Regio- and Diastereoselectivity in 1,3-Dipolar Cycloaddition Reactions of 2-Phenylisatogen and Its 3-Phenylimino Derivative with Electron-Deficient Alkenes[‡]

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The 1,3-dipolar cycloadditions of the cyclic nitrones 2-phenyl-3*H*-indole-3-one *N*-oxide (2-phenylisatogen, **1a**) and 2-phenyl-3-phenylimino-3*H*-indole *N*-oxide (**1b**) to several electron-deficient alkenes **2a–d** are reported. All the reactions studied are highly diastereoselective: the regioisomers with the ethoxycarbonyl group attached to the 4-position of the isoxazolidine moiety are the only products isolated, except in the reactions of nitrones **1a** and **1b** with ethyl acrylate **2a** where mixtures of the two different regioisomers are obtained. Crystal structures of compounds **3b**, **5a**, **5b**, **9a** and **10b** were determined by X-ray analysis, while the structure of the other cycloadducts was determined by spectroscopic analysis. Ab initio calculations were carried out showing that product distribution may be influenced by kinetic rather than thermochemical factors. Ab initio calculations of the ^{1}H NMR shielding tensor were performed on compounds **3b**, **4b**, **5a** and **6b** and the chemical shifts obtained are in perfect agreement with the experimental ones.

Introduction

Isoxazolidines, the products of 1,3-dipolar cycloaddition reactions between nitrones and dipolarophiles of different types, may be optically active compounds.[2] They are the precursors of biologically important products such as 1,3-amino alcohols[2] or β-lactams[3] in which the stereochemistry of the stereogenic centres of the cycloadducts is retained. For these reasons, asymmetric 1,3-dipolar cycloaddition reactions have received increasing attention and they can be approached either by the use of chiral nitrones[4] and of dipolarophiles having chiral auxiliary groups[5] or by a chiral catalyst.[2] Ab initio quantum mechanical calculations have been described extensively in the literature to model the stereochemical outcome of cycloaddition reactions.[6] Although the most used nitrones in cycloaddition reactions are acyclic ones, several papers have appeared in the last decades describing the reactions of cyclic nitrones.[7] We have recently studied the reactions between nitrones **1a** and **1b** and maleimides variously substituted at the nitrogen atom;[1] these reactions were diastereoselective since in each case both the *endo* and *exo* diastereomeric cycloadducts were isolated with different yields. The catalytic activity of metal cations such as Co^{II}, Ca^{II}, Zn^{II} and Ni^{II} in these reactions was also studied and it was found that in the presence of these cations, there was an increase in the yields of the reactions but no effect on their diastereoselectivity.

In this paper 1,3-dipolar cycloaddition reactions of 2-phenyl-3*H*-indole-3-one *N*-oxide (**1a**) and 2-phenyl-3-phenylimino-3*H*-indole *N*-oxide (**1b**) with electron-deficient asymmetric alkenes such as ethyl acrylate (**2a**), ethyl β-methyl crotonate (**2b**), ethyl crotonate (**2c**) and ethyl cinnamate (**2d**) are described (Scheme 1). It will be shown that these reactions are highly regio- and diastereoselective.

Results and Discussion

Aromatic *N*-oxides **1a** and **1b** were allowed to react with activated ethylenes **2a**−**d** that were also used as solvents and the expected cycloadducts were obtained, in some cases in very good yields. Regio- and stereochemical details of these additions along with reaction temperature and time, isolated yield and composition of the isomeric cycloadducts obtained are given in Table 1.

[‡] Part 2 of a series. Part 1: Ref.[1]

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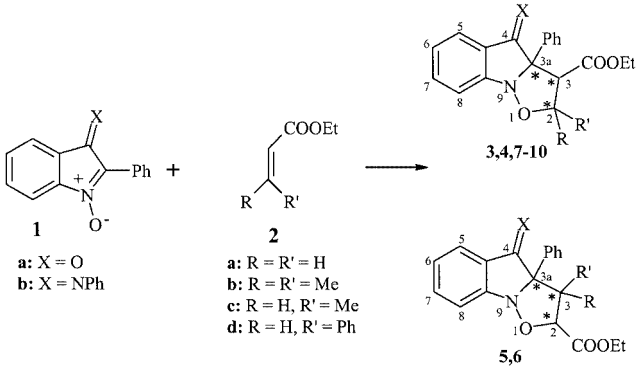
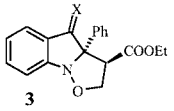
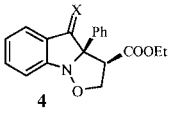
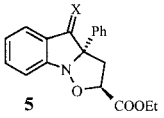
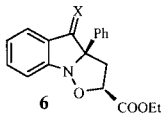
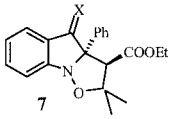
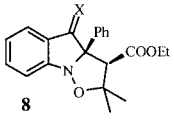
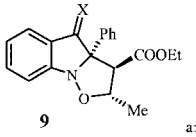
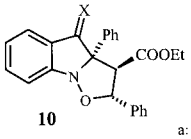


Scheme 1

Addition of ethyl acrylate (**2a**) to nitrones **1a** and **1b** afforded regioisomeric mixtures of all four possible adducts. The ^{1}H NMR spectra of the crude reaction products were used to assign the stereochemistry of the diastereomers and to determine the percentage composition of the mixtures by integrating the methyl signals of the ethoxycarbonyl groups (Table 1). From preparative chromatography, only compounds **3b**, **5a** and **5b** were obtained as racemic mixtures (see Exp. Sect.). The drawings included throughout the text only indicate the relative position of the different groups and not the absolute configuration.

The formation of the four diastereomers is in agreement with the tendency of electron-deficient monosubstituted olefins to give mixtures of 4- and 5-substituted isoxazolidines.[7d,8] Four different routes are open to planar dipolarophile ethyl acrylate (**2a**) in approaching *N*-oxides **1a** and **1b**, the ethoxycarbonyl group being oriented towards either the C-2 atom of the nitrone molecule or the oxygen atom of the *N*-oxide function. Two regioisomers are obtained and, in both of them, the ethoxycarbonyl group may be *syn* or *anti* with respect to the phenyl group of the indole moiety. The presence of the four possible diastereomeric cycloadducts identified in the reaction is fully justified by the existence of two chiral centres for both regioisomers. The reaction of nitrone **1a** is more regioselective than that of **1b**: in fact, in the former case, the two pairs of regioisomers are obtained in a 7:3 ratio, while in the latter, roughly in a 1:1 ratio (Table 1).

Table 1. Regio- and stereochemistry of cycloadditions of *N*-oxides **1a**−**b** to alkenes **2a**−**d**

Reaction	Time (h)	Temperature (°C)	Adducts and % Composition	Overall Yields (%)
1a + **2a**	4	80	 **3** a: 17.5% b: 37.5%  **4** a: 9.8% b: 12.0%	98
1b + **2a**	4	80	 **5** a: 48.8% b: 17.0%  **6** a: 23.9% b: 33.5%	94
1a + **2b**	8	130	 **7** a: 81.9% b: 83.3%  **8** a: 18.1% b: 16.7%	45
1b + **2b**	8	130		40
1a + **2c**	4	80	 **9** a: 100% b: 100%	85
1b + **2c**	4	80		90
1a + **2d**	10	130	 **10** a: 100% b: 100%	47
1b + **2d**	10	130		43

In our opinion, product distribution is determined by kinetic factors and not by thermodynamics. In fact, as already documented with ab initio studies for other molecular systems,[6] energy differences among the possible transition states may be responsible for product distribution. Unfortunately, our systems are too computationally demanding for such a systematic study and, to confirm our hypothesis, our investigation was limited to the thermochemistry of the reactions between **1b** and **2a** and between **2a** and **3c**, in particular (see Exp. Sect.). From the results obtained, collected in Table 2, it is clear that the small differences in the Gibbs free energy changes of the reaction do not account for the yields of the various isomers. This is particularly evident in the reaction between **1a** and **2c** whose thermodynamic data are very similar for the four different possible isomers, whereas only one diastereomer has been isolated. In this case, investigation was also extended to the two isomers with the ethoxycarbonyl group oriented toward the oxygen atom of the *N*-oxide function, indicated in Table 2 as **1a +2c-C** and **1a +2c-T**, which have never been detected in the reaction (see below).

