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Features of Reactions of 10-Methyl-9,10-dihydroacridine Heteroanalogs with Imines

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Abstract—Relying on the values of the energy of the highest occupied molecular orbitals calculated ab initio a series of reactivity was established for ylides isomeric to 10-methyl-9,10-dihydroacridine, dibenzopyran, dibenzothiopyran, 1,3-benzodithiol, and the tentative threshold value was determined for imines reaction with the mentioned heterocycles. One- or two-stage imines interaction with 10-methyl-9,10-dihydroacridine or dibenzopyran was confirmed by two reactions of ionic hydroheterylation of N-benzylideneaniline in the presence of sodium tetrahydroborate by the cation of 10-methyl-9,10-dihydroacridinium or the cation of dibenzopyrylium.

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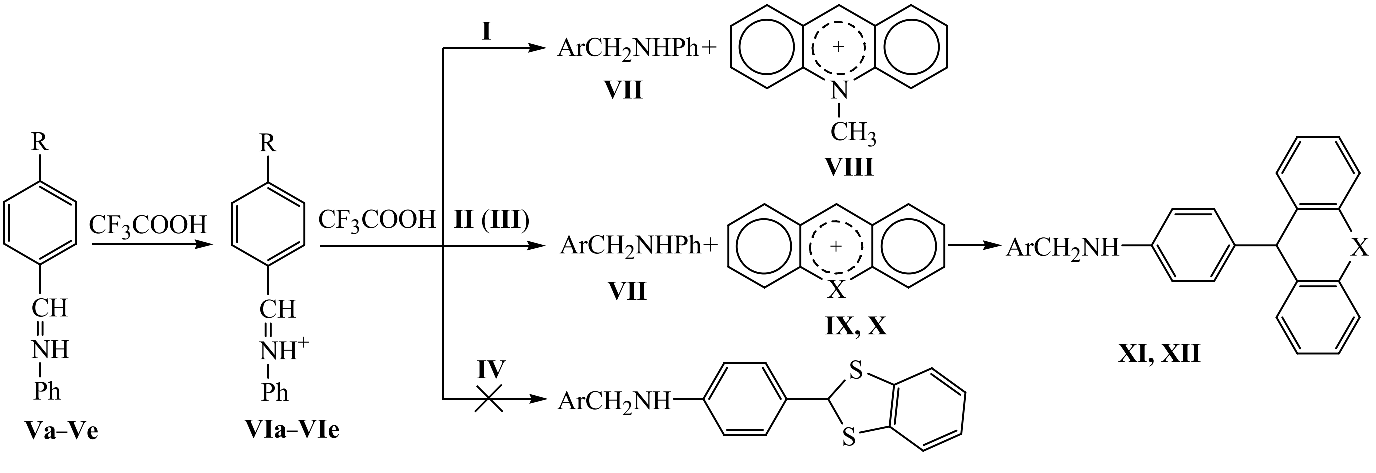
Among the heterocyclic compounds the 10-methyl-9,10-dihydroacridine and its heteroanalogs attract attention as compounds simulating the behavior of coenzyme NADH [1]. The investigation of dehydrogenation mechanisms of these H-nucleophiles extends the understanding of the hydride transfer reactions and supplements synthetic procedures [2–5].

We formerly demonstrated that the dehydrogeneration of 10-methyl-9,10-dihydroacridine (*N*-methylacridane) (**I**), dibenzopyran (xanthene) (**II**), dibenzothiopyran (thioxanthene) (**III**), and 1,3-benzodithiol (**IV**) with *N*-arylmethyleneanilines (imines) provided dissimilar results. For instance, *N*-methylacridane in the presence of trifluoroacetic acid reduced the C=N bond of imines **V** [6] (Scheme 1). Xanthene and thioxanthene under the same conditions formed products of reductive heterylation [7, 8]. 1,3-Benzodithiol in these conditions did not react with imines [9]; it was unexpected since compound **IV** in the known series of reactivity of these heterocycles [*N*-methylacridane > thioxanthene > 1,3-benzodithiol > xanthene (series 1)] took the third place. As hydride-ion acceptor here served tritylium cation and solvents pyridine

Scheme 1.



