Conformational Studies by Dynamic Nuclear Magnetic Resonance. Part 13.[1] Torsional Barriers and Conformational Analysis of *N*-Acylcarbazoles

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The ^{13}C n.m.r. spectra of *N*-acylcarbazoles at low temperature (between −5 and −140 °C) display non-equivalence of the aromatic carbons owing to restricted rotation about the N–COR bond. The free energies of activation were measured and the differences between the various substituents interpreted as due to steric effects in the alkyl, and to electronic properties in the aryl derivatives. A quantitative lanthanide-induced shift (LIS) investigation allowed a measure of the angle between the plane of the RCO group and the aromatic ring for R = Me (25°) and R = Bu^t (75°).

RESTRICTED motion around the N–COR bond has been detected in *N*-acyl pyrroles,[2,3] indoles,[4] and carbazoles;[4] in the latter series, however, the complexity of the ^1H n.m.r. spectra prevents accurate determinations of the torsional barriers, particularly if benzoyl derivatives have to be examined. On the other hand the simplicity of the C-13 patterns allows more reliable information to be obtained. There are three main advantages to a ^{13}C n.m.r. study of the stereodynamics of carbazoles. (i) It is not necessary to analyse two complex and overlapping ABCD spectra, nor use any approximation[4] since only two lines for each pair of non-equivalent carbons are observed.

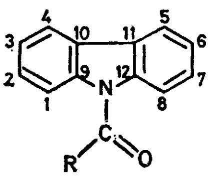
(ii) The larger chemical-shift differences allow the dynamic phenomenon to be followed over a wider range of temperatures, the errors due to uncertainties in the temperature measurements thus being reduced.

(iii) There are many coalescence temperatures within each spectrum, owing to the presence of various pairs of non-equivalent carbons with a variety of chemical-shift differences, so that the internal consistency of the measured $\Delta G^\ddagger$ values can be ascertained.

We thus undertook a ^{13}C study on the stereodynamical behaviour of the title compounds to check the dependence of the torsional barriers on the substituent R in the NCOR group and completed the investigation with a lanthanide-induced shift (LIS) study to determine the conformation of these molecules in two extreme cases (R = Me and R = Bu^t).

RESULTS AND DISCUSSION

The derivatives (1)—(7) have been investigated:



R
(1) = H
(2) = Me
(3) = Et
(4) = Pr^i
(5) = Bu^t
(6) = CF_3
(7) = Ph

(a) *Kinetics of the Dynamic Process.*—The spectra of derivatives (2), (3), (4), and (6) have quite similar behaviour with respect to temperature: a typical ^{13}C spectrum of the aromatic carbons in the two extreme situations is shown in Figure 1 for compound (2). At −30 °C in $CHFCl_2$ there are still six lines for the 12 aromatic carbons, since the rotation of the $CH_3CO–N$ bond is fast on the n.m.r. time scale; at −110 °C each line is split into a doublet since the pairs of carbons are no longer equivalent. In the case of compound (1) the situation is different in that the aromatic carbons are already non-equivalent at −5 °C, whereas equivalence is reached only above 100 °C. In contrast, for compound (7) the dynamic phenomenon is observed at much lower temperature; in Figure 2 it is evident that only