Table 2. Computed parameters for compounds **1, 2a, 2c**, **3b**−**6b** and **9a**

	H[a][b]	G[a][c]	$\Delta_r H^0_{298}$[d]	$\Delta_r G^0_{298}$[e]
1a	−743.840029	−743.893039	−	−
1b	−954.913948	−954.978262	−	−
2a	−345.652465	−345.694151	−	−
3b	−1300.585727	−1300.668201	−12.12	2.64
4b	−1300.580758	−1300.664883	−9.00	4.73
5b	−1300.584359	−1300.669700	−11.26	1.70
6b	−1300.584129	−1300.669936	−11.12	1.55
2c	−384.944372	−384.989993	−	−
9a-C[f]	−1128.797633	−1128.871203	−8.30	7.42
9a-T[f]	−1128.806010	−1128.879999	−13.56	1.90
1a +2c-C[f]	−1128.795288	−1128.869946	−6.83	8.21
1a +2c-T[f]	−1128.798277	−1128.873893	−8.71	5.73

[a] In Hartrees as obtained from the frequency calculations (1 Hartree = 627.5095 kcal) and related to the gas phase. [b] Sum of electronic and thermal enthalpies at 298.15 K. [c] Sum of electronic and thermal Gibbs free energies at 298.15 K. [d] Heat of reaction at 298.15 K in kcal. [e] Reaction Gibbs free energy changes at 298.15 K in kcal. [f] C denotes a *cis* relationship between the phenyl group of the indole moiety and the ethoxycarbonyl group; T denotes a *trans* relationship between the same two groups.

X-ray analysis of compounds **3b**, **5a** and **5b** was particularly useful in determining their stereochemistry (Figures 1, 2, and 3). In fact, the ^{1}H NMR spectrum of the crude reaction mixture (**1b +2a)** did not easily allow the identification of diastereomers **5b** and **6b** since the chemical shifts of their ester methyl groups are very similar (δ = 1.09 and 1.19 ppm, respectively). Using both techniques, it was possible to attribute the lowest chemical shift value to the methyl of **5b** and, consequently, the value of δ = 1.19 ppm to the methyl of **6b**. This difficulty was overcome in diastereomers **3b** and **4b** because the methyl signals fall far from each other, at δ = 1.36 and 0.95 ppm respectively.

Diastereomers **4b** and **6b** were identified on the basis of the ^{1}H NMR spectrum of the crude reaction mixture, because neither could be isolated. However, in the assignment it was taken into account that unfavourable steric effects deriving from the *cis* relationship between the ethoxycarbonyl and the phenyl groups in isomer **4b** may be responsible for the low yield of this cycloadduct.

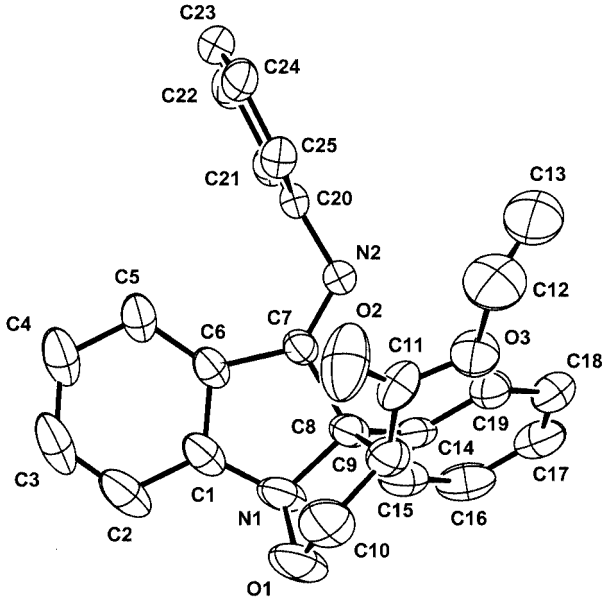


Figure 1. An ORTEP view (30% probability ellipsoids) of compound **3b** {ethyl (*anti*,3,3a)-3a-phenyl-4-[(*E*)-phenylimino]-2,3,3a,4-tetrahydroisoxazolo[2,3-*a*]indole-3-carboxylate}

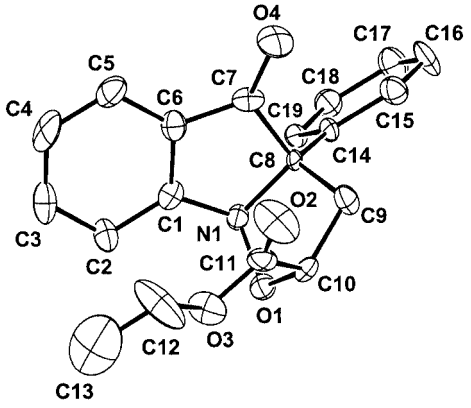


Figure 2. An ORTEP view (30% probability ellipsoids) of compound **5a** {ethyl (*anti*,2,3a)-4-oxo-3a-phenyl-2,3,3a,4-tetrahydroisoxazolo[2,3-*a*]indole-2-carboxylate}

Ab initio calculations of the ^{1}H NMR shielding tensors at the HF/6−31G(d) level, by means of the Gauge-Independent Atomic Orbital (GIAO) method,[9] starting from the full optimized geometries at the B3LYP/6−31G(d) level[10] of compounds **3b**, **4b**, **5b** and **6b**, were also performed. By subtracting the computed values from those arising from identical calculations on $SiMe_4$ as a reference, the chemical shift (in ppm) of each nucleus can be estimated. Table 3 shows that the computed values for the methyl groups mentioned are in good agreement with the experimental data.

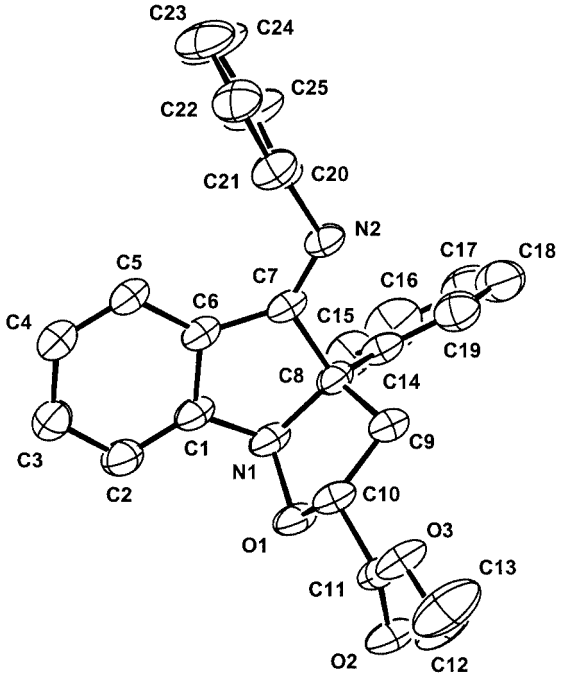


Figure 3. An ORTEP view (30% probability ellipsoids) of compound **5b** {ethyl -(*anti*,2,3a)-3a-phenyl-4-[(*E*)-phenylimino]-2,3,3a,4-tetrahydroisoxazolo[2,3-*a*]indole-2-carboxylate}

Table 3. Computed ^{1}H NMR $-CH_2-CH_3$ chemical shifts (in ppm) for compounds **3**−**6b**

	δ (calcd.)[a]	δ (exp.)[b]	Δδ (calcd. exp.)[c]
3b	1.37	1.36	0.01
4b	1.09	0.94	0.15
5b	1.26	1.10	0.16
6b	1.30	1.20	0.10

[a] Computed values. [b] Experimental values. [c] Difference between computed and experimental values.

The assignment of the structures of the diastereomers **3a**, **4a**, **5a** and **6a** may be solved as before, as the ^{1}H NMR spectra of the mixture of the four diastereomers are strictly similar to those of diastereomers **3b**, **4b**, **5b** and **6b**.

