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Liquid Crystalline Compounds Bearing Pyridine Ring: Azoxy Compounds with Alkyl Substituents

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Azoxy compounds bearing a 2,5-disubstituted pyridine ring as a principal constituent and at least one alkyl group at a molecular end were synthesized and their mesomorphic (nematic) ranges were examined. As for azoxy compounds containing an alkyl and an alkoxy group at both ends, respectively, mesomorphic ranges appeared with lower alkyl groups than those for azo compounds, their precursors. The ranges were also lower than those with both alkoxy ends. As regards an azoxy compound containing alkyl groups at both ends, no mesomorphic phenomenon appeared within the scope of this study.

Relatively few studies have been reported on liquid crystalline compounds bearing a pyridine ring as a principal constituent. A couple of studies on liquid crystalline Schiff bases[1,2] and phenylpyridines[3] can be found in the literature and we have reported 3-(4-alkoxyphenylazoxy)-6-alkoxypyridines as a novel liquid crystal series.[4] The replacement of the benzene ring by the pyridine, which exerts a sideward dipole moment, appears to profoundly affect the mesomorphic property of a compound.

In this study, we wish to report on the synthesis and the liquid-crystalline properties of azoxypyridines containing at least one terminal alkyl group in comparison with the known compounds containing only benzene rings, as well as the results of the previous study.[4]

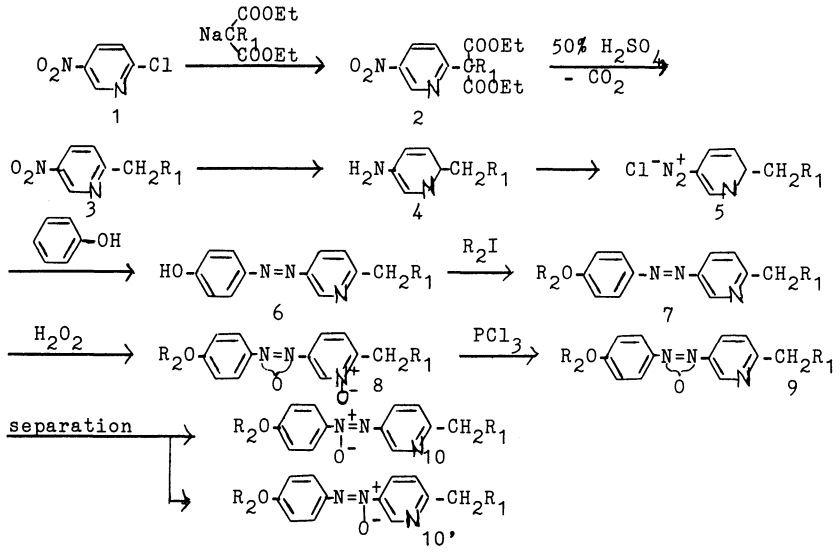
Two synthetic sequences (indicated in Schemes 1 and 2) were adopted.

Where R_1=CH_3, C_2H_5; R_2=CH_3, C_2H_5, n-C_6H_{13}; R_3=CH_3, n-C_4H_9.

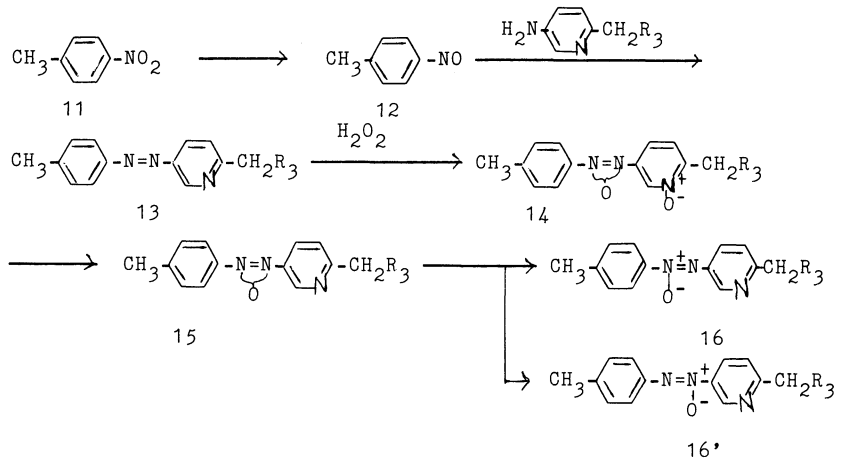
The mesomorphic behaviors of azoxy compounds **9**, **10**, **10′** and **15**, **16**, **16′** as well as those of azo compounds **7** and **13** were investigated.

