STERICALLY CROWDED HETEROCYCLES. VII. REDUCTION OF SOME (*Z*)-1,3-DIPHENYL-3-(2-PHENYLIMIDAZO[1,2-*a*]PYRIDIN-3-YL)-PROP-2-EN-1-ONES AS THEIR AXIAL CHIRALITY PROBE*

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Borohydride reduction of titled ketones **1a**–**1g** gave diastereoisomeric mixtures of (*Z*)-1,3-diphenyl-3-(2-phenylimidazo[1,2-*a*]pyridin-3-yl)prop-2-en-1-ols **2a**–**2g** and **3a**–**3g** in which the former ones prevailed. Only individual racemic products were obtained after borohydride reduction of (*E*)-1,3-diphenyl-3-(2-phenylimidazo[1,2-*a*]pyridin-3-yl)-prop-2-en-1-one **4** to corresponding 1-hydroxy derivative **5** and by conversion of (*Z*)-1-oxo derivative **1a** to 1,3-diphenyl-3-(2-phenylimidazo[1,2-*a*]-pyridin-3-yl)propan-1-one (**6**) with sodium hydrogenselenide. Diastereoselectivity of the borohydride reduction is discussed using the PM3 calculations of the molecules **1a**, **2a**, **2b**, **3a**, **3b**, **4**, **5**, and **6**.
Key words: Axial chirality; Diastereoisomerism; Borohydride reduction; Imidazo[1,2-*a*]pyridines.

It has been recently shown[2] that axial chirality of (*Z*)-1,3-diphenyl-3-(2-phenylimidazo-[1,2-*a*]pyridin-3-yl)prop-2-en-1-one (**1a**) is caused by restricted rotation about the C3–C3′ bond. Consequently, diastereoisomerism of related ketones substituted by an additional chiral group can be expected. In fact, this phenomenon has been observed in two cases of **1a**-like ketones prepared from different racemic precursors[3]. In this communication of the titled series (the preceding paper, see ref.[4]) reductions of the prochiral carbonyl group in sterically crowded (*Z*)-ketone **1a** and some of its derivatives were investigated. The results are then compared with some other reductive conversions.

Borohydride reductions of all investigated α,β-unsaturated ketones **1a**–**1g** were found to proceed 1′-regioselectively and (*Z*)-stereospecifically to corresponding (*Z*)-1,3-diphenyl-3-(2-phenylimidazo[1,2-*a*]pyridin-3-yl)prop-2-en-1-ols as mixture of diastereoisomeric pairs **2a**–**2g** and **3a**–**3g**, respectively (Table I).

Configurations of compounds **2a**–**2g** and **3a**–**3g** can be assigned on the basis of X-ray determined[4] relative configurations of the **2b**, **3b** couple. The assignments are possible

* A part of this work has been presented as a preliminary communication (ref.[1]).

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by means of the ^{13}C and ^{1}H NMR spectra of alcohols **2a**–**2g** and **3a**–**3g** interpreted per analogia to earlier assignments for **1**-like ketones[2]. Thus, signals of the C-1′, sp^3 carbons could be easily recognized in the region of δ 72.40–73.81 where all up-field shifted counterpart signals have been found to be typical for configuration **2** (see Experimental). Diastereoisomer types of **2** and **3** are also distinguishable by the H-1′ and H-2′ proton signals in the regions of δ 4.92–5.12 and δ 6.00–6.82, respectively, as shown by values of the relative chemical shifts $\Delta\delta = \delta(\mathbf{2}) - \delta(\mathbf{3})$ (Table II). It is evident that the H-1′ and H-2′ chemical shifts exhibit reverse shielding effects and different sensitivities to the configuration changes. As far as corresponding coupling constants are concerned, the relationship $^{3}J_{HH}(\mathbf{3}) > {}^{3}J_{HH}(\mathbf{2})$ is fulfilled except of the **2f**, **3f** couple where a conformational exclusiveness may be expected. In favour of this assumption, the H-1′ chemical shifts are observed to be extremely small (δ 6.00 and 6.14) and the H-2′ shifts extremely large (δ 5.18 and 5.12) in comparison with the same characteristics of other investigated couples of diastereoisomers.

