# Stereoselectivity of the Diels—Alder Cycloadditions, Sodium Borohydride Reduction and 1,3-Dipolar Cycloadditions to Furan Derivatives

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*N*-Phenyl- and *N*-(3,5-dichlorophenyl)maleimide react smoothly with furan to give *endo* and *exo* adducts depending on the reaction temperature. Semiempirical quantum-mechanical methods AM1 were used to rationalize this formation of adducts. The reduction of *exo* Diels—Alder adducts with sodium borohydride proceeds stereoselectively to yield the *exo* or *endo* hydroxylactams depending on the reaction temperature. 1,3-Dipolar cycloaddition of arylnitrile oxides to *exo* Diels—Alder adducts led exclusively to *exo-exo* cycloadducts.

With our effort to investigate the stereoselectivity of the cycloadditions to heterocyclic compounds [1—4] we have paid attention to the preparation of condensed isoxazolines based on the *exo* *N*-(3,5-dichlorophenyl)imide 7-oxabicyclo[2.2.1]hept-2-ene-5,6-dicarboxylates, since some compounds of dicarboximide type are reported to reveal effective systemic activity against *Botrytis cinerea, Cochliobolus miyabeanus*, and *Pellicularia sasaci* [5]. Reported here are the results of our studies on the stereoselectivity of the Diels—Alder cycloadditions to furan together with AM1 calculations, sodium borohydride reduction and 1,3-dipolar cycloadditions of arylnitrile oxides to furan adducts, which show that the corresponding *endo* or *exo* stereoselectivity depending on the reaction temperature can be achieved.

Maleimides are powerful dienophiles, reacting readily with a variety of dienes through a normal *endo* cycloaddition process [6, 7]. However, there are few publications relating to Diels—Alder cycloadditions of furan, acting as diene, mostly with *N*-phenylmaleimides [8, 9]. According to Ref. [8] furan (*I*) reacts with *N*-phenylmaleimide (*IIa*) to give *endo* adduct. Controversially, in our case furan reacts with *IIa* and *N*-(3,5-dichlorophenyl)maleimide (*IIb*), respectively, under mild conditions (room temperature) to furnish a mixture of *endo* adducts *IIIa, IIIb* and *exo* adducts *IVa, IVb*. An analysis of the $^1$H NMR spectra of the crude reaction mixture reveals the distribution of the individual products. Both, *endo-III* and *exo-IV* cycloadducts were formed in the mole ratio 78:22 (*IIa*) and 47:53 (*IIb*), respectively.

Elevated reaction temperature (reflux in ethyl acetate) gives rise exclusively to *exo* Diels—Alder adducts *IVa* and *IVb* in very good yields. The corresponding *endo* isomer *III* has not been detected in the crude reaction mixture by NMR spectroscopy (Scheme 1). Their structures have been assigned on the basis of the chemical shift data and multiplicity of signals in the $^1$H and $^{13}$C NMR spectra. The *exo* configuration of the imide moiety related to oxygen bridge in *III* has been deduced from the presence of singlets and the *endo* configuration in *IV* from the appearance of the H-6, H-5, H-1, and H-4 doublets in $^1$H NMR spectra.

Recently, an increasing interest in the synthesis of hydroxylactams has emerged [10, 11]. Partial reductions of cyclic imides with sodium borohydride to the corresponding hydroxylactams have been well studied [12—14], because of the importance of these products for the synthesis of alkaloids and other pharmacologically active compounds. Sodium borohydride reduction of the imide *IVa* in methanol at −20 °C gives exclusively *exo* hydroxylactam *Va*. Its structure has been assigned on the basis of the chemical shift data and multiplicity of signals in the $^1$H and $^{13}$C NMR spectra. The *exo* configuration of the C-9 hydroxyl group in *Va* has been deduced from the appearance of the H-9 doublet of doublets at $\delta = 5.79$ with the coupling constant $J_{1,9} = 7.0$ Hz and from the presence of an

