_{(3)}$ atom. In addition, if protonation proceeds precisely at this double bond, incorporation of a nitro group in the benzene ring of the subsituent would be likely.

It was found that nitration of 4-phenyl-2,3-dihydro-1H-1,5-benzodiazepin-2-one (I) by the action of potassium nitrate in concentrated sulfuric acid gives nononitro compound II, the acid hydrolysis of which leads to 4-nitro-o-phenylenediamine, indicating that the nitro group is attached to $C_{(7)}$ or $C_{(8)}$ of the diazepine portion of the molecule. The considerable yield of II and the absence in the reaction mixture of other substances are probably associated with protonation at the N_5 atom, as a result of which coordinated orientation of the protonated nitrogen atom and the acetamido group is observed [3]. The structure of this substance as precisely the 7 isomer was confirmed by alternative synthesis from N-(2,4-dinitrophenyl)benzoylacetamide (IV), the reductive

Dnepropetrovsk State University, Dnepropetrovsk 320625.

Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 4, pp. 525-528, April, 1977. Original article submitted April 26, 1976.