STERICALLY CROWDED HETEROCYCLES. XIII. AN INSIGHT INTO THE ABSOLUTE STEREOCHEMISTRY OF ATROPISOMERIC (*Z*)-3-(IMIDAZO[1,2-*a*]PYRIDIN-3-YL)PROP-2-EN-1-ONES

Radek POHL[a1], Jan SÝKORA[b1], Petr MALOŇ[c], Stanislav BÖHM[a2,*],
Bohumil KRATOCHVÍL[b2] and Josef KUTHAN[a]

[a] *Department of Organic Chemistry, Institute of Chemical Technology, Prague, 166 28 Prague 6, Czech Republic; e-mail: [1] pohlr@usa.net, [2] bohm@vscht.cz*
[b] *Department of Solid State Chemistry, Institute of Chemical Technology, Prague, 166 28 Prague 6, Czech Republic; e-mail: [1] jan.sykora@vscht.cz, [2] bohumil.kratochvil@vscht.cz*
[c] *Institute of Organic Chemistry and Biochemistry, Academy of Science of the Czech Republic, 166 10, Prague 6, Czech Republic; e-mail: malon@uochb.cas.cz*

Received August 23, 2000
Accepted September 21, 2000

The absolute configuration of the atropisomeric (*Z*)-3-(5-methyl-2-phenylimidazo-[1,2-*a*]pyridin-3-yl)-1,3-diphenylprop-2-en-1-one was evaluated to be *R* for the dextrorotatory and *S* for the laevorotatory enantiomers. The assignment is based on their two-step syntheses *via* atropodiastereoisomeric carbamates prepared from the corresponding atropodiastereoisomeric alcohols with (*R*)-(+)-α-phenylethyl isocyanate and by a complete X-ray space analysis of the quaternary triiodide obtained from the (*R*)-(+)-enantiomer. CD spectra and PM3 calculated heats of formation for selected compounds are discussed in relation to the found molecular configurations.

Key words: Imidazo[1,2-*a*]pyridines; Atropisomerism; Axial chirality; Absolute configuration; X-Ray analysis; CD spectroscopy; PM3 method; Semiempirical calculations; Racemization barriers.

During the last years it has been shown that the ferricyanide oxidation of suitable quaternary 2,4,6-triaryl- or 4-*tert*-butyl-2,6-diphenylpyridinium salts can be used for preparation of substituted imidazo[1,2-*a*]pyridine derivatives possessing sterically crowded atropisomeric molecules[1]. Axial chirality of these compounds was proved[2] by NMR chiral shift reagents, and by chemical transformations using the racemic forms. In addition, modified chiral HPLC methods involving a polarimetric detection as well as semiempirical PM3 calculations could be applied to determine appropriate barriers to rotation[3].

Racemic (*Z*)-3-(5-methyl-2-phenylimidazo[1,2-*a*]pyridin-3-yl)-1,3-diphenylprop-2-en-1-one (**1a**,**b**), easily accessible[1a] by the oxidation of 1-(6-methyl-pyridin-2-yl)-2,4,6-triphenylpyridinium perchlorate, may be considered to be the key stereochemical model for the sterically crowded imidazo[1,2-*a*]pyridines as it consists of two so far not separated enantiomers (*R*)-**1a** and (*S*)-**1b**, for which the barriers to racemization were determined by heating of their ethanolic solution in polarimetric detector[3a] to be 26.1 kcal/mol and calculated by PM3 (ref.[3b]) to be 22.9 and 28.4 kcal/mol (see Table I), and their sufficient optical stability may be expected under usual conditions[4].

In this paper, the absolute configurations are assigned to individual, separated enantiomers using procedures described below. Although absolute configurations for a number of atropisomeric heterocycles have been reported[5], no example of similar sterically hindered α,β-unsaturated carbonyl compounds have hitherto been reported to our knowledge in the literature.