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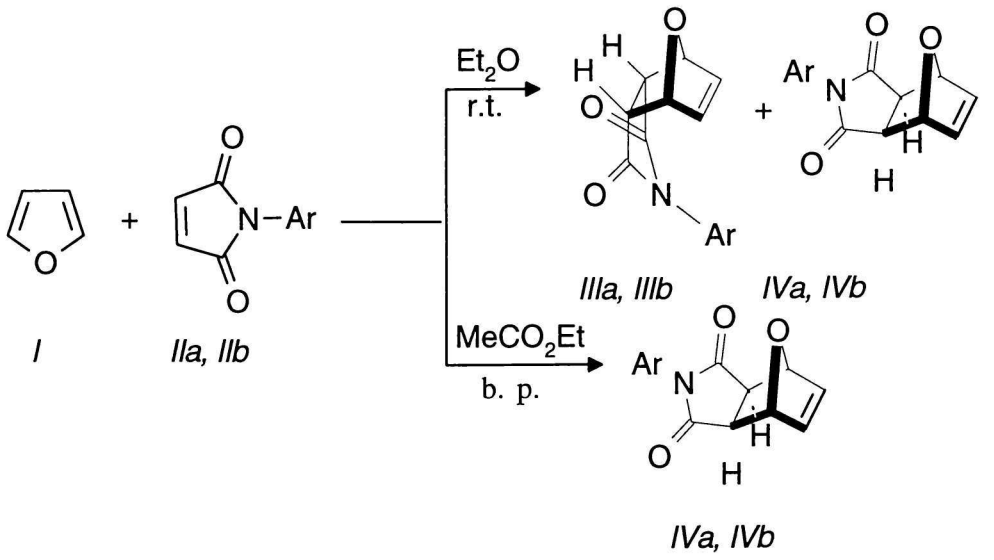
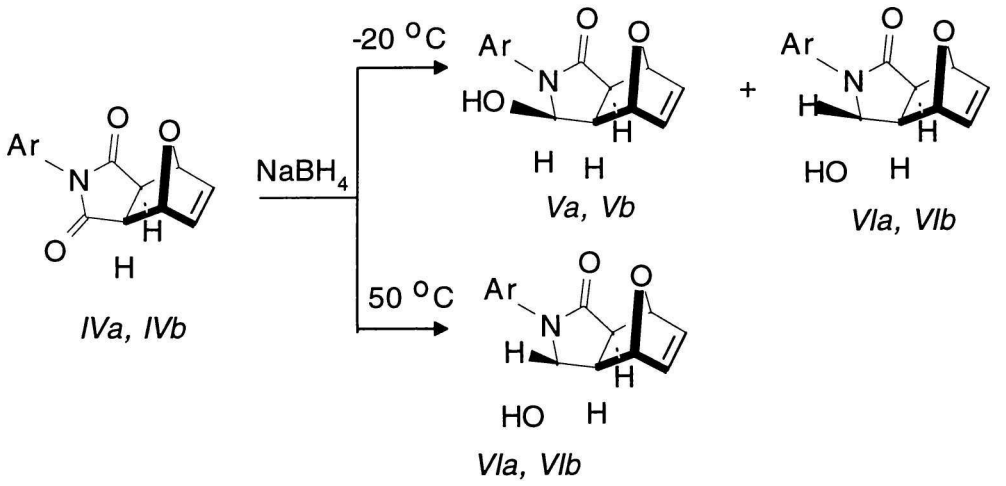
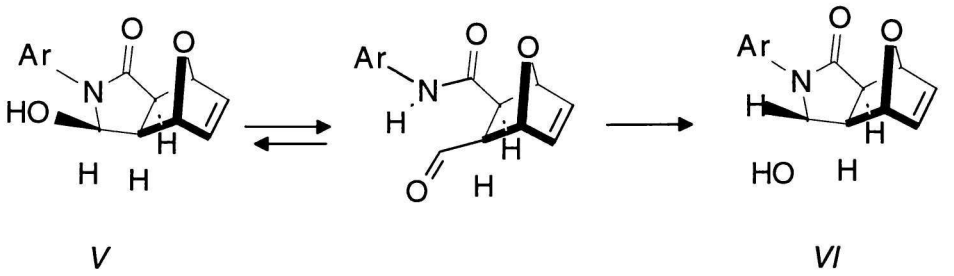



*Scheme 1.* *a* Ar = $C_6H_5$, *b* Ar = 3,5-$C_6H_3Cl_2$



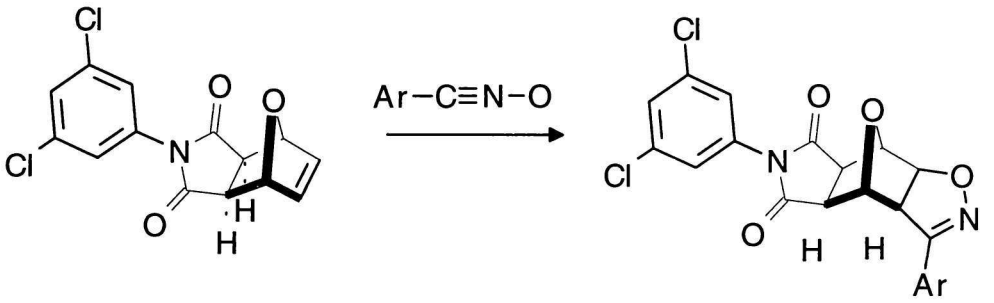




*Scheme 2.* *a* Ar = $C_6H_5$, *b* Ar = 3,5-$C_6H_3Cl_2$

OH doublet at $\delta = 6.32$ with the coupling constant $J_{9,OH} = 7.0$ Hz in $^1$H NMR spectra.