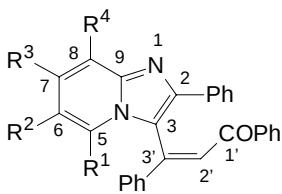
TABLE I
Physico-chemical characteristics of diastereoisomeric mixtures **2a–2g** and **3a–3g**

Diastereoisomers	M.p., °C Yield, %	Formula M.w.	Calculated/Found		
			% C	% H	% N
2a, 3a	143–145[a]	$C_{28}H_{22}N_2O$	83.56	5.51	6.96
	90	402.5	83.61	5.55	6.99
2b, 3b	223–227	$C_{29}H_{24}N_2O$	83.63	5.81	6.73
	~100	416.5	83.83	5.90	6.72
2c, 3c	148–150[a]	$C_{29}H_{24}N_2O$	83.63	5.81	6.73
	80	416.5	83.43	5.95	6.48
2d, 3d	158–160[a]	$C_{29}H_{24}N_2O$	83.63	5.81	6.73
	70	416.5	83.87	5.93	6.70
2e, 3e	150–152[a]	$C_{29}H_{24}N_2O$	83.63	5.81	6.73
	80	416.5	83.74	6.08	6.65
2f, 3f	176–178[a]	$C_{34}H_{28}N_2O$	84.97	5.87	5.83
	80	480.6	84.72	5.57	5.55
2g, 3g	205–207[a]	$C_{28}H_{21}IN_2O$	63.65	4.01	5.30
	80	528.4	63.67	4.27	5.12

[a] From diethyl ether.

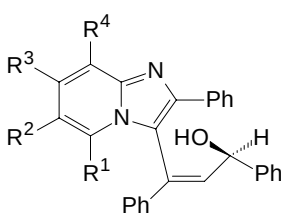
Temperature dependent ^{1}H NMR spectra of the **2e**, **3e** mixture in hexadeuteriodimethyl sulfoxide have shown that the axial chirality of the corresponding molecules is conserved at least up to 110 °C. For example, at 24 °C both diastereoisomers **2e** and **3e** exhibit multiplet 1′-methine signals at δ 4.68 and 4.80 splitted by couplings $^3J_{HH(O)}$ = 9.1 and 7.7 Hz and $^3J_{HH(C)}$ = 3.6 and 4.1 Hz, respectively. At 110 °C the both signals are still observed at δ 4.74 and 4.96 but as doublets ($^3J_{HH(C)}$ = 9.2 and 6.8 Hz) due to rapid intermolecular hydroxy proton exchanges. Hydroxy proton doublets originally being at δ 5.60 and 5.58 are simultaneously transformed to broad singlets at δ 5.21 and 5.11, respectively.

Stereoselectivity of the borohydride reductions is not high for ketones **1a**–**1e** and **1g** (**2a**–**2e** : **3a**–**3e** and **2g** : **3g** are ≈ 3 : 2) except of 5-phenyl derivative **1f** for which the ratio **2f** : **3f** is about 7 : 2. To interpret the preferred formation of major diastereoisomers **2a**–**2g** the molecular shape of the most stable *a*,*a*-conformer[2] of ketone **1a** should be considered. From Fig. 1 it follows that two different A- and B-faces can be recognized for a nucleophile approaching the 1′-carbonyl group. The 3-(2-phenylimidazo[1,2-*a*]pyridin-2-yl) moiety evidently makes the A-face approach resulting in minor product **3a** difficult. Provided that the productive conformers of precursors **1a**–**1g** are similar, then the general formation of major diastereoisomers **2a**–**2g** can be attributed to the B-face reactions. An uncertainty may arise regarding the productive

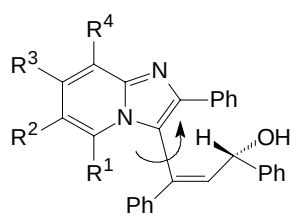


1a-1g

1-3	R^1	R^2	R^3	R^4
a	H	H	H	H
b	Me	H	H	H
c	H	Me	H	H
d	H	H	Me	H
e	H	H	H	Me
f	Ph	H	H	H
g	H	I	H	H



