# RESEARCH ON PERINONE COMPOUNDS

## V.* FORMATION OF 10- AND 11-SUBSTITUTED NAPHTHALOPERINONES

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11-Substituted 14H-benz[4,5]isoquinolino[2,1-a]perimidin-14-ones were synthesized, and their spectra were studied. In contrast to electron-acceptor substituents, electron-donor substituents have little effect on the shift of the absorption maxima. In the reactions of 1,8-naphthalenediamine with various 4-substituted naphthalic anhydrides, electron-donor substituents have little effect on the shift of the absorption maxima. In the reactions of 1,8-naphthalenediamine with various 4-substituted naphthalic anhydrides, electron-donor substituents lead primarily to 10-substituted naphthaloperinones, whereas electron-acceptor substituents lead primarily to 11-substituted naphthaloperinones. An assumption regarding the mechanism of the formation of 10- and 11-substituted naphthaloperinones is expressed.

Starting from the previously described 11-amino-14H-benz[4,5]isoquinolino[2,1-a]perimidin-14-one [2], as in the preparation of 10-substituted compounds [1], we used the Sandmeyer reaction to synthesize a number of new 11-substituted perinone compounds. The spectral data for the perinones obtained (Table 1) in comparison with the analogous data of unsubstituted naphthaloperinones show that the introduction of both electron-donor and electron-acceptor substituents leads to a bathochromic shift of the absorption maxima; an exception to this is the amino group, in which case a hypsochromic shift is observed. The correlation coefficients (Table 2) were calculated by comparison of the various types of $\sigma$ constants with the wave numbers of the absorption maxima of 11-substituted naphthaloperinones [3]. The improvement in the correlation when nucleophilic and electrophilic constants are used characterizes the prevailing influence of the mesomeric effect of substituents on the shift of the absorption maxima of these compounds as compared with unsubstituted naphthaloperinone. The observed substantial bathochromic shift of the long-wave absorption band in the case of acceptor substituents and the absence of a correlation for donor substituents constitute evidence that the heterocyclic ring of naphthaloperinone is an electron donor. There is a definite regularity in the change in the absorption maxima when substituents are introduced into the 10 and 11 positions of naphthaloperinone. It was established with the aid of the method of proportional response [4] that there is a linear correlation between the absorption maxima of the 10-and 11-isomers, and the corresponding points fall on two lines, one for the electron-acceptor substituents, and the other for the electron-donor substituents (Fig. 1). The presence of a proportional response between the absorption maxima of 10- and 11-R-naphthaloperinones is evidence for the monotypic character of the change in the electronic structure under the influence of the same substituent. Thus, the shift of the absorption maximum of the corresponding 10-substituted naphthaloperinone can be predicted from the shift of the absorption maximum of the 11-isomer.

The synthesis of the 10- and 11-isomers of the naphthaloperinones enabled us to discuss the orienting effect of substituents in naphthalic anhydride (II) on the isomeric composition of the naphthaloperinones formed during the reaction with 1,8-naphthalenediamine (I). It follows from the literature data that the question of the orienting effect of substituents in the reactions of dicarboxylic acid anhydrides with nucleophilic reagents is quite complex and that the isomer ratios depend not only on the nature of the reacting compound

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*See [1] for communication IV.

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TABLE 1. Spectral Characteristics of 11-Substituted Naphthaloperinones

| Compound | R | $\lambda_{max}$, nm | $\Delta\lambda=\lambda_R-\lambda_H$ | $\varepsilon\times10^3$ | $\nu_{C=O}$ |
|---|---|---|---|---|---|
| X | H | 472 | — | 0,45 | 1688 |
| XI | $NH_2$ | 456 | −16 | 0,75 | 1660 |
| XII | OH | 489 | 17 | 0,71 | 1661 |
| XIII | $OCH_3$ | 479 | 7 | 0,63 | 1686 |
| XIV | $NHCOCH_3$ | 488 | 16 | 0,59 | 1682 |
| XV | $NO_2$ | 546 | 74 | 0,88 | 1682 |
| XVI | CN | 520 | 48 | 0,79 | 1692 |
| XVII | $COOCH_3$ | 509 | 37 | 0,58 | 1691 |
| XVIII | COOH | 504 | 32 | 0,66 | 1695 |
| XIX | Br | 498 | 26 | 0,60 | 1688 |

