HYDROACRIDINES AND RELATED COMPOUNDS

XVI.* COMPARISON OF THE REDUCTIVE CAPACITIES OF 9,10-DISUBSTITUTED DECAHYDROACRIDINES

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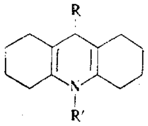
The effect of substituents in the 9 and 10 positions on the reductive capacities of 9,10-disubstituted decahydroacridines was established in the case of the reduction of organic dyes (Methylene Blue, Indigo Carmine, and Brilliant Green).

Continuing our research [2] on the reductive properties of N-substituted decahydroacridines, we ascertained the effect of the nature of the substituents in the 9 and 10 positions on the reductive activity of 9,10-disubstituted decahydroacridines (I-XXVI). Studies of this type have not been made for 1,4-disubstituted 1,4-dihydropyridines that do not contain electron-acceptor groups.

Most of the indicated decahydroacridines reduce the organic dyes Methylene Blue and Indigo Carmine, and some of them reduce Brilliant Green. Indigo Carmine is reduced in almost all cases only in acidic media (ionic hydrogenation), whereas the other two dyes, which contain cations, undergo reduction without the addition of acid.

The following orders (in the order of increasing decolorization time) were obtained with respect to the time required for decolorization of the dyes by various decahydroacridines in dimethylformamide (DMF). 1) Decolorization of Indigo Carmine: XV < XIV < XII < XIII ≪ XXI < II < I < XIX < XVI < XI < XXIV < VI < XXIII < XXII ≈ XXV. The last two members of the series did not decolorize Indigo Carmine under the experimental conditions. The Hantzsch ester (XXVII) decolorized it at about the same rate as VI and XXIII. 2) Decolorization of Methylene Blue: XV < XIV < XVIII < XIII < XVII < XI < VI < XXVII < III < IV < V < II < IX < I < XVI < XXVI. 3) Decolorization of Brilliant Green: XV < XVIII < XIV. The remaining decahydroacridines did not decolorize this dye.



I–XXVI

I R=R′=C_6H_5; II R=$C_6H_4OCH_3$-*p*, R′=C_6H_5; III R=$C_6H_4N(CH_3)_2$-*p*, R′=C_6H_5; IV R=α-furyl, R′=C_6H_5; V R=C_6H_5, R′=$C_6H_4OC_2H_5$-*p*; VI R=C_6H_5, R′=$C_6H_4N(C_2H_5)_2$-*p*; VII R=C_6H_5, R′=$C_6H_4NO_2$-*p*; VIII R=C_6H_5, R′=C_6H_4Br-*m*; IX R=C_6H_5, R′=$C_6H_4OCH_3$-*o*; X R=C_6H_5; R′=C_6H_4OH-*p*; XI R=$C_6H_4OCH_3$-*p*, R′=$C_6H_4N(C_2H_5)_2$-*p*; XII R=$C_6H_4OCH_3$-*p*, R′=$CH_2C_6H_5$; XIII R=C_6H_5, R′=$CH_2C_6H_5$; XIV R=CH_3, R′=$CH_2C_6H_5$; XV R=H, R′=$CH_2C_6H_5$; XVI R=C_6H_5, R′=$C_6H_4COOCH_3$-*p*; XVII R=CH_3, R′=$C_6H_4COOCH_3$-*p*; XVIII R=H, R′=$C_6H_4COOCH_3$-*p*; XIX R=C_6H_5, R′=C_6H_4OH-*o*; XX R=CH_3, R′=C_6H_4OH-*o*; XXI R=H, R′=C_6H_4OH-*o*; XXII R=C_6H_5, R′=$C_6H_4NH_2$-o; XXIII R=CH_3, R′=$C_6H_4NH_2$-*o*; XXIV R=H, R′=$C_6H_4NH_2$-*o*; XXV R=C_6H_5, R′=CH_2CH_2OH; XXVI R=C_6H_5, R′=cyclo-C_6H_{11}

The N-benzyl derivatives were the most active compounds. In particular, they decolorize Indigo Carmine in the presence of weak acids (oxalic and acetic), and XV decolorizes it even when acid is absent, whereas the other decahydroacridines decolorize it only when HCl is present and are inactive even in the presence of trifluoroacetic acid. The reductive capacities of the decahydroacridines depend on the nature

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* See [1] for communication XV.

