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1,3-Dipolar Cycloaddition of Azomethine Ylides Generated from Ketimines and Difluorocarbene to Symmetrically Substituted Olefins*

M. S. Novikov, A. F. Khlebnikov, and R. R. Kostikov

St. Petersburg State University, St. Petersburg, 198504, Russia

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Abstract—Iminiodifluoromethanides generated from difluorocarbene and benzophenone or fluorenone imines enter into reaction of 1,3-cycloaddition with electron-deficient alkenes to furnish pyrrolidone derivatives. The generation of iminiodifluoromethanides from alkyl *N*-benzhydrylidene glycinates in the presence of dipolarophiles is liable to complication by a concurrent proton shift in the initial imine giving NH-azomethine ylide also capable of 1,3-dipolar cycloaddition resulting in a side product of pyrrolidone series. The use of active lead instead of lead powder as reductant for dibromodifluoromethane in generation of difluorocarbene permits suppressing formation of the side products in these reactions.

Halogen-substituted nitrogen ylides are more and more extensively applied in heterocycles syntheses [1–7]. We formerly demonstrated that imines of aromatic and unsaturated aldehydes readily added dichloro- and difluorocarbenes yielding unstable *gem*-dichloro- [1, 2] and difluoro-substituted [3] azomethine ylides. These reactive intermediate are interesting for synthesis for they are capable of 1,3-dipolar cycloaddition to electron-deficient alkenes and alkynes providing respectively derivatives of pyrrolidones [8] and α-halopyrrolidones [9, 10]. Difluoromethylides are able besides to add to the carbonyl group of aldehydes affording oxazolidine derivatives [11]. The reactivity of ylides generated from dichlorocarbenes and ketimines is sufficiently studied [12–14]. It was shown that from aliphatic ketones at ylide configuration favorable for the intramolecular H-shift arose substituted formamides [12, 14]. Dichloro- and chlorofluoromethylides obtained from benzophenone imines always suffer 1,3-cyclization to yield gem-dihaloaziridines [13]. Interestingly in these cases the cyclization reaction occurred cleanly even in the presence of dipolarophiles, and the 1,3-dipolar cycloaddition of the intermediate ylides to multiple bonds is completely suppressed [14, 15]. It should be noted that the change of the benzylidene moiety in the ylide for a more sterically crowded benzhydrylidene one was not a sufficient condition of blocking cycloaddition reaction. For instance, ylides $Ph_2C{=}NH^+{-}C^-(X)CO_2R$ arising as a result of prototropic isomerization in *N*-benzhydrylidene derivatives of aminoacids readily add to activated double bonds even at X = CH_3 [16]. Thus it was presumable that decreasing the halosubstituted ylide fragment by changing chlorine for fluorine would permit occurrence of 1,3-dipolar cycloaddition also for ylides generated by reactions of benzophenone and fluorenone imines with halocarbenes.

We recently reported on the first example of 1,3-dipolar addition to dimethyl maleate of ylide **I** generated from difluorocarbene and ethyl-*N*-benzhydrilylidene glycinate (**II**) [15]. The isolated reaction product was pyrrolidone **III** originating from the hydrolysis of the primary cycloaddition adduct (Scheme 1).

In the present publication we report on results of investigation of 1,3-dipolar cycloaddition of ylides arising from difluorocarbene and benzophenone and fluorenone imines. As dipolarophiles we selected derivatives of maleic and fumaric acids. An attempt was made to estimate qualitatively the steric requirements for cycloaddition of ylide system $Ar_2C{=}N(R)^+{-}CF_2^-$ to electron-deficient alkenes.

Reactions of benzophenone *N*-methyl- (**IVa**) and *N*-benzylimines (**IVb**) with difluorocarbene generated by dibromodifluoromethane reduction with lead in the presence of tetrabutylammonium bromide [17] is

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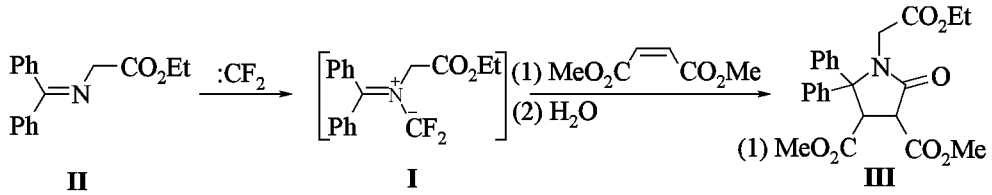
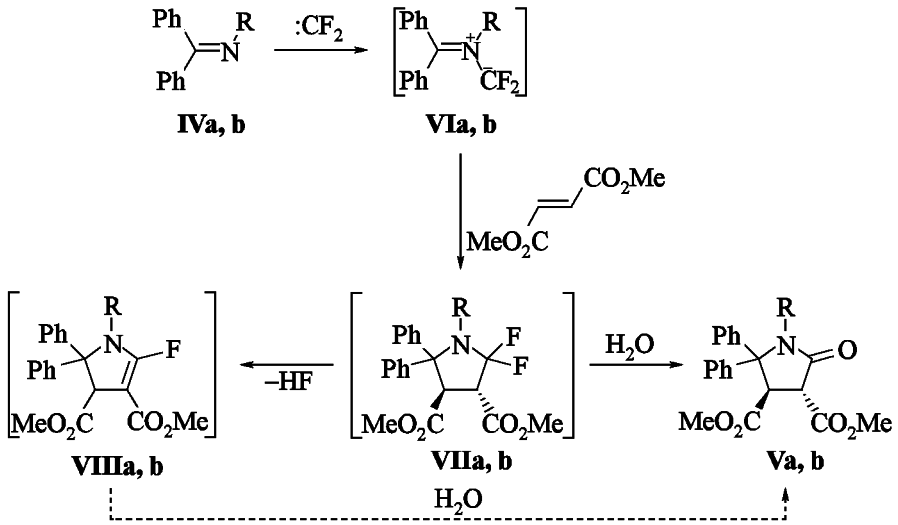
Scheme 1.