TABLE 2. Correlation of the Shifts of the Absorption Maxima of 11-R-Naphthaloperinones with Different Types of $\sigma$ Substituent Constants

| R | $\sigma$ | r* | $\rho$ |
|---|---|---|---|
| $NH_2$, $NHCOCH_3$, OH, $OCH_3$, H | $\sigma$ | 0,75109 | −13,159 |
| | $\sigma^+$ | 0,89080 | −8,5019 |
| | $\sigma_c^+$ | 0,84328 | −7,2570 |
| | $\sigma_I$ | — | — |
| $NO_2$, CN, $COOCH_3$, COOH, Br, H | $\sigma$ | 0,93890 | 46,334 |
| | $\sigma^-$ | 0,93560 | 28,332 |
| | $\sigma_c^-$ | 0,99852 | 34,234 |
| | $\sigma_I$ | 0,90351 | 59,256 |

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*Symbols: r is the correlation coefficient, and $\rho$ is the sensitivity coefficient; the Student $t_\alpha$ coefficient corresponds to reliability $\alpha=0.999$.

TABLE 3. Ratio (%) of 10- and 11-Isomeric Naphthaloperinones

| Substituent in the naphthalic anhydride | 11-Isomer, % | 10-Isomer, % |
|---|---|---|
| $NO_2$ | 78 | 22 |
| COOH | 59 | 41 |
| Br | 52 | 48 |
| $NH_2$ | 25 | 75 |
| OH | 35 | 65 |
| $OCH_3$ | 38 | 62 |

(specifically, on the nature of the substituent) but also on the conditions under which the reaction is carried out – temperature, solvent, etc. [5-8]. For example, the reactions of 3- and 4-nitro- and 3- and 4-acetamidophthalic anhydrides with o-phenylenediamine lead to a complex mixture of products, the quantitative ratios between which were not established. Nevertheless, the existence of an orienting effect of a substituent does not raise any doubts, and the carbonyl group in the ortho and para positions with respect to the substituent is more reactive in 3-ethyl-nitrophthalic anhydrides, whereas the acetamido group has the opposite effect [9].

We investigated the reaction of 1,8-naphthalenediamine with various 4-substituted naphthalic anhydrides. The ratios of the resulting 10- and 11-isomers of naphthaloperinones were determined from the absorption spectra of the mixtures obtained and those of two individual components [10]. The method was first checked with artificial mixtures, and an accuracy sufficient for our purposes was demonstrated [2]. The results (Table 3) show that electron-donor substituents lead primarily to 10-substituted naphthaloperinones, whereas electron-acceptor substituents lead primarily to 11-substituted naphthaloperinones. Krasovitskii and co-workers in a study of the mechanism of the reaction of o-phenylenediamine with naphthalic anhydride [11] showed that in the case of 3-nitrophthalic anhydride only one isomer – 3-nitro-7H-benzimidazo[2,1-a]benz[d,e]isoquinolin-7-one – is formed. This course of the reaction was explained by nucleophilic attack by the electrons of the amino group on the carbonyl carbon atom in conjugation with the nitro group. In analogy with [11], we expected the formation of 10-isomers of naphthaloperinones in the reactions of 1,8-naphthalenediamine with 4-substituted naphthalic anhydrides in the case of electron-acceptor substituents and 11-isomers in the case of electron-donor substituents. In fact, we obtained the opposite results.

