HETEROCYCLIC ANALOGS OF PLEIADIENE

43.* METALLATION OF THE 2-METHYL GROUP IN PERIMIDINES. KINETIC ACIDITIES OF 2-METHYL DERIVATIVES OF PERIMIDINE AND CONDENSED IMIDAZOLE SYSTEMS

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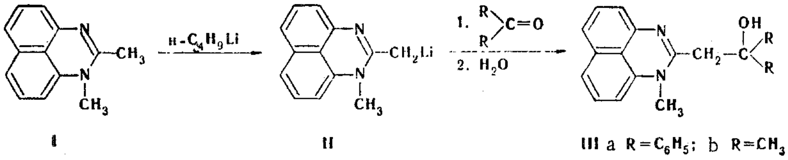
The 2-methyl group in perimidines has high CH acidity and is readily metallated, while only an addition reaction is realized in the case of the 1,2,3-trimethylperimidinium cation. The CH acidities of the 2-methyl groups of various imidazole systems under the conditions of basic deuterium exchange are compared.

It has been shown that, in contrast to N-substituted condensed imidazole systems, 1-substituted perimidines are not metallated by organometallic compounds but add them to the C = N bond to give 1,2-disubstituted 2,3-dihydroperimidines [1]. However, considering the high activity of the 2-methyl group of perimidines in reactions involving condensation with aldehydes [2, 3], one might have expected that products of metallation of the CH_3 group would be formed by the action of organometallic compounds on 1-substituted 2-methylperimidines.

We have established that metallation of the CH_3 group to give lithium derivative II in extremely high yield actually occurs in the reaction of n-butyllithium with 1,2-dimethylperimidine (I). Lithium derivative II can be detected by reaction with acetone or benzophenone, which leads to the previously unknown carbinols (III) of the perimidine series in ~70% yields. The IR spectra of alcohols III in dilute solutions of chloroform or CCl_4 show the presence of a chelated hydroxy group, and this confirms their structure. A strong intramolecular hydrogen bond is the reason for the weakening of the basis properties of the compounds obtained. For example, they form hydrochlorides with difficulty, and the hydrochlorides are hydrolyzed immediately when they are dissolved in water.

We were unable to establish the formation of organolithium compound II by means of other agents. Thus the starting compound is regenerated almost completely when carbon dioxide is used; this is evidently a consequence of the facile decarboxylation of the initially formed 1-methyl-2-perimidinylacetic acid (compare this with the data [4] on the instability of 2-perimidinylacetic acid). The reaction of aldehydes (benzaldehyde, acetaldehyde) with lithium derivative II leads to the formation of complex mixtures of substances that we were unable to separate.



It should be noted that the possibility of metallation of the 2-CH_3 group in perimidine I heretofore did not seem apparent. In fact, we have established [1] that 1-methyl-2-n-butylperimidine is converted only to 1-methyl-2,2-dibutyl-2,3-dihydroperimidine under the influence of n-butyllithium; an attempt to establish the possible product of metallation of the α-methylene group was unsuccessful. This confirms the previously expressed [5] idea that the ratio of the energies of activation of reactions involving the metallation and addition

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* See [9] for communication 42.

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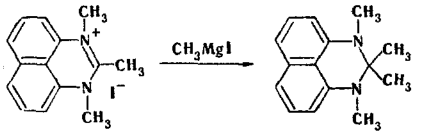
TABLE 1. Results of a Kinetic Study of Basic Deuterium Exchange for the 2-Methyl Groups of a Perimidine and Imidazoles

Compound	Temp., °C	$k \times 10^5$, sec^{-1}	E_a, kcal/mole	lg A	$-\lg k_{50}$
1,2-Dimethylperimidine	30 20 0	18,0 5,0 0,3	23,9	13,5	2,7
1,2-Dimethylnaphth[2,3-d]imidazole	35 20	15,0 2,3	22,4	12,1	3,0
2,3-Dimethylnaphth[1,2-d]imidazole	80 70	5,3 1,5	29,9	14,3	5,9
1,2-Dimethylbenzimidazole	70 55 40	13,0 2,0 0,24	28,5	15,3	5,0
1,2-Dimethylimidazole [7]	—	—	17,7	5,0	6,6

of organometallic compounds in the imidazole and perimidine series is extremely sensitive to the influence of various factors. The small decrease in the CH acidity of the α-methylene group in 1-methyl-2-n-butylperimidine evidently makes the metallation reaction more difficult as compared with the addition reaction. On the other hand, in the case of methylperimidine I metallation takes place initially, and the negative charge that develops on the methyl group makes the subsequent addition of butyllithium to the C = N bond of derivative II impossible. The energy balance again becomes directed in favor of the addition reaction in the reaction of the organometallic compounds with the 1,2,3-trimethylperimidinium cation. As we have established, 1,2,3-trimethylperimidinium iodide (IV) reacts with methylmagnesium iodide to give exclusively 1,2,2,3-tetramethyl-2,3-dihydroperimidine (V). This indicates that the onium center in salt IV favors the addition reaction to a greater degree than an increase in the acidity of the CH_3 group.



IV V

Since the methyl group in perimidine I is considerably more active in the reaction with butyllithium than, for example, 1,2-dimethylbenzimidazole [6], we made a comparison of the CH acidities of the 2-methyl groups in 1- and 2-methyl derivatives of various imidazole systems under the conditions of basic deuterium exchange. The results are presented in Table 1. The negative logarithms of the rate constants for H–D exchange reduced to 50°C (i.e., log k_{50}) provide evidence that the investigated compounds are arranged in the following order with respect to decreasing lability of the protons of the 2-CH_3 group: 1,2,-dimethylperimidine > 1,2-dimethylnaphth-[2,3-d]imidazole > 1,2-dimethylbenzimidazole > 2,3-dimethylnaphth[1,2-d]imidazole > 1,2-dimethylimidazole. The difference in the CH acidities between the most and least active compounds is approximately four orders of magnitude.