Results and Discussion

2-[1,1-Bis(ethoxycarbonyl)alkyl]-5-nitropyridines (**2**) were prepared in a conventional manner by replacing the activated chlorine atom of 2-chloro-5-nitropyridine (**1**) with the carbanion from diethyl alkylmalonate prepared with sodium metal in xylene in 45—70% yields. The hydrolysis and subsequent decarboxylation of **2** with sulfuric acid were carried out according to Champa[2] to give 2-alkyl-5-nitropyridine (**3**) in 40—73% yield. A reduction of nitro to amino groups with cyclohexene in the presence of Pd-C (5%) proceeded quantitatively to afford 2-alkyl-5-amino-pyridines (**4**). A diazotization of **4** followed by coupling with phenol in the conventional manner provided azo compound **6** in high yield (83—91%). Etherification of the phenolic hydroxyl group via phenoxide ion with R_2I in DMF at 20 °C for 48 h afforded crude 3-(*p*-alkoxyphenylazo)-6-alkylpyridine (**7**), which was purified by silica-gel (Wakogel C-300) column chromatography using benzene as the eluting solvent. The oxidative conversion of **7** to azoxy derivatives **8** with hydrogen peroxide in acetic acid took 4 h, until the orange color of the



Scheme 1.



Scheme 2.

solution faded to some extent. IR (1250 cm^{-1}) and mass spectrometry clearly showed that the product was azoxypyridine *N*-oxide (**8**). This took a longer time than in the case of a previous report.[4] *N*-Oxides **8** were converted to the aimed 3-(*p*-alkoxyphenylazoxy)-6-alkylpyridines (**9**) by refluxing in PCl_3-$CHCl_3$ (1 : 4 v/v) followed by the usual work-up and recrystallization from ethanol in reasonable yields. The results of IR, MS, and ^1H NMR studies indicated that **9** was obtained. Since azoxy compounds **9** included two isomers by TLC, silica-gel column chromatography using ether-hexane (1 : 5 v/v) as the eluting solvent was employed in order to separate these isomer mixtures (**10** and **10'**). Identifications of azoxy compounds, thus separated, were satisfactorily made by ^1H NMR signals (δ 9.1—9.2 for **10**; δ 9.4—9.5 for **10'**). The ratioes of **10**/**10'** in **9** (Table 1) were determined from ^1H NMR signals. A remarkable feature is that **10'** is produced exclusively in samples **9b**, **9d**, and **9e**, indicating that the electron-donating effect of R_2O makes the azoxy N-atom more distant from the benzene ring more electrophilic as a result of resonance.