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TABLE 1. Decahydroacridines II-XXVI

Compound	mp, °C	Found, %			Empirical formula	Calculated, %			Yield, %
		C	H	N		C	H	N	
II	114—116	83,8	8,0	4,0	$C_{26}H_{29}NO$	84,3	7,8	3,8	54
III	118—119	84,3	8,7	7,7	$C_{27}H_{32}N_2$	84,4	8,3	7,3	67
V	125—126	84,7	8,5	3,6	$C_{27}H_{31}NO$	84,2	8,1	3,6	35
VI	88—90	83,6	8,8	6,8	$C_{29}H_{36}N_2$	84,4	8,7	6,8	20
VII	132—134	77,4	6,9	7,0	$C_{25}H_{26}N_2O_2$	77,7	6,7	7,3	66
VIII	93—95	70,5	6,7	3,3	$C_{25}H_{30}NBr$	70,8	7,1	3,3	14
IX	133—135	83,6	7,9	3,8	$C_{26}H_{29}NO$	84,3	7,8	3,8	60
X	>100 (dec.)	83,2	7,5	3,2	$C_{25}H_{27}NO$	84,0	7,6	3,9	62
XI	136—137	—	—	6,9	$C_{30}H_{38}N_2O$	81,5	8,6	6,3	68
XII	67—69	83,3	8,3	4,2	$C_{27}H_{31}NO$	84,2	8,1	3,7	37
XIV	Oil	85,9	9,4		$C_{21}H_{27}N$	86,0	8,9	5,0	34
XV	37—38	86,6	8,4	5,1	$C_{20}H_{25}N$	86,0	9,2	4,9	34
XVII	80—82	78,1	8,3	4,4	$C_{22}H_{27}NO_2$	78,3	8,0	4,2	80
XXVI	94—96	85,8	9,7	4,0	$C_{25}H_{33}N$	86,5	9,5	4,0	58

TABLE 2. Conditions for the Reaction of Decahydroacridines with the Dyes

Dye	Decahydroacridines	Decahydroacridine concn., N	Decahydroacridine: dye ratio	Temp. °C	Acid
Indigo Carmine	I, II, VI, XI, XVI, XIX—XXV, XXVII	0,027	15 : 1	17	0,18M HCl
The same	XII, XIII, XV	0,015	15 : 1	25	0,3M $(COOH)_2$
Methylene Blue	I—VI, IX, XI, XVI, XVII, XXVI, XXVII	0,012	10 : 1	22	—
The same	XIII—XVIII	0,007	3 : 1	22	—
Brilliant Green	XIV, XV, XVIII	0,011	3 : 1	22	—

TABLE 3. Rate Constants for the Reduction of Methylene Blue

	I	II	III	V	VI	VII	VIII	X	XVI
k, liters · $mole^{-1}$ · sec^{-1}	10,3	14,9	32,2	15,0	50,8	0,44	1,9	14,2	1,3
k · 10^{-2}, sec^{-1}	1,0	1,7	2,4	2,0	5,7	—	0,2	—	0,2

of the substituent in the 9 position and decrease sharply in the substituent order H, CH_3, C_6H_5; this is in agreement with the data on the decrease in the reductive acitivity of 1,4-dihydropyridines when substituents are introduced in the 4 position [3]. Donor groups in the phenyl rings in both the 9 and 10 positions accelerate the reduction of the dyes, while acceptor groups slow it down. In particular, the diethylamino group slows down the reduction of Indigo Carmine in acidic media (I < VI) but accelerates the reduction of Methylene Blue when acid is absent (VI < I). The introduction of o-hydroxy and o-aminophenyl substituents in the 10 position leads to a decrease in the reductive activity of the decahydroacridines, evidently because of the five-ring structure of XIX-XXIV [4]. Opening of the azoline ring of these compounds, which is necessary for the manifestation of the reductive properties [4], evidently takes place with greater difficulty in the case of o-aminophenyldecahydroacridine than in the case of o-hydroxyphenyldecahydroacridine.