II **I** **III**

Scheme 2.



IVa, b **VIa, b**

VIIIa, b **VIIa, b** **Va, b**

H_2O

IV–**VIII**, R = Me (**a**), $PhCH_2$ (**b**).

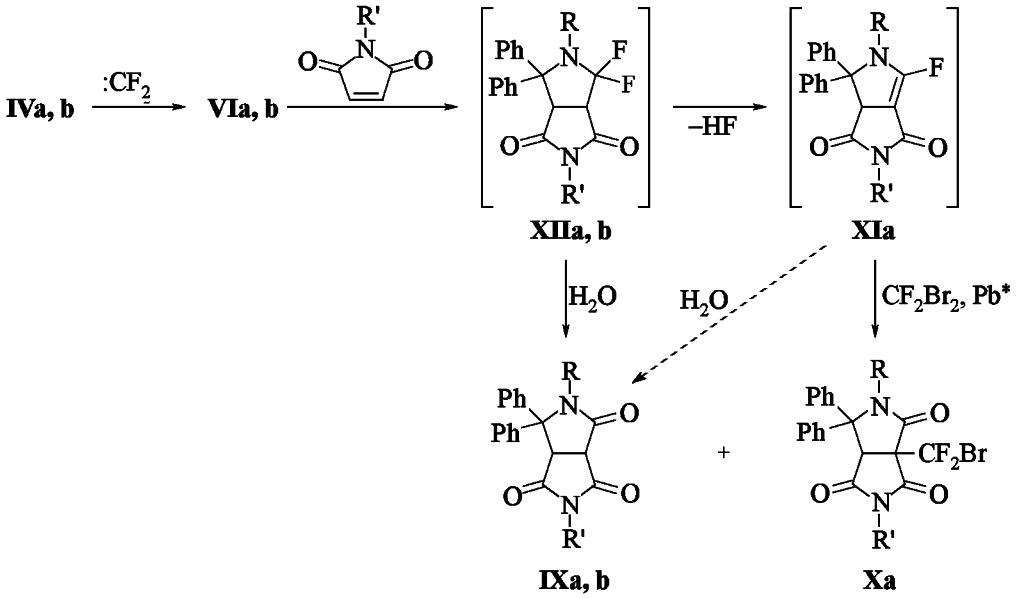
accompanied with notable tarring of the reaction mixtures and does not yield any stable products. However the reaction carried out in the presence of dimethyl fumarate gives rise to pyrrolidinones **Va, b** in 28 and 42% yield respectively. The reaction mechanism involves the difluorocarbene attack on the unshared electron pair of the imine nitrogen furnishing an unstable difluoromethylide **VIa** followed by 1,3-dipolar cycloaddition of the latter to the dimethyl fumarate. We failed to isolate the primary product of **VIa** addition since it suffered fast hydrolysis during the work-up of the reaction mixture affording the final pyrolidinone **V**. Apparently difluoropyrrolidines **VIIa, b** in the course of the reaction are totally or partially dehydrofluorinated to the corresponding pyrrolines, and the final pyrrolidinones arise from hydrolysis of these intermediates on silica gel. This assumption was concluded from the results of [18] where a reaction had been studied between the difluorocarbene and *N*-benzylidenebenzylamine in the presence of dimethyl fumarate, and in the reaction mixture alongside difluoropyrrolidines and pyrrolidinones had been found significant amounts of the corresponding 2-fluoro-Δ^2-pyrrolines.

The reactions of ylide **VIb** with *N*-ethyl and *N*-phenylmaleimides take a similar route and furnish bicyclic products **IXa, b**.

The reaction of methyl-*N*-benzhydrylidene glycinate (**XIII**) with difluorocarbene in the presence of *N*-ethylmaleimide occurred in a similar way and gave rise to diazabicyclo[3.3.0]octane (**XIVa**) which was isolated in 60% yield. However the same reaction carried out with *N*-aryl-substituted maleimides used as dipolarophiles was complicated by formation of a side product **XVb, c** that originated from addition of the substituted maleimide to azomethine ylide **XVI**. The latter arose as a result of a known azomethine–azomethine ylide tautomerism [19] observed in the series of alkylbenzhydrylidene glycinates [15, 16]. Imines of **XV** type form at boiling imine **XIII** in dichloromethane with the corresponding N-substituted maleimides for 1–2 days [16]. To suppress the unwanted formation of compounds **XV** the rate of difluoromethylide production depending on the efficiency of difluorocarbene generation should be increased.

We showed previously [10] that this can be achieved by the use for difluorocarbene generation instead

Scheme 3.



X–**XII**, R = Me, R' = Et (**a**), R = $PhCH_2$, R' = Ph (**b**).