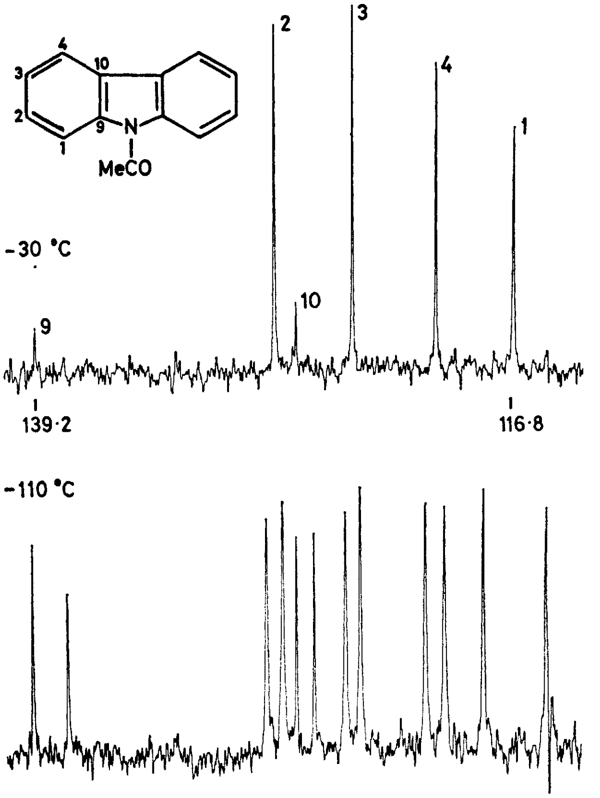


FIGURE 1 F.T. ^{13}C n.m.r. spectra (25.16 MHz) of the aromatic region of *N*-acetylcarbazole (2) in $CHFCl_2$ at −30 °C (upper) and −110 °C (lower)

at −130 °C does the C_6H_5CO–N rotation affect the line shape of the signals. Finally, for compound (5) not even at −160 °C could line broadening due to restricted rotation be detected. From the chemical-shift differences in the slow-exchange region and from the corresponding coalescence temperatures the kinetic constants for the rotational process were obtained and the corresponding $\Delta G^{\ddagger}$ values calculated[5] for all the molecules, with the exception of (5) (Table 1). The various coalescence temperatures were measured for each pair of doublet signals, and the free energies of activation reported in Table 1 are the average of these determinations. In one case we also checked by a total line shape analysis that $\Delta S^{\ddagger}$ is negligible for these processes as reported for many analogous situations.[6] From Table 1 it appears that the torsional barrier for (1; R = H) is much higher than for (1; R = Me, Et, Pr^i, or CF_3) whereas that of (7; R = Ph) is the lowest we could determine. In our opinion the low value of $\Delta G^{\ddagger}$ for (7) depends on the conjugative properties of the benzene ring. The restricted motion, in fact, is due to the partial double-bond character of structures like (A): when R = Ph structures like (B) become important, thus reducing the N–CO double-bond character and, consequently, the torsional barrier.

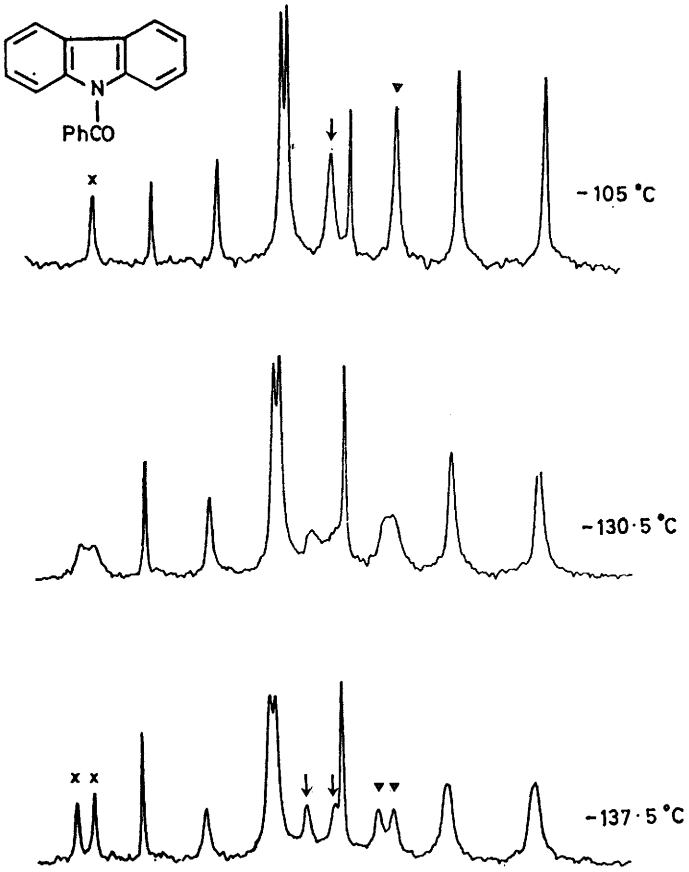


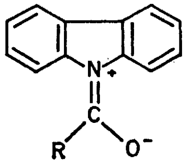
FIGURE 2 Variation of the 25.16 MHz ^{13}C spectrum of the aromatic region of *N*-benzoylcarbazole (7) with temperature. At −105 °C the ten lines expected for the ten equivalent carbons are observed; at −137 °C (in Me_2O) the three lines marked with the triangle, arrow, and cross are split in two owing to the restricted rotation of PhCO Since the lines could not be assigned to the individual carbons, the corresponding frequencies are not given in Table 3. The values in p.p.m. with respect to $SiMe_4$ are at −105°: 139.3, 136.2, 132.8, 129.55, 129.3, 127.0, 126.1, 123.7, 120.5, and 116.1