R = H (**a**), Cl (**b**), Br (**c**), OCH$_3$ (**d**), NO$_2$ (**e**); X = O (**IX, XI**), S (**X, XII**).

[10] or tetrahydrofuran [11]. Thus the reactivity order of the above heterocycles is strongly affected by the acceptor and the medium.

Another feature of these compounds dehydrogenetion by imines consists in the fact of greater reactivity of xanthene than thioxanthene. For instance, the thioxanthene unlike the xanthene did not react with *N*-benzylideneaniline and reacted only with imines containing electron-acceptor substituents (Cl, Br, NO_2) in the *para*-position of the benzene ring of the imine aldehyde fragment. The rate constants of reactions between 4-nitrobenzylideneaniline and xanthene or thioxanthene were equal to 4×10^{-4} and 1.3×10^{-4} l mol^{-1}s^{-1} respectively [6]. These data show the difference in the dehydrogenation mechanism of heterocyclic H-nucleophiles **I–IV** by a tritylium cation and by protonated imines.

In extension of this research we set a goal to establish the reason of the inconsistency between the reactivity of the N-methylacridane heteroanalogs and the known series (1), and to find the criteria governing the direction of the reaction, either imines reduction or their reductive heterylation.

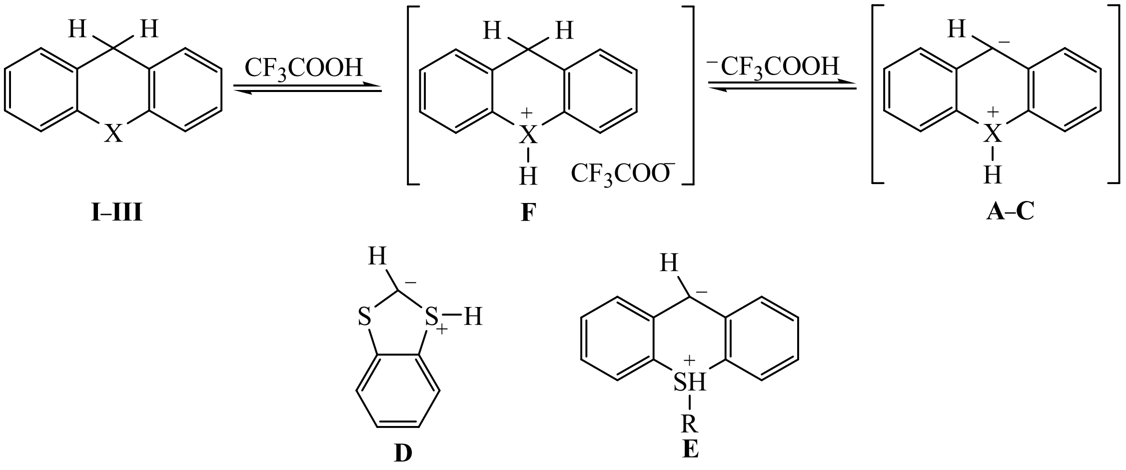
To elucidate the mechanism of hydrogen transfer to imines from the C–H group of *N*-methylacridane and its heteroanalogs we analyzed the energies of the frontier orbitals ΔE_{LUMO} of the protonated *N*-phenylmethyleneaniline (**VIa**), *N*-(4-chlorophenyl)methyleneaniline (**VIb**), *N*-(4-bromophenyl)methyleneaniline (**VIc**), *N*-(4-methoxyphenyl)methyleneaniline (**VId**), *N*-(4-nitrophenyl)methyleneaniline (**VIe**), ΔE_{HOMO} of heterocycles **I–IV** and their isomeric ylides of methylacridane **A**, xanthene **B**, thioxanthene **C,** 1,3-benzodithiola **D** calculated by nonempirical quantum-chemical method RHF/6-31G(d). We regard ylides as intermediate species in the reaction in question. The properties of such intermediates were considered by Kharchenko and Chalaya [12]. Describing the substituted thiabenzenes as very reactive and short-lived species they concluded that thiabenzenes were cyclic sulfonium ylides, e.g., ylide **E**. Our assumption on ylides involvement is also based on the important role of the trifluoroacetic acid for in its absence the reaction of the *N*-methylacridane heteroanalogs with the protonated imines does not occur.