The correct stereochemical assignment of hydroxylactam *Va* has been clearly proved by a complete epimerization of *Va* to the corresponding *endo* diastereoisomer *VIa* by crystallization of the former compound in boiling ethanol. The transformation *Va* → *VIa* can be explained by a ring opening/ring closure mechanism (Scheme 2).

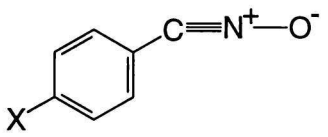
The suggested stereochemical arrangement is sup-




*IVb* *VIII*

| | | |
|---|---|---|
| *a* X = H | *e* X = 4-$NO_2$ | *i* X = 2-$NO_2$ |
| *b* X = 2,4,6-tri-$CH_3$ | *f* X = 4-Cl | *j* X = 2,4-$Cl_2$ |
| *c* X = 2-Cl | *g* X = 4-F | *k* X = 3-Cl |
| *d* X = 2-Br | *h* X = 3-$NO_2$ | *l* X = 4-$CH_3$ |

*Scheme 3*




*Formula 1*

ported by the different multiplicity of the H-9 proton in *Va* and *VIa*. The *endo* configuration of the C-9 hydroxyl group in *VIa* has been assigned on the basis of the presence of the H-9 doublet at $\delta = 5.42$ coupled solely only with the hydroxyl group. The reduction of *Va* in methanol at 50 °C results in the exclusive formation of *endo* product *VIa*. The reduction of dichloro derivative *Vb* (see Experimental) gives analogous results, only by the reduction at −20 °C an inseparable mixture of both epimers in the mole ratio of 83:17 in favour of *Vb* is formed.

When X-substituted benzenenitrile oxides were generated from the corresponding benzohydroximoyl chlorides and triethylamine in diethyl ether in the presence of *exo-IVb*, the *exo-exo* cycloadducts *VIIIa*—*VIIIl*, where X is H (*a*), 2,4,6-tri-$CH_3$ (*b*), 2-Cl (*c*), 2-Br (*d*), 4-$NO_2$ (*e*), 4-Cl (*f*), 4-F (*g*), 3-$NO_2$ (*h*), 2-$NO_2$ (*i*), 2,4-$Cl_2$ (*j*), 3-Cl (*k*), and 4-$CH_3$ (*l*), were formed together with the recovered starting material *IIb* and 3,4-diarylfuroxan, the nitrile oxide dimer [15] (Formula 1). The first prefix *exo* in *VIII* showed a relationship between imide moiety and oxygen bridge; the second one a relationship of isoxazoline moiety to oxygen bridge. The second possible *exo-endo* products have not been detected in the crude reaction mixture by NMR spectroscopy (Scheme 3).

The distinction between these possibilities was made on the basis of spectroscopic data, in particular using coupling constants and NOE experiments. For example, NMR spectrum of *VIIIa* showed the presence of doublets at $\delta = 3.46$, 3.62, 4.51, and 5.23, for H-4, H-3, H-6, and H-1 atoms. In *VIII* the zero coupling constants between H-1 and H-2 as well as between H-5 and H-6 are consistent only with *exo* stereochemistry, since in the *exo-endo* isomer the above-mentioned hydrogens would be nearly eclipsed, and would give rise to a much larger coupling constant. The NMR spectrum of the *exo-endo* stereoisomer would have doublet of doublets for the aforementioned H-1, H-2, H-5, and H-6 protons. This excludes the possibility that this is an *exo-endo* stereoisomer and proves that isolated adducts *VIII* result from the same kind of approach between nitrile oxide and dipolarophile *IVb*, namely that which binds the 1,3-dipole with the C=C double bond of *IVb* from the *exo* side to the oxygen bridge.

