1,3-Dipolar cycloaddition of nitrosonaphthols to 3-aroylaziridines. Novel syntheses of substituted naphtho[1,2-*d*]oxazoles and naphtho[2,1-*d*]oxazoles

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A series of 3-aroyl-2-arylaziridines underwent 1,3-dipolar cycloadditions in both orientations to the nitrogen–oxygen bond of 1-nitroso-2-naphthol. Spontaneous 1,3-cleavage of the intermediate oxadiazolidines to nitrones and cyclodehydration of the latter afforded both 2-aryl- and 2-aroylnaphtho-[1,2-*d*]oxazoles in good yields. The interpretation of the reaction received confirmation by independent, unambiguous synthesis of several 2-aroylnaphtho[1,2-*d*]oxazoles.

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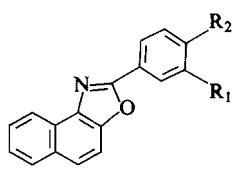
The thermal and photochemical cleavage of the carbon–carbon bond in aziridines to yield azomethine ylides and their subsequent [2 + 3] cycloaddition to reactive carbon–carbon multiple bonds, has been firmly established by several authors (1–14).

An interest in the general problem of synthesizing five and six membered ring heterocycles from the addition reactions of readily available small ring heterocycles led us to explore the analogous thermally induced additions of 3-aroylaziridines to heteromultiple bonds. We have reported the additions of 3-aroylaziridines and 3-carboalkoxyaziridines to the following heteromultiple bonds as dipolarophiles, (*i*) the C=S bond of aryl isothiocyanates with the formation of 4-aroyl-5-arylamino-4-thiazolines (15), (*ii*) the C=N bond of imines and sulfonylimines with the formation of imidazolidines (16), (*iii*) the C=O bond of diphenylcyclopropenone which ultimately affords 4-aroyl-4-oxazolines (17, 18), (*iv*) the C=O bond of aryl aldehydes and chloral to form oxazolidines (19), and (*v*) the C=N bond of cyclopropenimines to form imidazolines and imidazolidines (20).

We report full details of an examination of the 1,3-dipolar cycloaddition of 3-aroylaziridines to the N=O bond of isomeric nitrosonaphthols which produced substituted naphtho[1,2-*d*]-oxazoles and which in the case of 1-nitroso-2-naphthol provided compelling evidence for a concerted cycloaddition. These results have previously been published only in a preliminary form (21).

Treatment of 3-benzoyl-1-cyclohexyl-2-*p*-nitrophenylaziridine (22) with one equivalent of 1-nitroso-2-naphthol in refluxing benzene for 16 h resulted in the precipitation of 2-[4-nitrophenyl]-naphtho[1,2-*d*]oxazole (**1**), $C_{17}H_{10}N_2O_3$, m.p. 240° in 35.5% yield (R_1 = H; R_2 = NO_2). The infrared (i.r.) spectrum of **1** showed a 1532 cm^{-1} band characteristic of the nitro group.



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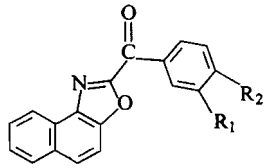