The results can apparently be explained by the fact that the direction of cyclization of III is determined primarily by intramolecular protonation of the carbonyl oxygen atom through the hydrogen of the amino group rather than by nucleophilic attack of the electrons of the amino group on the carbonyl carbon

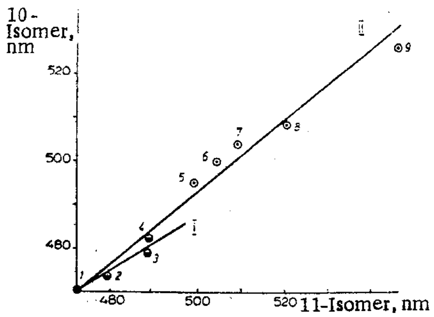


Fig. 1

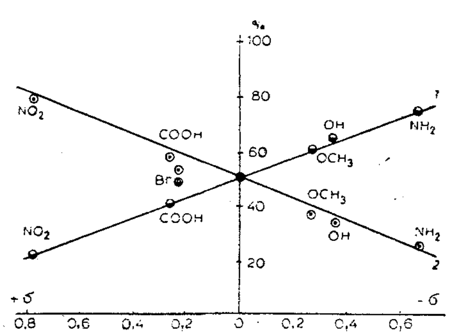


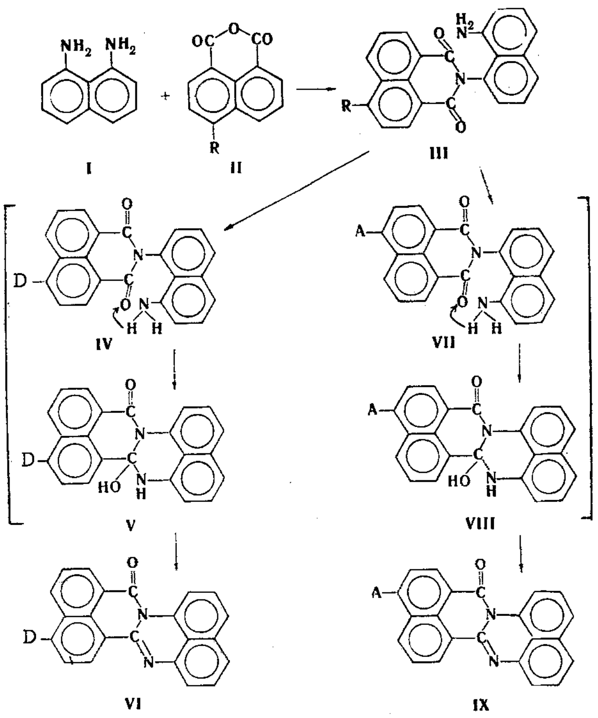
Fig. 2

Fig. 1. Comparison of the absorption maxima of 10- and 11-substituted naphthaloperinones: 1) H; 2) $OCH_3$; 3) $NHCOCH_3$; 4) OH; 11-H; 5) Br; 6) COOH; 7) $COOCH_3$; 8) CN; 9) $NO_2$ (I $r=0.994$, $\rho=1.11$; II $r=0.997$, $\rho=1.03$).

Fig. 2. Dependence of the amounts of 10- and 11-substituted naphthaloperinones formed on the $\sigma$ value of a substituent in naphthalic anhydride: 1) 1-substituted naphthaloperinones ($r=0.992$, $\rho=1.12$, and $s=0.44$); 2) 11-substituted naphthaloperinones ($r=0.989$, $\rho=1.02$, and $s=0.61$).

atom. Substituents with a +M effect in the para position relative to the carbonyl group intensify polarization of the $C=O$ double bond, and this causes the increased reactivity of the carbonyl oxygen atom with respect to electrophilic attack by the hydrogen of the amino group (IV → VI). Substituents with a −M effect reduce the electron density on both the carbonyl carbon atom and on the carbonyl oxygen atom, such that the reactivity with respect to electrophilic attack decreases. In the case of electron-acceptor substituents, the second molecule of water is therefore split out from III through the carbonyl oxygen atom that is not conjugated with the substituent to give VIII; this leads to the primary formation of 11-isomers (VII → IX).

Intramolecular protonation is also confirmed by the fact that when the reaction is carried out in both acetic acid and chlorobenzene the ratios of isomers formed are identical.