TABLE 1

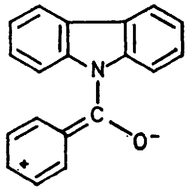
Torsional barriers obtained from the 25.16 MHz ^{13}C n.m.r. spectra of *N*-acylcarbazole. The free energies of activation ($\Delta G^{\ddagger}$) are given in kcal mol^{-1} (1 kcal = 4.186 74 kJ)

Compound (RCO–carbazole)	$\Delta G^{\ddagger}$
(1; R = H)	15.0 ± 0.1
(2; R = Me)	$9.4_5 \pm 0.1_5$
(3; R = Et)	9.6 ± 0.1
(4; R = Pr^i)	9.8 ± 0.1
(5; R = Bu^t)	Undetected
(6; R = CF_3)	9.1 ± 0.1
(7; R = Ph)	7.1 ± 0.1

(A)

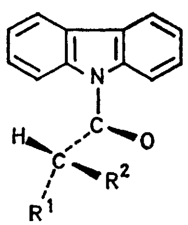


(B)



In contrast, the variation of $\Delta G^{\ddagger}$ in the aliphatic series has to be accounted for in terms of steric effects. The *N*-formylcarbazole (1; R = H) is expected to be planar, or very nearly so, in the ground state whereas the transition state of the rotational process has the HCO plane perpendicular to the carbazole ring. When the formyl hydrogen is replaced by a bulkier substituent the stability of the ground state is reduced in that the conformation becomes twisted, whereas the effect on the perpendicular transition state is expected to be very small; accordingly, there is a dramatic reduction (>5 kcal mol^{-1}) for compounds (2)—(5) with respect to (1). The value of the barriers does not change in an appreciable manner when R increases from Me to Et to Pr^i [$\Delta G^{\ddagger}$ being respectively 9.4_5, 9.6, and 9.8 kcal mol^{-1} for (2), (3), and (4)]. This invariance seems to indicate that in the twisted conformation the ground state has the hydrogen of the HCR^1R^2 moiety [$R^1 = R^2 = H$ in (2); R^1 = Me, R^2 = H in (3); $R^1 = R^2$ = Me in (4)] directed toward the plane of the carbazole ring as shown in (C).

(C)



In this situation the dimensions of R^1 and R^2 do not significantly affect the stability of the ground state since they interact little with H-1 and H-8. This

TABLE 2

Relevant features of the ^{13}C spectra and LIS experiments in $CDCl_3$ for *N*-acetyl- (2) and *N*-trimethylacetyl-carbazole (5). The values are in p.p.m.

R = Me (2)	Shift	LIS (Exper.)	LIS (computed) $\theta = 25°$	Undecoupled spectrum
CH_3	27.6	42.5	42.7	
C-1,8	116.1	20.0	20.2	broad
C-2,7	127.2	8.4	8.5	narrow
C-3,6	123.5	7.2	6.6	narrow
C-4,5	119.7	8.1	8.15	broad
C-9,11	138.5	25.0	24.7	
C-10,12	126.3	14.0	13.8	
R = Bu^t (5)			$\theta = 75°$	
Me_3C	43.4	7.3	7.3	
C-1,8	113.8	3.2	3.1_5	
C-2,7	126.3	0.7_5	0.7_5	
C-3,6	121.8	0.6_5	0.6	
C-4,5	120.0	0.8_5	0.8	
C-9,11	138.7	4.4	4.4	
C-10,12	124.5	1.9	2.0	

hypothesis seems supported by the behaviour of (5) where no hydrogen is left on the aliphatic carbon. Since (5) cannot adopt the conformational arrangement proposed in (C) the angle between Me_3CCO and the ring is forced to become much larger, thus approaching a perpendicular conformation. As a consequence the situation with respect to the less hindered carbazoles is reversed in that the ground state is now perpendicular, or very nearly so, and the transition state planar. Therefore, even if the rotation of Bu^tCO is slow on the n.m.r. time scale the symmetry of the ground state (perpendicular) would prevent the detection of any effect in the spectrum of (5) since the six pairs of carbons remain equivalent. Other examples of variation of the ground state from planar to perpendicular owing to steric effects have been recently discovered by means of ^{13}C n.m.r. and *X*-ray investigations.[7]