Cycloaddition reactions of nitrones **1a** and **1b** with polysubstituted olefins **2b**−**d** are much more regioselective than the ones with acrylate **2a**: i.e. they yield only the regioisomer(s) (Table 1) derived from the attack of the nucleophilic oxygen atom of the nitrone on the double bond on the opposite site to the electron-withdrawing group. The regiospecificity observed in these reactions is in perfect agreement with that usually observed when 1,2-disubstituted olefins bearing an electron-withdrawing group are used as dipolarophiles[8a,11] and, as previously stated, is not determined by thermodynamic factors (Table 2). The reactions of **1a** and **1b** with alkenes **2c**−**d** are not only regiospecific, but also diastereospecific. For example, the reaction of either ethyl crotonate (**2c**) or ethyl cinnamate (**2d**) afforded only one regioisomer and, at least at the detection limit of ^{1}H NMR spectroscopy, only one diastereoisomer. The structure of the cycloadducts **9a** and **10b** was determined by X-ray analysis (Figure 4 and 5) and by ^{1}H NMR spectroscopy; by analogy, the structure of the other two adducts (**9b** and **10a**) was also assigned. The complete stereoselectivity of addition obtained in the reactions with **2c** and **2d** is due to steric factors: in approaching the nitrones, the ester function of the (*E*)-dipolarophiles is in a *trans* relationship both with the phenyl group of the indole moiety and with the substituent of the alkene methylene, as shown in

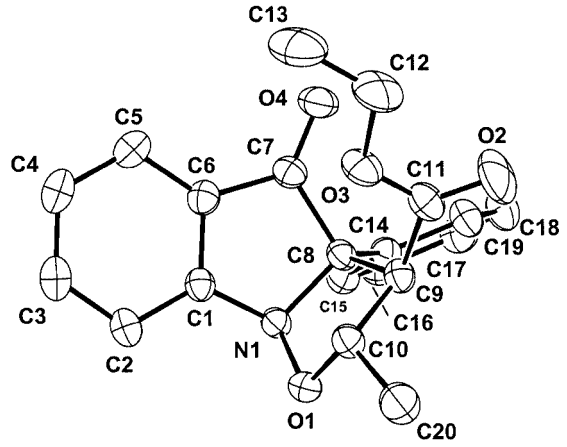


Figure 4. An ORTEP view (30% probability ellipsoids) of compound **9a** {ethyl (*syn*,2,3a;*anti*,2,3)-2-methyl-4-oxo-3a-phenyl-2,3,3a,4-tetrahydroisoxazolo[2,3-*a*]indole)-3-carboxylate}

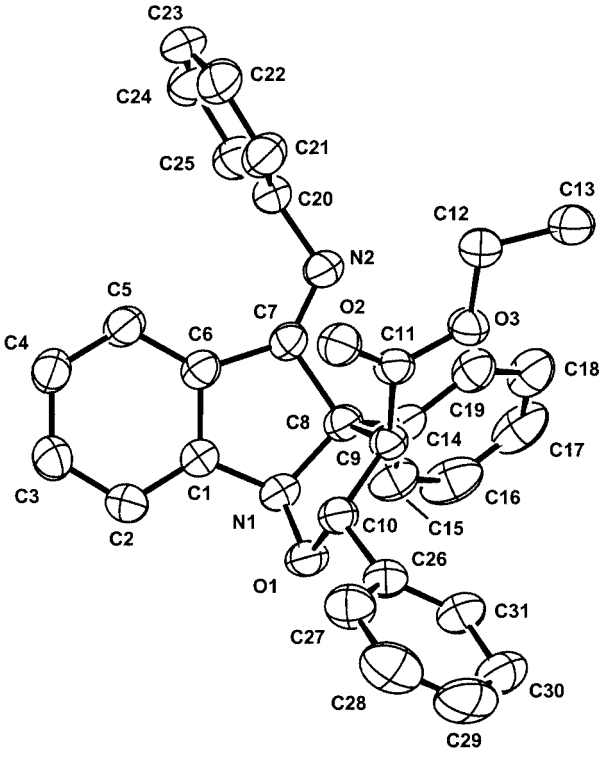
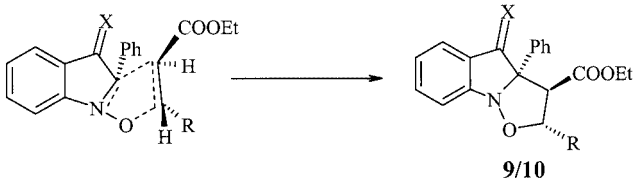


Figure 5. An ORTEP view (30% probability ellipsoids) of compound **10b** {ethyl (*syn*,2,3a;*anti*,2,3)-2,3a-diphenyl-4-[(*E*)-phenylimino]-2,3,3a,4-tetrahydroisoxazolo[2,3-*a*]indole-3-carboxylate}



Scheme 2

Scheme 2. The alternative orientation, i.e. the one with the phenyl and ethoxycarbonyl groups in a *cis* relationship, is so unfavourable that no traces of the corresponding isomer are observed in the ^{1}H NMR spectra of the crude reaction mixtures, whereas in the reactions of acrylate **2a** the same diastereomers (**4a,b**) were formed, although in low yields.

Even in the reaction of ethyl β-methylcrotonate (**2b**) with nitrones **1a** or **1b**, only one regioisomer was obtained as a pair of two diastereomers: the regioisomer comes from the attack of the oxygen atom of the nitrone on the β-ester carbon atom of the alkene, whereas the two diastereomers derive from different orientations of the ethoxycarbonyl group with respect to the phenyl group of the indole moiety. However, the reaction is still very diastereoselective, since the two adducts are obtained in different yields (see Table 1).

Conclusions

Nitrones **1a** and **1b** react diastereoselectively with ethyl acrylate: the four possible diastereomers are all obtained with different yields. When ethyl acrylate is substituted at the methylene carbon with an alkyl or phenyl group in *trans* configuration, addition reactions to nitrones **1a** and **1b** are regio- and diastereospecific, since only one regioisomer is obtained and, among the three possible diastereomers, only one can be isolated.

Experimental Section

Melting points are uncorrected and were measured with an electrochemical apparatus. IR solid-state spectra were measured with a Nicolet Fourier Transform Infrared 20-SX spectrophotometer equipped a Spectra Tech. "Collector" for DRIFT measurements. ^{1}H NMR spectra were recorded at room temperature in $CDCl_3$ or C_6D_6 solution with a Varian Gemini 200 spectrometer ($SiMe_4$ was taken as reference peak). Mass spectra were recorded with a Carlo Erba QMD 1000 mass spectrometer, equipped with a Fisons GC 8060 chromatograph.

Compounds **1a**,[12] and **1b**[13] were prepared and purified according to literature methods. Activated alkenes **2a**−**d** were purchased from Aldrich and used without further purification.

Reaction of 2-Phenyl-3*H*-indole-3-one *N*-Oxide (1a) and 2-Phenyl-3-phenylimino-3*H*-indole *N*-Oxide (1b) with Activated Alkenes 2a−d. General Procedure: Nitrone **1a** (223 mg, 1 mmol) or **1b** (298 mg, 1 mmol) was suspended in alkene (**2a**−**d**; 5 mL) and heated as detailed in Table 1. The reaction solution (0.5 mL) was evaporated to dryness under reduced pressure. The residue was taken up with toluene (1 mL) and the solvents evaporated to dryness; this treatment was repeated twice in order to completely eliminate the alkene. The residue was then dissolved in $CDCl_3$ and submitted to ^{1}H NMR spectroscopy for determining the diastereomers formed

Table 4. Experimental data for the X-ray diffraction studies on crystalline compounds **3b**, **5a**, **5b**, **9a**, and **10b**

