Oxazoles Formation During *O*-Alkylation of Isonitroso-naphthols. X-Ray Structure of [1,2]Naphthoquinone 1-[*O*-(4-*tert*-Butyl-benzyl)-oxime] and 2-(4-*tert*-Butyl-phenyl)Napth[1,2-*d*]Oxazole

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1-Nitroso-2-naphthol and 2-nitroso-1-naphthol, both in the isonitroso form, react with benzyl bromides in THF and in the presence of triethylamine affording, in low yields, the corresponding *O*-benzyl oximes and 2-aryl naphthoxazoles in a 1:1 ratio, approximately. The structures of *O*-benzyl oximes and naphthoxazoles isolated have been determined by X-ray analysis.

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Introduction.

Aminoxyls, both aliphatic and aromatic [1], are good precursors of *N*-alkoxyamines, which, in the last decades, have received great attention because of their importance as initiators and intermediates in "living"/controlled free radical polymerization [2]. Furthermore, the kinetics of polymerizations involving aminoxyl radicals are closely related to a general phenomenon, the so-called persistent radical effect, characterized by a highly specific formation of the cross-reaction products of transient and persistent radicals, when simultaneously formed in the reaction system [3].

Since iminoxyls are persistent radicals [4], alkylation of isonitroso-naphthols was attempted in order to obtain alkoxyimines to be possibly used, just like alkoxyamines, in radical polymerization. The reactions here described afforded the expected alkoxyimines, although in low yields, together with unexpected new naphthoxazoles.

Results and Discussion.

Compounds **1** and **2** react with benzylbromides **3a** and **3b** at room temperature in THF and in the presence of triethylamine giving the corresponding alkylated iminoxyls **4** and **6** and oxazoles **5** and **7** as shown in Scheme 1. Yields of the products isolated together with their analytical and spectroscopic data are reported in the experimental section.

X-Ray analyses were performed on compounds **4b** and **5b** in order to establish or confirm the structure of compounds **4**, **5**, **6** and **7**. X-Ray experimental details, selected bond distances and angles for compounds **4b** and **5b** are reported in Tables 1 and 2

The molecular geometry observed for both compounds is as expected. In particular, in compound **4b** (Figure 1) the values of the bond distances are consistent with a double bond character of the N1-C1 (1.302(3) Å), O1-C2 (1.220(3) Å), and C3-C4 (1.316(4) Å) bonds. These values are in good agreement with those reported in the literature for the corresponding bonds in naphthoquinone-1-oxime systems (mean values 1.36(2), 1.236(10), and 1.328(12) Å respectively, calculated over four entries [5] from the Cambridge Crystallographic Databank). The iminoxyl moiety deviates significantly from planarity, the maximum deviation being observed for the O1 atom (0.272(2) Å). The C12…C17 aromatic ring is oriented almost perpendicular to the least-square mean plane through the atoms of the iminoxyl moiety, the dihedral

Scheme 1

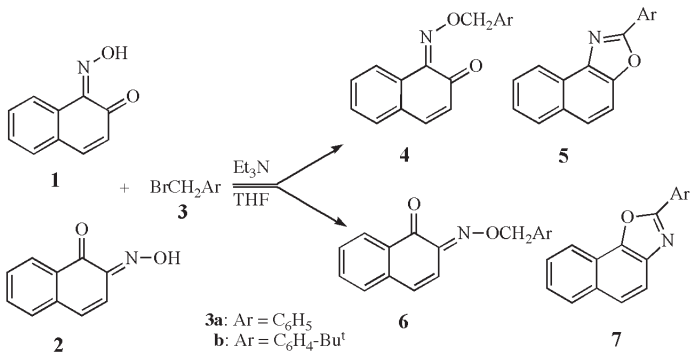

Table 1

Experimental Data for the X-ray Diffraction Study on Crystalline Compounds Compounds **4b** and **5b**

Compound	**4b**	**5b**
formula	$C_{21}H_{21}NO_2$	$C_{21}H_{19}NO$
a, Å	10.168(2)	13.637(3)
b, Å	15.292(3)	10.995(2)
c, Å	11.611(2)	11.209(2)
β, °	98.39(2)	90
V, Å^3	1786.1(6)	1680.7(6)
Z	4	4
formula weight	319.4	301.4
space group	$P2_1/c$	$Pca2_1$
t, °C	20	20
λ, Å	0.71073	1.54178
ρ_{calc}, g cm^{-3}	1.188	1.191
μ, cm^{-1}	0.76	5.66
transmission coefficient	0.984-0.989	0.873-0.903
R [a]	0.068	0.061
wR_2	0.148	0.155
GOF	1.016	1.137
N-observed [b]	1660	1107
N-independent [c]	3891	1688
N-refinement [d]	3234	1575
variables	214	203

[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 $I > 0$.

