1-AZABICYCLIC COMPOUNDS.

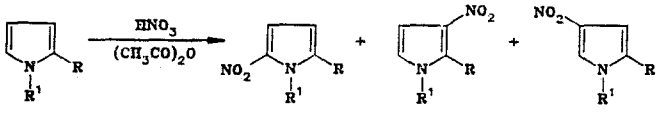
24.* SELECTIVITY OF POSITION OF NITRATION OF 1,2-DIHYDROPYRROLIZINE, 5,6,7,8-TETRAHYDROPYRROCOLINE AND PYRROLE HOMOLOGS

I. M. Skvortsov and L. N. Astakhova

UDC 547.742:542.958.1

The selectivity of the position of nitration of 1-methylpyrrole, 1,2-dimethylpyrrole, 1,2-dihydropyrrolizine, and 5,6,7,8-tetrahydropyrrocoline was found. In contrast to the selectivity of substitution during nitration of their carbocyclic analogs, o-xylene, indane and tetraline, the fraction of the α-nitro-isomer in the nitration products of 1,2-dimethylpyrrole is smaller than the fraction of α-nitro derivatives of 1,2-dihydropyrrolizine and 5,6,7,8-tetrahydropyrrocoline, and in the two latter cases the isomers are almost equally distributed. During nitration of the above bicyclic pyrroles, the Mills-Nixon effect does not appreciably influence the selectivity of the position of the reaction.

A study of the regioselectivity of the nitration reaction of pyrrole and its simplest homologs, for example compounds I-IV, helps to clarify the influence of hydrocarbon radicals on the activity of free positions in the ring [2-6] and also to solve the general problem of the reactivity of five-membered heterocycles [7], particulary pyrroles, as a function of structural factors. Depending on the symmetry of the initial compound, for pyrroles I-IV, in each case two V, IX (or XIII) and VII, XI (or XV), or three VI, X, XIV and VIII, XII, XVI isomeric mononitro derivatives can be formed.



I–IV, XVII, XVIII — V–VIII, XIX, XX — IX–XII, XXI, XXII — XIII–XVI, XXIII, XXIV

I, V, IX (XIII) R=R¹=H; II, VI, X, XIV R=CH₃, R¹=H; III, VII, XI (XV) R=H, R¹=CH₃; IV, VIII, XII, XVI R=R¹=CH₃; XVII, XIX, XXI, XXIII R+R¹=(CH₂)₃; XVIII, XX, XXII, XXIV R+R¹=(CH₂)₄

In the present work, our aim was to nitrate pyrrole homologs III and IV, and also cyclic analogs of 1,2-dialkylpyrroles, 1,2-dihydropyrrolizine (XVII), and 5,6,7,8-tetrahydropyrrocoline (XVIII) under the same conditions, to compare selectivity of the position of the reaction and to determine how a transition from a monocyclic compound IV to bicyclic compounds XVII and XVIII influences this selectivity. This transition is accompanied by the appearance of a strain in the bicyclic system, compared with the pyrrole homolog IV. By analogy with the data in [8] and from the examination of models and experimental data [9], it can be seen that system XVII is more strained than system XVIII.

For asymmetric initial pyrroles IV, XVII, XVIII, the reaction leads to the formation of all three mononitro-isomers, VIII, XII, XVI [6], XIX, XXI, XXIII [1], and XX, XXI, XXIV.

In the present work, the series of compounds for studying the selectivity of the position of nitration were selected in accordance with the data in [8] on a study of the selectivity of nitration of o-xylene, tetraline and indane. Increase in the reaction products of

*See [1] for Communication 23.

Institute of Biochemistry and Physiology of Plants and Microorganisms, Academy of Sciences of the USSR, Saratov 410015. N. G. Chernyshevskii Saratov State University, Saratov 410601. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 11, pp. 1489-1491, November, 1987. Original article submitted July 11, 1986.

0009-3122/87/2311-1189$12.50

TABLE 1. Distribution of Isomers with Different Position of Nitro Group in Nitration Products of Compounds I-IV, XVII, and XVIII

Initial compound	Reaction products (their content in mixture, %)	Ratio of content of α-isomer to β-isomer*	Method of determination of content of isomers	Literature
I	V (93), IX (XIII) (7)	13,3	Gravimetric	[2]
	V (80), IX (XIII) (20)	4	GLC	[3]
II	VI (85), X (15), XIV (0)	5,7	GLC	[4]
III	VII, XI (XV)	1,8	Gravimetric	[2]
	VII (76), XI (XV) (24)	3,2	not indicated	[5]
	VII (58±2), XI (XV) (42±2)	1,4	GLC	The present work
IV	VIII 50, XII (30), XVI (20)	1	NMR	[6]
	VIII (52±1), XII (31±2), XVI (17±1)	1,1	GLC	The present work
XVII	XIX (58±1), XXI (27±1), XXIII (15±1)	1,4	GLC	[1]
XVIII	XX (59±1), XXII (28±1), XXIV (13±2)	1,4	GLC	The present work

*In the case of formation of two β-isomers (see nitration of compounds IV, XVII, and XVIII), the ratio of the content of the α-isomers is given with respect to the overall amount of β-isomers.

the β-isomer* fraction in a given sequence of carbocycles was explained by the Mills-Nixon effect [8], which intensifies with the increase in the angular strain on transition from tetraline to indane. The authors of [10, 11] were doubtful of the existence of this effect. Nevertheless, it has been suggested that it may take place in the heterocyclic series [11]. Results were also described of a study of the electrophilic substitution reaction of fluorene, dibenzofuran, dibenzothiophene, and carbazole. The author of [12] concluded that decrease in the reactivity of the α-positions in condensed systems was caused by a strain in the ring at the stage of the transition state.