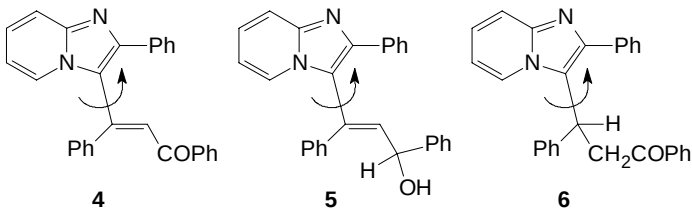
2a-2g



3a-3g

conformer of the more sterically crowded 5-phenyl derivative **1f**. However, a preliminary model analysis has shown that a more favourable attack at possible *s,s*-conformer of ketone **1f** can also result in the prevailing diastereoisomer **2f**.

Physico-chemical as well as spectral properties of alcohol **5** obtained by borohydride reduction of the (*E*)-enone **4** and ketone **6** indicate no diastereoisomerism. It can be therefore concluded that the molecules **5** and **6** exhibit no axial chirality and are racemic owing to occurrence of the asymmetric C1′-centres.



4 **5** **6**

Calculated heats of formation ΔH_f for the diastereosiomeric couples **2a**, **3a** and **2b**, **3b** show no significant energy preferences caused by different relative configurations at the asymmetric C-1′centre (Table III). Hence, the observed diastereoselectivity may be attributed rather to the kinetic controlled borohydride reductions of ketones **1**. On the other hand, the calculated rotation C3–C3′ barriers ΔE_{rot} exhibit remarkable variabilities owing to occurrence of the 5-methyl group and structure of the **3**-side chain as well. Differencies between the ΔE_{rot} values within the couples **2a**, **2b** and **3a**, **3b** (7.0 and 8.0 kcal/mol, respectively) are evidently due to a steric interaction of the 5-substituent with the 3′-phenyl group. The (*Z*) → (*E*) change of the C2′–C3′ double bond configuration in the PM3 models of the most stable conformers of (*Z*)-alcohols **2a**, **3a** and (*E*)-alcohol **5** is accompanied with the decrease of the ΔE_{rot} values as approximates

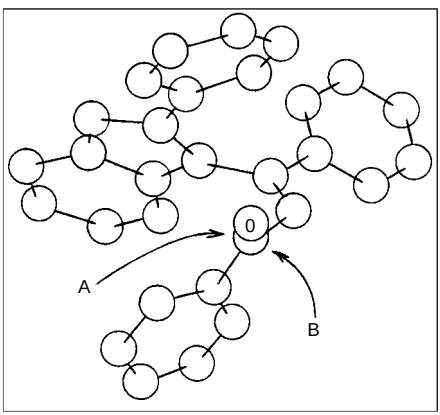


FIG. 1
Schematic picture of A- and B-face approaches with respect to the *a,a*-conformer of ketone **1a**

of true racemization barierrs from ca 18.5 to ca 8 kcal/mol (Table III). The energy effect of the C2′–C3′ bond saturation in the PM3 model of ketone **6** is almost the same (8.2 kcal/mol) in agreement with the lack of axial chirality observed in the NMR spectra of compounds **5** and **6**.

From the above mentioned results it can be concluded that the axial chirality in sterically crowded **1**-like heterocyclic compounds is conditioned by occurrence so as by *Z*-configuration of the C2′-C3′ double bond at least for the molecules in which R^1 = H. Thus, the current knowledge of antropoisomerism about sp^2–sp^2 bonds[5] has been extended to novel heterocyclic systems.

EXPERIMENTAL

The temperature data are uncorrected. Melting points were determined on a Boetius block. NMR spectra (δ, ppm; Hz) were taken on a GEMINI 300 HC instrument at 297 K. The working frequency

TABLE II
Comparison of some ^{13}C and ^1H NMR spectral characteristics of diastereoisomeric couples **2a–2g** and **3a–3g**[a]

Compounds	Δδ(C-1′)	Δδ(H-1′)	Δδ(H-2′)	$^3J_{HH}$, Hz	$\Delta\delta_{Me}$(C)	$\Delta\delta_{Me}$(H)
2a, 3a	0.20	0.05	–0.11	8.6 9.2	–	–
2b, 3b[b]	0.70	–0.05	–0.06	8.4 9.2	–0.56	–0.61
2c, 3c	0.55	0.01	–[c]	8.2 9.1	–0.12	–0.24
2d, 3d	0.32	0.03	–0.11	8.7 9.2	0.02	0.00
2e, 3e	0.12	0.04	–0.13	8.9 9.3	0.02	0.00
2f, 3f	1.31	0.06	–0.13	9.8 9.1	–	–
2g, 3g	0.59	0.02	–[c]	7.7 9.1	–	–

[a] Solutions in $CDCl_3$, Δδ = δ(**2**) – δ(**3**). [b] According to data given in ref.[1]. [c] Not recognized because of overlapping signals.