Compound	**3b**	**5a**	**5b**	**9a**	**10b**
Empirical formula	$C_{25}H_{22}N_2O_3$	$C_{19}H_{17}NO_4$	$C_{25}H_{22}N_2O_3$	$C_{20}H_{19}NO_4$	$C_{31}H_{26}N_2O_3$
a, Å	18.957(2)	21.839(5)	12.770(3)	31.040(6)	11.789(2)
b, Å	11.074(2)	8.212(2)	8.282(2)	8.070(2)	16.720(3)
c, Å	20.885(2)	18.814(4)	20.635(5)	15.871(3)	12.688(3)
α, °	90	90	90	90	90
β, °	104.63(2)	90	104.14(2)	119.42(2)	91.54(2)
γ, °	90	90	90	90	90
V, Å^3	4236.1(11)	3374.1(13)	2116.3(9)	3462.9(14)	2500.0(9)
Z	8	8	4	8	4
Molecular mass	398.5	323.3	398.5	337.4	474.6
Space group	$P2_1/n$ (no. 14)	*Pbcn* (no. 60)	$P2_1/n$ (no. 14)	$C2/c$ (no. 15)	$P2_1/n$ (no. 14)
T, °C	25	25	25	25	25
λ, Å	0.71069	0.71069	1.54178	1.54178	1.54178
$\rho_{calcd.}$, g cm^{-3}	1.250	1.273	1.251	1.294	1.261
μ, cm^{-1}	0.83	0.90	6.65	8.39	6.50
Transmission coefficient	0.998−1.000	0.997−1.000	0.848−1.000	0.997−1.000	0.998−1.000
R[a]	0.054	0.046	0.084	0.047	0.049
wR_2	0.149	0.057	0.223	0.135	0.125
GOF	1.140	0.736	1.020	1.107	0.820
N-observed[b]	4833	589	2152	2365	1738
N-independent[c]	9007	2973	4004	3282	4736
N-refinement[d]	4833	2109	2152	2365	3840
Variables	541	217	272	226	325

[a] Calculated on the observed reflections having $I > 2\sigma(I)$. [b] *N*-observed is the total number of the independent reflections having $I > 2\sigma(I)$. [c] *N*-independent is the number of independent reflections. [d] *N*-refinement is the number of reflection used in the refinement having $I > 0$ for 5a, 10b and $I > 2\sigma(I)$ for 3b, 5b, 9a.

and their relative ratios. The whole reaction mixture was then evaporated to dryness and the residue chromatographed on a column of silica eluting with cyclohexane/ethyl acetate (95:5); further purification was carried out by preparative TLC using the same eluent. The yields of the isolated products are reported in Table 1; m.p., crystallisation solvents and spectroscopic data are reported below.

X-ray Crystallography for Compounds 3b, 5a, 5b, 9a and 10b: Crystal data and details associated with structure refinement are given in Table 4. Data collections for all compounds were carried out at room temperature (298 K). Data for **3b** were collected with a Bruker AXS 100 CCD by using Mo-K_α radiation. Data for **5a** were collected with a Philips PW1100 diffractometer using graphite-monochromatized Mo-K_α radiation, those for **5b** with a Siemes AED diffractometer using graphite-monochromatized Cu-K_α radiation, and those for **9a**, **10b** with a Enraf−Nonius CAD4 diffractometer by using graphite-monochromatized Cu-K_α radiation. The solutions and refinements were carried out using the programs SIR97 [14] and SHELX97.[15] Selected bond lengths and angles are quoted in Table 5. A comparison of relevant conformational parameters is given in Table 6.

CCDC-200978 to -200982 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge at www.ccdc.cam.ac.uk/conts/retrieving.html [or from the Cambridge Crystallographic Data Centre, 12 Union Road,

Table 5. Selected bond lengths [Å] and angles[°] for compounds **3b**, **5a**, **5b**, **9a**, and **10b**

	3b		**5a**	**5b**	**9a**	**10b**
	Mol. A	Mol. B				
O(1)−N(1)	1.430(5)	1.435(3)	1.457(7)	1.461(3)	1.443(3)	1.438(4)
O(1)−C(10)	1.418(6)	1.432(3)	1.458(8)	1.432(5)	1.445(2)	1.431(4)
N(1)−C(1)	1.419(6)	1.421(3)	1.420(8)	1.429(5)	1.418(3)	1.421(4)
N(1)−C(8)	1.499(6)	1.498(3)	1.509(7)	1.499(5)	1.499(5)	1.492(4)
C(1)−C(2)	1.404(6)	1.389(4)	1.395(9)	1.365(6)	1.390(5)	1.369(5)
C(1)−C(6)	1.380(5)	1.382(3)	1.382(10)	1.400(6)	1.383(5)	1.397(5)
C(2)−C(3)	1.355(7)	1.377(5)	1.383(11)	1.392(6)	1.383(3)	1.378(5)
C(3)−C(4)	1.378(8)	1.392(5)	1.398(11)	1.392(6)	1.387(5)	1.380(5)
C(4)−C(5)	1.383(6)	1.378(6)	1.370(11)	1.359(7)	1.378(5)	1.360(5)
C(5)−C(6)	1.399(6)	1.396(5)	1.408(10)	1.412(5)	1.393(3)	1.394(5)
C(6)−C(7)	1.468(4)	1.467(3)	1.446(9)	1.466(6)	1.418(3)	1.462(4)
C(7)−C(8)	1.533(5)	1.542(3)	1.570(9)	1.548(5)	1.499(5)	1.557(3)
C(7)-X[a]	1.271(4)	1.272(3)	1.217(7)	1.272(5)	1.212(5)	1.268(4)
C(8)−C(9)	1.566(5)	1.568(3)	1.561(7)	1.556(6)	1.561(4)	1.555(4)
C(8)−C(14)	1.525(6)	1.522(3)	1.507(8)	1.516(6)	1.514(5)	1.537(5)
C(9)−C(10)	1.515(7)	1.523(4)	1.524(8)	1.513(6)	1.532(5)	1.526(5)
C(9)−C(11)	1.505(5)	1.511(3)	−	−	1.509(4)	1.522(5)
C(10)−Y[b]	−	−	1.508(9)	1.510(6)	1.503(4)	1.499(4)
N(1)−O(1)−C(10)	104.1(4)	104.5(2)	106.5(4)	103.8(3)	105.0(2)	105.4(2)
O(1)−N(1)−C(1)	112.0(3)	111.4(2)	111.3(4)	109.3(2)	111.7(2)	112.7(2)
O(1)−N(1)−C(8)	106.6(3)	106.9(2)	107.8(4)	107.1(2)	107.4(2)	106.3(2)
C(1)−N(1)−C(8)	107.3(3)	106.9(2)	107.9(5)	107.8(3)	107.2(2)	107.7(2)
N(1)−C(1)−C(2)	126.9(4)	125.1(2)	125.8(6)	125.3(4)	125.6(2)	126.1(3)
N(1)−C(1)−C(6)	112.6(4)	112.2(2)	112.8(5)	111.5(3)	112.5(2)	111.2(3)
C(2)−C(1)−C(6)	120.4(4)	122.6(2)	121.2(6)	123.1(4)	121.6(3)	122.4(3)
C(1)−C(2)−C(3)	118.3(4)	116.9(3)	117.1(6)	117.8(4)	116.6(3)	117.5(3)
C(2)−C(3)−C(4)	122.4(5)	121.7(3)	121.7(7)	120.1(4)	122.3(2)	121.5(3)
C(3)−C(4)−C(5)	119.8(4)	120.5(3)	121.3(8)	122.1(4)	120.8(3)	120.7(3)
C(4)−C(5)−C(6)	118.9(4)	118.9(3)	117.3(6)	118.7(4)	117.7(3)	119.7(3)
C(1)−C(6)−C(5)	120.1(4)	119.3(2)	121.3(6)	118.2(4)	121.0(2)	118.3(3)
C(1)−C(6)−C(7)	107.2(3)	108.0(2)	108.7(6)	108.8(4)	108.5(3)	108.7(3)
C(5)−C(6)−C(7)	132.7(3)	132.6(2)	129.9(6)	133.0(4)	130.5(2)	133.0(3)
X−C(7)−C(6)	132.3(2)	133.8(2)	130.5(5)	133.7(4)	129.3(3)	133.8(3)
X−C(7)−C(8)	119.9(3)	119.3(2)	122.0(5)	119.7(3)	124.0(3)	119.8(2)
C(6)−C(7)−C(8)	107.8(2)	106.8(2)	107.5(5)	106.7(3)	106.7(2)	106.2(2)
N(1)−C(8)−C(7)	102.6(3)	103.2(2)	102.6(4)	104.1(3)	103.4(2)	103.3(2)
N(1)−C(8)−C(9)	103.7(3)	103.6(2)	103.8(4)	103.7(3)	103.7(2)	103.7(2)
N(1)−C(8)−C(14)	111.8(3)	111.1(2)	111.4(5)	111.3(3)	111.4(2)	111.0(3)
C(7)−C(8)−C(9)	114.0(3)	113.9(2)	111.3(4)	111.2(3)	114.5(2)	113.7(2)
C(7)−C(8)−C(14)	112.6(3)	110.8(2)	110.6(5)	111.4(3)	108.2(2)	112.3(2)
C(9)−C(8)−C(14)	111.4(3)	113.4(2)	116.0(4)	114.4(3)	115.0(2)	112.2(3)
C(8)−C(9)−C(10)	101.9(3)	102.7(2)	104.9(4)	102.7(3)	103.2(2)	104.0(2)
C(8)−C(9)−C(11)	115.3(3)	113.7(2)	−	−	115.9(2)	114.3(2)
C(10)−C(9)−C(11)	113.1(4)	112.6(2)	−	−	113.0(3)	112.5(2)
O(1)−C(10)−C(9)	104.8(4)	103.9(2)	103.6(4)	103.7(3)	102.9(2)	103.1(2)
O(1)−C(10)−Y	−	−	114.1(5)	108.2(3)	108.3(2)	108.3(2)
C(9)−C(10)−Y	−	−	112.4(5)	116.1(3)	115.1(3)	117.4(3)