In an earlier paper[6] it has been shown that borohydride reduction of the racemic (*Z*)-ketone **1a**,**b** afforded two secondary alcohols, namely major[7], lower-melting (m.p. 174–176 °C) racemate **2a**,**b** and minor[7], higher-melting (m.p. 245–247 °C) racemate **3a**,**b**, the relative configuration of which was determined by X-ray[6]. The both substances have been independently allowed to react with (*R*)-(+)-α-phenylethyl isocyanate to form corresponding carbamates (Scheme 1). While the alcohol **2a**,**b** gave two chromatographically separable carbamates, for which only the atropodiastereoisomeric configurations (*R*,1*R*,α*R*)-**4a** and (*S*,1*S*,α*R*)-**4b** come into account, the analogous products from the alcohol **3a**,**b** have prowed to be preparatively hardly separable under the conditions used.

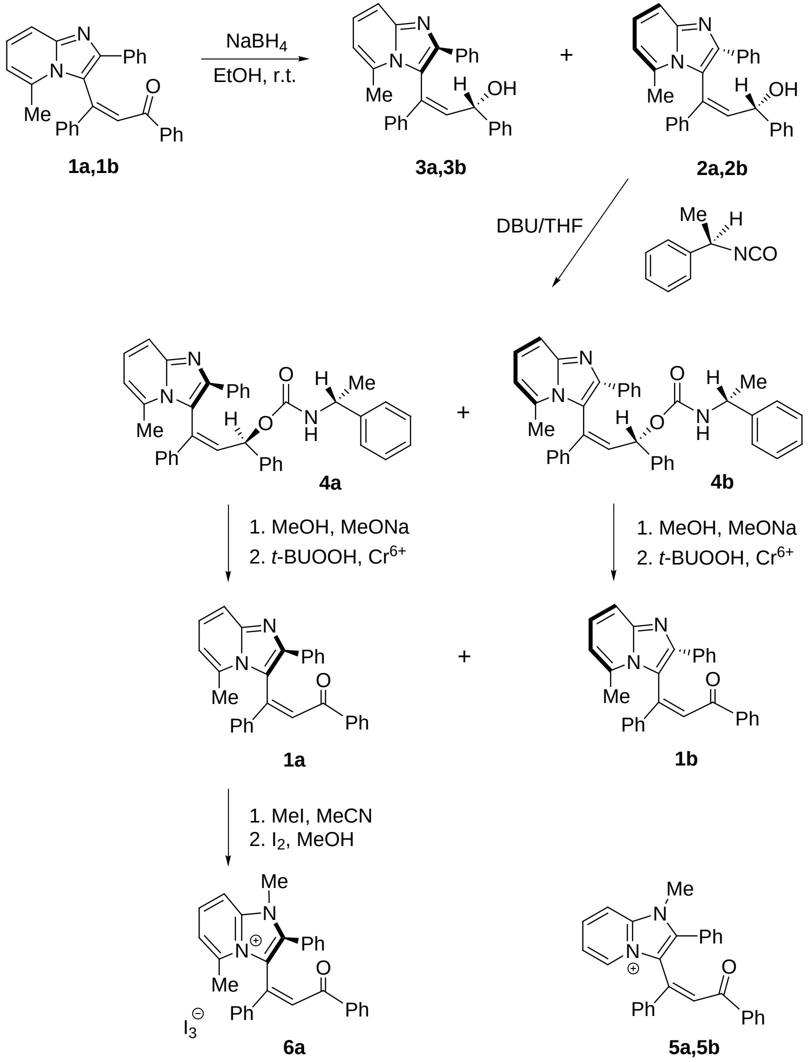
TABLE I

Selected isomerization barriers calculated by PM3 method (ΔE_1, ΔE_2) and kinetically measured ($\Delta G^{\neq}$)

Compound	ΔE_1, kcal mol^{-1}	ΔE_2, kcal mol^{-1}	$\Delta G^{\neq}$, kcal mol^{-1}
1	28.4	22.9	26.1[a]
2	31.4	26.5	29.7[b], 30.3[c]
3	22.5	31.0	29.9[b], 30.5[c]
6	33.2[d]	23.8[d]	–

[a] By on-line polarimetric detection[3a] (EtOH, 60 °C). [b] By ^{1}H NMR in DMSO-d_6 solution at 110 °C. [c] By ^{1}H NMR in DMSO-d_6 solution at 150 °C. [d] Only for the cationic moiety.