TABLE III
Heats of formation and rotation barierrs[a] calculated by the PM3 method for the most stable conformers (all data are given in kcal/mol)

Compound	ΔH_f	ΔE_{rot}	Compound	ΔH_f	ΔE_{rot}
2a	100.7	18.7	**2b**	92.7	35.1
3a	100.7	18.2	**3b**	93.7	28.9
5	99.6	8.0	**6**	92.3	8.2

[a] Bond C3–C3′.

was 300 MHz for ^{1}H and 75 MHz for ^{13}C. IR spectra ($\tilde{\nu}$, cm^{-1}) were measured on a FTIR spectrometer NICOLET 740.

Preparation of starting ketones **1a**–**1g** was reported in preceding contributions[2,6,7].

Borohydride Reduction of Ketones **1a**–**1g**

A mixture of the ketone **1** (0.5 g) and sodium borohydride (0.2 g) in ethanol (20 ml) was stirred at 20 °C until dissolution of the starting compound and decolouration of the solution were observed (1 to 2 h). Under prolonged stirring the reaction mixture was decomposed by dropwise addition of aqueous 10% NH_4Cl (10 ml). Then the solid product was precipitated with water (200 ml), sucked off, washed with water (100 ml) and finally dried in vacuo. The crude mixture of diastereoisomeric alcohols **2** and **3** was purified by dissolution in diethyl ether (ca 10 ml), filtration and crystallization. Melting temperatures and elemental analyses are given in Table I.

*(Z)-1,3-Diphenyl-3-(2-phenylimidazo[1,2-a]pyridin-3-yl)prop-2-en-1-ols **2a** and **3a***. IR spectrum ($CHCl_3$): 1 635 (C=C), 3 153 and 3 594 (OH). ^{1}H and ^{13}C NMR spectral characteristics, see ref.[1].

*(Z)-3-(5-Methyl-2-phenylimidazo[1,2-a]pyridin-3-yl)-1,3-diphenylprop-2-en-1-ols **2b** and **3b***. IR spectrum ($CHCl_3$): 1 637 (C=C), 3 562 and 3 595 (OH). ^{1}H and ^{13}C NMR data of individual diastereoisomers, see ref.[1].

*(Z)-3-(6-Methyl-2-phenylimidazo[1,2-a]pyridin-3-yl)-1,3-diphenyl-prop-2-en-1-ols **2c** and **3c***. IR spectrum ($CHCl_3$): 1 603 (C=C), 3 596 (HO). ^{1}H NMR spectrum ($CDCl_3$): 2.00 s, 3 H (CH_3-6, **2c**); 2.12 s, 3 H (CH_3-6, **3c**); 3.56 brs, 1 H (HO-1′, **2c**); 4.38 brs, 1 H (HO-1′, **3c**); 4.97 d, 1 H, J = 9.1 (H-1′, **3c**); 4.98 d, 1 H, J = 8.2 (H-1′, **2c**); 6.83–7.34 m (Ph); 7.38 d, 1 H, J = 9.6 (H-8, **3c**); 7.42 d, 1 H, J = 9.0 (H-8, **3c**); 7.63 s, 1 H (H-5, **3c**); 7.66–7.72 m, 2 H (*o*-Ph2, **3c**); 7.93–7.99 m, 2 H (*o*-Ph2, **2c**). ^{13}C NMR spectrum ($CDCl_3$): 18.57 CH_3 (**2c**), 18.81 CH_3 (**3c**), 72.37 CH (C-1′, **2c**), 72.92 CH (C-1′, **3c**), 116.94 CH, 117.25 C, 117.55 C, 121.91 CH, 122.28 CH, 122.33 C, 122.68 C, 126.59 CH, 126.62 CH, 126.68 CH, 126.82 CH, 127.7 CH, 127.80 CH, 127.87 CH, 128.06 CH, 128.44 CH, 128.58 CH, 128.71 CH, 128.77 CH, 128.84 CH, 129.05 CH, 129.09 CH, 129.24 CH, 129.49 CH, 129.57 CH, 130.38 C, 130.71 C, 134.23 C, 134.47 C, 138.03 C, 138.08 CH, 138.21 C, 139.70 CH, 142.86 C, 143.14 C, 143.34 C, 143.93 C, 144.75 C.