In the 2nd series, *p*-nitrotoluene (**11**) was converted to *p*-nitrosotoluene (**12**) via *p*-tolylhydroxylamine in usual manner.[5] The yield of *p*-nitrosotoluene was 40% on the basis on the starting *p*-nitrotoluene. **12** was reacted with **4** in acetic acid to give the corresponding azo compound **13** in low yield. The oxidation of **13** with hydrogen peroxide took 6 h (this time), and refluxing with PCl_3 afforded crude 3-(*p*-tolylazoxy)-6-alkylpyridine (**15**). A purification of the crude product with column chromatography eluted (hexane-benzene 5 : 1 v/v) the purified product in 21% yield (**15b**; R_3=C_4H_9). The ratio of two isomers in **15**(**16**/**16'**) was also determined from ^1H NMR signals (δ 9.1—9.2 for **16**; δ 9.5—9.6 for **16'**). For **15a**, the separation of two isomers was carried out by centrifugal liquid chromatography using hexane-ether (5 : 1 v/v) as the eluting solvent to afford isomers **16** and **16'**. These azoxy compounds indicated no mesomorphic range, presumably due to the presence of a very short methyl group at the one end.

Tables 1—3 summarize the transition temperatures of **9**, **10**, **10'**, and their precursors **7**, together with the values of the molar absorptivity (ε) in ethanol at the absorption maxima.

It can be recognized from Tables 1 and 2 that the azoxy compounds with relatively short R_2 chains such as Nos. **9a**, **9b**, **10a**, **10'a**, and **10'b** indicate no mesomorphic ranges when R_1=Me; however, the conventional azoxy compounds containing only benzene rings exhibit mesomorphic phases, even in the case of a compound corresponding to **9a**(C37N71I).[6] Therefore, it appears that the introduction of 2,5-

Table 1. Transition Temperature of Azoxy Compound **9** and **15**

No.	R_1	R_2	Yield / %	**10**/**10'** Molar ratio	Transition[a] temperature / °C	ε / $\times 10^4$ $m^3 cm^{-1} mol^{-1}$
9a	CH_3	CH_3	33	0.8	C43-46I	1.76(352)[c]
9b	CH_3	C_2H_5	47	0	C76-77I	2.43(361)[c]
9c	CH_3	C_6H_{13}	51	0.5	C37N76I	2.30(348)[c]
9d	C_2H_5	C_2H_5	32	0	C68N91I	2.32(361)[c]
9e	C_2H_5	C_6H_{13}	64	0	C51N85I	Undetermined
15a	CH_3[b]	—	36	1.6[d]	C27-28I	2.03(372)[c]
15b	C_4H_9[b]	—	21	0.3[d]	C39-40I	Undetermined

a) C, crystal; N, nematic; I, isotropic. b) R_3. c) Figures in parentheses indicate absorption maxima (EtOH) in nm. d) **16**/**16'**.

Table 2. Transition Temperature of Azoxy Compound **10** and **10′**, **16** and **16′**

No.	R_1	R_2	Transition temperature °C	ε $\times 10^4$ m^3 cm^{-1} mol^{-1}
10a	CH_3	CH_3	C60–62I	2.03(339)
10′a	CH_3	CH_3	C55–56I	2.38(359)
10′b	CH_3	C_2H_5	C76–77I	2.43(361)
10c	CH_3	C_6H_{13}	C56N85I	2.32(241)
10′c	CH_3	C_6H_{13}	C43N85I	2.59(361)
10′d	C_2H_5	C_2H_5	C68N89I	2.32(361)
10′e	C_2H_5	C_6H_{13}	C51N85I	Undetermined
16a	CH_3[a)]	—	C52I	1.26(324)
16′a	CH_3[a)]	—	C22I	3.47(333)

a) R_3. Figures in parentheses indicate absorption maxima (EtOH) in nm.

Table 3. Transition Temperature of Azo Compound **7** and **13**

No.	R_1	R_2	Yield %	Transition temperature °C	ε $\times 10^4$ m^3 cm^{-1} mol^{-1}
7a	CH_3	CH_3	62	C47–48I	2.64(353)
7b	CH_3	C_2H_5	43	C81–83I	2.55(355)
7c	CH_3	C_6H_{13}	31	C58–59I	2.38(355)
7d	C_2H_5	C_2H_5	73	C74N81I	2.53(355)
7e	C_2H_5	C_6H_{13}	59	C57N75I	2.68(355)
13a	CH_3[a)]	—	11	C63I	2.32(327)
13b	C_4H_9[a)]	—	10	C64–65I	Undetermined

a) R_3. Figures in parentheses indicate absorption maxima (EtOH) in nm.

disubstituted pyridine in place of the usual benzene ring in the alkyl-substituted azoxy compounds gives rise to a sideward polar effect on a molecule due to the unshared electron pair present on the 2,5-disubstituted pyridine ring; longer alkyl chains are required than the conventional azoxy compounds[5,7] to exhibit mesomorphism.