Table 2

Selected Bond Distances (Å) and Angles (°) for Compounds **4b** and **5b**

Compound	**4b**	**5b**
O1-C2	1.220(3)	1.385(6)
O1-C11	-	1.378(6)
O2-N1	1.385(2)	-
O2-C11	1.473(2)	-
N1-C1	1.302(3)	1.402(5)
N1-C11	-	1.295(6)
C1-C2	1.524(3)	1.370(6)
C1-C10	1.463(3)	1.420(6)
C2-C3	1.437(3)	1.391(6)
C3-C4	1.316(4)	1.361(8)
C2-O1-C11	-	104.0(3)
N1-O2-C11	107.5(1)	-
O2-N1-C1	114.1(2	-
C1-N1-C11	-	104.4(4)
N1-C1-C2	109.5(2)	109.3(4)
N1-C1-C10	131.1(2)	130.7(4)
C2-C1-C10	119.4(2)	120.0(4)
O1-C2-C1	121.7(2)	107.6(4)
O1-C2-C3	122.4(2)	127.6(4)
C1-C2-C3	115.9(2)	124.8(4)
C2-C3-C4	122.6(2)	115.6(4)

angle they form being 94.4(1)°. The presence of an oxazole moiety in compound **5b** (Figure 2) is confirmed by the aromaticity of the C1…C10 system and by the double bond character of the N1-C11 bond (1.295(6) Å). The oxazole ring system is almost planar (maximum deviation from planarity: 0.042(5) Å for C6 and C7). The C12…C17 aromatic ring is nearly co-planar with the oxazole system, the dihedral angle they form being 2.8(1)°. Conformation and geometry of the naphthoxazole compare well with those found in the literature [6].

For both compounds, crystal packing is mainly determined by van der Waals interactions, the shortest hydrogen contacts observed being C9…O2, 2.786(4) Å; H9…O2, 2.20 Å; C9-H9…O2, 120.8° and C17…O1, 2.816(6) Å; H17…O1, 2.50 Å; C17-H17…O1, 100.2° for **4b** and **5b**, respectively.

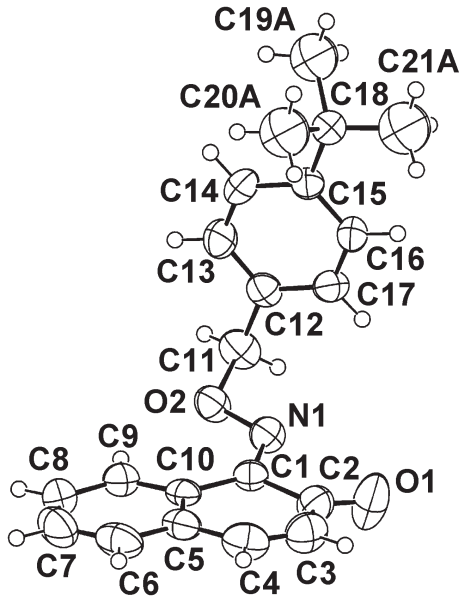

Figure 1. An ORTEP view (50% probability ellipsoids) of compound **4b**. Disorder affecting the *t*-Bu group has been omitted for clarity.

In order to improve the selectivity of the reactions and therefore to obtain higher yields of the alkylated oxime or of the oxazole, different combinations of solvents and bases were used, *i.e.* DMSO in the presence of KOH or acetone in the presence of K_2CO_3. However, the selectivity was not improved and both products were obtained in lower yields together with high reaction tar.

Alkylated iminoxyls **4** and **6** were tested in "living"/controlled radical polymerization of styrene, but it was established that homolytic cleavage of the oxygen-carbon bond, responsible for their activity, does not occur up to 170 °C in DMSO or chlorobenzene. Such a high temperature for oxygen-carbon bond cleavage prevents their use because styrene can be thermally polymerized at 140 °C without catalysis [7].

Thus, the formation of oxazoles **5** and **7** in these reactions may be considered the most interesting result because of the biological activity described for some benzoxazole [8] and naphthoxazole [9] derivatives.

Mechanicistic studies on these reactions are currently underway and will be reported in due course.