In order to rationalize the above cycloadditions, we have carried out quantum-mechanical calculations. Inspection of energy levels of furan (*I*) as well as *IIa* calculated by the AM1 method [16] shows that the cycloaddition is governed by the $HOMO_{diene}$ ($HOMO_I = -9.31$ eV, $HOMO_{IIa} = -9.06$ eV, $LUMO_{IIa} = -1.27$ eV, and $LUMO_I = 0.72$ eV) as the most of the Diels—Alder cycloadditions of maleimides [6, 7]. We tried to elucidate the formation of adducts through the relative thermodynamic stability. The geometries of all compounds *III* and *IV* were fully optimized by the AM1 method. The relative thermodynamic stabilities (kJ $mol^{-1}$) of *IIIa* (0.0) and *IVa* (7.8) calculated by AM1 showed that the *exo* derivative *IIIa* is a more stable one. Thus, AM1 results are in a very good agreement with experimental results.

## EXPERIMENTAL

Melting points are uncorrected, the $^1H$ and $^{13}C$ NMR spectra of deuterochloroform solutions were measured with Varian VXR 300 instrument, tetra-

methylsilane being the internal reference. Mass spectra were recorded at 70 eV on an AEI MS 902 spectrometer equipped with direct inlet system. All reagents were purified and dried if necessary prior to use. TLC analyses were carried out with $UV_{254}$ silica gel plates (Lachema, Brno).

### *N*-Arylimide 7-Oxabicyclo[2.2.1]hept-2-ene-5,6-dicarboxylates (*III* and *IV*)

To a solution of *N*-arylmaleimide *II* (70 mmol) in ethyl acetate (50 $cm^3$) furan (*I*) (105 mmol) was added (Scheme 1). The reaction mixture was refluxed for about 5 h (TLC) and then it was evaporated under diminished pressure, dried, and separated by chromatography on a silica gel column and purified by crystallization.

*exo-IVa*: Yield = 84 %, m.p. = 163—165 °C. For $C_{14}H_{11}NO_3$ ($M_r$ = 241.25) $w_i$(calc.): 69.70 % C, 4.60 % H, 5.81 % N; $w_i$(found): 69.65 % C, 4.36 % H, 5.62 % N. $^1$H NMR spectrum, $\delta$: 7.14—7.54 (m, 5H, $H_{arom}$), 6.63 (s, 2H, H-2 and H-3), 5.28 (s, 2H, H-1 and H-4), 3.10 (s, 2H, H-5 and H-6).

*exo-IVb*: Yield = 78 %, m.p. = 131—132 °C. For $C_{14}H_9Cl_2NO_3$ ($M_r$ = 308.99) $w_i$(calc.): 54.37 % C, 2.94 % H, 4.53 % N; $w_i$(found): 54.55 % C, 2.86 % H, 4.81 % N. $^1$H NMR spectrum, $\delta$: 7.28—7.73 (m, 3H, $H_{arom}$), 6.63 (s, 2H, H-2 and H-3), 5.29 (s, 2H, H-1 and H-4), 3.14 (s, 2H, H-5 and H-6).

Cycloaddition of *IIa* to furan at room temperature in ether afforded a mixture of *IIIa* and *IVa* in the mole ratio 78:22, yield = 80 %. Some relevant signals corresponding to *endo-IIIa* were also clearly observed in the spectra of some fractions containing additionally *IVa*. $^1$H NMR spectrum, $\delta$: 7.08—7.44 (m, 5H, $H_{arom}$), 6.63 (s, 2H, H-2 and H-3), 5.40 (d, 2H, H-1 and H-4), 3.71 (d, d, 2H, H-5 and H-6).

Cycloaddition of *IIb* to furan at room temperature in ether afforded a mixture of *IIIb* and *IVb* in the mole ratio 47:53, yield = 76 %. Some relevant signals corresponding to *endo-IIIb* were also clearly observed in the spectra of some fractions containing additionally *IVb*. $^1$H NMR spectrum, $\delta$: 7.24—7.75 (m, 3H, $H_{arom}$), 6.68 (s, 2H, H-2 and H-3), 5.43 (d, 2H, H-1 and H-4), 3.74 (d, d, 2H, H-5 and H-6).

### Reduction of *IV* with Sodium Borohydride to Hydroxylactams *V* and *VI*

Sodium borohydride (4.0 g; 106 mmol) was added to a stirred solution of *IV* (71 mmol) in methanol (50 $cm^3$) at −20 °C or 50 °C. Then a saturated aqueous ammonium chloride solution was added after stirring for 2 h and stirring was continued for 1 h. Methanol was removed from the mixture under reduced pressure, and the remaining aqueous solution was extracted with chloroform (3×20 $cm^3$), then with ethyl acetate (3×20 $cm^3$). The combined organic layers were dried with sodium sulfate and the solvent was removed *in vacuo*. The residue was separated on a silica gel column by using chloroform—methanol ($\varphi_r$ = 20:1) as the solvent.