We believe that in acid medium heterocycles **I–IV** are protonated to give salt **F** (for structures **I–III**) that can transform into the ylides **A–C** isomeric to the heterocycles (Scheme 2).

The calculated data (see the table) demonstrated a considerable increase in values of E_{HOMO}, in dipole moments and the negative charges on atoms C^9 or C^2 in ylides **A–D** compared with the same characteristics of heterocycles **I–IV** indicating the higher reactivity of the ylide structures.

Analysis of calculated values of the energy gaps between the protonated imines **VIa–VIe** and structures **I–IV**, **A–D** shows a considerable approach to each other of HOMO and LUMO energies of compounds **VIa–VIe** and ylides **A–D** compared to the energy difference of the fromtier orbitals of the same imines and heterocycles **I–IV**. For instance, the energy differences ΔE of reagent **VId** with N-methylacridane and N-methylacridane ylide

Scheme 2.



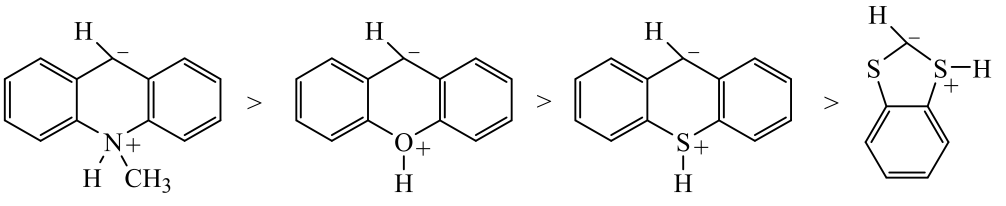
X = NCH_3 (I, **A**), O (II, **B**), S (III, **C**).

Energies of the highest occupied molecular orbitals (ΔE_{HOMO}), charges on atoms C^9 of structures **I–III**, **A–C**, or C^2 (**IV**, **D**) (*q*), dipole moments (μ), and energy gaps ΔE_{HOMO}(**I–IV**, **A–D**) – ΔE_{LUMO}(**VIa–VIe**) ($|\Delta E|$)

Compound	E_{HOMO}, eV	*q*, e	μ, D	$\lvert\Delta E_1\rvert$, eV[a]	$\lvert\Delta E_2\rvert$, eV[b]	$\lvert\Delta E_3\rvert$, eV[c]	$\lvert\Delta E_4\rvert$, eV[d]	$\lvert\Delta E_5\rvert$, eV[e]
I	–7.781	–0.310	0.917	5.222	4.852	4.663	4.662	4.400
II	–7.972	–0.291	1.176	5.413	5.043	4.854	4.853	4.591
III	–7.964	–0.378	1.709	5.405	5.035	4.846	4.845	4.583
IV	–7.994	–0.646	1.090	5.435	5.065	4.876	4.875	4.613
A	–5.153	–3.389	4.719	2.594	2.224	2.035	2.034	1.772
B	–5.455	–0.387	3.161	2.896	2.526	2.337	2.336	2.074
C	–5.666	–0.404	2.388	3.107	2.737	2.548	2.547	2.285
D	–6.949	–0.721	3.474	4.390	4.020	3.831	3.830	3.568