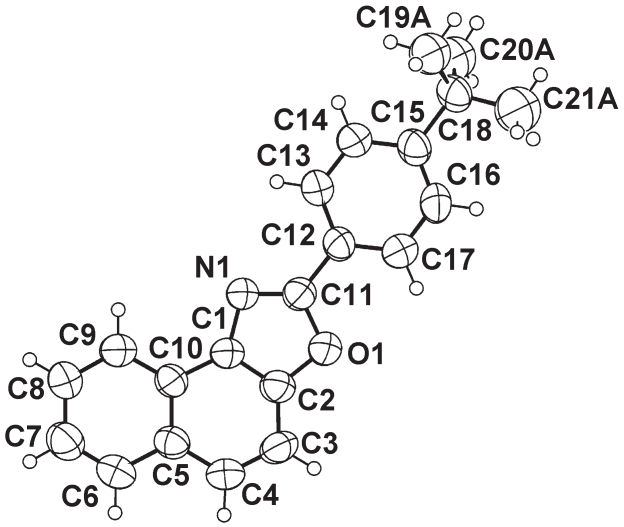

Figure 2. An ORTEP view (50% probability ellipsoids) of compound **5b**. Disorder affecting the *t*-Bu group has been omitted for clarity.

EXPERIMENTAL

Melting points are uncorrected and were measured with an Electrothermal apparatus. IR spectra were recorded on a Nicolet Fourier Transform Infrared 20-SX spectrophotometer equipped with a Spectra Tech Collector for DRIFT measurements. ^{1}H NMR spectra were recorded at room temperature in $CDCl_3$ solution on a Varian Gemini 200 spectrometer (δ in ppm referred to tetramethylsilane). Mass spectra were performed on a Carlo Erba QMD 1000 mass sperctrometer in EI^+ mode. Elemental analyses were performed with a Carlo Erba CHNSO E.A. 1108 elemental analyser.

Nitroso-naphthols **1** and **2**, alkyl halides **3a-b** and triethylamine were Aldrich commercial reagent grade products and used as received. Potassium carbonate, potassium hydroxide and all solvents were Carlo Erba or Aldrich RP-ACS grade.

General Procedure for the Reaction of Nitroso-naphthols **1** and **2** with Alkyl Halides **3a-b** in THF in the Presence of Triethylamine.

Alkyl halide (3 mmoles in 1 mL of THF) was added to a solution of nitroso-naphthol (2 mmoles in 3 mL of THF containing 5 mmoles of triethylamine) under stirring at room temperature. After 3 hrs the reaction mixture was poured into 20 mL of water and extracted with chloroform (2x20 mL). The organic layer was dried over anhydrous sodium sulfate and evaporated to dryness; the residue was chromatographed on silica gel column eluting with cyclohexane/ethyl acetate 8:2. The isolated products were subsequently purified on preparative plates eluting with the same solvents.

The reaction carried out in acetone/K_2CO_3 under reflux afforded the same products in low yields whereas those in DMSO/KOH at room temperature were much faster but with more impurities.

[1,2]Naphthoquinone 2-(*O*-Benzyl-oxime) (**4a**).

This compound was obtained as yellowish needles, 136 mg (0.5 mmol, 26%), mp 87-88 °C (ligroin); FT-IR: 1659 (C=O), 1519 (C=N), 987 (N-O) cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C): δ = 5.60 (s, 2H, CH_2), 6.38-6.43 (m, 1H, CH); 7.36-7.48 (m, 9H, aromatic), 8.69 (m, 1H, CH); MS (EI^+): *m/z* = 263 (5), 246 (48), 156 (28), 91 (100).

Anal. Calcd for $C_{17}H_{13}NO_2$: C, 77.55; H, 4.98; N, 5.32. Found: C, 77.53; H, 5.02; N, 5.36.

[1,2]Naphthoquinone 1-[*O*-(4-*tert*-Butyl-benzyl)-oxime] (**4b**).

This compounds was obtained as yellowish needles, 96 mg (0.3 mmol, 15%), mp 124-125 °C (ligroin); FT-IR: 1666 (C=O), 1526 (C=N), 987 (N-O) cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C): δ = 1.33 (s, 9H, *t*-Bu), 5.57 (s, 2H, CH_2), 6.39-6.44 (m, 1H, CH); 7.37-7.47 (m, 9H, aromatic), 8.69 (m, 1H, CH); MS (EI^+): *m/z* = 319 (2), 302 (45), 156 (35), 147 (100).

Anal. Calcd for $C_{21}H_{21}NO_2$: C, 78.97; H, 6.63; N, 4.39. Found: C, 78.95; H, 6.60; N, 4.41.

2-Phenyl-naphth[1,2-*d*]oxazole (**5a**).