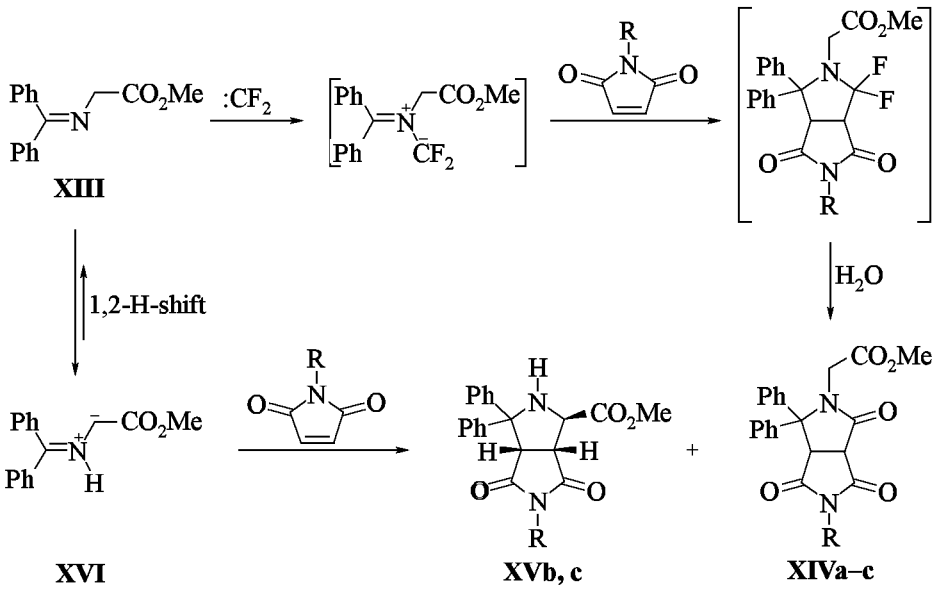
of lead filings an active lead produced by reduction of lead acetate with sodium borohydride. These reaction conditions were tested on the synthesis of compound **XVIc**: We found that conversion of lead significantly accelerated (reaction time decreased from 14 to 3 h), and the side product **XVc** did not form (see table).

We attempted in the same mode to reduce the process time in the above mentioned reactions of imines **IV** with difluorocarbene in the presence of N-substituted maleimides. However in this case the application of the active lead to the synthesis of compound **IX** was not justified. For instance, in the reaction of imine **IVa** with difluorocarbene in the presence of *N*-ethylmaleimide alongside the usual cycloaddition product **IXa** obtained in 58% yield formed a significant amount (16%) of side product **Xa** (Scheme 3). Trace amounts of cycloadducts with bromodifluoromethyl substituent attached to the nodal atom of the bicyclic system were detected in products of cycloaddition reactions to N-substituted maleimides

Yields of products and conditions of reaction between *N*-alkylketimines of general formula $Ar_2C{=}NCH_2R$ and difluorocarbene in the presence of dipolarophiles

Imine	R	Dipolarophile	Ratio imine : dipolarophile	Method-of :CF_2 generation	Reaction time, h	Reaction product	Yield, %
IVa	H	Dimethyl fumarate	1 : 2.5	*a*	13	**Va**	42
IVa	H	*N*-Ethylmaleimide	1 : 2.5	*a*	18	**IXa**	68
IVa	H	*N*-Ethylmaleimide	1 : 1.7	*b*	5	**IXa**	58
						Xa	16
IVb	Ph	Dimethyl fumarate	1 : 2.5	*a*	45	**Vb**	42
IVb	Ph	*N*-Phenylmaleimide	1 : 2	*a*	20	**IXb**	40
XIII	CO_2Me	*N*-Ethylmaleimide	1 : 2	*a*	23	**XIVa**	60
XIII	CO_2Me	*N*-(4-Methoxyphenyl)maleimide	1 : 2	*a*	33	**XIVb**	33
						XVb	28
XIII	CO_2Me	*N*-(4-Chlorophenyl)maleimide	1 : 2	*a*	14	**XIVc**	32
						XVc	14
XIII	CO_2Me	*N*-(4-Chlorophenyl)maleimide	1 : 2	*b*	3	**XIVc**	48
						XVc	0
XVIII	H	*N*-Ethylmaleimide	1 : 1.7	*b*	3	**XIX**	54
						XX	9

Scheme 4.



R = Et (**a**), 4-$MeOC_6H_4$ (**b**), 4-ClC_6H_4 (**c**).