Conformational Analysis by LIS Effect.—In order to confirm with quantitative data the conformational conclusions drawn from the dynamic n.m.r. study, experiments with lanthanide complexes were also performed. We examined in particular (2; R = Me) to obtain the twisting angle for derivatives with a barrier of *ca.* 9 kcal mol^{-1} and (5; R = Bu^t) to ascertain whether the suggestion of an almost perpendicular conformation is actually correct.

The lanthanide-induced shift (LIS) has been widely used for gaining information on molecular arrangement in solution.[8] The method requires that chemical shifts be measured in the presence of increasing amounts of an organic derivative of a lanthanide.[8] The plot of the variations of the C-13 shifts *versus* the molar ratio: lanthanide complex/investigated molecule gives a linear relationship with a slope depending on the distances of carbons from the lanthanide.[8] Assuming a standard geometry for the rigid part of the molecule it is possible to fit, with computer programs,[9] the experimental LIS values as function of the lanthanide position (three unknowns[8,9] are required if the CO ··· Ln distance is taken[8,9] to be equal to 3 Å) and of the twisting angle of RCO. As a lanthanide complex we used $Yb(dpm)_3$ which gives a LIS value of 100 p.p.m. for CO in (2): this value is far larger than that of other carbons thus indicating that the carbonyl is the site of attack of $Yb(dpm)_3$. Since, however, this value is independent of the conformation it has not been used in the best fitting procedure: the seven experimental values obtained from the straight lines of Figure 3 overcome the number of unknowns (four) thus making the problem overdetermined.

In order to reproduce the observed equivalence within each pair of carbons at room temperature the computed LIS values were averaged over two topomers having the CO group respectively *syn* to C-1 and to C-8. An unambiguous assignment of the ^{13}C frequencies is also required to correlate the computed with the experimental LIS values. Carbons 9,12, and 10,11 are easily assigned to quaternary carbons owing to the low intensity and to the lack of splitting in off-resonance experiments; the closeness to nitrogen and the larger separation for the doublet at low temperature (Table 3 and Figure 1) indicates that the low-field signal belongs to C-9, C-12, thus leaving the upfield to C-10, C-11.

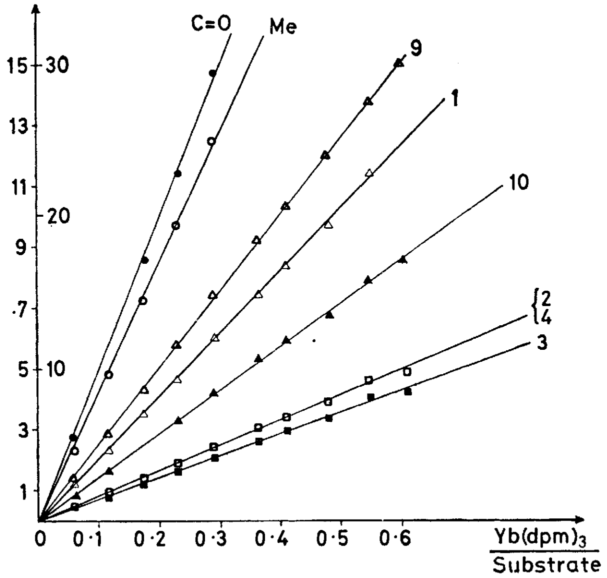


FIGURE 3 Dependence of the chemical shifts (p.p.m.) of carbons of *N*-acetylcarbazole (substrate) *versus* the $Yb(dpm)_3$/substrate values. The internal scale (30 p.p.m.) refers to the carbon of CO, the external (15 p.p.m.) to all the other carbons

Among the other four pairs of carbons C-1, C-8 can be identified because they give a larger internal difference at low temperature (Table 3, Figure 1). Furthermore in (6; R = CF_3) they are the only aromatic carbons coupled with fluorine ($J_{CF} = 2.9$ Hz): this effect is due to ' through space ' coupling which is only possible for C-1, C-8, the aromatic carbons closest to fluorine.[10] Furthermore when this signal is split in two (at −110 °C) only one (that upfield, at 115 p.p.m., in Table 3) of the two signals maintains the CF splitting whereas the other (at 118.1 p.p.m., in Table 3) is a