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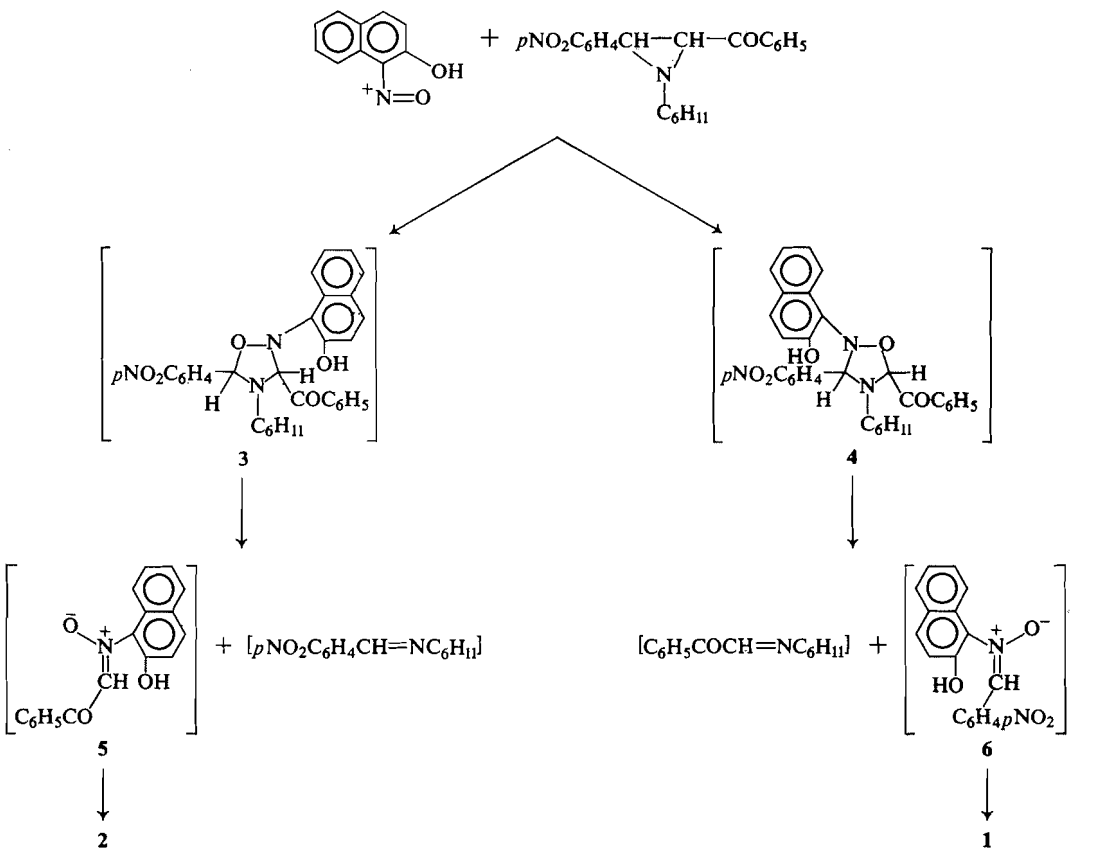
Concentration of the filtrate and chromatographic separation on alumina afforded the pale green solid 2-benzoylnaphtho[1,2-*d*]oxazole (**2**; R_1, R_2 = H), $C_{18}H_{11}NO_2$, m.p. 123° in 41.5% yield. The i.r. of **2** showed a strong band at 1660 cm^{-1} characteristic of a diaryl ketone (23). The absorption spectrum showed intense maxima at 264 and 356 mμ.

In view of the precedents for thermal carbon–carbon bond cleavage of aziridines quoted above, and the strong analogies for the subsequent concerted [2 + 3] cycloaddition to heteromultiple bonds also described, we interpret the reaction as proceeding by 1,3-dipolar addition of the intermediate azomethine ylide to the N=O bond in both possible orientations. Subsequent 1,3-cleavage of the intermediate oxadiazolidines **3** and **4** gives initially the nitrones **5** and **6** (Scheme 1).

The neighboring hydroxyl groups in **5** and **6** cyclize to the polarized azomethine bond with loss of water to produce **2** and **1** respectively. The secondary products of the 1,3-cleavage of the oxadiazolidines, which were expected to be the Schiff bases, could not be isolated. It has been our experience however that Schiff bases of



SCHEME 1

cyclohexylamine seldom survive elimination reactions of this type. For example in the 1,3-dipolar additions of 4-aroyl-4-oxazolines with olefinic and acetylenic dipolarophiles, the extruded cyclohexylamine Schiff base was isolated in only one case, but far more frequently was very easily hydrolyzed during the work-up procedure (24, 25). The oxadiazoline which results from the 1,3-dipolar addition of a nitrile ylide to nitrosobenzene similarly cannot be isolated and suffers a 1,3-cleavage to give a nitrone and benzonitrile (26). As far as we are aware the isolation of an oxadiazolidine has been reported only once in the literature by Agosta and that example was shown to be unstable (27).