A = an electron-acceptor substituent
D = an electron-donor substituent

A dependence of the amounts of isomers formed on the Jaffe $\sigma$ constants of the substituents in the 4 position of naphthalic anhydride (Fig. 2) was established, and its "predictive strength" was verified. According to Fig. 2, from the methyl ester of 4-carboxynaphthalic anhydride one should expect the formation of 67% 11-carbomethoxy- and 33% 10-carbomethoxynaphthaloperinone; however, 62% of the 11-isomer and 38% of the 10-isomer were actually obtained experimentally. In the case of 4-acetamidonaphthalic anhydride the expected amounts of isomers will be 48% of the 11-substituted compound and 52% of the 10-substituted compounds; 41% of the 11-isomer and 59% of the 10-isomer were actually obtained. Thus from the $\sigma$ value of the substitutent one can with sufficient accuracy predict the isomeric composition of naphthaloperinones formed in the reactions of 1,8-naphthalenediamine with 4-substituted naphthalic anhydrides.

The above-presented peculiarities of the effect of substituents on the formation of naphthaloperinones and the properties of the products of the reaction of aromatic dicarboxylic acids with o-phenylenediamine and perinaphthalenediamine show the substantial difference between naphthoylenebenzimidazoles and perinones, and the union of them in a single class that is encountered in the literature [12] does not seem to us to be completely valid.

## EXPERIMENTAL

The UV spectra of chlorobenzene solutions of the compounds were recorded with an SF-14 spectrophotometer. The IR spectra of mineral-oil suspensions were recorded with a UR-10 spectrometer. Anhydrous aluminum oxide was used for the chromatography.

11-Acetamido-14H-benz[4,5] isoquinolino[2,1-a]perimidin-14-one (XIV). A solution of 0.42 g (1.12 mmole) of 11-aminonaphthaloperinone in 13 ml of acetic anhydride was refluxed for 2 h, after which it was cooled and filtered, and the precipitate was washed with hot water and dried. The compound obtained was dissolved in acetone, and the solution was passed through a column filled with aluminum oxide [cyclohexane–acetone (1 : 1)]. The first fraction was collected, and the solvent was evaporated to give 0.22 g (51%) of XIV in the form of brown needles with mp 265-266°. Found: N 11.5%. $C_{24}H_{15}N_3O_2$. Calculated: N 11.2%.

11-Bromo-14H-benz[4,5]isoquinolino[~~2,1-a~~]perimidin-14-one (XIX). A mixture of 1.68 g (6 mmole) of 11-aminonaphthaloperinone and a 15% solution of sulfuric acid was refluxed for 30 min, after which it was cooled to 0°. A solution of 0.42 g of sodium nitrite in 2 ml of water was added slowly dropwise, and the reaction mixture was stirred at 0° for 45 min. It was then poured gradually into a solution of 1 g of cuprous bromide, 5 g of potassium bromide, and 8 ml of 48% hydrobromic acid in 25 ml of water. The resulting mixture was stirred for 1 h, after which it was heated to 80°. After 30 min, it was filtered, and the precipitate on the filter was washed with water and dried. It was then dissolved in chlorobenzene, and the solution was passed through a column filled with aluminum oxide. The first fraction was collected, one-third of the chlorobenzene was removed by distillation, the solution was cooled, and the resulting precipitate was filtered and dried to give 1.47 g (74.6%) of XIX as red-brown needles with mp 246-247°. Found: Br 20.5%. $C_{22}H_{11}BrN_2O$. Calculated: Br 20.0%.

11-Cyano-14H-benz[4,5]isoquinolino[~~2,1-a~~]perimidin-14-one (XVI). A solution of 1.86 g (56 mmole) of 11-aminonaphthaloperinone in 50 ml of 15% sulfuric acid was refluxed for 10 min, after which it was cooled to 0°, and a solution of 0.5 g of sodium nitrite in 4 ml of water was added dropwise. The mixture was stirred at 0° for 1 h, the excess nitrite was removed by the addition of urea, and the mixture was neutralized to pH 5.5-6.0 with potassium carbonate. The resulting suspensions were poured into a solution of 4 g of sodium cyanide and 5.9 g of copper cyanide in 55 ml of water, and the resulting mixture was stirred at room temperature for 3 h and at 70° for 1 h. The resulting precipitate was removed by filtration, washed with water, dried, and dissolved in chloroform. The chloroform solution was passed twice through a column filled with aluminum oxide. The blue fraction was collected, the solvent was evaporated, and the residue was recrystallized from chlorobenzene to give 0.6 g (31.6%) of nitrile XVI as blue needles with mp 275-276°. Found: N 11.9%. $C_{23}H_{11}N_3O$. Calculated: N 12.3%.