*(Z)-(7-Methyl-2-phenylimidazo[1,2-a]pyridin-3-yl)-1,3-diphenylprop-2-en-1-ols **2d** and **3d***. IR spectrum ($CHCl_3$): 1 603 and 1 648 (C=C), 3 593 (OH). ^{1}H NMR spectrum ($CDCl_3$): 2.33 s, 3 H (CH_3-7, **3d**); 2.35 s, 3 H (CH_3-7, **3d**); 5.00 d, 1 H, J = 9.2 (H-1′, **3d**); 5.03 d, 1 H, J = 8.7 (H-1′, **2d**); 6.37 dd, 1 H, J = 7.0 and ≈1.5 (H-6, **2d**); 6.45 dd, 1 H, J = 7.0 and ≈1.5 (H-6, **3d**); 6.71 d, 1 H, J = 8.7 (H-2′, **2d**); 6.82 d, 1 H, J = 9.2 (H-2′, **3d**); 6.88–6.94 m, 2 H (*o*-Ph, **3d**); 6.96–7.45 m (Ph); 7.66 d, 1 H, J = 7.0 (H-5, **3d**); 7.70–7.76 m, 2 H (*o*-Ph2, **3c**); 7.96–8.07 m, 2 H (*o*-Ph2, **2c**). ^{13}C NMR spectrum ($CDCl_3$): 21.95 CH_3 (**2d**, **3d**), 72.56 (C-1′, **3d**), 72.88 CH (C-1′, **2d**), 115.63 CH (**2d**), 115.75 CH (**3d**), 116.30 CH (**3d**), 116.43 CH (**2d**), 116.95 C (**3d**), 117.31 C (**2d**), 123.67 CH (**2d**), 123.95 CH (**3d**), 126.41 CH, 126.68 CH, 126.92 CH, 126.98 CH, 127.91 CH, 128.03 CH, 128.17 CH, 128.82 CH, 128.93 CH, 129.02 CH, 129.23 CH, 129.36 CH, 129.50 CH, 129.61 CH, 129.76 CH, 130.78 C, 131.24 C, 134.46 C, 134.73 C, 136.58 C, 137.81 CH, 138.29 C, 138.40 C, 138.95 CH, 143.02 C, 143.07 C, 143.63 C, 144.15 C, 146.31 C, 146.49 C.

*(Z)-3-(8-Methyl-2-phenylimidazo[1,2-a]pyridin-3-yl)-1,3-diphenylprop-2-en-1-ols **2e** and **3e***. IR spectrum ($CHCl_3$): 1 603 and 1 631 (C=C), 3 593 (OH). ^{1}H NMR spectrum ($CDCl_3$, 24 °C): 2.73 s, 3 H, (CH_3-8, **2e**); 2.75 s, 3 H (CH_3-8, **3e**); 4.98 d, 1 H, J = 9.3 (H-1′, **3e**); 5.02 d, 1 H, J = 8.9 (H-1′, **2e**); 6.49 dd, 1 H, J = 6.8 and 6.8 (H-6, **2e**); 6.61 dd, 1 H, J = 6.8 and 6.8 (H-6, **3e**); 6.67 d, 1 H, J = 8.9 (H-2′, **2e**); 6.80 d, 1 H, J = 9.3 (H-2′, **3e**); 6.84–6.90 m, 2 H (*o*-Ph, **3e**); 6.95–7.46 m (Ph); [$(CD_3)_2SO$, at 24 and *110 °C]: 2.60 s, *2.61 s, 3 H (CH_3-8, **3e**); 2.63 s, *2.66 s, 3 H (CH_3-8, **2e**); 4.68 dd, J = 9.1 and 3.6, 1 H, *4.74 d, *J = 9.2, *1 H (H-1′, **2e**); 4.80 dd, 1 H, J = 7.7 and 4.1, *4.86 d,