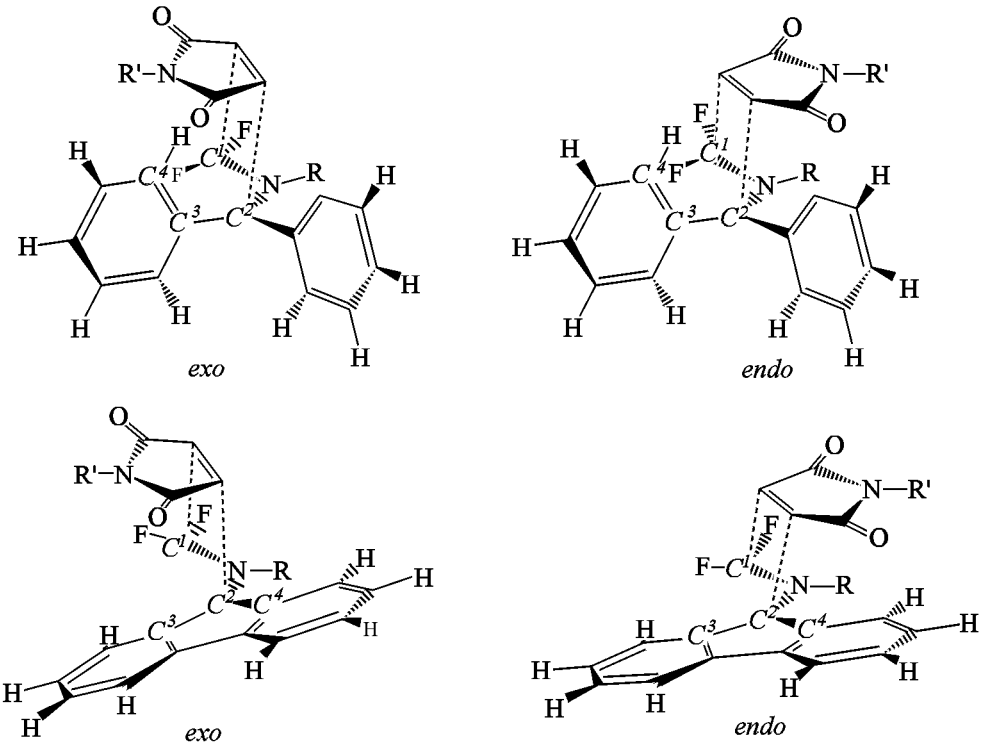
of difluoromethylides produced from aldimines under conditions of difluorocarbene generation by dibromodifluoromethane reduction with active lead [19]. Apparently the side process resulting in compound **Xa** consists in dibromodifluoromethane addition to the bicyclic fluoropyrroline intermediate **XI** that may arise from dehydrofluorination of difluoropyrrolidine intermediate **XIIa**. Due to angular strain these compounds should be considerably more active in addition reactions than monocyclic analogs of **VIII** type that do not give such addition products.

The addition of the N-substituted maleimides to ylides **IVa, b** can proceed only through an *endo*-transition state. The *exo*-transition state is unfavorable for benzene rings sterically hamper the approach of the dipolarophile: according to PM3 calculations the benzene rings form an angle of 81–87° to the plane of dipole C^1–N–C^2. The growing bulk of the N-substituent in the ylide should make the endo-addition also hardly probable. Actually, azomethine ylides generated by difluorocarbene addition to *N*-benzhydrylidenecyclohexylamine or methyl-*N*-benzhydrylidene alaninate do not enter into the cycloaddition reaction. Note however that elimination of one of the geminal phenyl substituents in ylide significantly increases its reactivity and allows bringing into cycloaddition reaction substrates with so bulky N-substituents as, e.g., cyclohexyl or *tert*-butyl [18].

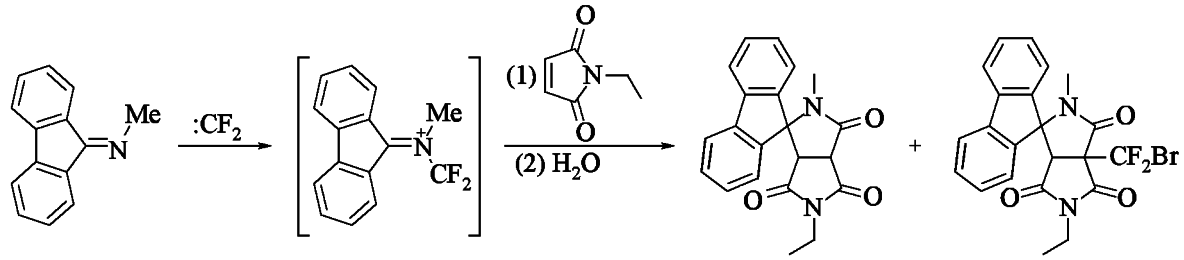
In difluoromethylide **XVII** the benzene rings lie in the same plane whose dihedral angle with the plane of dipole C^1–N–C^2 is 39.6°. Therefore unlike the case of benzophenone analog **IVa** the approach of dipolarophile is here basically probable both from the *endo*- and *exo*-side. Ylide **XVII** was generated from fluorenone *N*-methylimine (**XVIII**) and difluorocarbene in the presence of *N*-ethylmaleimide as dipole trap. From the reaction mixture were isolated by column chromatography cycloaddition products **XIX** and **XX** in 54 and 9% yield respectively. At the same time the reaction of difluorocarbene with fluorenone N-cyclohexylimine in the presence of *N*-ethylmaleimide did not yield any cycloaddition product. This fact is apparently due to the hindered approach of dipolarophile both from the *endo*- and *exo*-side at replacement of methyl substituent by cyclohexyl one as is mentioned above for benzophenone analogs.

Here the greater bulk of the N-substituent and the larger angle between the plane of the aromatic system C^3–C^2–C^4 and that of ylide C^1–N–C^2 (according to PM3 calculations the dihedral angle is 50.1°) inevitably result in shielding of the reaction sites of the dipole with H^1 and H^8 of the fluorene moiety.

Thus difluoromethylides generated by reaction of difluorocarbene with benzophenone and fluorenone N-alkylimines undergo 1,3-dipolar cycloaddition to electron-deficient alkenes yielding pyrrolidone derivatives when the initial imines contain primary alkyl substituents at the nitrogen. The branching at the α-carbon of the substituent results in total inhibition of the cycloaddition. Iminiodifluoromethanides generation from alkyl-*N*-benzhydrylidene glycinates in the presence of polarophiles is complicated by



concurrent prototropic isomerization of the initial imine into NH-azomethine ylide also capable of 1,3-dipolar cycloaddition providing a side product of pyrrolidine series. The use of active lead instead of lead powder as reductant for dibromodifluoromethane in generation of difluorocarbene permits suppressing formation of the side products in these reactions.