*exo-Va*: Yield = 55 %, m.p. = 119—122 °C. For $C_{14}H_{13}NO_3$ ($M_r$ = 243.26) $w_i$(calc.): 69.12 % C, 5.39 % H, 5.76 % N; $w_i$(found): 68.98 % C, 5.24 % H, 5.52 % N. $^1$H NMR spectrum, $\delta$: 7.10—7.51 (m, 5H, $H_{arom}$), 6.53 (s, 2H, $H_{vinyl}$), 6.32 (d, $J_{9,OH}$ = 7.0 Hz, 1H, OH), 5.79 (dd, $J_{1,9}$ = 7.0 Hz, 1H, H-9), 5.26 (s, 1H, H-2), 5.08 (s, 1H, H-5), 2.45—2.71 (m, 2H, H-1 and H-6). IR spectrum, $\tilde{\nu}$/$cm^{-1}$: 3343 $\nu$(OH), 1690 $\nu$(C=O).

*endo-VIa*: Yield = 48 %, m.p. = 160—163 °C. For $C_{14}H_{13}NO_3$ ($M_r$ = 243.26) $w_i$(calc.): 69.12 % C, 5.39 % H, 5.76 % N; $w_i$(found): 69.08 % C, 5.54 % H, 5.82 % N. $^1$H NMR spectrum, $\delta$: 7.15—7.63 (m, 5H, $H_{arom}$), 6.50 (s, 2H, $H_{vinyl}$), 6.46 (d, $J_{9,OH}$ = 9.6 Hz, 1H, OH), 5.42 (d, 1H, H-9), 5.14 (s, 1H, H-2), 5.01 (s, 1H, H-5), 2.80 (d, $J_{1,6}$ = 7.0 Hz, 2H, H-1), 2.16 (d, 1H, H-6). IR spectrum, $\tilde{\nu}$/$cm^{-1}$: 3337 $\nu$(OH), 1673 $\nu$(C=O).

*endo-VIb:* Yield = 50 %, m.p. = 172—173 °C. For $C_{14}H_{11}Cl_2NO_3$ ($M_r$ = 311.01) $w_i$(calc.): 54.02 % C, 3.56 % H, 4.50 % N; $w_i$(found): 53.98 % C, 3.28 % H, 4.72 % N. $^1$H NMR spectrum, $\delta$: 7.40—7.83 (m, 3H, $H_{arom}$), 6.69 (d, $J_{9,OH}$ = 8.6 Hz, 1H, OH), 6.52 (s, 2H, $H_{vinyl}$), 5.61 (d, 1H, H-9), 5.18 (s, 1H, H-2), 5.06 (s, 1H, H-5), 2.90 (d, $J_{1,6}$ = 7.0 Hz, 2H, H-1), 2.21 (d, 1H, H-6). $^{13}$C NMR spectrum, $\delta$: 172.67 (s, C=O), 140.08, 136.75, 135.86, 134.02, 124.03, 119.52 ($C_{arom}$ and $C_{vinyl}$), 85.51 (d, C-9), 81.73 (d, C-5), 80.73 (d, C-2), 49.17 (d, C-6), 46.64 (d, C-1). IR spectrum, $\tilde{\nu}$/$cm^{-1}$: 3358 $\nu$(OH), 1676 $\nu$(C=O).

Reduction of *IVb* at −20 °C afforded a mixture of *Vb* and *VIb* in the mole ratio 83:17, yield = 66 %. Some relevant signals corresponding to *exo-Vb* were also clearly observed in the spectra of some fractions containing additionally *VIb*. $^1$H NMR spectrum, $\delta$: 7.38—7.65 (m, 3H, $H_{arom}$), 6.51 (s, 2H, $H_{vinyl}$), 5.87 (d, $J_{1,9}$ = 7.0 Hz, 1H, H-9), 5.29 (s, 1H, H-2), 5.10 (s, 1H, H-5), 2.70 (dd, $J_{1,6}$ = 8.0 Hz, 2H, H-1), 2.47 (d, 1H, H-6).