Table 1 gives the literature data on the isomeric composition of the compounds obtained by nitration of pyrroles I-IV, and our results on the nitration of compounds III, IV, XVII, and XVIII under similar conditions. It is seen that, in accordance with the data in [2, 5], the introduction of a methyl radical to the nitrogen atom appreciably increases the fraction of the β-isomers in the mixture of mononitropyrroles, compared with the distribution of the isomers in the nitration products of pyrrole [2, 3] and 2-methylpyrrole [4]. Their content increases sharply in particular in the simultaneous presence of methyl groups at the 1- and 2-positions [6].

Comparison of the distribution of the isomers in the nitration products of compounds IV, XVII, and XVIII (Table 1) shows that on transition from an acyclic homolog of pyrrole IV to cyclic analogs XVII and XVIII (among which the former is more strained than the latter), an increase in the content of the α-isomers is observed in the isomeric mixtures of the nitro derivatives. It is significant that the bicyclic compounds XVII and XVIII give almost equivalent results with respect to the distribution of the nitro derivatives. Thus, in contrast to o-xylene–tetraline–indane carbocyclic series, no increase in the fraction of

*The α- and β-isomers differ in the position of the nitro group in the aromatic ring. In the former, the nitro group is located at the ortho-position to the methyl group, tri- or tetramethylene chain, and in the latter it is in the meta-position.

the β-isomers is observed in the reaction products on transition from monocyclic compound IV to the corresponding bicyclic compounds XVII and XVIII. In the group of pyrrole compounds that we selected an almost opposite effect is evident.

Hence, in the case of pyrroles XVII and XVIII, the factors defined as the Mills–Nixon effect are either not effective or only weakly effective.

EXPERIMENTAL

The conditions of nitration of compounds III, IV, XVII, and XVIII, the preparation of the reaction products for analysis, their chromatographic analysis, and the statistical treatment of the measurement results are similar to those described in [1].

For the investigation we used 1-methylpyrrole (Ferak, Berlin), purified by distillation. 1,2-Dimethylpyrrole (IV) was prepared by a method described in [13], bp 138-139°C, n_D^{20} 1.4920, yield 41%. 1,2-Dihydropyrrolizine (XVII) and 1-(2-furyl)-4-aminobutane (XXV) were synthesized by the methods in [1, 14].

5,6,7,8-Tetrahydropyrrocoline (XVIII) was obtained by catalytic dehydration of 11.7 g (0.08 mole) of amine XXV [14] by the scheme described in [15]. Commercial aluminum oxide (GOST 8136-56), ground to 3-mm granules, was used as the catdalyst. Dehydration temperature was 390°C. The method of dehydration and isolation of the compound is similar to that described in [16]. Yield 2.4 g (24%), bp 87-90.5 (13 mm), n_D^{20} 1.5320.

LITERATURE CITED

1. L. N. Astakhova, I. M. Skvortsov, L. V. Safonova, and V. I. Makukhina, Khim. Geterotsikl. Soedin., No. 3, 320 (1986).
2. H. J. Anderson, Can. J. Chem., 35, 21 (1957).
3. A. R. Cooksey, K. J. Morgan, and D. P. Morrey, Tetrahedron, 26, 5101 (1970).
4. P. E. Sonnet, J. Heterocycl. Chem., 7, 399 (1970).
5. G. Doddi, P. Mencarelli, A. Razzini, and F. Stegel, J. Org. Chem., 44, 2321 (1979).
6. L. Grehn, Chem. Scr., 13, 67 (1978-1979).
7. L. I. Belen'kii, Khim. Geterotsikl. Soedin., No. 12, 1587 (1979).
8. J. Vaughan, G. J. Welch, and G. J. Wright, Tetrahedron, 21, 1665 (1965).
9. J. M. Patterson, J. Brasch, and P. Drenchko, J. Org. Chem., 26, 4712 (1961).
10. G. M. Badger, Q. Rev., 5, 147 (1951).
11. P. J. Garratt and D. N. Nicolaides, J. Org. Chem., 39, 2222 (1974).
12. R. J. Taylor, J. Chem. Soc. B, No. 12, 1559 (1968).
13. F. P. Doyle, M. D. Mehta, G. S. Sach, and J. L. Pearson, J. Chem. Soc., No. 12, 4458 (1958).
14. I. P. Skvortsov, N. A. Buntyakova, A. A. Stolyarchuk, and N. I. Ivanova, Khim.-Farm. Zh., No. 5, 66 (1977).
15. J. M. Patterson, J. Brasch, and P. Drenchko, J. Org. Chem., 27, 1652 (1962).
16. I. M. Skvortsov and I. V. Antipova, Khim. Geterotsikl. Soedin., No. 6, 764 (1978).