[a] X should be read N(2) for **3b**, **5b**, **10b**; O(4) for **5a**, **9a**. [b] Y should be read C(11) for **5a**, **5b**; C(20) for **9a**; C(26) for **10b**.

Table 6. Comparison of relevant conformational parameters for compounds **3b**, **5a**, **5b**, **9a** and **10b**

	3b		**5a**	**5b**	**9a**	**10b**
	Mol. A	Mol. B				
			Out-of-plane distances within the indole ring [Å]			
N(1)	0.137(4)	0.137(2)	0.068(5)	0.059(3)	0.058(1)	0.141(3)
C(1)	0.002(4)	0.010(2)	−0.012(7)	−0.028(4)	−0.042(3)	−0.011(3)
C(2)	−0.050(4)	−0.083(2)	−0.043(6)	−0.071(5)	−0.080(3)	−0.065(4)
C(3)	−0.044(4)	−0.099(4)	−0.042(7)	−0.045(5)	−0.046(3)	−0.056(4)
C(4)	0.001(4)	−0.013(4)	0.045(9)	0.012(5)	0.030(3)	0.003(4)
C(5)	0.034(4)	0.059(4)	0.048(7)	0.043(4)	0.066(3)	0.061(4)
C(6)	0.015(3)	0.053(2)	0.022(7)	0.017(4)	0.013(3)	0.023(3)
C(7)	−0.001(2)	0.004(2)	−0.029(5)	−0.014(4)	−0.029(3)	−0.002(3)
C(8)	−0.122(4)	−0.132(2)	−0.032(5)	−0.092(4)	−0.135(3)	−0.115(3)
			Out-of-plane distances within the isoxazole ring (Å)			
O(1)	0.191(4)	0.207(2)	0.109(3)	0.153(2)	0.162(2)	0.201(2)
N(1)	−0.136(4)	−0.139(2)	−0.143(5)	−0.103(2)	−0.114(2)	−0.192(3)
C(8)	0.043(4)	0.033(2)	0.015(6)	0.071(4)	0.070(2)	0.037(3)
C(9)	0.058(4)	0.077(2)	0.120(5)	0.157(4)	0.144(2)	0.114(3)
C(10)	−0.342(5)	−0.310(3)	−0.302(6)	−0.358(4)	−0.332(2)	−0.246(3)
Dihedral angles (°):						
N(1),C(1)···C(8) C(14)···C(19)	121.8(1)	107.8(1)	107.7(2)	112.0(1)	102.1(1)	124.6(1)
N(1),C(1)···C(8) C(20)···C(25)	90.9(1)	97.5(1)	–	93.1(2)	–	92.6(1)
Torsion angles (°):						
X−C(7)−C(8)−CC(14) [a]	−47.2(4)	−51.5(3)	−58.0(7)	−54.4(5)	−52.1(4)	−53.7(4)
C(14)−C(8)−C(9)−C(11)	107.8(4)	108.4(2)	–	–	101.3(3)	110.7(3)
C(14)−C(8)···C(10)−C(11)	–	–	170.7(6)	20.1(8)	–	–
C(14)−C(8)···C(10)−Y [b]	–	–	–	–	18.6(6)	17.8(5)

[a] X should be read N(2) for **3b**, **5b**, **10b**; O(4) for **5a**, **9a**. [b] Y should be read C(20) for **9a** and C(26) for **10b**.

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Ab-initio Calculations: Ab initio calculations were carried out by means of a Gaussian[16] package at the B3LYP/6−31G(d) level for geometry optimization and frequencies calculations. For all computed geometries the structures from X-ray analysis were employed as the initial guess; the results are referred to the gas phase but, since the studied reactions were carried out in solution, we believe that the computed structures should be considered rather than those obtained from the solid state which are usually affected by constraints due to crystal packing. In any case, negative values were never found in these calculations (imaginary frequencies), confirming that the computed geometries were always referred to a minimum.

Physical and Spectroscopic Data of Isolated Compounds

Compound 3b: $C_{25}H_{22}N_2O_3$; isolated 140 mg (yield 35%); m.p. 132−134 °C (ligroin 60−80 °C). ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C): δ = 1.36 (t, *J* = 7.2 Hz, 3 H, $-CH_2CH_3$), 4.03 (q, *J* = 10.9 Hz, 2 H, $-CH_2CH_3$), 4.25 (q, *J* = 7.2 Hz, 2 H, $-CH_2-$), 6.38 (d, *J* = 8.0 Hz, 1 H, arom.), 6.86 (d, *J* = 7.6 Hz, 1 H, arom.), 7.12 (pseudo-t, *J* = 7.3 Hz, 1 H, arom.), 7.28−7.50 (m, 7 H, arom.), 7.97 (d, *J* = 7.6 Hz, 2 H, arom.) ppm. IR (KBr): ṽ = 1734 (−COO−), 1669 (−C=N−), 1592 (−C=C−) cm^{-1}. MS (EI$^+$): *m*/*z* = 398 (3) [M$^+$], 325 (20), 297 (26), 282 (100), 205 (22.5), 179 (92). $C_{25}H_{22}N_2O_3$ (398.47): calcd. C 75.36, H 5.57, N 7.03; found C 75.41, H 5.48, N 7.12.

Compound 5a: $C_{19}H_{17}NO_4$; isolated 190 mg (yield 48%); m.p. 104−106 °C (diethyl ether/petroleum ether). ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C): δ = 1.09 (t, *J* = 7.1 Hz, 3 H, $-CH_2CH_3$), 2.98−3.29 (m, 2 H, $-CH_2-$), 4.77 (pseudo-q, *J* = 8.0, 5.1 Hz, 1 H, −CH−), 7.22−7.47 (m, 4 H, arom.), 7.58−7.78 (m, 4 H, arom.) ppm. IR (KBr): ṽ = 1730 (−COO−), 1602 (−C=O) cm^{-1}. MS (EI$^+$): *m*/*z* = 323 (22) [M$^+$], 250 (80), 222 (100), 193 (34). $C_{19}H_{17}NO_4$ (323.35): calcd. C 70.58, H 5.30, N 4.33; found C 70.41, H 5.38, N 4.27.