This compound was obtained as white prisms, 142 mg (0.58 mmol, 29%), mp 133-135 °C (ligroin); FT-IR: 1551 and 1485 (C=N), 1238 (C-O) cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C): δ = 7.53-7.82 (m, 7H, aromatic), 7.98 (d, 1H, J = 8.3 Hz, aromatic), 8.32-8.39 (m, 2H, aromatic), 8.61 (d, 1H, J = 8.3 Hz, aromatic); MS (EI^+): *m/z* = 245 (100), 114 (52).

Anal. Calcd for $C_{17}H_{11}NO$: C, 83.25; H, 4.52; N, 5.71. Found: C, 83.28; H, 4.55; N, 5.74.

2-(4-*tert*-Butyl-phenyl)naphth[1,2-*d*]oxazole (**5b**).

This compound was obtained as white prisms, 156 mg (0.52 mmol, 26%), mp 134-135 °C (ligroin); FT-IR: 1495 (C=N) 1270 (C-O) cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C): δ = 1.39 (s, 9H, *t*-Bu), 7.57 (d, 2H, J = 8.4 Hz, aromatic), 7.63-7.85 (m, 4H, aromatic), 8.01 (d, 1H, J = 8.4 Hz, aromatic), 8.29 (d, 2H, J = 8.4 Hz, aromatic), 8.63 (d, 1H, J = 8.4 Hz, aromatic); MS (EI^+): *m/z* = 301 (80), 286 (100), 258 (30), 114 (40).

Anal. Calcd for $C_{21}H_{19}NO$: C, 83.69; H, 6.35; N, 4.65. Found: C, 83.71; H, 6.32; N, 4.67.

[1,2]Naphthoquinone 2-(*O*-Benzyl-oxime) (**6a**).

This compound was obtained as greenish needles, 142 mg (0.54 mmol, 27%), mp 108-110 °C (ligroin); FT-IR: 1675 (C=O), 1590 (C=N), 971 (N-O) cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C): δ = 5.52 (s, 2H, CH_2), 6.84 (d, 1H, J = 10.4 Hz, CH), 7.11 (d, 1H, J = 10.4 Hz, CH), 7.31-7.61 (m, 8H, aromatic), 8.19-8.23 (m, 1H, aromatic); MS (EI^+): *m/z* = 263 (3), 246 (79), 157 (20), 91 (100).

Anal. Calcd for $C_{17}H_{13}NO_2$: C, 77.55; H, 4.98; N, 5.32. Found: C, 77.58; H, 4.96; N, 5.34.

[1,2]Naphthoquinone 2-[*O*-(4-*tert*-Butyl-benzyl)-oxime] (**6b**).

This compound was obtained as yellowish needles, 179 mg (0.56 mmol, 28%), mp 93-94 °C (ligroin); FT-IR: 1673 (C=O),

1520 (C=N), 963 (N-O) cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$, 25 °C): δ = 1.33 (s, 9H. *t*-Bu), 5.49 (s, 2H, CH_2), 6.82 (d, 1H, J = 10.1 Hz, CH), 7.11 (m., 1H, J = 10.1 Hz, CH), 7.28-7.62 (m, 7H, aromatics), 8.20 (m, 1H, aromatic); MS (EI^+): *m/z* = 319 (15), 302 (45), 147 (100), 132 (66).

Anal. Calcd for $C_{21}H_{21}NO_2$: C, 78.97; H, 6.63; N, 4.39. Found: C, 78.99; H, 6.65; N, 4.37.

2-Phenyl-naphth[2,1-*d*]oxazole (**7a**).

This compound was obtained as white prisms, 98 mg (0.4 mmol, 20%), mp 87-88 °C (ligroin); FT-IR: 1548 and 1485 (C=N), 1250 (C-O); ^1H NMR (200 MHz, $CDCl_3$, 25 °C): δ = 7.55-7.60 (m, 4H, aromatic), 7.62-7.71 (m, 1H, aromatic), 7.78-7.9 (m, 2H, aromatic), 7.97-8.02 (m, 1H, aromatic), 8.31-8.38 (m, 3H, aromatic); MS (EI^+): *m/z* = 245 (100), 114 (52).

Anal. Calcd for $C_{17}H_{11}NO$: C, 83.25; H, 4.52; N, 5.71. Found: C, 83.28; H, 4.55; N, 5.74.

2-(4-*tert*-Butyl-phenyl)naphth[2,1-*d*]oxazole (**7b**).

This compound was obtained as white prisms, 210 mg (0.7 mmol, 35%), mp 118-119 °C (ligroin); FT-IR: 1495 (C=N), 1270 (C-O); ^1H NMR (200 MHz, $CDCl_3$, 25 °C): δ = 1.40 (s, 9H, *t*-Bu), 7.55-7.57 (m, 4H, aromatic), 7.77-7.89 (m, 2H, aromatic), 7.97-8.01 (m, 1H, aromatic), 8.25-8.35 (m, 3H, aromatic); MS (EI^+): *m/z* = 301 (85), 286 (100), 258 (60), 114 (53).