### 1,3-Dipolar Cycloaddition of *IV* to Cycloadducts *VIII*

Triethylamine (13 mmol) in ether (30 $cm^3$) was added to a stirred solution of arylhydroximoyl chloride (10 mmol) and the dipolarophile *IVb* (10 mmol) in ether (30 $cm^3$) at 0—5 °C within 1 h. The reaction mixture was stirred overnight at room temperature, the separated triethylammonium chloride was filtered off, removed by dissolving in water and organic material was evaporated under diminished pressure, dried, and separated by chromatography on a silica gel column and purified by crystallization.

*VIIIa*: Yield = 32 %, m.p. = 285—288 °C. For $C_{21}H_{14}Cl_2N_2O_4$ ($M_r$ = 429.26) $w_i$(calc.): 58.76 % C, 3.29 % H, 6.53 % N; $w_i$(found): 58.98 % C, 3.24 % H,

6.39 % N. $^1$H NMR spectrum, $\delta$: 7.37—7.83 (m, 8H, $H_{arom}$), 5.23 (d, $J_{1,6}$ = 8.4 Hz, 1H, H-1), 5.00 (s, 1H, H-2), 4.78 (s, 1H, H-5), 4.51 (d, 1H, H-6), 3.62 (d, $J_{3,4}$ = 7.2 Hz, 1H, H-3), 3.46 (d, 1H, H-4). $^{13}$C NMR spectrum, $\delta$: 175.36 (s, C=O), 175.20 (s, C=O), 154.83 (s, C-7), 134.38, 130.57, 129.34, 128.59, 128.29, 127.05, 125.85 ($C_{arom}$), 85.47 (d, C-1), 84.97 (d, C-2), 80.63 (d, C-5), 57.10 (d, C-6), 48.60 (d, C-3), 45.33 (d, C-4).

*VIIIb*: Yield = 40 %, m.p. = 239—243 °C. For $C_{24}H_{20}Cl_2N_2O_4$ ($M_r$ = 471.34) $w_i$(calc.): 61.16 % C, 4.28 % H, 5.94 % N; $w_i$(found): 61.33 % C, 4.44 % H, 6.11 % N. $^1$H NMR spectrum, $\delta$: 6.96—7.73 (m, 5H, $H_{arom}$), 5.19 (d, $J_{1,6}$ = 8.1 Hz, 1H, H-1), 5.04 (s, 1H, H-2), 4.48 (s, 1H, H-5), 4.30 (d, 1H, H-6), 3.43 (d, $J_{3,4}$ = 7.2 Hz, 1H, H-3), 3.33 (d, 1H, H-4), 2.26 (s, 3H, $CH_3$), 2.20 (s, 6H, 2 × $CH_3$). $^{13}$C NMR spectrum, $\delta$: 175.20 (s, C=O), 174.94 (s, C=O), 154.70 (s, C-7), 138.44, 136.67, 134.10, 128.64, 128.44, 128.31, 126.58, 125.52, 124.89 ($C_{arom}$), 84.72 (d, C-1), 84.00 (d, C-2), 79.59 (d, C-5), 60.59 (d, C-6), 48.14 (d, C-3), 45.29 (d, C-4), 20.68 (q, 2 × $CH_3$), 19.50 (q, $CH_3$).

*VIIIc*: Yield = 65 %, m.p. = 174—177 °C. For $C_{21}H_{13}Cl_3N_2O_4$ ($M_r$ = 463.70) $w_i$(calc.): 54.39 % C, 2.83 % H, 6.04 % N; $w_i$(found): 54.61 % C, 2.74 % H, 6.38 % N. $^1$H NMR spectrum, $\delta$: 7.28—7.68 (m, 7H, $H_{arom}$), 5.25 (d, $J_{1,6}$ = 8.1 Hz, 1H, H-1), 5.02 (s, 1H, H-2), 4.60 (s, 1H, H-5), 4.59 (d, 1H, H-6), 3.50 (d, $J_{3,4}$ = 7.2 Hz, 1H, H-3), 3.39 (d, 1H, H-4). $^{13}$C NMR spectrum, $\delta$: 175.03 (s, C=O), 174.88 (s, C=O), 153.92 (s, C-7), 134.14, 131.91, 131.52, 131.14, 130.57, 128.33, 127.63, 127.32, 125.59 ($C_{arom}$), 85.03 (d, C-1), 84.66 (d, C-2), 79.85 (d, C-5), 59.14 (d, C-6), 48.14 (d, C-3), 45.19 (d, C-4).