XVIII **XVII** **XIX** **XX**

EXPERIMENTAL

IR spectra of compounds solutions in $CHCl_3$ were measured on spectrophotometer UR-20, cell thickness 400μ. NMR spectra were registered on spectrometer Bruker DPX-300 at operating frequencies 300 (^1H) and 75 (^{13}C) MHz. Elemental analyses were carried out on CHN-analyzed HP-185B. The reaction progress was monitored by TLC on Silufol-254 plates. The separation of reaction mixture by column chromatography was performed with the use of silica gel LS 5/40 (Chemapol).

N-Methyl- (**IVa**) and *N*-cyclohexylbenzhydrylideneamines (**IVb**) and *N*-methylhexafluorenylideneamine (**XVIII**) [20], *N*-cyclohexylfluorenylideneamine [21], *N*-benzylbenzhydrylideneamine [22], methyl-*N*-benzhydrylidene glycinate and methyl-*N*-benzhydrylidene alaninate [23] were prepared by published procedures.

Preparation of active lead. To a solution of 6.5 g (0.02 mol) of lead acetate in 20 ml of 2M solution of acetic acid at cooling with ice water was added dropwise while stirring a solution of 1.66 g (0.04 mol) of sodium borohydride in 5 ml of water. Then to the reaction mixture was added 20 ml of 2M acetic acid and dropwise was added another portion of the solution of 1.66 g (0.04 mol) of sodium borohydride in 5 ml of water. The precipitated black lead powder

was washed by decanting in succession with 1 M solution of acetic acid (3 × 30 ml), with water (3 × 5 ml), ethanol (3 × 5 ml), and dichloromethane (3 × 5 ml). After drying at 60–70°C (10 mm Hg) the active lead was at once used in reactions.

Imines reactions with difluorocarbene in the presence of derivatives of fumaric and maleic acids. (a) Into a flask of 50 ml capacity filled with argon was charged in succession 1.2 g (5.8 mmol) of fresh lead filings, 1.9 g (6.0 mmol) of tetrabutylammonium bromide, 10 ml of dichloromethane, 0.55 g 2.8 mmol) of imine **IVa**, 1.00 g (6.9 mmol) of dimethyl fumarate, and 1.92 g (9.2 mmol) of dibromodifluoromethane. Then the flask was tightly stoppered, and the mixture was stirred at 45°C till the lead was fully consumed. Into the mixture was added 3.8 g of silica gel (LS 40/100, Chemapol), the solvent was evaporated to dryness in a vacuum, and the powder obtained was charged into a chromatographic column packed with silica gel (LS 5/40, Chemapol). Elution was performed with hexane–ethyl acetate mixture. After recrystallization from a mixture Et_2O–hexane we obtained 0.43 g (42%) of **dimethyl (±)-(3*R*,4*R*)-1-methyl-5-oxo-2,2-diphenylpyrrolidine-3,4-dicarboxylate (Va)**, mp 146–148°C. IR spectrum (CCl_4), cm^{-1}: 3065 w, 3035 w, 2960, 1740 s, 1710 s, 1450, 1420 w, 1375, 1325 w, 1270, 1230, 1180, 1010. ^1H NMR spectrum ($CDCl_3$), δ, ppm: 2.52 s (3H, CH_3N), 3.44 s (3H, CH_3O), 3.85 s (3H, O–CH_3), 4.03 d (1H, H^3, *J* 10.8 Hz), 4.69 d (1H, H^4, *J* 10.8 Hz), 7.0–7.5 m (15H, H arom). ^{13}C NMR spectrum, δ, ppm: 27.2 (CH_3N), 48.9 (C^3), 51.8, 52.5, 52.8 (C^4, $2CH_3O$), 72.6 (C^2); 127.4, 128.1, 128.2, 128.2, 128.4, 128.9, 136.7, 138.0 (C_{Ph}); 167.5, 168.8, 168.9 (CO). Found, %: C 68.70; H 5.79; N 3.73. $C_{21}H_{21}NO_5$. Calculated, %: C 68.65; H 5.76; N 3.81.

(b) Into a flask of 50 ml capacity containing 1.8 g (8.7 mmol) of active lead under argon atmosphere was charged in succession 12 ml of anhydrous dichloromethane, 2.9 g (9.0 mmol) of tetrabutylammonium bromide, 1.08 g (4.3 mmol) of imine **XIII**, and 1.78 g (8.0 mmol) of *N*-ethylmaleimide. The mixture was cooled to 10–15°C with cold water, 3.0 g (14.3 mmol) of dibromodifluoromethane was added, the flask was tightly stoppered, and the reaction mixture was stirred at 45°C till complete consumption of lead (3 h). After work-up of the reaction mixture and products isolation by the same procedure as in method (a) above the product was recrystallized from ethyl–dichloromethane mixture. **Yield of methyl 2-[(±)-(3*aR*,6*aS*)-3,4,6-trioxo-1,1-diphenyl-5-(4-chlorophenyl)perhydropyrrolo[3,4-*c*]pyrrol-2-yl]-acetate (XIVc)** 1.01 g (48%), mp 232–234°C (Et_2O_CH2Cl2). IR spectrum ($CHCl_3$), cm^{-1}: 3070 br.w, 2955 w, 1785 w, 1730 s, 1495, 1450 w, 1410 w, 1370, 1290 w, 1100, 1020 w. ^1H NMR spectrum ($CDCl_3$), δ, ppm: 3.52 s (3H, CH_3O), 3.47 d (1H, CH_2, *J* 17.1 Hz), 4.33 d (1H, H^{6a}, *J* 9.2 Hz), 4.36 d (1H, CH_2, *J* 17.1 Hz), 4.71 d (1H, H^{3a}, *J* 9.2 Hz), 6.6–7.5 m (14H, H arom). ^{13}C NMR spectrum, δ, ppm: 43.2 (CH_2), 48.7, 51.0, 51.7 (C^{3a}, C^{6a}, CH_3O), 74.1 (C^1); 127.0, 128.2, 128.4, 128.7, 128.8, 129.3, 134.1, 136.8, 138.8 (C_{Ph}); 165.7, 166.7, 168.6, 172.1 (CO). Found, %: C 66.41; H 4.36; N 5.78. $C_{27}H_{21}N_2O_5$. Calculated, %: C 66.33; H 4.33; N 5.73.