Hence, only the carbamates **4a** and **4b** have been used in further experiments. The dextrorotatory isomer ([α]$_D$ +197.5) was obtained in a crystalline form affording no satisfactory X-ray structural results while the second laevorotatory isomer ([α]$_D$ –153.9) was isolated only as a solid foam substance. However, methanolyses of both substances with 5% NaOMe–MeOH led to enantiomeric alcohols of the alternative configurations (*R*,1*R*)-**2a** and



SCHEME 1

(*S*,1*S*)-**2b**, which were oxidized in crude states with *tert*-butylhydroperoxide under chromium(VI) oxide catalysis to optically active (*Z*)-enones, $[\alpha]_D$ +290 and –306, of possible configurations (*R*)-**1a** and (*S*)-**1b**, respectively. Optical purity of enantiomers **1a** and **1b** was checked by ^{1}H NMR measurements of atropodiastereoisomeric solvates with (–)-1-(9-anthryl)-2,2,2-trifluoroethan-1-ol, and was determined as higher than 98% e.e. in both cases.

The CD curves of the obtained (*Z*)-enones shown in Fig. 1 exhibit perfect mirror shapes and suggest comparable optical purities of both substances. In the region λ = 260–500 nm at least four simply observable Cotton effects are detected. The broad CD band above 400 nm is undoubtedly associated with the nπ* absorption of the ketone chromophore, while other, lower lying CD bands are mainly due to the presence of optically active ππ* absorptions of the aromatic chromophoric system in the molecules. Except of the region 280–300 nm all Cotton effects belonging to one enantiomer seem to be of one sign.

Since the molecules of enantiomeric (*Z*)-enones **1a** and **1b** contain no heavy atoms making easier the X-ray absolute configuration determination[8] at least one of the enantiomers had to be transformed into a suitable derivative. We have therefore utilized the earlier findings[9] that sterically crowded imidazo[1,2-*a*]pyridines of the type **1** can be easily quaternized at the N(1) nitrogen with methyl iodide and by subsequent reaction with iodine afford crystalline triiodide **5**. Considering the fact that the PM3 calculations of the barriers to rotation for the cation part of the salt **6** show no

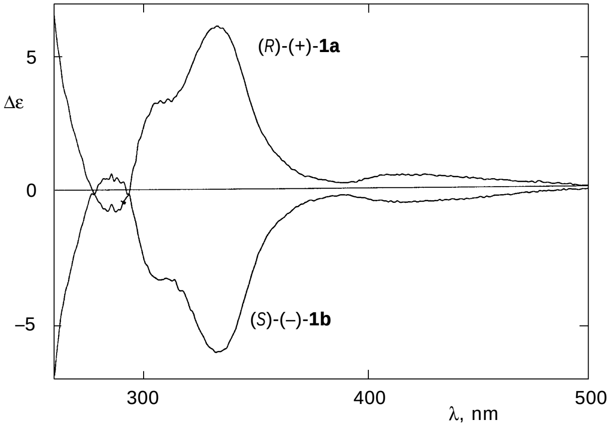


FIG. 1
CD curves of the enantiomeric (*Z*)-enones **1a** and **1b** in the region 260–500 nm

significant difference to the corresponding free (*Z*)-enone base (see Table I), it may be concluded that no racemization of **1a** and **1b** would take place during their quaternization and the absolute configuration will be conserved.

To prove this assumption, the dextrorotatory (*Z*)-enone (**1a**) was transformed with methyl iodide and iodine to the corresponding quaternary triiodide **6a**. As shown in the X-ray structure in Fig. 2 its enantiomeric crystals (see Experimental) contain exclusively the same (*R*)-cations which is recognizable from various directions of view represented by the formula **6a**. It may be noted that the salt **6a** exhibits in the solid state practically the same conformation as racemic triiodide **5** (see ref.[9]) with the characteristic close proximity between the carbonyl oxygen and heterocyclic N(4) nitrogen atom.

Consequently, the absolute configuration of the starting dextrorotatory enantiomer must be (*R*)-(+)-**1a** and (*S*)-(–)-**1b** of the remaining laevorotatory one. Absolute configurations of the intermediate carbamates **4a** and **4b** follow from the performed transformations (*R*,1*R*,α*R*)-(+)-**4a** → (*R*,1*R*)-**2a** → (*R*)-(+)-**1a** and (*S*,1*S*,(*R*)-**4b** → (*S*,1*S*)-**2b** → (*S*)-(–)-**1b**.