Thus, our study showed that the 2-methyl group in perimidines has extremely high CH acidity and is easily metallated; this fact can be used for preparative purposes.

EXPERIMENTAL

The IR spectra of solutions of the compounds in chloroform and carbon tetrachloride were obtained with a UR-20 spectrometer. The PMR spectrum was obtained with a Tesla spectrometer (the solvent was $CDCl_3$, and the internal standard was hexamethyldisiloxane). The method used to study the exchange reaction has been previously described [8].

General Method for Metallation and Preparation of Alcohols III. A solution of 1.9 g (0.01 mole) of 1,2-dimethylperimidine in 40 ml of absolute toluene was added to a cooled (to 0°C) ether solution of n-butyllithium obtained from 4.1 g (0.03 mole) of butyl bromide and 0.42 g (0.06 g-atom) of lithium in an inert atmosphere, and the mixture was stirred at 0°C for 1 h. A solution of 0.03 mole of the corresponding ketone in 20 ml of ether was then added, the cooling bath was removed, and stirring was continued for another hour. Water (20 ml) was added, and the precipitate was removed by filtration, washed successively with water and ether, and chromatographed with a column filled with aluminum oxide with collection of the first fraction (elution with benzene).

1-Methyl-2-(2,2-diphenyl-2-hydroxyethyl)perimidine (IIIa). This compound was obtained in 74% yield in the form of yellow crystals with mp 134-135°C (from benzene with octane). IR spectrum: 3370 cm^{-1} (OH, broad band of medium intensity). Found: C 82.5; H 5.8; N 7.1%. $C_{26}H_{22}N_2O$. Calculated: C 82.5; H 5.9; N 7.4%.

1-Methyl-2-(2-methyl-2-hydroxypropyl)perimidine (IIIb). This compound was obtained in 68% yield in the form of yellow crystals with mp 107-108°C (from petroleum ether). IR spectrum: 3380 cm^{-1} (OH, broad band of medium intensity). Found: C 76.1; H 7.3; N 10.8%. $C_{16}H_{18}N_2O$. Calculated: C 75.6; H 7.1; N 11.0%.

1,2,2,3-Tetramethyl-2,3-dihydroperimidine (V). A 1.1-g (0.003 mole) sample of 1,2,3-trimethylperimidinium iodide (IV) was added to a solution of methylmagnesium iodide obtained from 0.25 g (0.01 g-atom) of magnesium and 2.65 g (0.015 mole) of methyl iodide in 50 ml of absolute ether, and the suspension was refluxed with stirring until the solution became colorless. It was then cooled and treated with 40 ml of water, and the ether layer was separated and dried with calcium chloride. The ether was removed by distillation to give colorless crystals of V, which were recrystallized from alcohol to give 0.5 g (75%) of a product with mp 59-60°C. PMR spectrum: 1.32 (s, 6H, $C-CH_3$), 2.88 (s, 6H, $N-CH_3$), 6.55 (q, 2H, 4-H, 9-H), and 7.2 ppm (m, 4-H, 5-H, 6-H, 7-H, 8-H). Found: C 78.8; H 8.3; N 12.2%. $C_{15}H_{18}N_2$. Calculated: C 79.2; H 8.0; N 12.4%.

LITERATURE CITED

1. A. F. Pozharskii, L. P. Smirnova, B. A. Tertov, I. S. Kashparov, and V. I. Sokolov, Khim. Geterotsikl. Soedin., No. 12, 1682 (1975).
2. V. A. Anisimova and A. F. Pozharskii, Khim. Geterotsikl. Soedin., No. 1, 137 (1974).
3. S. I. Drusvyatskaya, B. V. Lopatin, A. F. Bekhli, A. I. Krotov, and A. S. Naidenova, Khim.-Farm. Zh., No. 5, 61 (1976).
4. R. F. Smith and M. M. Holmer, J. Chem. Soc., No. 12, 7531 (1965).
5. A. I. Belyashova, N. N. Zatsepina, E. N. Malysheva, A. F. Pozharskii, L. P. Smirnova, and I. F. Tupitsyn, Khim. Geterotsikl. Soedin., No. 11, 1544 (1977).
6. B. A. Tertov, A. S. Morkovnik, and Yu. G. Bogachev, Khim. Geterotsikl. Soedin., No. 12, 1699 (1976).
7. N. N. Zatsepina and I. F. Tupitsyn, Khim. Geterotsikl. Soedin., No. 12, 1587 (1974).
8. N. N. Zatsepina, I. F. Tupitsyn, and L. S. Éfros, The Chemistry and Technology of Isotopes [in Russian], Vol. 56, Khimiya, Leningrad (1967).
9. A. F. Pozharskii and G. G. Yurchuk, Khim. Geterotsikl. Soedin., No. 3, 418 (1979).

HETEROCYCLIC ANALOGS OF PLEIADIENE

44.* AMBIDENT CHARACTER OF THE N ANION OF PERIMIDINE IN REACTIONS WITH BENZYL AND ALLYL HALIDES

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It is shown that the N anion of perimidine displays ambident character in its reactions with benzyl and allyl halides and gives products of C alkylation in the 4 position in addition to N-substituted perimidines.

The N anion (I) of perimidine differs from the N anions of other N-heteromatic systems with respect to its extremely facile oxidizability under the influence of air oxygen, which leads to the formation of an insoluble black substance [2]. There is no doubt that this peculiarity of the N anion of perimidine is a consequence of its exceptionally high π-surplus character, which is characteristic of even the neutral perimidine molecule [3].

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* See [1] for communication 43.

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