Anal. Calcd for $C_{21}H_{19}NO$: C, 83.69; H, 6.35; N, 4.65. Found: C, 83.67; H, 6.37; N, 4.62.

Crystal data for [1,2]Naphthoquinone 1-[*O*-(4-*tert*-Butyl-benzyl)-oxime] **(4b)** (CCDC-225801).

$C_{21}H_{21}NO_2$, M_r = 319.4, monoclinic, space group $P2_1/c$, *a* = 10.168(2), *b* = 15.292(3), *c* = 11.611(2) Å, β = 98.39(2)°, *V* = 1786.1(6) $Å^3$, *Z* = 4, ρ = 1.188 g cm^{-3}; λ(Mo-Kα) = 0.71073 Å, μ(Mo-Kα) = 0.76 cm^{-1}: yellow prism, crystal dimensions 0.15 x 0.18 x 0.32 mm. The structure was solved by direct methods (SIR97) [10] and anisotropically refined for all the non-H atoms. The methyl carbon atoms of the *t*-Bu group were found to be disordered over two positions (called A and B) anisotropically refined with site occupation factors of 0.75 and 0.25, respectively. During the refinement the C-C bond distances involving the disordered atoms were constrained to be 1.54(1) Å. The hydrogen atoms were put in geometrically calculated positions and introduced as fixed contributors in the last stage of refinement with U_{iso} assigned to be 1.2 times those of the attached C atoms. The structure was refined on F^2 values (SHELX93) [11] by using the weighting scheme $w = 1/[\sigma^2(F_o^2)+(0.074\ P)^2]$ (with $P = (F_o^2 + 2\ F_c^2)/3$). For 1660 unique reflections having $I > 2(I)$ collected at *T* = 293(2) K on a Philips PW1100 diffractometer ($3 < 2\theta < 54°$) the final *R* is 0.068 (*wR2* = 0.148 calculated over 3234 reflections having $I > 0$; *S* = 1.016).

Crystal data for 2-(4-*tert*-Butyl-phenyl)naphth[1,2-*d*]oxazole **(5b)** (CCDC-225802).

$C_{21}H_{19}NO$, M_r = 301.4, orthorhombic, space group $Pca2_1$, *a* = 13.637(3), *b* = 10.995(2), *c* = 11.209(2) Å, *V* = 1680.7(6) $Å^3$, *Z* = 4, ρ = 1.191 g cm^{-3}; λ(Cu-Kα) = 1.54178 Å, μ(Cu-Kα) = 5.66 cm^{-1}: pale yellow prism, crystal dimensions 0.18 x 0.20 x 0.40 mm. The structure was solved by direct methods (SIR97) [10] and anisotropically refined for all the non-H atoms except for the methyl carbon atoms of the *t*-Bu group, which were found to be disordered over two positions (called A and B) isotropically refined with site occupation factors of 0.75 and 0.25, respectively. During the refinement the C-C bond distances involving the disordered atoms were constrained to be 1.54(1) Å. The hydrogen atoms were put in geometrically calculated positions and introduced as fixed contributors in the last stage of refinement with U_{iso} assigned to be 1.2 times those of the attached C atoms. The structure was refined on F^2 values (SHELX93) [11] by using the weighting scheme $w = 1/[\sigma^2(F_o^2)+(0.109\ P)^2]$ (with $P = (F_o^2 + 2\ F_c^2)/3$). For 1107 unique reflections having $I > 2(I)$ collected at *T* = 293(2) K on a Enraf-Nonius CAD4 diffractometer ($3 < 2\theta < 140°$) the final *R* is 0.061 (*wR2* = 0.155 calculated over 1575 reflections having $I > 0$; *S* = 1.137). The choice of the noncentrosymmetric space group ($Pca2_1$) should be considered correct on the basis of the successful structure refinement. Moreover, although the molecule shows a C_m pseudo-symmetry, the corresponding centrosymmetric space group (*Pbcm*) results incompatible with the orientation of the molecule within the unit cell.

REFERENCES AND NOTES

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[1] On the basis of their reactivity, we divide stable aminoxyls into two different classes: aliphatic aminoxyls with the nitroxide function between two sp^3 carbons, such as tetramethyl-piperidino, pyrrolidino and imidazolino derivatives and aromatic aminoxyls whose nitroxide function is conjugated with an aromatic ring, such as indolinonic and quinolinic derivatives.

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