TABLE 3

Chemical shifts (in p.p.m. from $SiMe_4$) of the carbons of compounds (1)—(6)

	Solvent	Temperature (°C)	1,8	2,7	3,6	4,5	9,12	10,11	CO	CH_3	Other
(1; R = H)	C_2Cl_4	+100	112.9	126.7	123.6	119.6	137.3	125.7	155.8		
		−6	109.6, 116.5	126.4, 127.2	123.4, 123.9	119.2, 120.0	*a*	*a*	156.1		
(2; R = Me)	$CHFCl_2$	−30	116.8	128.1	124.4	120.5	139.2	127.0	171.2	28.1	
		−110	115.2, 118.2	127.6, 128.3	123.9, 124.6	119.9, 120.8	137.8, 139.4	126.1, 126.9	171.7	28.4	
(3; R = Et)	$CHFCl_2$	−30	117.0	128.0	124.3	120.5	139.0	126.9	175.4	9.1	33.4
		−110	115.8, 118.1	127.6, 128.4	123.9, 124.6	120.0, 120.9	137.6, 139.7	126.3, 127.0	175.5	9.1	33.4
(4; R = Pr^i)	$CHFCl_2$	−30	117.0	128.0	124.2	120.4	139.1	127.0	179.7	19.8	36.1
		−110	115.7, 118.1	127.7, 128.2	123.8, 124.4	119.8, 120.4	137.1, 139.7	126.1, 127.0	179.8	19.8	36.0
(5; R = Bu^t)	$CHFCl_2$ }	−30	114.4	127.1	122.6	120.7	139.8	125.4	*b*	28.6	44.3
	CCl_2F_2 }	−150	114.9	127.2	122.8	120.8	139.9	125.2	185.6	28.4	44.3
(6; R = CF_3)	$CHFCl_2$	−30	116.7 [c]	128.2	125.9	120.3	137.9	127.4	*b*		*b*
		−110	115.0,[c] 118.1	127.6, 128.3	125.4, 126.0	119.7, 120.4	135.4, 138.7	126.3, 127.0	155.0 [d]		*b*

[a] Not detected at this temperature. They became visible at −110° (in Me_2O) C-9,C-12 at 137.3, 138.5 and C-10,C-11 at 125.7, 126.5. [b] Not detected at this temperature. [c] Quartet with $J_{CF} = 2.9$ Hz. [d] Quartet with $J_{CF} = 43.2$ Hz.

sharp singlet. This is in agreement with ' through space ' coupling since when CF_3CO is locked only one carbon (C-1 in the diagram) is now close to CF_3. Thus we suggest that in the whole series the carbon opposite (C-1) is upfield with respect to the carbon close (C-8) to the carbonyl oxygen.

The assignment of the other pairs of carbons cannot be made unambiguously: we attempted, therefore, to reproduce the experimental LIS values with all the possible permutation of these three shifts. It turned out that only assigning the LIS = 7.2 to C-3, C-6 the correct sequence is reproduced, whatever the conformation adopted. On the other hand C-2 and C-4 could not be unambiguously assigned in this way. Depending on their assignment the angle can be 25 or 35°, giving confirmation of the non-planarity of the molecule. To solve this final uncertainty the spectrum of (2) was recorded without proton decoupling. Each aromatic carbon bonded to a hydrogen gives a large ($J_{CH} = 163$ Hz) and a small ($J_{CCCH} = 7.5$) doublet: further fine structure could be also detected although not enough first order for a complete interpretation. It has been recently observed and explained that in asymmetrically *ortho*-disubstituted benzenes the undecoupled ^{13}C spectra display two types of patterns:[11] those broad and complex belong, most likely, to the carbons corresponding to C-1 and C-4 of derivative (2), whereas the simpler and narrower to C-2 and C-3. Since we observed that the undecoupled signals of (2) at 118.7 p.p.m. are as broad and complex as those of C-1 they were assigned to C-4, whereas those at 127.2, being simple and narrow like C-3, were assigned to C-2 (see Table 2). Consequently to this assignment, the twisting angle of (2) is 25°.