Along procedure (a) from imine **XIII** and *N*-(4-chlorophenyl)maleimide was obtained compound **XIVb** (32%) and **methyl (±)-(3*aR*,6*aS*)-4,6-dioxo-3,3-diphenyl-5-(4-chlorophenyl)perhydropyrrolo-[3,4-*c*]-pyrrole-1-carboxylate (XVc)** (14%), mp 147–149°C (Et_2O_CH_2Cl_2). IR spectrum ($CHCl_3$), cm^{-1}: 3350 w, 3070 br.w, 2955 w, 1780 w, 1740, 1710 s, 1495, 1460 w, 1400, 1340 w, 1320 w, 1135 w, 1095. ^1H NMR spectrum ($CDCl_3$), δ, ppm: 2.91 d (1H, NH, *J* 6.2 Hz), 3.72 d.d (1H, H^{6a}, *J* 7.1, 7.5 Hz), 3.84 s (3H, CH_3O), 3.91 d.d (1H, H^1, *J* 6.2, 7.1 Hz), 4.32 d (1H, H^{3a}, *J* 7.5 Hz), 7.0–7.5 m (14H, H arom). ^{13}C NMR spectrum, δ, ppm: 48.6, 52.1, 52.4, 59.7 (C^1, C^{3a}, C^{6a}, CH_3O), 73.3 (C^3); 126.0, 126.9, 127.1, 127.5, 127.6, 127.7, 128.5, 128.9, 129.7, 133.9, 141.0, 144.0 (C_{Ph}); 170.2, 173.4, 174.4 (CO). Found, %: C 67.79; H 4.62; N 6.18. $C_{26}H_{21}ClN_2O_4$. Calculated, %: C 67.75; H 4.59; N 6.08.

The yields of compounds obtained and the conditions of reactions are given in the table.

Dimethyl (±)-(3*R*,4*R*)-1-benzyl-5-oxo-2,2-diphenylpyrrolidine-3,4-dicarboxylate (Vb). mp 187–189°C (Et_2O). IR spectrum (CCl_4), cm^{-1}: 3065 w, 3030 w, 2950 w, 1740, 1685 s, 1650 s, 1485, 1445, 1420, 1380, 1350, 1205, 1175, 1140, 960. ^1H NMR spectrum ($CDCl_3$), δ, ppm: 3.43 s (3H, CH_3), 3.72 d (1H, CH_2, *J* 15.0 Hz), 3.86 s (3H, CH_3), 3.97 d (1H, H^3, *J* 11.3 Hz), 4.77 d (1H, H^4, *J* 11.3 Hz), 4.92 d (1H, CH_2, *J* 15.0 Hz), 6.6–7.5 s (15H, H arom). ^{13}C NMR spectrum, δ, ppm: 45.3 (CH_2), 48.5 (C^3), 51.8 (CH_3), 52.3 (C^4), 52.8 (CH_3), 73.1 (C^2); 126.2, 127.3, 127.4, 127.5, 127.8, 128.1, 128.3, 128.4, 129.4, 136.3, 137.0, 137.1 (C_{Ph}); 168.5, 168.6, 168.9 (CO). Found, %: C 73.32; H 5.76; N 2.92. $C_{27}H_{25}NO_5$. Calculated, %: C 73.12; H 5.68; N 3.16.

(±)-(3*aR*,6*aS*)-5-Methyl-6,6-diphenyl-2-ethylperhydropyrrolo[3,4-*C*]pyrrole-1,3,4-trione (IXa). mp 197–199°C (Et_2O–CH_2Cl_2). IR spectrum ($CHCl_3$), cm^{-1}: 3045 br.w, 2940 w, 1780 w, 1715 s, 1450 w, 1400 w, 1380, 1350 w, 1250 w, 1120 w. ^1H NMR spectrum ($CDCl_3$), δ, ppm: 0.81 t (3H, CH_3C, *J* 7.2 Hz), 2.56 s (3H, CH_3N), 3.28 t (2H, CH_2, *J* 7.2 Hz), 4.01 d (1H, H^{6a}, *J* 9.2 Hz), 4.26 d (1H, H^{3a}, *J* 9.2 Hz), 7.1–7.4 m (10H, H arom). ^{13}C NMR spectrum, δ, ppm: 12.0 ($\underline{C}H_3C$), 28.3 ($\underline{C}H_3N$), 33.7 (CH_2), 49.0 and 51.6 (C^{3a}, C^{6a}), 73.8 (C^6); 127.6, 127.9, 128.2, 128.4, 136.2, 140.3 (C_{Ph}); 165.8, 169.9, 172.9 (CO). Found, %: C 72.64; H 5.78; N 7.80. $C_{21}H_{20}N_2O_3$. Calculated, %: C 72.40; H 5.79; N 8.04.