In Fig. 3 the CD curves in the region 190–370 nm for the (*Z*)-enones **1a** and **1b** and the carbamates **4a** and **4b** are compared. It is evident that, except of the small region 275–295 nm, all CD bands are of the same sign, *i.e.* the positive for (*R*)-(+)-**1a** and the negative for (*S*)-(–)-**1b**. In addition, CD of the atropodiastereoisomeric carbamates **4a** and **4b** are almost perfectly mir-

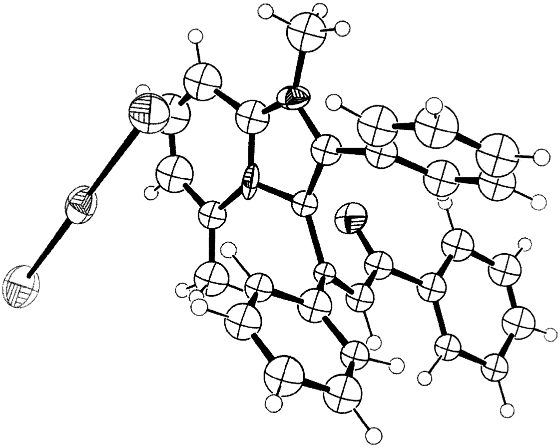


FIG. 2
X-Ray crystal structure of triiodide **6**

ror shaped. Hence, it may be concluded that the atropisomeric chromophore involving hindered rotation between heterocyclic and –C(Ph)=CH– side chain parts of the molecules exhibits a dominant effect on the general shape of the CD spectra and thus reflects the *R* or *S* configurations. On the other hand, the nature of the carbonyl chromophores in the region 290–400 nm seems to be of lesser significance.

It may be expected that various alkyl and simple aryl substituents in the series of **1**-like molecules will not significantly affect the shape of the CD curves and analogous absolute configuration assignments should be possible only on the basis of the CD measurements.

To support the conservation of axial chirality relationships during the presented stereochemical correlations, theoretical barriers to rotation of the key intermediates **2a**,**b** and **3a**,**b** were calculated using the recently reported[3b] procedure.

EXPERIMENTAL

The temperature data are uncorrected. Melting points were determined on a Boetius block. NMR spectra (δ, ppm; *J*, Hz) were taken on a Unity 500 HC instrument at 297 K. The working frequency was 500 MHz for ^{1}H and 125 MHz for ^{13}C. Elemental analyses were performed on Perkin–Elmer 240 analyser. IR spectra (ν, cm^{-1}; CHCl$_3$ solutions) were measured on a FTIR spectrometer Nicolet 740. X-Ray analysis was perfomed on an Enraf CAD4 diffractometer. Optical rotation was measured on an Opton polarimeter using a 10 cm

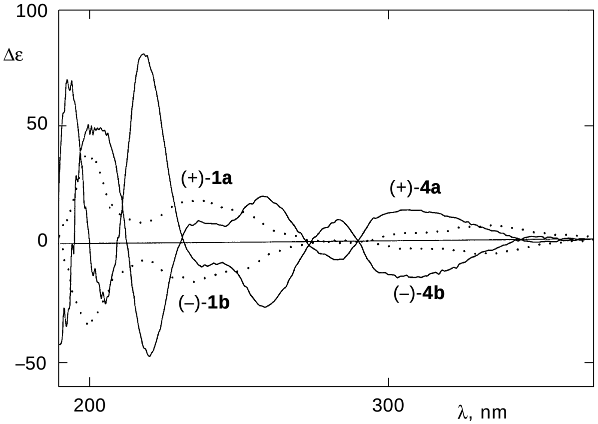


FIG. 3
Comparison of CD curves of (*Z*)-enones **1a** and **1b** with those of the corresponding carbamates **4a** and **4b**