The mesomorphic ranges shown in Tables 1 and 2 were comparatively low, even with longer R_2, such as **9e** and **10′e**, as compared with those of the corresponding azoxy compounds with alkoxy groups at both ends.[4] This difference appears to be caused by the fact that alkyl group did not produce any polar effects on the arrays of molecules, as compared with polar alkoxy type. It can also be recognized from Table 3 that azo compounds **7** are inferior to azoxy types in the mesomorphic range formation, since even **7c** with long alkoxy chain does not afford any mesomorphic range. This may be caused by the fact that the polar character of azoxy at the central portion of the molecule would play a role in the appearance of mesomorphism. Generally, ONN isomers had higher CN and CI temperatures than NNO ones, presumably due to the more balanced polarities of the formers (Table 2), where ONN and NNO mean that the nitrogen atom on the benzene ring side and that on the pyridine side were oxidized, respectively. These azo-azoxy series are, more or less, colored; therefore, the values of molar absorptivity (ε) at absorption maxima are shown in Tables 1—3. However, the differences of ε and the absorption maxima are generally small, although visual colors are considerably different due to the difference in the expansion of absorption spectrum.

Experimental

IR, ^{1}H NMR, and mass spectra were recorded on a Hitachi 215 spectrophotometer, a JNM-PMX60 spectrometer, and a Hitachi RMU-6 spectrometer, respectively, under standard conditions. Elemental analyses and centrifugal liquid chromatography were carried out with Perkin-Elmer 250 and Hitachi CLC-5 instruments.

The transition temperatures were determined by means of either a Yamato MP-21 melting-point apparatus or an optical microscope, both equipped with crossed polarizers.

2-[1,1-Bis(ethoxycarbonyl)alkyl]-5-nitropyridine (2). Diethyl alkylmalonate (30 mmol) was stirred with a sand-like suspension of sodium metal(0.7 g, 30 mmol) in xylene (50 ml) at 50 °C until sodium metal completely disappeared (0.5—1 h). The resulting mixture was heated under reflux with 2-chloro-5-nitropyridine (**1**; 4.8 g, 30 mmol) for 4 h. Xylene was distilled off from the reaction mixture and the residue was extracted with ether-water. The organic layer was washed with water, dried over anhydrous sodium sulfate, and concentrated on a rotary evaporator, followed by distillation under reduced pressure (152—210 °C, 0.1 mmHg†) to give a fluid. Yield: 68% for R_1=Me, 50% for Et, 45% for C_4H_9. IR ($CHCl_3$) 1740 (C=O), 1350 (NO_2) cm^{-1}. ^{1}H NMR ($CDCl_3$) δ=0.9—2.4 (m, alkyl), 4.3 (q, 4H, $2CH_2O$), 8.0 (d, 1H, pyridine), 8.5 (q, 1H, pyridine), 9.4 (d, 1H, pyridine).

2-Alkyl-5-nitropyridine (3). These compounds were prepared according to a known method.[2] A solution of **2** (30

† 1 mmHg=133.322 Pa.

mmol) in 50% H_2SO_4 was stirred at 110 °C until the generation of carbon dioxide gas was no longer discernible (2 h). The usual work-up and distillation under reduced pressure (100 °C/0.1 mmHg) gave a pure product. Yield: 61% for R_1=Me, 73% for Et, 40% for C_4H_9.