The rate of decolorization of the dyes depends on the solvent used: in the case of the reduction of Indigo Carmine and Methylene Blue with I, V, and XVI the decolorization time increased in the solvent order ethanol < acetone < DMF, and the order of decreasing reagent activity (V > I > XVI) was retained in all of the solvents. The decolorization time increased in the solvent order dioxane < ethanol < acetone < benzene < DMF in the reduction of Brilliant Green with XVIII. In general a certain tendency for acceleration of reduction in more polar solvents is traced; the particular activity of dioxane is probably due to this ability to form complexes

In order to quantitatively evaluate the effect of substituents in the phenyl rings of 9,10-diaryldecahydroacridine we investigated the kinetics of the reduction of Methylene Blue with two series of compounds: series A, composed of I, V-VIII, X, and XVI, and Series B, composed of I-III. The data obtained in ethanol at a decahydroacridine-to-Methylene Blue molar ratio of 2 : 1 with superimposition of the rate constants from a second-order rate equation showed that the log (k/k_0) values obtained (where k_0 is the rate constant in the case of I) correlate satisfactorily with the σ^0 constants of the corresponding substituents (Fig. 1). For series A, ρ =

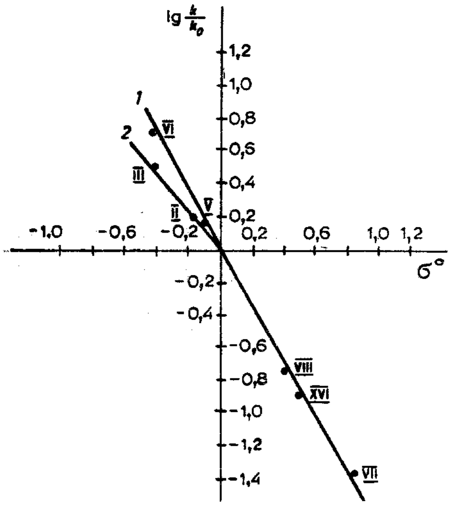

Fig. 1. Dependence of log (k/k_0) on σ^0: 1) series A; 2) series B.

-1.7, as compared with -1.1 for series B. This correlation is retained in the reduction in DMF at a decahydroacridine-to-Methylene Blue ratio of 10 : 1 in the case of calculation of the rate constants from a first-order rate equation (a pseudomonomolecular reaction). In this case $\rho = -1.8$ for series A, and $\rho = -0.9$ for series B. The data obtained may serve as an indication that hydride-ion transfer from the decahydroacridine to the compound undergoing reduction occurs in the bimolecular complex in the rate-determining step of the reduction; this is, in general, characteristic for 1,4-dihydropyridines [5]. Substituents in the phenyl rings of 9,10-diaryldecahydroacridine have only an inductive effect on the transition state, and this effect is stronger in the 10 position than in the 9 position.

EXPERIMENTAL

The solvents used in this research were purified by the method in [6]. Compounds I, IV, XIII, XVI, and XVIII-XXV were previously obtained in [4, 7, 8]. The remaining decahydroacridines, except for XV, were obtained for the first time from 2,2'-methylenedicyclohexanone (XXVIII) and 4-substituted 2,3-tetramethylenebicyclo[3.3.1]nonan-2-ol-9-ones (R = CH_3, C_6H_5) by reaction with the appropriate primary amines by a similar method (by refluxing with water separation in xylene for II, III, V, VI, IX-XI, XVII, and XXVI and in benzene for VIII, VII, and XII-XIV).

10-Benzyldecahydroacridine (XV). A 5.2-g (0.025 mole) of XXVIII and 3 g (0.028 mole) of benzylamine were dissolved in 10 ml of ethanol, and the solution was allowed to stand at room temperature in an argon atmosphere for 24 h, during which the initially formed oil gradually crystallized. The reaction product (XV) was removed by filtration and purified by freezing out from acetone–ethanol (1 : 3) at −50°. The compound rapidly turned brown in air. All of the spectra of the decahydroacridines obtained for the first time contain a characteristic double band at 1660-1690 cm^{-1}.

Kinetics of the Reduction of Methylene Blue. 1) Determined with a KF-5 colorimeter with a green-light filter at a cuvette thickness of 1 mm in a dry box in an argon atmosphere at 20°. The dihydroacridine-to-Methylene Blue molar ratio was 2 : 1, and the solvent was absolute ethanol. 2) Determined with an FÉK-M colorimeter with a green-light filter at a cuvette thickness of 5 mm at 20°. The dihydroacridine-to-Methylene Blue molar ratio was 10 : 1 and the solvent was DMF. The rate constants found by these methods are presented in Table 3.

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