cuvette at 293 and 298 K, specific rotation values $[\alpha]_D$ are given in 10^{-1} deg cm^2 g^{-1}. CD measurements were performed using a Jobin Yvon Mark VI dichrographe. HPLC analyses were performed using an Ecom LCP 4000 chromatograph with an LCD 2082 UV/VIS detector, column was Nucleosil C-18 Macherey–Nagel column, the mobile phase was $CH_3OH–H_2O$ (8 : 2 or 7 : 3). Samples for HPLC analyses were dissolved in MeOH. Commercial Silufol plates (Kavalier Sázava, Czech Republic) were used for TLC. Merck 40 and Merck 60 PF 254 silica gels were used for column and preparative TLC chromatography, respectively. Eluent for column or TLC chromatography was CH_2Cl_2–EtOH (98 : 2 for TLC, gradient for column chromatography). (*R*)-α-Phenylethyl isocyanate was purchased from Fluka. THF was distilled from benzophenone ketyl prior to use.

(*R*,1*R*)-(*Z*)-3-(5-Methyl-2-phenylimidazo[1,2-*a*]pyridin-3-yl)-1,3-diphenylprop-2-en-1-yl *N*-(*R*)-α-Phenylethyl Carbamate (**4a**) and (*S*,1*S*)-(*Z*)-3-(5-Methyl-2-phenylimidazo[1,2-*a*]pyridin-3-yl)-1,3-diphenylprop-2-en-1-yl *N*-(*R*)-α-Phenylethyl Carbamate (**4b**)

DBU (180 μl, 183 mg, 1.20 mmol) was added to a stirred solution of racemic alcohol-**2a**,**b** (ref.[5]; 1.00 g, m.p. 174–176 °C, 2.40 mmol) in dry THF (35 ml). After 5 min of stirring (*R*)-α-phenylethyl isocyanate (507 μl, 530 mg, 3.60 mmol) was added to the solution *via* syringe at room temperature. The reaction mixture was then stirred overnight at room temperature. Solvent was evaporated off and the residue was subjected to chromatography on reversed phase column to remove the unreacted starting alcohol (Fluka, Silica gel 100, C_{18}-Reversed phase; eluent methanol–water, 4 : 1). Fractions containing a mixture of carbamates **4a** and **4b** were evaporated to yield 1.43 g (100%) of crude product. This mixture was chromatographed on column (150 g silica gel; eluent dichloromethane–ethanol, 98 : 2). Less polar fractions contained the lower melting carbamate which was isolated as a solid foam (this product was later identified as the (*S*,1*S*,α*R*)-**4b**). Yield 384 mg (28%), m.p. 83–86 °C, $[\alpha]_D^{20}$ –153.91 (*c* 1.016, $CHCl_3$). ^{1}H NMR ($CDCl_3$): 1.30 d, 3 H, *J* = 6.6 (CH_3); 2.00 brs, 3 H (5-CH_3); 4.45–4.55 m, 2 H (CH + NH); 5.88 d, 1 H, *J* = 7.4 (H-1′); 6.22 brs, 1 H; 6.62–7.40 m, 20 H; 7.55 d, 1 H, *J* = 9.2; 7.95 d, 2 H, *J* = 7.8. ^{13}C NMR ($CDCl_3$): 19.37 CH_3; 22.25 CH_3; 50.40 CH; 75.56 CH; 113.21 CH; 115.60 CH; 117.02 C; 124.82 CH; 125.85 CH; 126.37 CH; 127.15 CH; 127.53 CH; 127.73 CH; 127.85 CH; 128.23 CH; 128.40 CH; 128.48 CH; 129.10 CH; 133.91 C; 134.16 C; 136.51 C; 139.51 C; 140.48 C; 143.26 C; 143.87 C; 146.97 C; 153.93 CO (three CH signals were overlapped). IR: ν(–O–CO–NH–) 1 723; ν(–NH–) 3 445. For $C_{38}H_{33}N_3O_2$ (563.7) calculated: 80.97% C, 5.90% H, 7.46% N; found: 80.73% C, 6.35% H, 7.22% N.