The results of IR and NMR were satisfactory.

2-Alkyl-5-aminopyridine (4). A solution of **3** (10 mmol) and cyclohexene (5 ml) in absolute ethanol (70 ml) was heated under reflux with the addition of 5% Pd-C (1 g) for 2 h with stirring. The reaction mixture was filtered and the filtrate was concentrated on a rotary evaporator to leave a fluid.

^{1}H NMR ($CDCl_3$) δ=0.9—3.0 (m, alkyl), 3.7 (b, 2H, amine), 6.9 (d, 2H, pyridine), 8.0 (b, 1H, pyridine).

3-(*p*-Hydroxyphenylazo)-6-alkylpyridine (6). To a solution of **4** (10 mmol) in a mixture of hydrochloric acid (4.5 ml) and water (10 ml) was added under ice cooling a solution of sodium nitrite (0.7 g) in water (10 ml), followed by stirring for a while. A solution of phenol (10 mmol) and sodium hydroxide (1.0 g) in water (20 ml) was dropped at 0—5 °C under ice-water cooling. Stirring was continued for one hour; then the solution was neutralized with sodium hydrogencarbonate, and the resulting precipitate was picked up by filtration. Recrystallization was carried out from chloroform-hexane. Yield; 91% for R_1=Me, 83% for Et. Mp 182—183 °C for R_1=Me, 151—151 °C for Et.

R_1	C%	H%	N%	MS(*m*/*z*)
CH_3	68.53(68.72)	5.86(5.73)	18.60(18.50)	227(M^+)
C_2H_5	69.57(69.71)	6.25(6.22)	17.28(17.43)	241(M^+)

Figures in parentheses indicate the calcd values.

IR($CHCl_3$) 3600—3150 (OH) cm^{-1}. ^{1}H NMR ($CDCl_3$) δ= 0.9—2.0 (m, alkyl), 2.9 (q, or t, 2H, $ArCH_2$), 6.9—8.1 (m, 6H, ArH+pyridine), 8.9 (d, 1H, pyridine), 10.0 (b, 1H, OH).

3-(4-Alkoxyphenylazo)-6-alkylpyridine (7). **6** (10 mmol) was dissolved in a solution of potassium hydoxide (12 mmol) in methanol (20 ml). Methanol was then removed on a rotary evaporator and the residue was dissolved in anhydrous DMF (20 ml). Alkyl iodide (12 mmol) was dropped and the mixture was stirred at 20 °C for 48 h. A 1 M[††] sodium hydroxide solution was then added and the mixture was extracted with chloroform. The organic layer was first washed with an aqueous sodium hydroxide solution and then with water. It was next dried over anhydrous sodium sulfate and evaporated on a rotary evaporator. Column (SiO_2, Wakogel C-300) chromatography using benzene as the eluting solvent was employed for purification.

No.	R_1	R_2	Yield/%
7a	CH_3	CH_3	62
7b	CH_3	C_2H_5	43
7c	CH_3	C_6H_{13}	31
7d	C_2H_5	C_2H_5	73
7e	C_2H_5	C_6H_{13}	59

No.	C/%	H/%	N/%	MS(*m*/*z*)
7a	69.43(69.71)	6.23(6.22)	17.47(17.43)	241(M^+)
7b	71.03(70.59)	7.01(6.67)	16.18(16.47)	255(M^+)
7c	73.20(73.31)	8.08(8.04)	13.42(13.50)	311(M^+)
7d	71.47(71.38)	7.12(7.06)	15.45(15.61)	269(M^+)
7e	73.48(73.85)	8.53(8.31)	12.65(12.92)	325(M^+)

Figures in parentheses indicate calcd values.

[††] 1 M=1 mol dm^{-3}.

^{1}H NMR ($CDCl_3$) δ=0.9—3.0 (m, alkyl), 3.8 for **7a** (s, 3H, CH_3O), 4.0 for others (q or t, 2H, CH_2O), 6.8—8.2 (m, 6h, ArH+pyridine), 9.0 (d, 1H, pyridine).