Reactions between pyridinium or sulfonium ylides and aryl nitroso compounds to form nitrones have been reported previously (28–31) (e.g. eq. [1]). Accordingly, compound **2***a* was synthesized unambiguously by treating a mixture of 1-nitroso-2-naphthol and one equivalent of *N*-phenacylpyridinium bromide (32) with an equivalent of *N* aqueous sodium hydroxide at $-20°$. The yield of **2** was quantitative (see eq. [2]). The analytical and spectral data on several 2-aryl and 2-aroyl naphtho[1,2-*d*]oxazoles obtained by the 1,3-dipolar addition of 1-nitroso-2-naphthol with the appropriate 3-aroylaziridines are summarized in Tables 1 and 2. 2-Nitroso-1-naphthol reacted with 3-benzoyl-1-cyclohexyl-2-*p*-nitrophenylaziridine to give 2-*p*-nitrophenylnaphtho-[2,1-*d*]oxazole (**7**) in 8.0% yield. While the

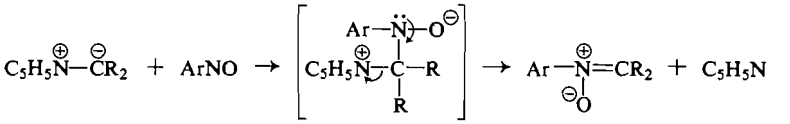
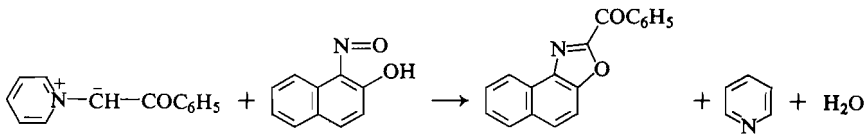
[1] 

TABLE 1
2-Arylnaphtho[1,2-*d*]oxazoles*

No. 1	R_1	R_2	Melting point (°C)	Yield (%)	Observed C	H	N	Molecular ion (mass spectrum)	Calculated C	H	N	Molecular ion (mass spectrum)	Infrared spectrum Nujol (NO_2)
a	H	NO_2	240	35.5	70.18	3.64	9.66	290.0694	70.34	3.47	9.65	290.0691	1535 1350
b	NO_2	H	237–239	32	70.14	3.26	9.66	290.0694	70.34	3.47	9.65	290.0691	1529 1348
c	H	H	125–130	40	67.98	3.40	8.99	245.0840	67.94	3.17	8.86	245.0841	—

*Numbering of substituents refers to structure 1.

[2] 

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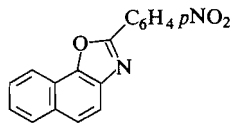
corresponding 2-aroylnaphtho[2,1-*d*]oxazole **8** was not obtained in this reaction, it was however prepared by the second procedure with *p*-bromophenacyl pyridinium bromide and sodium hydroxide (31) so that the two methods were quite complementary.



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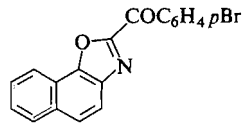

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2-Nitroso-1-naphthol gave lower yields of the 2-arylnaphtho[2,1-*d*]oxazole in reaction with aziridines than did 1-nitroso-2-naphthol. This appears to be due to competing reactions including the formation of a product tentatively assigned as a naphtho[2,1-*f*]-1,3,5-oxadiazepine which is currently under further investigation.

The isolation of naphthoxazoles of both types **1** and **2** represents the first reported example of addition of a heteromultiple bond to an aziridine in both possible orientations and provides good evidence that the reaction involved is a 1,3-dipolar addition. Since **1** and **2** are obtained in approximately equal yields it is clear that the steric influence on orientation in the reactions with 1-nitroso-2-naphthol is negligible. A similar conclusion has very recently been reached by Kresze *et al.* in a study of the Diels–Alder additions of nitrosobenzene to substituted dienes (33).

In contrast, the 1,3-dipolar cycloadditions of 3-aroylaziridines to dipolarophiles containing heteromultiple bonds all took place exclusively in one orientation presumably due to more stringent steric control, for example in addition to the C=S bond in aryl isothiocyanates (15), the C=N bond in imines and sulfonylimines (16) and iminocyclopropenes (20), and the C=O bond in aryl aldehydes, chloral (19), and diphenylcyclopropenone (17, 18).

One isolated example of the addition of an aryl nitroso compound to an aziridine had previously been reported by Heine and his coworkers, involving the addition of nitrosobenzene to 1,1*a*-dihydro-1-(*p*-nitrophenyl)-2-phenylazirino-[1,2-*a*]quinoxaline (**9**) (14) (see eq. [3], Ar = *p*-$NO_2C_6H_4$—). The formation of the products, 2-phenylquinoxaline (**13**) and the nitrone **12** was interpreted either in terms of 1,3-dipolar addition via **10** or via the dipolar intermediate **11**. It seems likely that in this particular reaction, the orientation of the addition is dictated by the stability of the product quinoxaline **13** and the nitrone **12**.