The more polar fractions were evaporated and the residue was crystallized from acetone–hexane affording white crystals of the higher melting carbamate (this product was later identified as the (*R*,1*R*,α*R*)-**4a**). Yield 420 mg (31%), m.p. 154–158 °C, $[\alpha]_D^{20}$ +197.47 (*c* 1.008, $CHCl_3$). ^{1}H NMR ($CDCl_3$): 1.27 d, 3 H, *J* = 6.6 (CH_3); 1.96 s, 3 H (5-CH_3); 4.56 brs, 2 H (CH + NH); 5.83 d, 1 H, *J* = 7.6 (H-1′); 6.22 brd, 1 H, *J* = 6.5; 6.65–7.33 m, 20 H; 7.53 d, 1 H, *J* = 9.3; 7.89 d, 2 H, *J* = 7.1. ^{13}C NMR ($CDCl_3$): 19.32 CH_3; 22.29 CH_3; 50.36 CH; 75.78 CH; 113.19 CH; 115.58 CH; 117.01 C; 124.82 CH; 125.93 CH; 126.37 CH; 127.22 CH; 127.50 CH; 127.68 CH; 127.88 CH; 128.13 CH; 128.38 CH; 128.49 CH; 129.19 CH; 133.76 C; 134.23 C; 136.45 C; 139.57 C; 140.53 C; 143.31 C; 145.83 C; 146.97 C; 153.91 CO (three CH signals were overlapped). IR: ν(–O–CO–NH–) 1 721; ν(–NH–) 3 446. For $C_{38}H_{33}N_3O_2$ (563.7) calculated: 80.97% C, 5.90% H, 7.46% N; found: 81.22% C, 5.93% H, 7.38% N.

(*R*)-(*Z*)-3-(5-Methyl-2-phenylimidazo[1,2-*a*]pyridin-3-yl)-1,3-diphenylprop-2-en-1-one ((*R*)-**1a**)

A solution of (*R*,1*R*,α*R*)-**4a** (280 mg, 0.497 mmol) in 5% MeONa–MeOH (20 ml) was heated to reflux for 2 h. The reaction mixture was poured into water (150 ml) and extracted with 4 × 10 ml of dichloromethane, the collected organic extracts were dried with sodium sulfate and evaporated. The residue was chromatographed using preparative TLC (20 × 20 cm sheet, 16 g of silica gel; eluent petroleum ether–acetone, 9 : 1) affording alcohol (*R*,1*R*)-**2a**, which was subsequently oxidized without further purification. The oxidation procedure was following: *tert*-butyl hydroperoxide solution (70% in water, 273 μl, 256 mg, 1.99 mmol) and catalytic amount of chromium(VI) oxide (2.5 mg, 0.05 mmol) were added to a solution of alcohol **2a** in dichloromethane (5 ml). The reaction mixture was then stirred in dark at room temperature for 48 h. The mixture was then washed with a solution of sodium sulfite (5%, 5 ml) and the organic phase was separated. Volatile components were evaporated off and the residue was chromatographed using preparative TLC (20 × 20 cm sheet, 16 g of silica gel; eluent dichloromethane–ethanol, 99 : 1) affording enone **1a**. The analytical sample was crystallized from ethanol. Yield 90 mg (44%), m.p. 178–180 °C, $[\alpha]_D^{25}$ +290.0 (*c* 0.800, $CHCl_3$). The NMR spectra correspond to those published earlier[1a] for racemic compound **1a**,**b**.

(*S*)-(*Z*)-3-(5-Methyl-2-phenylimidazo[1,2-*a*]pyridin-3-yl)-1,3-diphenylprop-2-en-1-one ((*S*)-**1b**)

Enantiomer (*S*)-**1b** was prepared by the same method used for the preparation of the enone (*R*)-**1a**. The reaction was started from carbamate (*S*,1*S*,α*R*)-**4b** (210 mg, 0.373 mmol) and yielded enone (*S*)-**1b**. Yield 66 mg (43%), m.p. 178–180 °C, $[\alpha]_D^{25}$ –306.2 (*c* 1.016, $CHCl_3$). The NMR spectra correspond to those published earlier[1a] for racemic compound **1a**,**b**.