3-[(4-Alkoxyphenyl)-NON-azoxy]-6-alkylpyridine *N*-Oxide (8). A solution of **7** (5 mmol) and 30% hydrogen peroxide (17 ml) in glacial acetic acid (100 ml) were heated at 65 °C until the color of the solution faded to some extent (4 h). The solution was poured onto ice and the resulting precipitate was picked up by filtration. The precipitate was recrystallized from ethanol-water.

No.	R_1	R_2	Mp(θ_m/°C)	Yield/%
8a	CH_3	CH_3	117—118	32
8b	CH_3	C_2H_5	156—157	12
8c	CH_3	C_6H_{13}	80—82	46
8d	C_2H_5	C_2H_5	123—125	35
8e	C_2H_5	C_6H_{13}	136—137	27

No.	C/%	H/%	N/%	ε / ×10⁴ m^3 cm^{-1} mol^{-1}
8a	61.79	5.63	15.29	2.00
	(61.54)	(5.49)	(15.38)	(364)
8b	62.56	5.96	14.48	2.25
	(62.72)	(5.92)	(14.63)	(367)
8c	66.65	7.30	12.25	2.41
	(66.47)	(7.29)	(12.24)	(367)
8d	63.55	6.36	13.79	2.35
	(63.79)	(6.31)	(13.95)	(368)
8e	67.12	7.51	11.69	2.18
	(67.23)	(7.56)	(11.76)	(366)

The figures to the far right of the parentheses indicate the absorption maxima in nm. MS (*m*/*z*) of all compounds provided molecular ion peaks. IR (KBr) 1250 (*N*-oxide) cm^{-1}. ^{1}H NMR ($CDCl_3$) δ=0.9—3.0 (m, alkyl), 3.9 for **8a** (s, 3H, CH_3O), 3.8—4.2 for others (q or t, 2H, CH_2O), 6.9—8.5 (m, 6H, ArH+pyridine), 9.3 (d, 1H, pyridine).

3-[(4-Alkoxyphenyl)-NON-azoxy]-6-alkylpyridine (9). A mixture of **8** (0.3 mmol) and phosphorus trichloride (2.5 ml) in chloroform (10 ml) was refluxed for 4 h. To the reaction mixture were added ice and sodium hydroxide in order to make the solution alkaline. The whole was extracted with chloroform. The combined extracts were washed with water, dried over anhydrous sodium sulfate, and evaporated to dryness on a rotary evaporator. Recrystallization from ethanol provided a purified product.

No.	R_1	R_2	Yield/%
9a	CH_3	CH_3	33
9b	CH_3	C_2H_5	47
9c	CH_3	C_6H_{13}	51
9d	C_2H_5	C_2H_5	32
9e	C_2H_5	C_6H_{13}	64

No.	C/%	H/%	N/%
9a	65.00(65.42)	5.85(5.84)	16.18(16.35)
9b	66.35(66.42)	6.29(6.27)	15.43(15.50)
9c	69.86(69.72)	7.76(7.65)	12.85(12.84)
9d	66.91(67.37)	6.59(6.67)	14.92(14.74)
9e	70.22(70.44)	8.04(8.00)	12.26(12.32)

Mass spectra fo all azoxy compounds indicated molecular ion peaks.

^{1}H NMR ($CDCl_3$) δ=0.9—3.0 (m, alkyl), 3.9 for **9a** (s, 3H, CH_3O), 4.1 for others (q or t, 2H, CH_2O), 6.9—8.8 (m, 6H, ArH+pyridine), 9.2, 9.5 (1H, pyridine).

Separation of Isomers. Column (silica gel, Wako C-300) chromatography was applied to **9** using ether-hexane (1 : 5 v/v) as an eluting solvent to afford NNO-azoxy, then ONN-azoxy isomers.