An analogous LIS experiment carried out on (5) (assuming the same assignment) yielded a twisting angle of 75° (Table 2). Even considering the uncertainty in this kind of determination (see Experimental section) the hypothesis drawn from the dynamic n.m.r. experiments is confirmed, and the impossibility of detecting the barrier of (5) even at −160 °C is due to the symmetry of its ground state (almost perpendicular). In other words whereas the profile of the energy as a function of the twisting angle in the less hindered carbazoles like (2) has a perpendicular transition state and a ground state almost planar, that of (5) has a reverse trend in that the transition state is now planar whereas the ground state is almost perpendicular.

EXPERIMENTAL

Spectral Measurements.—The ^{13}C spectra were recorded at 25.16 MHz on JEOL PS 100 and Varian XL-100 NMR instruments in the F.T. (Fourier-transform) mode. The samples for low temperatures measurements were prepared by condensing with liquid nitrogen the gaseous solvents ($CHFCl_2$, CF_2Cl_2, and Me_2O) into the 10-mm n.m.r. tubes connected to a vacuum line: the samples were subsequently sealed and introduced in the precooled probe of the instruments. Small amounts of $(CD_3)_2CO$ were added to provide a deuteron lock signal. The temperatures were measured after each spectral accumulation (*ca.* 500 transients) by means of a thermocouple inserted into the probe in a dummy tube.

The LIS experiments were run on a Varian CFT-20 NMR instrument (operating at 20 MHz) at probe temperature in the case of (2). In the case of (5) the LIS values were too small to be detected at room temperature, most likely because the steric hindrance of Bu^t makes difficult the attack of $Yb(dpm)_3$ to carbonyl. At −20 °C however the equilibrium $CO \cdots Ln \rightleftharpoons CO + Ln$ is shifted enough to the left-hand side to make the LIS values large enough to be appreciated. Even at this temperature, however, larger $Yb(dpm)_3$: carbazole ratios had to be used for compound (2). As a consequence the LIS values were much smaller for (5) (see Table 2) and their accuracy lower than for (2). A modified version of the computer program MOLA[8] was employed for the determination of the twisting angle: the DNMR program was also used for simulating some of the temperature-dependent ^{13}C spectra. Both programs were run on the computer facilities of the University of Bologna.

Materials.—*N*-Acetyl-[12] and *N*-trifluoroacetyl-carbazole[13] were available from previous studies. *N*-Formyl-[14] and *N*-benzoyl-carbazole[15] were prepared according to reported methods. *N*-Propionyl[16] and *N*-(2-methylpropionyl)carbazole {m.p. 44 °C, $\delta[(CD_3)_2SO]$, 1.36 (6 H, d, CMe_2), 3.75 (1 H, septet, C–H), 7.20—7.70 (4 H, m, 2,3,6,7-H), and 7.95—8.30 (4 H, m, 1,4,5,8-H)} were prepared by reaction of carbazolylmagnesium bromide with the corresponding acid chloride according to ref. 16. The mass spectrum yields the expected molecular weight and elemental analysis was correct.

N-*Trimethylacetylcarbazole*.—This compound was prepared by treatment of the sodium salt of carbazole with trimethylacetyl chloride, after unsuccessful attempts with Grignard reagents and potassium salt.

A suspension of sodium hydride (1.5 g, 62 mmol) in anhydrous *NN*-dimethylformamide (20 ml) was added dropwise with carbazole (10 g, 56 mmol) in anhydrous *NN*-dimethylformamide (20 ml). The mixture was heated for 1 h at reflux and then trimethylacetyl chloride (9 g, 74.6 mmol) was added dropwise and the mixture refluxed for 3 h. The mixture was poured into saturated aqueous $NaHCO_3$ and extracted with diethyl ether; the organic layer was separated, dried (Na_2SO_4), filtered, and evaporated. The yellow residue was chromatographed on deactivated silica and eluted with light petroleum (b.p. 40—60 °C) to give 5 g of a crystalline white solid, m.p. 45 °C (yield 32%); $\delta(CCl_4)$ 1.45 (9 H, s, CMe_3), 6.90—7.60 (6 H, m, 1,2,3,6,7,8-H), 7.70—7.90 (2 H, m, 4,5-H). The molecular weight (mass spectrometry) and elemental analysis were as expected.

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