Compound 5b: $C_{25}H_{22}N_2O_3$; isolated 63 mg (yield 16%); m.p. 113−115 °C (ligroin 60−80 °C). ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C): δ = 1.09 (t, *J* = 7.2 Hz, 3 H, $-CH_2CH_3$), 3.3 (dd, *J* = 12.8, 5.9 Hz, 2 H, $-CH_2-$), 3.82−4.02 (m, 2 H, $-CH_2CH_3$), 4.77 (pseudo-q, *J* = 8.0 Hz, 1 H, −CH−), 6.38 (d, *J* = 7.8 Hz, 1 H, arom.), 6.70 (d, *J* = 7.8 Hz, 2 H, arom.), 7.13 (pseudo-t, *J* = 1.4 Hz, 1 H, arom.), 7.28−7.67(m, 7 H, arom.), 7.83(d, *J* = 1.4 Hz, 2 H, arom.) ppm. IR (KBr): ṽ = 1727 (−COO−), 1677 (−C=N−), 1591 (−C=C−) cm^{-1}. MS (EI$^+$): *m*/*z* = 398 (2) [M$^+$], 368 (12), 323 (34), 295 (92), 282 (100), 205 (30), 79 (96). $C_{25}H_{22}N_2O_3$ (398.47): calcd. C 75.36, H 5.57, N 7.03; found C 75.29, H 5.63, N 7.15.

Compound 7a: $C_{21}H_{21}NO_4$; isolated 130 mg (yield 37%); m.p. 96−98 °C (petroleum ether). ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C): δ = 1.13 (s, 3 H, $-CH_3$), 1.21 (t, *J* = 7.2 Hz, 3 H, $-CH_2CH_3$), 1.37 (s, 3 H, $-CH_3$), 3.71 (s, 1 H, $-CH$COOEt), 4.16 (q, *J* = 7.2 Hz, 2 H, $-CH_2CH_3$), 7.20−7.42 (m, 4 H, arom.), 7.52 (d, 1 H, arom.), 7.60−7.76 (m, 4 H, arom.) ppm. IR (KBr): ṽ = 1723 (−COO−), 1602 (−C=O) cm^{-1}. MS (EI$^+$): *m*/*z* = 351 (11) [M$^+$],

322 (16), 294 (7), 248 (29), 223 (100), 193 (29), 179 (42), 105 (35), 77(28). $C_{21}H_{21}NO_4$ (351.41): calcd. C 71.78, H 6.02, N 3.99; found C 71.68, H 6.11, N 4.05.

Compound 7b: $C_{27}H_{26}N_2O_3$; isolated 133 mg (yield 33%); m.p. 160−162 °C (ligroin 60−80 °C). ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C): δ = 1.17 (s, 3 H, $-CH_3$), 1.26 (t, J = 7.2 Hz, 3 H, $-CH_2CH_3$), 1.37 (s, 3 H, $-CH_3$), 4.23 (dq, J = 7.2, 1.6 Hz, 2 H, $-CH_2CH_3$), 6.38 (d, J = 7.6 Hz, 1 H, arom.), 6.70−7.86 (m, 2 H, arom.), 7.1 (pseudo-t, 1 H, arom.), 7.27−7.47 (m, 7 H, arom.), 7.85 (pseudo-q, 2 H, arom.) ppm. IR (KBr): ṽ = 1736 (−COO−), 1670 (−C=N−), 1593 (−C=C−) cm^{-1}. MS (EI$^+$): m/z = 426 (2.3) [M$^+$], 411 (21.5), 368 (6.5), 323 (46.5), 295 (100), 282 (5), 223 (13), 105 (40). $C_{27}H_{26}N_2O_3$ (426.51): calcd. C 76.03, H 6.14, N 6.57; found C 76.10, H 6.18, N 6.51.

Compound 9a: $C_{20}H_{19}NO_4$; isolated 287 mg (yield 85%); m.p. 133−135 °C (ligroin 60−80 °C). ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C): δ = 1.32 (d, 3 H, $-CH_3$), 1.33 (t, 3 H, $-CH_2CH_3$,), 3.38 (d, 1 H, *CH*COOEt), 4.18−4.43 (m, 3 H, $-CH_2CH_3$ + $-CHCH_3$), 7.23−7.44 (m, 4 H, arom.), 7.53−7.87 (m, 5 H, arom.) ppm. ^{1}H NMR (200 MHz, C_6D_6, 25 °C): δ = 0.97 (d, 3 H, $-CH_3$), 1.07 (t, 3 H, $-CH_2CH_3$), 3.43 (d, 1 H, *CH*COOEt), 3.92−4.23 (m, 2 H, $-CH_2CH_3$), 4.43−4.58 (m, 1 H, $-CHCH_3$), 6.78 (pseudo-t, 1 H, arom.), 7.05−7.30 (m, 4 H, arom.) 7.40 (pseudo-d, 1 H, arom.), 7.48 (pseudo-d, 1 H, arom.), 8.2 (pseudo-d,2 H, arom.) ppm. IR (KBr): ṽ = 1730 (−COO−), 1605 (−C=O) cm^{-1}. MS (EI$^+$): m/z = 337 (27) [M$^+$], 223 (87), 179 (100), 105 (40). $C_{20}H_{19}NO_4$ (337.38): calcd. C 71.20, H 5.68, N 4.15; found C 71.15, H5.70, N 4.11.

Compound 9b: $C_{26}H_{24}N_2O_3$; isolated 371 mg (yield 90%); m.p. 178−179 °C (ligroin 60−80 °C). ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C): δ = 1.34−1.38 (d + t, J = 7.2 Hz, 6 H, $-CH_3$ + $-CH_2CH_3$), 3.55 (d, J = 10.4 Hz, 1 H, *CH*COOEt), 4.28−4.45 (q + d, J = 7.2, 10.3 Hz, 3 H, $-CH_2CH_3$ + $-CHCH_3$), 6.37 (pseudo-q, 1 H, arom.), 6.73 (pseudo-q, 1 H, arom.), 6.78−6.88 (m, 1 H, arom.), 7.26−7.47 (m, 8 H, arom.), 7.92 (pseudo-d, 2 H, arom.) ppm. IR (KBr): ṽ = 1734 (−COO−), 1665 (−C=N−), 1596 (−C=C−) cm^{-1}. MS (EI$^+$): m/z = 413 (3) [M$^+$ + 1], 368 (12), 323 (24), 295 (65), 282 (72), 205 (19.5), 179 (55.%) 77 (100). $C_{26}H_{24}N_2O_3$ (412.49): calcd. C 75.71, H 5.86, N 6.79; found C 75.75, H 5.79, N 6.82.

Compound 10a: $C_{25}H_{21}NO_4$; isolated 188 mg (yield 47%); m.p. 119−121 °C (benzene/petroleum ether). ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C): δ = 1.30 (t, J = 7.1 Hz, 3 H, $-CH_2CH_3$), 3.75 (d, J = 10.4 Hz, 1 H, −CH−), 4.2 (q, J = 7.1 Hz, 2 H, $-CH_2CH_3$), 5.28 (d, J = 10.4 Hz, 1 H, −CH−), 7.22−7.48 (m, 9 H, arom.), 7.6−7.82 (m, 3 H, arom.), 7.92 (pseudo-q, 2 H, arom.) ppm. IR (KBr): ṽ = 1729 (−COO−), 1604 (−C=O) cm^{-1}. MS (EI$^+$): m/z = 399 (10) [M$^+$], 326 (6.5), 223 (100), 105 (41.5),77 (48.5). $C_{25}H_{21}NO_4$ (399.45): calcd. C 75.17, H 5.30, N 3.51; found C 75.22, H 5.34, N 3.56.