[a] ΔE_{LUMO} (**VId**) –2.559 eV. [b] ΔE_{LUMO} (**VIa**) –2.929 eV. [c] ΔE_{LUMO} (**VIc**) –3.118 eV. [d] ΔE_{LUMO} (**VIb**) –3.119 eV. [e] ΔE_{LUMO} (**VIe**) –3.381 eV

were 5.222 and 2.594 eV respectively. The comparison of the energy gaps values between the same protonated imine and ylides **A–D** shows that the minimum ΔE value always corresponds to the pair protonated imine–N-methylacridane ylide, and the maximum value, to the pair with the 1,3-benzodithiol ylide. Thus the ΔE_2 values calculated for the protonated N-phenylmethyleneaniline and ylides of N-methylacridane or 1,3-benzodithiol amount to 2.224 and 4.020 eV repectively. Besides the energy gaps between E_{LUMO} of protonated imine imine **VIa** and E_{HOMO} of xanthene ylide is significantly smaller (ΔE 2.526 eV) than the analogous difference with the E_{HOMO} of thioxanthene ylide (ΔE 2.737 eV) in agreement with the experimentally established fact of the partial transformation of the series (1): xanthene in the reaction of reductive heterylation is more active than thioxanthene. Consequently, by the reactivity the ylides of heterocycles **I–IV** form a series (2):



A **B** **C** **D**

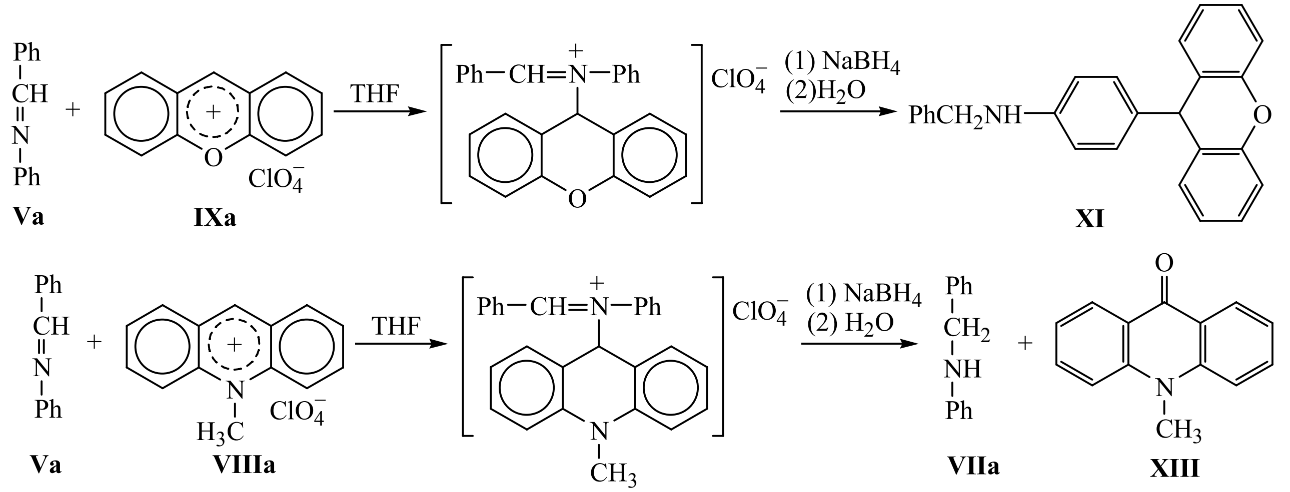
In series (2) 1,3-benzodithiol ylide **D** is on the last place and thus possesses the lowest reactivity. This is the reason why 1,3-benzodithiol (**IV**) does not react with imines under the studied conditions.

The calculated values of energy gaps ΔE for the reactions of ylides **A–D** with protonated imines containing electron-acceptor substituents (NO_2) are considerably lesser than for imines with the electron-donor substituents (OCH_3) in agreement with the experimental data on the reaction kinetics for imines and xanthene [6].

The value ΔE 2.737 eV characterizing the reaction of the protonated N-benzylideneaniline with the thioxanthene in the trifluoroacetic acid that leads to the formation of product traces can be tentatively regarded as the threshold value: Below this value the imine reactions with N-methylacridane heteroanalogs are possible, at higher values the reaction is impossible. It is important for the prediction of new reactions.