Further studies of arylnitroso compounds with 3-aroylaziridines leading to imidazolidines and Schiff's bases will be reported subsequently.

Experimental

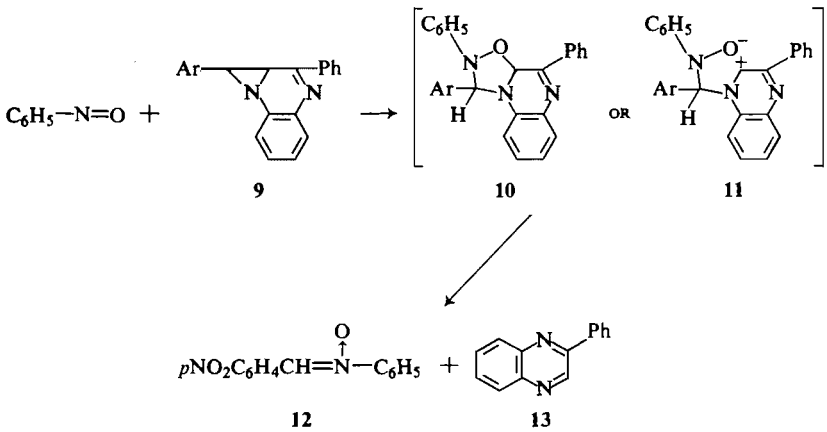
Melting points were determined on a Fisher–Johns apparatus and are uncorrected. The i.r. spectra were recorded on a Perkin–Elmer model 421 spectrophotometer, and only the principal, sharply defined peaks are reported. Nuclear magnetic resonance (n.m.r.) spectra

TABLE 2

2-Aroylnaphtho-[1,2-*d*]oxazoles*

No. 2	R_1	R_2	Melting point (°C)	Yield (%)	Observed					Calculated					Infrared spectrum $CHCl_3$ (C=O)	Nuclear magnetic resonance spectrum ($CDCl_3$) δ	
					C	H	N	Br	Molecular ion (mass spectrum)	C	H	N	Br	Molecular ion (mass spectrum)		Aryl protons	2-*p*-Aroyl substituent
a	H	H	124	41.5† 100‡	78.90	3.97	5.17	—	273.0793	79.11	4.06	5.13	—	273.0790	1658	7.2–8.8 (11H) m	—
b	H	CH_3	114	32.3†	79.55	4.49	5.15	—	287.0946	79.41	4.56	4.88	—	287.0946	1652	7.2–8.3 (10H) m	2.46 (3H) s
c	H	OCH_3	124–125	41.5†	75.45	4.48	4.83	—	303.0893	75.25	4.32	4.62	—	303.0895	1651	6.9–8.5 (10H) m	3.98 (3H) s
d	H	NO_2	223–225	31.5† 76.5‡	67.68	3.23	9.26	—	318.0639	67.94	3.17	8.86	—	318.0641	1663	7.1–8.5 (10H) m	—
e	NO_2	H	167	50.5‡	67.92	3.14	8.89	—	318.0638	67.94	3.17	8.86	—	318.0641	1652	7.0–8.4 (10H) m	—
	H	Br	164	68.5‡	61.19	2.78	4.06	23.30	350.9893	61.41	2.86	3.98	22.70	350.9895	1655	6.9–8.3 (10H) m	—

*Numbering of substituents refers to structure 2.
†Method *A*.
‡Method *B*.

[3] 

were recorded on Varian A-60 and A-100 analytical spectrometers. The spectra were measured on approximately 10–15% (w/v) solutions in $CDCl_3$, with tetramethylsilane as a standard. Line positions are reported in parts per million from the reference. Absorption spectra were recorded in 'spectro'-grade solvents on a Beckman DB recording spectrophotometer. Mass spectra were determined on an Associated Electrical Industries MS-9 double focusing high resolution mass spectrometer. The ionization energy, in general, was 70 eV. Peak measurements were made by comparison with perfluorotributylamine at a resolving power of 15 000. Kieselgel DF-5 (Camag, Switzerland) and Eastman Kodak precoated sheets were used for thin-layer chromatography. Microanalyses were carried out by Dr. D. Daesslé, Organic Microanalysis Ltd , Montreal, Quebec and by Mrs. D. Mahlow of this department.