*1 H, *J = 6.8 (H-1′, **3e**); 5.58 d, 1 H, *J* = 4.5, *5.11 brs, *1 H (HO-1′, **3e**); 5.60 d, 1 H, *J* = 4.0, *5.21 brs, *1 H (HO-1′, **2e**); 6.49 dd, 1 H, *J* = 7.0 and 6.7, *6.47 dd, *1 H, *J = 6.9 and 6.8 (H-6, **3e**); 6.81–7.36 m *6.90–7.35 m (Ph); 7.41 dd, 2 H, *J* = 7.5 and 7.5, *7.40 dd, *2 H, *J = 7.8 and 7.5 (*m*-Ph, **3e**); 7.70–7.77 m, 2 H *7.73–7.79 m, *2 H (*o*-Ph2, **2e**); 7.89 d, 2 H, *J* = 6.7, *7.92 d, *1 H, *J = 6.7 (H-5, **2e**); 8.13 d, 2 H, *J* = 7.2, *8.13 d, *2 H, *J = 7.3 (*o*-Ph2, **3e**). ^{13}C NMR spectrum ($CDCl_3$): 17.76 CH_3 (**2e**, **3e**), 72.71 CH (C-1′, **3e**), 72.83 CH (C-1′, **2e**), 113.08 CH, 113.25 CH, 117.82 C, 118.28 C, 122.41 CH, 122.55 CH, 124.43 CH, 126.37 CH, 126.61 CH, 126.97 CH, 127.01 CH, 128.03 CH, 128.10 CH, 128.13 C, 128.18 CH, 128.27 CH, 128.43 CH, 128.88 CH, 128.94 CH, 128.98 CH, 129.05 CH, 129.27 CH, 129.37 CH, 129.53 CH, 129.61 CH, 129.76 CH, 130.92 C, 131.50 C, 134.48 C, 134.80 C, 137.50 CH, 138.31 C, 138.69 CH, 142.74 C, 142.57 C, 143.57 C, 146.54 C.

*(Z)-3-(2,5-Diphenylimidazo[1,2-a]pyridin-3-yl)-1,3-diphenyl-3-yl)-1,3-diphenylprop-2-en-1-ols **2f** and **3f***. IR spectrum ($CHCl_3$): 1 602 and 1 631 (C=C), 3 554 (OH). ^{1}H NMR spectrum ($CDCl_3$): 5.12 d, 1 H, *J* = 9.1 (H-1′, **3f**); 5.18 d, 1 H, *J* = 9.8 (H-1′, **2f**); 6.00 d, 1 H, *J* = 9.8 (H-2′, **2f**); 6.14 d, 1 H, *J* = 9.1 (H-2′, **3f**); 6.20 dd, 1 H, *J* = 7.3 and 7.3 (**2f**); 6.36–6.75 m (Ph); 6.77 dd, 1 H, *J* = 7.4 and 7.4 (**2f**); 6.89 dd, 1 H, *J* = 7.4 and 7.4 (**3f**); 6.95–7.50 m (Ph); 7.61 dd, 2 H, *J* = 8.1 and 1.9 (*o*-Ph2, **3f**); 7.66 d, 2 H, *J* = 7.9 (H-8, **3f**); 7.77 d, 1 H, *J* = 8.9 (H-8, **2f**); 7.82–7.90 m, 2 H (*o*-Ph2, **2f**). ^{13}C NMR spectrum ($CDCl_3$): 72.50 CH, (C-1′, **3f**), 73.81 CH (C-1′, **2f**), 116.47 CH, 117.21 CH, 118.71 C, 125.71 CH, 126.11 CH, 126.53 CH, 126.73 CH, 127.73 CH, 128.40 CH, 128.45 CH, 128.65 CH, 128.75 CH, 128.88 CH, 128.98 CH, 129.03 CH, 129.25 CH, 129.31 CH, 129.46 CH, 129.56 CH, 130.31 CH, 132.34 C, 134.21 CH, 134.29 C, 134.69 C, 135.23 C, 139.40 C, 139.87 C, 140.50 C, 141.98 C, 146.20 C, 148.33 C.