Compound 10b: $C_{31}H_{26}N_2O_3$; isolated 204 mg (yield 43%); m.p. 166−167 °C (benzene/petroleum ether). ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C): δ = 1.29 (t, J = 7.1 Hz, 3 H, $-CH_2CH_3$), 3.94 (d, J = 10.4 Hz, 1 H, −CH−), 4.3 (q, J = 7.1 Hz, 2 H, $-CH_2CH_3$), 5.28 (d, J = 10.4 Hz, 1 H, −CH−), 6.42 (d, J = 8.0 Hz, 1 H, arom.), 6.78 (pseudo-q, J = 7.9 Hz, 2 H, arom.), 6.83−6.94 (m, 1 H, arom.), 7.12 (t, J = 7.4 Hz, 1 H, arom.), 7.28−7.52 (m, 12 H, arom.), 8.01 (pseudo-d, J = 7.2 Hz, 2 H, arom.) ppm. IR (KBr): ṽ = 1733 (−COO−), 1662 (−C=N−), 1592 (−C=C−) cm^{-1}. MS (EI$^+$): m/z = 475 (6) [M$^+$ +1], 368 (24), 323 (46.5), 295 (100), 281 (23.5), 267 (25). $C_{31}H_{26}N_2O_3$ (474.56): calcd. C 78.46, H 5.25, N 5.90; found C 75.50, H 5.22, N 5.95.

Selected ^{1}H NMR Spectroscopic Data of Compounds Observed in the Reaction Mixture

Compound 3a: ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C): δ = 1.33 (t, J = 7.3 Hz, 3 H, $-CH_2CH_3$) ppm

Compound 4a: ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C): δ = 0.94 (t, J = 7.3 Hz, 3 H, $-CH_2CH_3$) ppm.

Compound 6a: ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C): δ = 1.20 (t, J = 7.1 Hz, 3 H, $-CH_2CH_3$), 2.89−3.28 (m, 2 H, $-CH_2-$), 4.13 (q, J = 7.1 Hz, 2 H, $-CH_2CH_3$), 4.56 (pseudo-q, J = 9.1 and 7 Hz, 1 H,−CH−) ppm.

Compound 4b: ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C): δ = 0.95 (t, J = 7.3 Hz, 3 H, $-CH_2CH_3$) ppm.

Compound 6b: ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C): δ = 1.19 (t, J = 7 Hz, 3 H, $-CH_2CH_3$), 3.12−3.37.(m, 2 H, $-CH_2-$), 4.13 (q, J = 7.2 Hz, 2 H, $-CH_2CH_3$), 4.62 (pseudo-q, J = 8.9, 7.2 Hz, 1 H, ,−CH−) ppm.

Compound 8a: ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C): δ = 0.99 (t, 3 H, $-CH_2CH_3$), 1.0 (s, 3 H, $-CH_3$) 1.38 (s, 3 H, $-CH_3$), 3.86 (q, 2 H, $-CH_2CH_3$), 3.93 (s, 1 H, $-CH$COOEt) ppm.

Compound 8b: ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C): δ = 0.9 (t, 3 H, $-CH_2CH_3$), 1.18 (s, 3 H, $-CH_3$) 1.38 (s, 3 H, $-CH_3$), 3.86 (q, 2 H, $-CH_2CH_3$), 3.72 (s, 1 H, $-CH$COOEt) ppm.

Crystal Data for Ethyl (*anti*,3,3a)-3a-Phenyl-4-[(*E*)-phenylimino]-2,3,3a,4-tetrahydroisoxazolo[2,3-*a*]indole-3-carboxylate (3b) (CCDC-200978): $C_{25}H_{22}N_2O_3$, M_r = 398.5, monoclinic, space group $P2_1/n$, a = 18.957(2), b = 11.074(2), c = 20.885(2) Å, β = 104.63(2)°, V = 4236.1(11) Å^3, Z = 8, ρ = 1.250 g cm^{-3}; λ(Mo-K_α) = 0.71069 Å, μ(Mo-K_α) = 0.83 cm^{-1}: colourless plate, crystal dimensions 0.06 × 0.19 × 0.30 mm. The structure was solved by direct methods (SIR97) and anisotropically refined for all the non-H atoms. The hydrogen atoms were localized from a difference Fourier map and introduced as fixed contributors in the last stage of refinement (U_{iso} = 0.08 Å^2). The structure was refined on F^2 values (SHELX97) by using the weighting scheme $w = 1/[\sigma^2(F_o^2) + (0.0928P)^2]$ (with $P = (F_o^2 + 2F_c^2)/3$). For 4833 unique observed reflections [$I > 2\sigma(I)$] collected at T = 298(3) K on a Bruker AXS 100 CCD diffractometer ($3 < 2\theta < 54°$) the final R is 0.054 ($wR2$ = 0.149; S = 1.140). The structure contains two crystallographically independent molecules showing a very similar geometry.

Crystal Data for Ethyl 4-Oxo-3a-phenyl-2,3,3a,4-tetrahydroisoxazolo[2,3-*a*]indole-2-carboxylate (5a) (CCDC-200979): $C_{19}H_{17}NO_4$, M_r = 323.3, orthorhombic, space group $Pbcn$, a = 21.839(5), b = 8.212(2), c = 18.814(4) Å, V = 3374.1(13) Å^3, Z = 8, ρ = 1.273 g cm^{-3}; λ(Mo-K_α) = 0.71069 Å, μ(Mo-K_α) = 0.90 cm^{-1}: pale yellow plate, crystal dimensions 0.10 × 0.28 × 0.45 mm. The structure was solved by direct methods (SIR97) and anisotropically refined for all the non-H atoms. The hydrogen atoms were localized from a difference Fourier map and introduced as fixed contributors in the last stage of refinement (U_{iso} = 0.08 Å^2). The structure was refined on F^2 values (SHELX97) by using the weighting scheme $w = 1/\sigma^2(F_o^2)$. For 589 unique observed reflections [$I > 2\sigma(I)$] collected at T = 298(3) K on a Philips PW1100 diffractometer ($3 < 2\theta < 50°$) the final R is 0.046 ($wR2$ = 0.057 for 2109 unique reflections with $I > 0$ used in the refinement; S = 0.736).

Crystal Data for Ethyl (*anti*,2,3a)-3a-Phenyl-4-[(*E*)-phenylimino]-2,3,3a,4-tetrahydroisoxazolo[2,3-*a*]indole-2-carboxylate (5b) (CCDC-200980): $C_{25}H_{22}N_2O_3$, M_r = 398.5, monoclinic, space

group $P2_1/n$, a = 12.770(3), b = 8.282(2), c = 20.635(5) Å, β = 104.14(2)°, V = 2116.3(9) Å^3, Z = 4, ρ = 1.251 g·cm^{-3}; λ(Cu-K_α) = 1.54178 Å, μ(Cu-K_α) = 6.65 cm^{-1}: colourless plate, crystal dimensions 0.12 × 0.30 × 0.42 mm. The structure was solved by direct methods (SIR97) and anisotropically refined for all the non-H atoms. The hydrogen atoms were put in geometrically calculated positions and introduced as fixed contributors in the last stage of refinement (U_{iso} = 0.10 Å^2). The structure was refined on F^2 values (SHELX97) by using the weighting scheme $w = 1/[\sigma^2(F_o^2) + (0.2079P)^2]$; with $P = (F_o^2 + 2F_c^2)/3$. For 2152 unique observed reflections [$I > 2\sigma(I)$] collected at T = 298(3) K on a Siemens AED diffractometer ($3 < 2\theta < 140°$) the final R is 0.084 ($wR2$ = 0.223; S = 1.020).

Crystal Data for Ethyl (*syn*,2,3a;*anti*,2,3)-2-Methyl-4-oxo-3a-phenyl-2,3,3a,4-tetrahydroisoxazolo[2,3-*a*]indole3-carboxylate (9a) (CCDC-200981): $C_{20}H_{19}NO_4$, M_r = 337.4, monoclinic, space group $C2/c$, a = 31.040(6), b = 8.070(2), c = 15.871(3) Å, β = 119.42(2)°, V = 3462.9(14) Å^3, Z = 8, ρ = 1.294 g cm^{-3}; λ(Cu-K_α) = 1.54178 Å, μ(Cu-K_α) = 8.39 cm^{-1}: colourless prism, crystal dimensions 0.20 × 0.22 × 0.28 mm. The structure was solved by direct methods (SIR97) and anisotropically refined for all the non-H atoms. The hydrogen atoms were put in geometrically calculated positions and introduced as fixed contributors in the last stage of refinement (U_{iso} = 0.08 Å^2). The structure was refined on F^2 values (SHELX97) by using the weighting scheme $w = 1/[\sigma^2(F_o^2) + (0.0844P)^2]$; with $P = (F_o^2 + 2F_c^2)/3$. For 2365 unique observed reflections [$I > 2\sigma(I)$] collected at T = 298(3) K on a Enraf−Nonius CAD4 ($3 < 2\theta < 140°$) the final R is 0.047 ($wR2$ = 0.135; S = 1.107).