11-Carboxy-14H-benz[4,5]isoquinolino[~~2,1-a~~]perimidin-14-one (XVIII). A mixture of 1 g of nitrile XVI, 10 ml of acetic acid, 10 ml of sulfuric acid, and 10 ml of water was stirred and refluxed, after which the mixture was poured into 100 ml of water, and the resulting precipitate was removed by filtration, washed with water, and reprecipitated from 50 ml of 5% sodium carbonate solution. The precipitate was crystallized twice from pyridine to give 0.3 g (28.4%) of acid XVIII as dark-blue plates. The purity of the product was monitored by chromatography of a solution of it on paper in pyridine–isoamyl alcohol–water (1.3 : 1 : 1). Found: N 7.5%. $C_{23}H_{12}N_2O_3$. Calculated: N 7.7%.

11-Carbomethoxy-14H-benz[4,5]isoquinolino[2,1-a]perimidin-14-one (XVII). A 0.27-g (0.7 mmole) sample of acid XVIII was refluxed in 10 ml of chlorobenzene with 0.5 ml of thionyl chloride for 2 h, after which the excess thionyl chloride was removed by distillation, 5 ml of methanol was added, and the mixture was refluxed for 8 h. It was then cooled, and the resulting precipitate was removed by filtration and dissolved in benzene. The solution was chromatographed on aluminum oxide [cyclohexane–acetone (1 : 1)]. Evaporation of the solvent gave 0.16 g (57.2%) of ester XVII as blue plates with mp 213-214°. Found: N 7.6%. $C_{24}H_{14}N_2O_3$. Calculated: N 7.4%.

11-Hydroxy-14H-benz[4,5]isoquinolino[2,1-a]perimidin-14-one (XII). A 0.9-g (2.7 mmole) sample of 11-aminonapththaloperinone was refluxed for 30 min in 20 ml of 15% sulfuric acid, after which the mixture was cooled to 0°, and a solution of 0.44 g of sodium nitrite in 3 ml of water was added slowly. The mixture was stirred for 1 h, after which the excess sodium nitrite was removed by the addition of urea, and the mixture was refluxed for 6 h. The precipitate was removed by filtration, washed with water, and dried. Two crystallizations from pyridine gave 0.41 g (45.6%) of red-brown needles of XII. Found: N 8.1%. $C_{22}H_{12}N_2O_2$. Calculated: N 8.3%.

11-Methoxy-14H-benz[4,5]isoquinolino[2,1-a]perimidin-14-one (XIII). A 0.5-ml sample of 10% sodium hydroxide solution was added to a solution of 0.4 g (1.2 mmole) of XII in 20 ml of acetone. The mixture was stirred, and 1 ml of freshly distilled dimethyl sulfate was added, after which the mixture was held at 40° for 1 h. Dimethyl sulfate (0.5 ml) was then added, and after 30 min the mixture was poured into water. The resulting precipitate was removed by filtration, washed with water, and dried. The product was dissolved in benzene and chromatographed with a column filled with aluminum oxide [benzene–ethyl acetate (1 : 1)]. Evaporation of the solvent gave 0.11 g (26.4%) of brown needles of XIII with mp 237-238°. Found: N 8.2%. $C_{23}H_{14}N_2O_2$. Calculated: N 8.0%.

Reaction of 1,8-Naphthalenediamine with 4-Substituted Naphthalic Anhydride. A 0.01-mole sample of 1,8-naphthalenediamine and 0.01 mole of substituted naphthalic anhydride were refluxed in 25 ml of glacial acetic acid for 12 h, after which the mixture was cooled and poured into 100 ml of water. The resulting precipitate was removed by filtration, washed with water, and dried. The percentages of 10- and 11-substituted naphthaloperinones in the mixture were calculated from the absorption spectra of the mixture of 10- and 11-isomers and two individual compounds. The results are presented in Table 3.

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