(±)-(3*aR*,6*aR*)-3*a*-Bromodifluoromethyl-5-methyl-6,6-diphenyl-2-ethylperhydropyrrolo-[3,4-*C*]pyrrole-1,3,4-trione (Xa). mp 198–199.5°C (Et_2O–CH_2Cl_2). IR spectrum ($CHCl_3$), cm^{-1}: 3050 br.w, 2945 w, 1785 w, 1725 s, 1450 w, 1400 w, 1375, 1350, 1245 w, 1130 w, 1045 w. ^1H NMR spectrum ($CDCl_3$), δ, ppm: 0.82 t (3H, CCH_3, *J* 7.3 Hz), 2.64 s (3H, CH_3N), 3.13–3.37 s (2H, CH_2), 4.39 s (1H, H^{6a}), 7.0–7.5 s (10H, H arom). ^{13}C NMR spectrum, δ, ppm: 11.6 (CH_3), 29.4 ($\underline{C}H_3N$), 34.5 (CH_2), 56.8 (C^{6a}), 65.9 d.d (C^{3a}, $^2J_{CF}$ 22.7, 19.9 Hz), 72.3 (C^6), 127.6, 118.1 d.d (CF_2Br, $^1J_{CF}$ 316.2, 312.9 Hz); 127.9, 128.2, 128.5, 128.6, 128.8, 135.8, 139.1 (C_{Ph}); 160.7, 165.0, 171.1 (CO). Found, %: C 55.20; H 4.15; N 5.75. $C_{22}H_{19}BrF_2N_2O_3$. Calculated, %: C 55.36; H 4.01; N 5.87.

(±)-(3*aR*,6*aS*)-5-Benzyl-2,6,6-triphenylperhydropyrrolo[3,4-*C*]pyrrole-1,3,4-trione (IXb). mp 259–260°C (Et_2O–CH_2Cl_2). IR spectrum ($CHCl_3$), cm^{-1}: 3070 w, 3050 w, 3015 w, 2950 br.w, 1780 w, 1725 s, 1690, 1500, 1450 w, 1405 w, 1375, 1350, 1290 w, 1140 w. ^1H NMR spectrum ($CDCl_3$), δ, ppm: 3.80 d (1H, CH_2, *J* 14.9 Hz), 4.21 d (1H, H^{6a}, *J* 9.5 Hz), 4.56 d (1H, H^{3a}, *J* 9.5 Hz), 4.91 d (1H, CH_2, *J* 14.9 Hz), 6.5–7.4 m (10H, H arom). ^{13}C NMR spectrum, δ, ppm: 46.3 (CH_2), 48.7, 52.4 (C^{3a}, C^{6a}), 74.8 (C^6); 125.7, 126.5, 127.5, 127.8, 128.1, 128.3, 128.3, 128.6, 128.8, 129.1, 130.7, 136.1, 136.5, 139.2 (C_{Ph}); 166.1, 168.8, 172.5 (CO). Found, %: C 78.87; H 5.11; N 6.01. $C_{27}H_{22}N_2O_5$. Calculated, %: C 78.80; H 5.12; N 5.93.

Methyl 2-[(±)-(3*aR*,6*aS*)-3,4,6-trioxo-1,1-diphenyl-5-ethylperhydropyrrolo[3,4-*c*]pyrrol-2-yl]-acetate (XIVa). mp 190–191.5°C (Et_2O–CH_2Cl_2). IR spectrum ($CHCl_3$), cm^{-1}: 3070 w, 3010 w, 3015 w, 2955 w, 1785, 1765, 1720 s, 1695 w, 1450, 1405 w, 1390, 1380, 1350, 1290 w, 1190 w, 1095 w. ^1H NMR spectrum ($CDCl_3$), δ, ppm: 0.77 t (3H, CCH_3 *J* 7.1 Hz), 3.26 q (2H, CH_2, *J* 7.1 Hz), 3.36 s (3H, OCH_3), 3.47 d (1H, CH_2, *J* 17.2 Hz), 4.08 d (1H, H^{6a}, *J* 9.1 Hz), 4.26 d (1H, CH_2, *J* 17.2 Hz), 4.45 d (1H, H^{3a}, *J* 9.1 Hz), 7.1–7.4 m (10H, H arom). ^{13}C NMR spectrum, δ, ppm: 12.0 (CH_3), 33.8 (CH_2), 43.3 ($\underline{C}H_2CO$), 48.6, 50.9, 51.7 (C^{3a}, C^{6a}, CH_3O), 73.8 (C^1); 128.0, 128.1, 128.4, 128.6, 128.6, 136.7, 139.4, (C_{Ph}); 165.9, 166.7, 169.4, 172.8 (CO). Found, %: C 67.89; H 5.45; N 6.93. $C_{23}H_{22}N_2O_5$. Calculated, %: C 67.97; H 5.46; N 6.89.