Source of Nitrosonaphthols

1-Nitroso-2-naphthol and 2-nitroso-1-naphthol were obtained as practical grade chemicals from Eastman Organic Chemicals and were purified by recrystallization from petroleum ether.

General Preparation of 3-Aroylaziridines

The compounds used in this study were prepared by the Gabriel synthesis involving Claisen–Schmidt condensations to form chalcones, then addition of bromine to form the dibromochalcones and treatment of the dibromochalcones with a three molar proportion of a primary aliphatic amine to provide 3-aroylaziridines (15 and references therein).

Preparation of 2-Aryl- and 2-Aroylnaphtho[1,2-d]-oxazoles and 2-Aryl- and 2-Aroylnaphtho-[2,1-d]oxazoles

Representative examples of the preparation of naphthooxazoles of the four different types by the two methods, (*A*) reaction with a 3-aroylaziridine and (*B*) reaction with a phenacyl pyridinium halide and base, are described in detail.

The analytical and spectral data on further examples prepared in a similar fashion are summarized in Tables 1, 2, and 3.

TABLE 3

Absorption spectra of 2-aroylnaphtho[1,2-*d*]oxazoles in CH_2Cl_2

No. **2**	λ_{max}	log ε	λ_{max}	log ε
a	356	4.19	264	4.19
b	356	4.25	286	4.12
*c**	349	4.20	306	4.16
d	380	4.16	272	4.49
e	372	4.18	260	4.40
f	363	4.25	276	4.32

*Spectrum recorded in CH_3CN.

Method A

Reaction of 3-Benzoyl-1-cyclohexyl-2-p-nitrophenylaziridine with 1-Nitroso-2-naphthol

A solution of 1.75 g (0.005 mole) of 3-benzoyl-1-cyclohexyl-2-*p*-nitrophenylaziridine and 0.865 g (0.005 mole) of 1-nitroso-2-naphthol in 50 ml of dry benzene was stirred and heated under reflux for 24 h during which time the solution turned a dark brown. Upon cooling of the solution, a green–brown solid which had precipitated, 0.51 g (32% yield), was collected and purified by extraction of the impurities with hot ethyl acetate, m.p. 240°, representing 2-*p*-nitrophenylnaphtho[1,2-*d*]oxazole.

Anal. Calcd. for $C_{17}H_{10}N_2O_3$ (mol. wt. 290.0691): C, 70.34; H, 3.47; N, 9.65. Found (290.0694 (mass spectrum)): C, 70.18; H, 3.64; N, 9.66.

The i.r. spectrum ν_{max}(KBr disk): 1535, 1350 cm^{-1} (NO_2).

The filtrate was concentrated *in vacuo* and the residual oil was subjected to chromatography on alumina (B.D.H.) with benzene as eluant. Removal of the solvent and trituration of the resulting green oil with hexane gave 2-benzoylnaphtho[1,2-*d*]oxazole as a light yellow solid, 0.52 g (41.5% yield), m.p. 124° (benzene–hexanes).

Anal. Calcd. for $C_{18}H_{11}NO_2$ (mol. wt. 273.0790): C, 79.11; H, 4.06; N, 5.13. Found (273.0788 (mass spectrum)): C, 78.90; H, 3.97; N, 5.17.

The i.r. spectrum ν_{max}($CHCl_3$): 1659 cm^{-1} (C=O); n.m.r. spectrum: δ_{TMS}($CDCl_3$): 7.2–8.8 (11H, multiplet,

aromatic protons); absorption spectrum $\lambda_{max}(CH_2Cl_2)$: 264 (log ε 4.19); 356 mμ (log ε 4.19).

Reaction of 3-Benzoyl-1-cyclohexyl-2-p-nitrophenylaziridine with 2-Nitroso-1-naphthol

A solution of 1.75 g (0.005 mole) of 3-benzoyl-1-cyclohexyl-2-*p*-nitrophenylaziridine and 0.865 g (0.005 mole) of 2-nitroso-1-naphthol in 50 ml of dry benzene was stirred and heated under reflux for 24 h during which time the solution turned purple–black. The solution was concentrated *in vacuo* and the dark oil produced was subjected to chromatography on alumina (B.D.H.) Elution with benzene afforded as the first fraction (after removal of the solvent and trituration of the resulting red oil with a few drops of ethyl acetate and a greater amount of hexane) 2-*p*-nitrophenylnaphtho-[2,1-*d*]-oxazole as a red solid, 0.21 g (8.4% yield) m.p. 152–153° (ethyl acetate – hexanes).