Hence the assumption of the oxidation with the protonated imines of ylides isomeric to the heterocycles is in agreement with the experimental data and the quantum-chemical calculations; therewith the ab initio procedure better fits to the experiment (in the case of 1,3-benzodithiol) than the preliminary analysis of the

Scheme 3.



reaction between imines and *N*-methylacridane heteroanalogs performed by the AM1 procedure [6].

In order to elucidate the reasons governing the direction of imine reactions with heterocycles **I–III** it was presumed that the reaction of *N*-arylmethyleneanilines **V** with H-nucleophiles (Scheme 1) proceeded in one or two stages. The first one-stage mechanism involves the ionic hydrogenation of imines in the system H-nucleophile–trifluoroacetic acid leading to the formation of *N*-arylmethylaniline **VII** and aromatic cation [*N*-methylacridinium (**VIII**), xanthylium (**IX**), thioxanthylium (**X**)]. Further cations **IX** or **X** react with amine **VII** to give *N*-arylmethyl-4-[(thio)xanthen-9-yl]-anilines **XI** and **XII**.

We compared the calculated values of electron affinity ($A = -E_{\mathrm{LUMO}}$) of cations N-methylacridinium (3.287 eV), xanthylium (3.955 eV), 1,3-benzodithiolium (4.007 eV), and thioxanthylium (4.089 eV. As seen, *N*-methylacridinium cation is a weaker electron acceptor than thioxanthylium cation. That is why the *N*-methylacridane only reduces the imines and the xanthylium and thioxanthylium cations formed in the course of the reaction effect the heterylation of secondary amines. To confirm experimentally the dependence of the reaction direction on the electron affinity of cation we studied the hydrogenation of N-benzylideneaniline (**Va**) in two systems: xanthylium perchlorate (**IXa**)–$NaBH_4$ and *N*-methylacridinium perchlorate (**VIIIa**)–$NaBH_4$ (Scheme 3) under the conditions we had described before [9].

We established that the first reaction proceeded as ionic hydroheterylation and afforded *N*-benzyl-4-(xanthen-9-yl)aniline (**XIa**) identical to the sample obtained by procedure [7]. The second reaction led only to reduction of imine **Va** to *N*-benzylaniline (**VIIa**) and to the formation of acridone **XIII**. In the latter case the role of cation **VIIIa** consisted only in the imine activation. The control experiment showed that in the absence of N-methylacridinium cation the *N*-benzylideneaniline was not reduced by sodium tetrahydroborate within 1 h. Thus the experiment confirms the dependence of the process described in Scheme 1 on the electron affinity of cations **VIII** and **IX**.

EXPERIMENTAL

***N*-Benzyl-4-(xanthen-9-yl)]aniline (XI).** To a mixture of 0.36 g (2 mmol) of imine **Va** and 0.56 g (2 mmol) of perchlorate **IXa** in 30 ml of THF was added 0.08 g (2.1 mmol) of $NaBH_4$ while stiring at 20°C, reaction time 30 min. The reaction mixture was poured into water, the separated precipitate was recrystallized from ethanol. Yield 0.51 g (70%), colorless crystals, mp 145–146°C [7].

***N*-Benzylaniline (VIIa).** To a mixture of 0.18 g (1 mmol) of imine **Va** and 0.29 g (1 mmol) of perchlorate **VIIIa** in 10 ml of THF while stiring at 20°C was added 0.08 g (2 mmol) of $NaBH_4$, reaction time 1 h. The precipitate was filtered off. The precipitate and the filtrate were diluted with water. From the filtrate a precipitate settled, *N*-benzylaniline (**VIIa**), colorless crystals, mp 38°C (37–38°C [13]). The hydrolysis of the precipitate provided 10-methyl-9*H*-acridone (**XIII**), yellow crystals, mp 201°C [14].

The quantum-chemical calculations were performed using software GAUSSIAN 03 W [15].