*VIIId*: Yield = 73 %, m.p. = 189—192 °C. For $C_{21}H_{13}BrCl_2N_2O_4$ ($M_r$ = 508.16) $w_i$(calc.): 49.64 % C, 2.58 % H, 5.51 % N; $w_i$(found): 49.93 % C, 2.51 % H, 5.42 % N. $^1$H NMR spectrum, $\delta$: 7.40—7.85 (m, 7H, $H_{arom}$), 5.26 (d, $J_{1,6}$ = 8.4 Hz, 1H, H-1), 5.04 (s, 1H, H-2), 4.60 (s, 1H, H-5), 4.57 (d, 1H, H-6), 3.49 (d, $J_{3,4}$ = 6.9 Hz, 1H, H-3), 3.39 (d, 1H, H-4). $^{13}$C NMR spectrum, $\delta$: 175.11 (s, C=O), 174.93 (s, C=O), 154.97 (s, C-7), 134.13, 131.71, 131.34, 129.54, 128.39, 128.15, 125.66, 121.44 ($C_{arom}$), 84.98 (d, C-1), 84.69 (d, C-2), 79.71 (d, C-5), 59.38 (d, C-6), 48.15 (d, C-3), 45.18 (d, C-4).

*VIIIe*: Yield = 80 %, m.p. = 238—239 °C. For $C_{21}H_{13}Cl_2N_3O_6$ ($M_r$ = 474.26) $w_i$(calc.): 53.18 % C, 2.76 % H, 8.86 % N; $w_i$(found): 52.97 % C, 2.94 % H, 8.59 % N. $^1$H NMR spectrum, $\delta$: 7.36—8.34 (m, 7H, $H_{arom}$), 5.34 (d, $J_{1,6}$ = 7.8 Hz, 1H, H-1), 5.04 (s, 1H, H-2), 4.85 (s, 1H, H-5), 4.55 (d, 1H, H-6), 3.62 (d, $J_{3,4}$ = 7.2 Hz, 1H, H-3), 3.48 (d, 1H, H-4). $^{13}$C NMR spectrum, $\delta$: 175.05 (s, C=O), 174.92 (s, C=O), 153.94 (s, C-7), 148.17, 134.30, 134.19, 134.16, 128.40, 128.27, 125.63, 124.28 ($C_{arom}$), 86.47 (d, C-1), 84.66 (d, C-2), 80.31 (d, C-5), 56.42 (d, C-6), 48.42 (d, C-3), 45.09 (d, C-4).

*VIIIf*: Yield = 70 %, m.p. = 231—233 °C. For $C_{21}H_{13}Cl_3N_2O_4$ ($M_r$ = 463.70) $w_i$(calc.): 54.39 % C, 2.83 % H, 6.04 % N; $w_i$(found): 54.22 % C, 2.67 % H, 6.28 % N. $^1$H NMR spectrum, $\delta$: 7.36—7.86 (m, 7H, $H_{arom}$), 5.25 (d, $J_{1,6}$ = 7.8 Hz, 1H, H-1), 5.00 (s, 1H, H-2), 4.79 (s, 1H, H-5), 4.49 (d, 1H, H-6), 3.60 (d, $J_{3,4}$ = 6.6 Hz, 1H, H-3), 3.40 (d, 1H, H-4). $^{13}$C NMR spectrum, $\delta$: 175.04 (s, C=O), 174.89 (s, C=O), 153.86 (s, C-7), 134.89, 134.11, 129.15, 128.55, 128.31, 126.98, 125.56 ($C_{arom}$), 85.57 (d, C-1), 84.66 (d, C-2), 80.28 (d, C-5), 56.69 (d, C-6), 48.34 (d, C-3), 45.02 (d, C-4).

*VIIIg*: Yield = 72 %, m.p. = 236—238 °C. For $C_{21}H_{13}FCl_2N_2O_4$ ($M_r$ = 447.25) $w_i$(calc.): 56.40 % C, 2.93 % H, 6.26 % N; $w_i$(found): 56.15 % C, 3.20 % H, 6.39 % N. $^1$H NMR spectrum, $\delta$: 7.33—7.91 (m, 7H, $H_{arom}$), 5.24 (d, $J_{1,6}$ = 8.4 Hz, 1H, H-1), 4.99 (s, 1H, H-2), 4.79 (s, 1H, H-5), 4.49 (d, 1H, H-6), 3.66 (d, $J_{3,4}$ = 7.2 Hz, 1H, H-3), 3.41 (d, 1H, H-4). $^{13}$C NMR spectrum, $\delta$: 175.06 (s, C=O), 174.92 (s, C=O), 153.74 (s, C-7), 134.11, 129.24, 128.31, 125.57, 124.64, 116.30, 116.01 ($C_{arom}$), 85.36 (d, C-1), 84.69 (d, C-2), 80.28 (d, C-5), 56.90 (d, C-6), 48.34 (d, C-3), 45.02 (d, C-4).