Anal. Calcd. for $C_{17}H_{10}N_2O_3$ (mol. wt. 290.0691): C, 70.34; H, 3.47; N, 9.65. Found (290.0690 (mass spectrum)): C, 70.04; H, 3.13; N, 9.67.

The i.r. spectrum $\nu_{max}(CHCl_3)$: 1522, 1342 cm^{-1} (NO_2); n.m.r. spectrum: $\delta_{TMS}(CDCl_3)$: 7.3–8.6 (10H, multiplet, aromatic protons).

Further elution with 40:60 chloroform–benzene gave after removal of the solvent *in vacuo* a bright red solid, 0.21 g (8.4% yield), m.p. 220° (ethyl acetate).

Anal. Calcd. for $C_{31}H_{27}N_3O_4$ (mol. wt. 505.2002): C, 73.64; H, 5.38; N, 8.31. Found (505.1998 (mass spectrum)): C, 73.23; H, 5.13; N, 7.87.

Further elution with chloroform gave after removal of solvent a purple solid, 0.5 g m.p. 160° (ethylacetate–hexane).

Anal. Calcd. for $C_{20}H_{12}N_2O_2$ (mol. wt. 312.0899): C, 76.91; H, 3.88; N, 8.97. Found (312.0901 (mass spectrum)): C, 76.87; H, 4.04; N, 8.41.

These compounds are currently under further investigation.

Method B

2-Benzoylnaphtho-[1,2-d]oxazole

A solution of 1.73 g (0.01 mole) 1-nitroso-2-naphthol in 50 ml 95% ethanol was added to 2.78 g (0.01 mole) phenacyl pyridinium bromide in 5 ml of water. The solution was stirred at 0° to −10° during addition of 10 ml of 1 *N* sodium hydroxide over 1/2 h. After 5 min, the solution turned dark red and after 2 h of stirring, 20 ml of water was added and the dark red solid which had precipitated was collected and dried. The solid was dissolved in benzene and subjected to chromatography on alumina (B.D.H.) with benzene as eluant. Removal of the solvent and trituration of the resulting green oil with hexane gave 2-benzoylnaphtho-[1,2-*d*]oxazole as a light yellow solid, 2.70 g (100% yield), m.p. 124° (benzene–hexanes).

This compound was shown by mass, i.r., and n.m.r. spectroscopy to be identical in all respects to the compound prepared above by method *A*.

2-p-Bromobenzoylnaphtho-[2,1-d]oxazole

A solution of 1.73 g (0.01 mole) 2-nitroso-1-naphthol in 50 ml 95% ethanol was added to 3.23 g (0.01 mole) of *p*-bromophenacyl pyridinium bromide in 5 ml water. The solution was stirred at 0° to −10° during addition of 10 ml of 1 *N* sodium hydroxide over 1/2 h. After 5 min, the solution turned dark and after 2 h of stirring, 20 ml of water was added and the dark brown solid which had precipitated was collected and dried. The solid was chromatographed on alumina with benzene–chloroform (1:1) as eluant. Removal of the solvent and trituration of the resulting yellow oil with hexane gave 2-*p*-bromobenzoylnaphtho-[2,1-*d*]oxazole as a yellow solid, 0.13 g (2.6% yield), m.p. 191° (benzene–hexanes).

Anal. Calcd. for $C_{18}H_{10}BrNO_2$ (mol. wt. 350.9895): C, 61.41; H, 2.86; N, 3.98; Br, 22.70. Found (350.9895 (mass spectrum)): C, 61.53; H, 2.85; N, 4.17; Br, 22.72.

The i.r. spectrum $\nu_{max}(CHCl_3)$: 1658 cm^{-1} (C=O); n.m.r. spectrum: $\delta_{TMS}(CDCl_3)$: 7.2–8.8 (10H, multiplet, aromatic protons); absorption spectrum $\lambda_{max}(CH_2Cl_2)$: 278 (log ε 4.28), 316 (log ε 4.17), 365 mμ (log ε 4.09).

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