*(Z)-3-(6-Iodo-2-phenylimidazo[1,2-a]pyridin-3-yl)-1,3-diphenylprop-2-en-1-ols **2g** and **3g***. IR spectrum ($CHCl_3$): 1 602 and ≈1 625 (C=C), 3 595 (OH). ^{1}H NMR spectrum ($CDCl_3$): 4.92 d, 1 H, *J* = 9.1 (H-1′, **3g**); 4.94 d, 1 H, *J* = 7.7 (H-1′, **2g**); 6.83–6.96 m, 7.03–7.22 and 7.24–7.47 m (Ph); 7.71–7.77 m, 2 H (*o*-Ph2, **3g**); 7.98–8.04 m, 2 H (*o*-Ph2, **2g**); 8.08 s, 1 H (H-5, **3g**). ^{13}C NMR spectrum ($CDCl_3$): 72.83 CH (C-1′, **3g**), 73.42 CH (C-1′, **2g**); 75.99 C (C-6, **2g**); 76.18 C (C-6, **3g**); 117.53 C, 117.96 C, 118.92 CH, 119.03 CH, 126.60 CH, 126.63 CH, 126.66 CH, 126.93 CH, 127.95 CH, 128.40 CH, 128.56 CH, 128.72 CH, 129.08 CH, 129.15 CH, 129.24 CH, 129.59 CH, 129.80 CH, 129.90 CH, 130.23 C, 130.88 C, 133.46 CH, 133.68 CH, 134.01 C, 137.50 C, 137.73 C, 138.07 CH, 140.21 CH, 142.67 C, 142.91 C, 143.64 C, 144.35 C, 144.45 C, 144.81 C.

(*E*)-1,3-Diphenyl-3-(2-phenylimidazo[1,2-*a*]pyridin-3-yl)prop-2-en-1-ol (**5**)

Borohydride reduction of (*E*)-ketone **4** (ref.[8], 0.1 g, 0.25 mmol) was carried out in the same way as in the case of compounds **1a**–**1g**. The crude product was crystallized from diethyl ether. Yield 0.85 g (85%) of (*E*)-alcohol **5**, white crystals, m.p. 205–207 °C. For $C_{28}H_{22}N_2O$ (402.5) calculated: 83.56% C, 5.51% H, 6.96% N; found: 83.42% C, 5.60% H, 6.92% N. IR spectrum ($CHCl_3$): 1 635 (C=C), 3 591 (OH). ^{1}H NMR spectrum ($CDCl_3$): 5.69 d, 1 H, *J* = 9.7 (H-1′); 6.16 d, 1 H, *J* = 9.7 (H-2′); 6.57 dd, 1 H, *J* = 6.9 and 6.9 (H-6); 7.09–7.16 m, 1 H; 7.17–7.47 m, 13 H; 7.55 d, 1 H, *J* = 6.7 (H-5); 7.61 d, 1 H, *J* = 9.0 (H-8); 7.79–7.85 m, 2 H. ^{13}C NMR spectrum ($CDCl_3$): 71.78 CH (C-1′), 112.89 CH, 118.14 CH, 122.44 C, 124.83 CH, 125.40 CH, 126.93 CH, 128.25 CH, 129.48 CH, 129.64 CH, 129.68 CH, 131.92 C, 134.69 C, 137.31 C, 138.30 C, 143.11 C (C-2), 145.54 C (C-9) (one signal was overlapped).

1,3-Diphenyl-3-(2-phenylimidazo[1,2-*a*]pyridin-3-yl)propan-1-one (**6**)