Racemic 1,5-Dimethyl-3-[(*Z*)-3-oxo-1,3-diphenylprop-1-en-1-yl]-2-phenylimidazo-[1,2-*a*]pyridin-4-ium Triiodide (**6a**,**b**)

Racemate of enone **1a**,**b** (100 mg, 0.241 mmol) was dissolved in acetonitrile (4 ml). Methyl iodide (3 ml) was added to the solution and the reaction mixture was then stirred in dark at room temperature for 48 h. The reaction mixture was evaporated to dryness and white yellow residue was crystallized from solution of iodine (60 mg, 0.241 mmol) in methanol (20 ml). The crystals were collected to give 133 mg (68%) of triiodide **6a**,**b** with m.p. 215–217 °C. ^1H NMR (DMSO-d_6): 2.58 s, 3 H (C-CH_3); 3.83 s, 3 H (N-CH_3); 7.15 dd, 2 H, *J* = 1.3, 8.3; 7.27 dd, 2 H, *J* = 7.7, 8.1; 7.38–7.53 m, 7 H; 7.66 tt, 1 H, *J* = 1.2, 7.4; 7.74 dt, 2 H, *J* = 1.3, 6.7; 7.79 dd, 2 H, *J* = 1.2, 8.4; 8.10 dd, 1 H, *J* = 7.2, 9.2; 8.25 s, 1 H (H-2′); 8.31 dt, 1 H, *J* = 1.1, 9.2. ^{13}C NMR (DMSO-d_6): 19.11 CH_3; 32.69 CH_3; 109.96 CH; 118.90 CH; 121.38 C; 124.58 C; 127.96 CH; 128.66 CH; 128.92 CH; 128.93 CH; 129.61 CH; 129.84 CH; 130.77 CH; 131.13 CH; 131.20 CH; 134.02 CH; 134.07 CH; 134.92 C; 136.87 C; 137.85 C; 138.72 C; 139.73 C; 140.99 C; 190.80 C. IR: ν(C=O) 1 659. For $C_{30}H_{25}I_3N_2O$ (810.3) calculated: 44.47% C, 3.11% H, 46.99% I, 3.46% N; found: 44.25% C, 3.43% H, 46.89% I, 3.34% N.

(*R*)-1,5-Dimethyl-3-[(*Z*)-3-oxo-1,3-diphenylprop-1-en-1-yl]-2-phenylimidazo[1,2-*a*]pyridin-4-ium Triiodide ((*R*)-**6a**)

The title compound was prepared as described above for preparation of the racemic triiodide. The reaction was started from homochiral (*R*)-**1a** (21 mg, 0.05 mmol) and yielded 17 mg (42%) of triiodide (*R*)-**6a** with m.p. 168–169 °C. The NMR spectra correspond to above showed spectra of racemic triiodide. A suitable crystal for X-ray analysis was obtained using slow crystallization from methanol.

CD Measurements

CD measurements were performed using Jobin Yvon Mark VI dichrographe. The spectra were recorded in ethanolic solutions at room temperature. Quartz cells with the pathlength of 0.01–0.1 cm and sample concentrations $1 \cdot 10^{-3}$ mol/l were used. The spectra were normalized with respect to pure solvent and replotted using Spetracalc and Gramms (Galaxy Industries) software packages.

X-Ray Difraction Analysis of Triiodide **6a**

$C_{30}H_{25}I_3N_2O_1$, M_f = 810.26, orthorhombic system, space group $P2_12_12_1$, a = 9.70(1) Å, b = 10.87(1) Å, c = 56.64(1) Å, Z = 8, V = 5 972(3) Å^3, D_{calc} = 1.8 g/cm^3, μ(CuKα) = 24.84 mm^{-1}, crystal dimensions of 0.15 × 0.2 × 0.2 mm. Data were measured at 293 K on an Enraf–Nonius CAD4 diffractometer with graphite monochromated CuKα radiation. The structure was solved by direct methods[10]. Due to the presence of heavy atoms of iodine the carbon atoms were refined only isotropically. The whole structure was refined by full matrix least-squares on F values[11] to final R = 0.089 and R_w = 0.0977 using 5 325 independent reflections (θ_{max} = 60°). Hydrogen atoms were located from expected geometry and were not refined. The absolute configuration was proved by Flack's enantiopole parameter converging[8] to value 0.01(2). Psi scan was used for the absorption correction. Crystallographic data for the structure of triiodide **6a** reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication number CCDC-146519. Copies of the data can be obtained free of charge on application to CCDC, e-mail: deposit@ccdc.cam.ac.uk.