No.	R_1	R_2	ONN-azoxy (**10**) NMR/δ	NNO-azoxy (**10'**) NMR/δ
10(10')a	CH_3	CH_3	9.2(d, 1H, 2-pyridine)	9.5(d, 1H, 2-pyridine)
10'b	CH_3	C_2H_5	—	9.4(d, 1H, 2-pyridine)
10(10')c	CH_3	C_6H_{13}	9.1(d, 1H, 2-pyridine)	9.4(d, 1H, 2-pyridine)
10'd	C_2H_5	C_2H_5	—	9.5(d, 1H, 2-pyridine)
10'e	C_2H_5	C_6H_{13}	—	9.5(d, 1H, 2-pyridine)

MS (m/z) of all isomers indicated molecular ion peaks.

***p*-Nitrosotoluene (12).** *p*-Nitrosotoluene (**12**) was prepared via *p*-tolylhydroxylamine in a conventional manner.[5] Thus, starting with *p*-nitrotoluene (**11**; 13.7 g, 100 mmol), reduction (Zn, NH_4Cl) to the hydroxylamine (yield, 58%), and subsequent oxidation with sodium dichromate and sulfuric acid gave **12** in 40% overall yield. Mp 45 °C. The results of IR and NMR were satisfactory.

3-(4-Methylphenylazo)-6-alkylpyridine (13). To the solution of 2-alkyl-5-aminopyridine (**4**; 0.8 g, 5 mmol) in warm acetic acid (5 ml) was added **12** (0.6 g, 5 mmol) at 20 °C with shaking. The solution was stirred at 50 °C for 24 h. The reaction mixture was made alkaline with a sodium carbonate solution including ice and extracted with chloroform. The organic layer was concentrated on a rotary evaporator. The residue was subjected to SiO_2 column chromatography using hexane-ether (5 : 1 v/v) as the eluting solvent to give a purified product. Yield: 11% for R_3=CH_3; 10% for C_4H_9.

No.	R_3	C/%	H/%	N/%
13a	CH_3	74.17	6.64	18.67
		(74.64)	(6.71)	(18.65)
13b	C_4H_9	76.23	7.75	15.67
		(76.40)	(7.86)	(15.73)

No.	^{1}H NMR
13a	1.4(t, 3H, Me), 2.5(s, 3H, Me), 3.0(q, 2H, CH_2), 7.3—8.4(m, ArH+Rpyridine), 9.3(d, 1H, pyridine)
13b	0.9—2.0(m, 9H, alkyl), 2.4(s, 1H, Me), 2.9(t, 2H, CH_2), 7.0—8.1(m, 6H, ArH+pyridine), 9.0(d, 1H, pyridine)

Mass spectra of these azo compounds indicated molecular ion peaks.

3-(4-Methylphenyl-NON-azoxy)-6-alkylpyridine (15). The same procedure as that for **9** was applied to **13** with the exception that the reaction time was prolonged to 6 h at 65 °C.

No.	R_3	C/%	H/%	N/%
15a	CH_3	66.64	6.26	17.52
		(66.69)	(6.27)	(17.41)
15b	C_4H_9	76.58	7.71	9.90
		(76.60)	(7.80)	(9.93)

No.	MS(m/z)	^{1}H NMR
15a	241(M^+)	9.2, 9.6 (d, 2-pyridine)
15b	283(M^+)	9.1, 9.5 (d, 2-pyridine)

The separation of isomers was tried for the azoxy compound (**15a**; R_3=CH_3) with centrifugal liquid chromatography (CLC) using hexane-ether (5 : 1 v/v) as the eluting solvent. NNO, and then the ONN isomers, were eluted. ^{1}H NMR indicated characteristic peaks at δ 9.2 and 9.6 for ONN (**16a**) and NNO (**16'a**) isomers, respectively.

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