A solution of the reduction agent[9] was obtained by stirring of selenium (1.2 g, 15 mmol) and sodium borohydride (0.7 g, 18 mmol) in absolute ethanol (30 ml) under nitrogen at 0 °C for 1.5 h. A half of

the solution was added to (*Z*)-ketone **1a** (2 g, 5 mmol) in ethanol (5 ml) and the resulting mixture was refluxed under nitrogen for 3 h. Then the remaining portion of the reduction agent was added and the heating was prolonged for 5 h. After cooling the reaction mixture was treated with a 2 M solution of hydrochloric acid (15 ml), stirred under air oxygen overnight, diluted with water (300 ml), alkalized with solid potassium hydroxide and finally extracted with chloroform (3 × 100 ml). The collected extracts were washed with water (100 ml), dried over sodium sulfate, and evaporated at diminished pressure. The residue was treated with a small amount of diethyl ether and let to crystallize. It was obtained 1.7 g (85%) of ketone **6**, m.p. 165–167 °C (ethanol). For $C_{28}H_{22}N_2O$ (402.5) calculated: 83.56% C, 5.51% H, 6.96% N; found: 83.48% C, 5.58% H, 6.90% N. IR spectrum ($CHCl_3$): 1 666 (C=O). ^{1}H NMR spectrum ($CDCl_3$): 3.77 dd, 2 H, *J* = 7.0 and 2.1 (H_2C-2′); 5.58 dd, 1 H, *J* = ≈7.0 and ≈7.0 (HC-3′); 6.70 dd, 1 H, *J* = 6.8 and 6.8 (H-6); 7.13–7.20 m, 1 H; 7.21–7.37 m, 10 H; 7.44–7.51 m, 1 H; 7.57–7.67 m, 5 H, 7.82 d, 1 H, *J* = 6.8 (H-5). ^{13}C NMR spectrum ($CDCl_3$): 36.20 CH (C-3′), 42.86 CH_2 (C-2′), 112.78 CH, 118.41 CH, 121.56 C, 124.44 CH, 124.69 CH, 127.63 CH, 127.77 CH, 128.48 CH, 128.86 CH, 129.06 CH, 129.67 CH, 130.03 CH, 133.78 CH, 135.85 C, 136.89 C, 141.20 C, 144.85 C (C-2), 145.34 C (C-9), 197.81 C (C-1′).

Attempt at Reduction of (*E*)-Ketone **1b**

The reaction of compound **1b** (0.5 g, 1.2 mmol) with the selenium reduction agent[9] was carried out in the same manner as in the above mentioned case of ketone **1a**. The preparative procedure resulted only in 0.42 g (84%) of starting compound **1b**, m.p. 154–156 °C, besides several minor components (TLC), which according to ^{1}H NMR measurements did not contain the CH-CH_2 moiety.

CALCULATIONS

The molecular geometries of structures **2a**, **2b**, **3a**, **3b**, **5** and **6** were obtained by the PM3 (ref.[10]) optimization. Rotation barriers around the C3–C3′ bonds are calculated starting from a given optimized conformer geometry by stepwise change (± 5°) of the dihedral C2–C3–C3′–C2′ angle. All other degrees of freedom were optimized in every of the steps. Calculated geometry and energy characteristics are given in Table II.

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REFERENCES

1. Kubik R., Nemecek J., Bohm S., Hradilek M., Kuthan J.: Mendeleev Commun. *1995*, 29.
2. Bohm S., Kubik R., Hradilek M., Nemecek J., Husak M., Kratochvil B., Kuthan J.: Collect. Czech. Chem. Commun. *60*, 115 (1995).
3. Kubik R., Kuthan J.: Collect. Czech. Chem. Commun. *61*, 615 (1996).
4. Cejka J., Kubik R., Kratochvil B., Kuthan J.: Collect. Czech. Chem. Commun., in press.
5. Eliel E. L., Wilen S. H., Mander L. N. in: *Stereochemistry of Organic Compounds*, Chapter 14.5.b. Wiley, New York 1994.
6. Bohm S., Kubik R., Novotny J., Ondracek J., Kratochvil B., Kuthan J.: Collect. Czech. Chem. Commun. *56*, 2326 (1991).

7. Kubik R., Bohm S., Ruppertova I., Kuthan J.: Collect. Czech. Chem. Commun. *61*, 126 (1996).
8. Kubik R., Bohm S., Cejka J., Havlicek V., Strnad T., Kratochvil B., Kuthan J.: Collect. Czech. Chem. Commun., in press.
9. Nishyama Y., Yoshida M., Ohkawa S., Hamanaka S.: J. Org. Chem. *56*, 6720 (1991).
10. Stewart J. J. P.: J. Comput. Chem. *10*, 209, 221 (1989).