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REFERENCES

1. Matern, A.I., Charushin, V.N., and Chupakhin, O.N., *Usp. Khim.,* 2007, vol. 76, p. 27.
2. Yasui, S. and Ohno, A. *Bioorg. Chem.,* 1986, vol. 14, p. 70.
3. Parnes, Z.N. and Kursanov, D.N., *Reaktsii gidridnogo peremeshcheniya v organicheskoi khimii* (Reactions of Hydride Transition in Organic chemistry), Moscow: Nauka, 1969, p. 164.
4. Gronert, S. and Keeffe, J.R., *J. Am. Chem. Soc.,* 2005, vol. 127, p. 2324.
5. Pankratov, A.N. and Drevko, B.J., *J. Serb. Chem. Soc.,* 2004, vol. 69, p. 431.
6. Yunnikova, L.P. and Yunnikov, A.L., Dep. VINITI. Perm, 2002, no. 1909-V2002; *Ref. Zh. Khim.,* 2003, 13Zh56.
7. Yunnikova, L.P.*, Zh. Org. Khim*., 1995, vol. 31, p. 76.
8. Yunnikova, L.P., *Khim. Geterotsikl. Soedin.,* 1995, p. 1003.
9. Yunnikova, L.P. and Makhova, T.V., *Zh. Org. Khim.,* 2006, 42, p. 1872.
10. Izmail'skii, V.A., Ivanov, G.E., and Davydovskaya, Yu.A., *Zh. Obshch. Khim*., 1973, vol. 43, p. 2505.
11. Yunnikova, L.P. and Makhova, T.V., *Khim. Geterotsikl. Soedin.*, 2006, p. 1736.
12. Kharchenko, V.G. and Chalaya, S.N., *Tiopirany soli tiopiriliya i rodstvennye soedineniya* (Thiopyrans, Thiopirillium Salts and Related Compounds), Saratov: Izd. Saratov. Univ., 1987, p. 134.
13. Zechmeister, L. and Truka, J*., Ber.,* 1930, vol. 63, p. 2883.
14. Charbit, J.J., Galy, A.M., Galy, J.P., and Barbe, J., *J. Chem. Eng. Data,* 1989, vol. 34, p. 136.
15. Frisch, M.J., Trucks, G.W., Schlegel, H.B., Scuseria, G.E., Robb, M.A., Cheeseman, J.R., Montgomery, J.A. Jr., Vreven, T., Kudin, K.N., Burant, J.C., Millam, J.M., Iyengar, S.S., Tomasi, J., Barone, V., Mennucci, B., Cossi, M., Scalmani, G., Rega, N., Petersson, G.A., Nakatsuji, H., Hada, M., Ehara, M., Toyota, K., Fukuda, R., Hasegawa, J., Ishida, M., Nakajima, T., Honda, Y., Kitao, O., Nakai, H., Klene, M., Li, X., Knox, J.E., Hratchian, H.P., Cross, J.B., Bakken, V., Adamo, C., Jaramillo, J., Gomperts, R., Stratmann, R.E., Yazyev, O., Austin, A.J., Cammi, R., Pomelli, C., Ochterski, J.W., Ayala, P.Y., Morokuma, K., Voth, G.A., Salvador, P., Dannenberg, J.J., Zakrzewski, V.G., Dapprich, S., Daniels, A.D., Strain, M.C., Farkas, O., Malick, D.K., Rabuck, A.D., Raghavachari, K., Foresman, J.B., Ortiz, J.V., Cui, Q., Baboul, A.G., Clifford, S., Cioslowski, J., Stefanov, B.B., Liu, G., Liashenko, A., Piskorz, P., Komaromi, I., Martin, R.L., Fox, D.J., Keith, T., Al-Laham, M.A., Peng, C.Y., Nanayakkara, A., Shallacombe, M., Gill, P.M.W., Johnson, B., Chen, W., Wong, M.W., Gonzalez, C., and Pople, J.A., *Gaussian 03. Revision D.1,* Gaussian, Inc., CT 2005.