*VIIIh*: Yield = 68 %, m.p. = 254—257 °C. For $C_{21}H_{13}Cl_2N_3O_6$ ($M_r$ = 474.26) $w_i$(calc.): 53.18 % C, 2.76 % H, 8.86 % N; $w_i$(found): 53.55 % C, 3.04 % H, 9.14 % N. $^1$H NMR spectrum, $\delta$: 7.36—8.56 (m, 7H, $H_{arom}$), 5.33 (d, $J_{1,6}$ = 8.1 Hz, 1H, H-1), 5.03 (s, 1H, H-2), 4.88 (s, 1H, H-5), 4.61 (d, 1H, H-6), 3.66 (d, $J_{3,4}$ = 6.9 Hz, 1H, H-3), 3.43 (d, 1H, H-4). $^{13}$C NMR spectrum, $\delta$: 175.04 (s, C=O), 174.87 (s, C=O), 153.70 (s, C-7), 148.30, 134.11, 133.09, 130.70, 129.76, 128.31, 125.54, 121.10 ($C_{arom}$), 86.15 (d, C-1), 84.64 (d, C-2), 80.13 (d, C-5), 56.42 (d, C-6), 48.30 (d, C-3), 45.01 (d, C-4).

*VIIIi*: Yield = 85 %, m.p. = 207—209 °C. For $C_{21}H_{13}Cl_2N_3O_6$ ($M_r$ = 474.26) $w_i$(calc.): 53.18 % C, 2.76 % H, 8.86 % N; $w_i$(found): 53.27 % C, 2.94 % H, 8.63 % N. $^1$H NMR spectrum, $\delta$: 7.40—8.21 (m, 7H, $H_{arom}$), 5.32 (d, $J_{1,6}$ = 7.4 Hz, 1H, H-1), 5.06 (s, 1H, H-2), 4.69 (s, 1H, H-5), 4.43 (d, 1H, H-6), 3.45 (m, 2H, H-3 and H-4).

*VIIIj*: Yield = 78 %, m.p. = 179—182 °C. For $C_{21}H_{12}Cl_4N_2O_4$ ($M_r$ = 498.15) $w_i$(calc.): 50.63 % C, 2.43 % H, 5.62 % N; $w_i$(found): 50.38 % C, 2.66 % H, 5.43 % N. $^1$H NMR spectrum, $\delta$: 7.34—7.75 (m, 6H, $H_{arom}$), 5.26 (d, $J_{1,6}$ = 8.0 Hz, 1H, H-1), 5.01 (s, 1H, H-2), 4.65 (s, 1H, H-5), 4.49 (d, 1H, H-6), 3.71 (m, 2H, H-3 and H-4).

*VIIIk*: Yield = 48 %, m.p. = 250—253 °C. For $C_{21}H_{13}Cl_3N_2O_4$ ($M_r$ = 463.70) $w_i$(calc.): 54.39 % C, 2.83 % H, 6.04 % N; $w_i$(found): 54.58 % C, 3.11 % H, 5.82 % N. $^1$H NMR spectrum, $\delta$: 7.23—7.91 (m, 7H, $H_{arom}$), 5.29 (d, $J_{1,6}$ = 8.0 Hz, 1H, H-1), 5.03 (s, 1H, H-2), 4.84 (s, 1H, H-5), 4.51 (d, 1H, H-6), 3.67 (d, $J_{3,4}$ = 7.0 Hz, 1H, H-3), 3.43 (d, 1H, H-4).

*VIIIl*: Yield = 70 %, m.p. = 284—286 °C. For $C_{22}H_{16}Cl_2N_2O_4$ ($M_r$ = 443.29) $w_i$(calc.): 59.61 % C, 3.64 % H, 6.32 % N; $w_i$(found): 59.83 % C, 3.46 % H, 6.19 % N. $^1$H NMR spectrum, $\delta$: 7.26—7.78 (m,

7H, $H_{arom}$), 5.21 (d, $J_{1,6}$ = 8.0 Hz, 1H, H-1), 5.00 (s, 1H, H-2), 4.79 (s, 1H, H-5), 4.49 (d, 1H, H-6), 3.64 (d, $J_{3,4}$ = 7.0 Hz, 1H, H-3), 3.41 (d, 1H, H-4), 2.38 (s, 3H, $CH_3$).

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