Crystal Data for Ethyl (*syn*,2,3a;*anti*,2,3)-2,3a-Phenyl-4-[(*E*)-phenylimino]-2,3,3a,4-tetrahydroisoxazolo[2,3-*a*]indole-3-carboxylate (10b) (CCDC-200982): $C_{31}H_{26}N_2O_3$, M_r = 474.6, monoclinic, space group $P2_1/n$, a = 11.789(2), b = 16.720(3), c = 12.688(3) Å, β = 91.54(2)°, V = 2500.0(9) Å^3, Z = 4, ρ = 1.261 g cm^{-3}; λ(Cu-K_α) = 1.54178 Å, μ(Cu-K_α) = 6.50 cm^{-1}: pale yellow prism, crystal dimensions 0.16 × 0.18 × 0.40 mm. The structure was solved by direct methods (SIR97) and anisotropically refined for all the non-H atoms. The hydrogen atoms were put in geometrically calculated positions and introduced as fixed contributors in the last stage of refinement (U_{iso} = 0.08 Å^2). The structure was refined on F^2 values (SHELX97) by using the weighting scheme $w = 1/[\sigma^2(F_o^2) + (0.0512P)^2]$; with $P = (F_o^2 + 2F_c^2)/3$. For 1738 unique observed reflections [$I > 2\sigma(I)$] collected at T = 298(3) K on an Enraf−Nonius CAD4 ($3 < 2\theta < 140°$) the final R is 0.049 ($wR2$ = 0.125 for 3840 unique reflections with $I > 0$ used in the refinement; S = 0.820).

[1] L. Greci, G. Tommasi, P. Bruni, P. Sgarabotto, L. Righi, *Eur. J. Org. Chem.* **2001**, 3147−3153.

[2] [2a] K. V. Gothelf, K. A. Jørgensen, *Chem. Rev.* **1998**, *98*, 863−909. [2b] M. Frederickson, *Tetrahedron* **1997**, *53*, 403−425.

[3] S. Kobayashi, M. Kawamura, *J. Am. Chem. Soc.* **1998**, *120*, 5840−5841.

[4] [4a] P. Merino, J. Revuelta, T. Tejero, U. Chiacchio, A. Rescifina, A. Piperno, G. Romeo, *Tetrahedron: Asymmetry* **2002**, *13*, 167−172. [4b] S. Hanessian, M. Bayrakdarian, *Tetrahedron Lett.* **2002**, *43*, 967−971. [4c] N. Katagiri, M. Okada, Y. Morishita, C. Kaneko, *Tetrahedron* **1997**, *53*, 5725−5746.

[5] [5a] A. Brandi, S. Cicchi, A. Goti, K. M. Pietrusiewicz, M. Zablocka, W. Wieniewski, *J. Org. Chem.* **1991**, *56*, 4383−4388. [5b] P. Bravo, L. Brochè, A. Farina, G. Fronza, S. V. Meille, A. Merli, *Tetrahedron: Asymmetry* **1993**, *4*, 2131−2134. [5c] H. Ina, M. Ito, C. Kibayashi, *J. Org. Chem.* **1996**, *61*, 1023−1029.

[6] [6a] M. A. Silva, J. M. Goodman, *Tetrahedron* **2002**, *58*, 3667−3671. [6b] P. Merino, J. A. Mates, J. Revuelta, T. Tejero, U. Chiacchio, G. Romeo, D. Iannazzo, R. Romeo, *Tetrahedron: Asymmetry* **2002**, *13*, 173−190.

[7] [7a] F. Pisaneschi, C. Della Monica, F. M. Cordero, A. Brandi, *Tetrahedron Lett.* **2002**, *43*, 5711−5714. [7b] R. C. F. Jones, J. N. Martin, P. Smith, *Syn. Lett.* **2000**, *7*, 967−970. [7c] R. C. Bernotas, J. S. Sabol, L. Sing, D. Friedrich, *Syn. Lett.* **1999**, *5*, 653−655. [7d] S. A. Ali, M. I. M. Wazeer, *J. Chem. Soc., Perkin Trans. 1* **1988**, 597−605.

[8] [8a] J. J. Tufariello, *1,3-Dipolar Cycloaddition Chemistry*, John Wiley & Sons: New York, **1984**. [8b]A. Padwa, L. Fisera, K. F. Koehler, A. Rodriguez, G. S. K. Wong, *J. Org. Chem.* **1984**, *49*, 276−281. [8c] T. Tejero, A. Dondoni, I. Rojo, F. L. Merchán, P. Merino, *Tetrahedron* **1997**, *53*, 3301−3318.

[9] J. R. Cheeseman, G. W. Trucks, T. A. Keith, M. J. Frisch, *J. Chem. Phys.* **1996**, *104*, 5497−5509.

[10] [10a] K. Wolinski, J. F. Hinton, P. Pulay, *J. Am. Chem. Soc.* **1990**, *112*, 8251−8260. [10b] J. L. Dodds, R. McWeeny, A. J. Sadlej, *Mol Phys.* **1980**, *41*, 1419. [10c] R. Ditchfield, *Mol Phys.* **1974**, *27*, 789. [10d] McWeeny, *Phys. Rev.* **1962**, *126*, 1028−1034. [10e] F. London, *J. Phys. Radium, Paris* **1937**, *8*, 397.

[11] [11a] F. Busquè, P. de March, M. Figueredo, J. Font, M. Monsalvatje, A. Virgili, A. Álvarez-Larena, J. F. Piniella, *J. Org. Chem.* **1996**, *61*, 8578−8585. [11b] R. Albiés, F. Busquè, P. de March, M. Figueredo, J. Font, T. Parella, *Tetrahedron* **1998**, *54*, 10857−10878. [11c] M. P. S. Ishar, G. Singh, K. Kumar, R. Singh, *Tetrahedron* **2000**, *56*, 7817−7828.

[12] C. C. Bond, M. Hooper, *Synthesis* **1974**, *6*, 443.

[13] L. Marchetti, L. Greci, G. Tosi, *Gazz. Chim. Ital.* **1970**, *100*, 770−776.

[14] A. Altomare, M. C. Burla, M. Camalli, G. Cascarano, C. Giacovazzo, A. Guagliardi, A. G. G. Moliterni, G. Polidori, R. Spagna, *J. Appl. Cryst.* **1999**, *32*, 115−119.

[15] G. M. Sheldrick, SHELXL97, *Program for crystal structure refinement*, University of Göttingen, Germany, **1997**.

[16] Gaussian 98, Revision A.9, M. J. Frisch, G. W. Trucks, H. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, V. G. Zakrzewski, J. A. Montgomery Jr., R. E. Stratmann, J. C. Burant, S. Dapprich, J. M. Millam, A. D. Daniels, K. N. Kudin, M. C. Strain, O. Farkas, J. Tomasi, V. Barone, M. Cossi, B. Cammi, C. Mennucci, C. Pomelli, S. Adamo, J. Clifford, G. A. Ochterski, P. Y. Petersson, Q. Ayala, K. Cui, R. Morokuma, D. K. Malick, A. D. Rabuck, K. Raghavachari, J. B. Foresman, J. Cioslowski, J. V. Ortiz, A. G. Baboul, B. B. Stefanov, G. Liu, A. Liashenko, P. Piskorz, I. Komaromi, R. Gomperts, R. L. Martin, D. J. Fox, T. Keith, M. A. Al-Laham, C. Y. Peng, A. Nanayakkara, M. P. Challacombe, M. W. Gill, B. Johnson, W. Chen, M. W. Wong, J. L. Andres, C. Gonzalez, M. Head-Gordon, E. S. Replogle, J. A. Pople, Gaussian, Inc., Pittsburgh PA, **1998**.

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