Methyl 2-[(±)-(3*aR*,6*aS*)-5-(4-methoxyphenyl)-3,4,6-trioxo-1,1-diphenylperhydropyrrolo-[3,4-*c*]-pyrrol-2-yl]acetate (XIVb). mp 201–203°C (Et_2O–CH2Cl2). IR spectrum ($CHCl_3$), cm^{-1}: 3070 br.w, 2960 w, 2845 w, 1790 w, 1730 s, 1610 w, 1520, 1445 w, 1380, 1300 w, 1260, 1040 w. ^1H NMR spectrum ($CDCl_3$), δ, ppm: 3.36 s (3H, CH_3), 3.48 d (1H, CH_2, *J* 17.2 Hz), 3.76 s (3H, CH_3), 4.26 d (1H, H^{6a}, *J* 9.3 Hz), 4.37 d (1H, CH_2, *J* 17.2 Hz), 4.66 d (1H, H^{3a}, *J* 9.3 Hz), 6.5–7.5 m (14H, H arom). ^{13}C NMR spectrum, δ, ppm: 43.2 (CH_2), 48.6, 51.0, 51.7, 55.1 (C^{3a}, C^{6a}, $2CH_3O$), 74.1 (C^1); 113.9, 123.4, 126.9, 128.2, 128.3, 128.4, 128.7, 136.8, 139.0, 159.1 (C_{Ph}); 165.8, 166.8, 168.9, 172.5 (CO). Found, %: C 69.37; H 5.00; N 5.79. $C_{28}H_{24}N_2O_6$. Calculated, %: C 69.41; H 4.96; N 5.78.

Methyl (±)-(3*aR*,6*aS*)-5-(4-methoxyphenyl)-4,6-dioxo-3,3-diphenylperhydropyrrolo-[3,4-*c*]pyrrole-1-carboxylate (XVb). mp 174–176°C (Et_2O–CH_2Cl_2). IR spectrum ($CHCl_3$), cm^{-1}: 3350 w, 3070 br.w, 2955 w, 2845 w, 1780 w, 1740, 1710 s, 1610 w, 1520, 1445, 1390, 1340 w, 1305 w, 1260, 1170, 1135, 1040. ^1H NMR spectrum ($CDCl_3$), δ, ppm: 2.93 d (1H, NH, *J* 7.0 Hz), 3.71 t (1H, H^{6a}, *J* 7.5 Hz), 3.79 s (3H, OCH_3), 3.84 s (3H, OCH_3), 3.91 d.d (1H, H^1, *J* 7.0, 7.5 Hz), 4.32 d (1H, H^{3a}, *J* 7.5 Hz), 6.8–7.4 m (14H, H arom). ^{13}C NMR spectrum, δ, ppm: 48.7, 52.0, 52.5, 55.1, 59.8 (C^1, C^{3a}, C^{6a}, $2CH_3O$), 73.3 (C^3); 114.0, 124.0, 126.1, 126.9, 127.1, 127.3, 127.4, 127.6, 128.5, 141.1, 144.2, 159.1 (C_{Ph}); 170.3, 173.8, 174.8 (CO). Found, %: C 70.90; H 5.32; N 6.14. $C_{27}H_{24}ClN_2O_5$. Calculated, %: C 71.04; H 5.30; N 6.14.

(±)-(3*aR*,6*aS*)-2-methyl-5-ethylspiro(perhydropyrrolo[3,4-*c*]pyrrole-1,9′-fluorene)-3,4,6-trione (XIX). mp 161–163°C (Et_2O–CH_2Cl_2). IR spectrum ($CHCl_3$), cm^{-1}: 3040 br.w, 2950 w, 1780 w, 1720 s, 1450 w, 1400 w, 1390, 1380, 1350, 1250 w, 1125 w, 1105 w, 1075 w. ^1H NMR spectrum ($CDCl_3$), δ, ppm: 1.18 t (3H, CCH_3, *J* 7.2 Hz),

2.30 s (3H, NCH_3), 3.54 m (2H, CH_2), 3.80 d (1H, $H^{3'a}$, *J* 9.2 Hz), 4.16 d (1H, $H^{6'a}$, *J* 9.2 Hz), 6.9–7.8 m (8H, H arom). ^{13}C NMR spectrum, δ, ppm: 12.5 ($\underline{C}H_3C$), 25.9 (CH_3N), 34.1 (CH_2), 47.5 and 48.8 ($C^{3'a}$, $C^{6'a}$), 73.1 ($C^{6'}$), 120.5, 122.3, 123.5, 127.3, 128.4, 129.7, 129.9, 139.5, 140.1, 140.7, 145.6 (C_{Ph}), 166.0, 170.3, 172.7 (CO). Found, %: C 72.88; H 5.22; N 7.90. $C_{22}H_{18}N_2O_3$. Calculated, %: C 72.82; H 5.24; N 8.09.

(±)-(3*aR*, 6*aS*)-3*a*-bromodifluoromethyl-2-methyl-5-ethylspiro(perhydropyrrolo[3,4-*c*]pyrrole-1,9'-fluorene)-3,4,6-trione (XX). mp 202–206°C (Et_2O–CH_2Cl_2). IR spectrum ($CHCl_3$), cm^{-1}: 3045 br.w, 2945 w, 2880 w, 1790 w, 1730 s, 1705, 1605 w, 1450, 1400 w, 1375, 1350, 1170 w, 1130, 1080 w, 1045 w, 1035 w. ^1H NMR spectrum ($CDCl_3$), δ, ppm: 1.21 t (3H, CH_3C, *J* 6.7 Hz), 2.38 s (3H, CH_3N), 3.57 m (2H, CH_2), 4.01 C (1H, H^{6a}), 6.8–7.8 m (8H, H arom). ^{13}C NMR spectrum, δ, ppm: 12.0 ($\underline{C}H_3C$), 26.6 (CH_3N), 34.8 (CH_2), 52.3 (C^{6a}), 66.0 d.d (C^{3a}, $^2J_{CF}$ 23.5, 19.1 Hz), 71.3 (C^1), 118.0 d.d (CF_2Br, $^1J_{CF}$ 317.9, 311.3 Hz), 120.5–145.6 (C_{Ph}), 160.5, 165.6 d ($^4J_{CF}$ 5.5 Hz), 170.4 (CO).

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