Calculations

All heats of formation were calculated by the semiempirical PM3 method[12] and the approximate procedure[3b] was used to calculate barriers to intramolecular rotations.

REFERENCES AND NOTES

1. a) Kubík R., Böhm S., Ruppertová I., Kuthan J.: *Collect. Czech. Chem. Commun.* **1996**, *61*, 126; b) Böhm S., Strnad T., Ruppertová I., Kuthan J.: *Collect. Czech. Chem. Commun.* **1997**, *62*, 1599; c) Pohl R., Böhm S., Kuthan J.: *Collect. Czech. Chem. Commun.* **1999**, *64*, 1274.
2. a) Böhm S., Kubík R., Hradilek M., Němeček J., Hušák M., Kratochvíl B., Kuthan J.: *Collect. Czech. Chem. Commun.* **1995**, *60*, 115; b) Kubík R., Němeček J., Böhm S., Hradilek M.,

Kuthan J.: *Mendeleev Commun.* **1995**, *29*; c) Kubík R., Böhm S., Kuthan J.: *Collect. Czech. Chem. Commun.* **1996**, *61*, 1018.

3. a) Mannschreck A., Pustet N.: Personal communication; b) Böhm S., Pohl R., Kuthan J.: *Collect. Czech. Chem Commun.* **1999**, *64*, 1761.
4. Õki M.: *Top. Stereochem.* **1983**, *14*, 1.
5. a) Dai X., Wong A., Virgil S. C.: *J. Org. Chem.* **1998**, *63*, 2597; b) Tulinsky J., Mizsak S. A., Watt W., Dolak L. A., Judge T., Gammil R. B.: *Tetrahedron Lett.* **1995**, *36*, 2017; c) Ikeura Y., Ishimaru T., Doi T., Kawada M., Fujishima A., Natsugari H.: *Chem. Commun.* **1998**, 2141; d) Brandt E. V., Young D. A., Young E., Ferreira D.: *J. Chem. Soc., Perkin Trans. 2* **1987**, 1365; e) Li H., Nehira T., Hagiwara M., Harada N.: *J. Org. Chem.* **1997**, *62*, 7222; f) Brunner H., Olschewski G., Nuber B.: *Synthesis* **1999**, *3*, 429; g) Slany M., Stang P. J.: *Synthesis* **1996**, 1019; h) Ohno A., Kunitomo J., Kawai Y.: *Tetrahedron* **1997**, *53*, 4601; i) Ohno A., Kunitomo J., Kawai Y., Kawamoto T., Tomishima M., Yoneda F.: *J. Org. Chem.* **1996**, *61*, 9344; j) Gelpke A. E. S., Fraanje J., Goubitz K., Schenk H., Hiemstra H.: *Tetrahedron* **1997**, *53*, 5899.
6. Čejka J., Kubík R., Kratochvíl B., Kuthan *J.: Collect. Czech. Chem. Commun.* **1996**, *61*, 1380.
7. A more accurate HPLC investigation of the crude mixture of the atropodiastereoisomeric mixture (Macherey–Nagel Nucleosil 120-5 C_{18} column, detector UV 254 nm; mobile phase methanol–water, 7 : 3, flow 1 ml/min) has shown that, contrary to the preliminary report[2b], the higher melting racemate is in fact minor (R_t = 11.30 min, 40%) while the lower metlting form is major (R_t = 9.59 min, 55%) component.
8. Flack H. D.: *Acta Crystallogr., Sect. A: Fundam. Crystallogr.* **1983**, *39*, 876.
9. Böhm S., Kubík R., Hradilek M., Něměček J., Hušák M., Pakhomova S., Ondráček J., Kratochvíl B., Kuthan J.: *Collect. Czech. Chem. Commun.* **1994**, *59*, 2677.
10. Altomare A., Cascarano G., Giacovazzo G., Guagliardi A., Burla M. C., Polidori G., Camalli M.: *J. Appl. Crystallogr.* **1994**, *27*, 435.
11. Watkin D. J., Prout C. K., Carruthers R. J., Betteridge P.: *CRYSTALS*, Issue 10. Chemical Crystallography Laboratory Oxford, Oxford 1996.
12. Stewart J. J. P.: *J. Comput. Chem.* **1989**, *10*, 209.