A Novel and Chemoselective Preparation of Chlorosulphonyl-containing Azo-dyes with Phosphoryl Chloride–*N*,*N*-Dimethylacetamide

By **Shinsaku Fujita**, Research Laboratories, Ashigara, Fuji Photo Film Co. Ltd., Minami-Ashigara, Kanagawa, 250-01, Japan

Azo dyes containing a chlorosulphonyl group (1b)—(10b) have been prepared by the reaction of the corresponding sodium sulphonates (1a)—(10a) with phosphoryl chloride–*N*,*N*-dimethylacetamide (in acetonitrile); the chemoselectivity of this reagent is superior to phosphoryl chloride, phosphoryl chloride–*N*,*N*-dimethylformamide, and thionyl chloride–*N*,*N*-dimethylformamide. By-products of the latter reactions have been isolated and characterized.

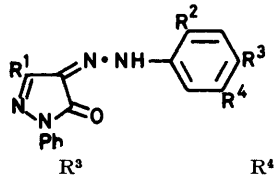
RECENTLY, azo-dyes containing *o*-sulphonamidophenol [1] and *p*-sulphonamidonaphthol functions [2] have been proposed as dye releasers (or dye-releasing redox compounds) in instant photography.[3] Since sulphonyl chlorides are key intermediates both for the synthesis of such dye releasers as well as sulphonyl-containing drugs of commercial importance,[4] our synthetic efforts require mild and chemoselective reagents for the chlorination of sulphonic acids. Although the preparations of several chlorosulphonyl-containing dyes by the use of phosphorus pentachloride or chlorosulphonic acid have been reported,[5] the reagents are difficult to handle, especially, on a large-scale. Thionyl chloride–*N*,*N*-dimethylformamide ($SOCl_2$–DMF) has been widely used for the preparation of aromatic sulphonyl chlorides.[6] However, this reagent often suffers from the formation of by-products, when applied to the chlorination of sulphonyl-containing azo-dyes. Here we describe a convenient method of preparing sulphonyl chlorides with phosphoryl chloride–*N*,*N*-dimethylacetamide ($POCl_3$–DMA), the chemoselectivity of which is superior to $POCl_3$–DMF or $SOCl_2$–DMF.

Preparation of Chlorosulphonyl-containing Azo-dyes with $POCl_3$–DMA.—Tables 1 and 2 show chlorosulphonyl-containing azo-dyes prepared with $POCl_3$–DMA. Chlorosulphonyl-containing pyrazolone azo-dyes (1b)—(7b) and naphthol azo-dyes (8b)—(10b) have been obtained by this method without affecting other functional groups. The procedures are simple and afforded good yields of sulphonyl chlorides of high purity. Thus, the corresponding sodium sulphonates (1a)—(10a) were suspended in acetonitrile (and/or sulpholane) containing an excess of DMA (*ca.* 4 mol per 1 mol of the sodium sulphonate) and then treated with phosphoryl chloride (*ca.* 4 mol). DMA played an important role both as a reagent and as a co-solvent to give smooth chlorination. When a catalytic quantity of DMA was used, the reaction was retarded and its chemoselectivity was affected. The reactive species of this chlorination was presumed to be a Vilsmeier-type complex of $POCl_3$ and DMA.[7] The applicability of this method to other types of azo-dye sulphonic acids is under investigation.

Chemoselectivity of $POCl_3$–DMA. *Comparison with* $POCl_3$, $POCl_3$–DMF, *and* $SOCl_2$–DMF.—Several other reagents were studied in order to clarify the chemoselectivity of the $POCl_3$–DMA reagent. When the chlorination of (2a) was carried out with $POCl_3$ in the absence of DMA (using acetonitrile–sulpholane as a solvent), the resulting chloride (2b) was contaminated with two by-products, one of which was isolated and characterized as having structure (11). Its molecular formula was established as $C_{17}H_{13}Cl_2N_5O_3S$ from mass spectral evidence [*m*/*e* 437 (M^+) and (M + 1) peak (*m*/*e* 438) of field desorption mass spectrum] and its elemental analysis. ^{1}H N.m.r. signals at δ 8.62 (CONH) and at δ 2.87 and 2.85 (CH_3N) showed the presence of

TABLE 1

Chlorosulphonyl-containing pyrazolone azo-dyes prepared with $POCl_3$–DMA [a]



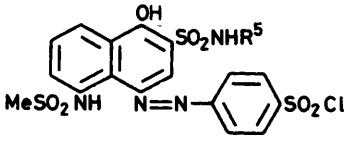
Compd.	R¹	R²	R³	R⁴	Yield (%)	M.p. °C
(1b)	$CONH_2$	OMe	H	SO_2Cl	93	226—227 (decomp.)
(2b)	CONHMe	H	SO_2Cl	H	94	244—245 (decomp.)
(3b)	CONHMe	OMe	H	SO_2Cl	90	227—228 (decomp.)
(4b)	CONHMe	Me	SO_2Cl	H	70 (91) [b]	217—218 (decomp.)
(5b)	CONHMe	H	SO_2Cl	Me	95	188—193 (decomp.)
(6b)	CN	H	OCH_2CH_2OMe	SO_2Cl	95	182—183
(7b)	CN	OMe	H	SO_2Cl	81 (97) [b]	235—236 (decomp.)

[a] A mixture of the corresponding sodium sulphonate (1a)—(7a) (0.01 mol), acetonitrile (20 ml as a solvent), DMA (3.6 ml), and $POCl_3$ (3.6 ml) was stirred at 50—55 °C for 1.5 h. [b] The yield in parentheses was obtained using acetonitrile (10 ml)–sulpholane (10 ml) as a solvent.

an *N*-methylcarbamoyl group. Moreover, its electronic spectrum contained a hypsochromically shifted absorption band at $\lambda_{max.}$ 346 nm, which revealed that the enol group of pyrazolone was displaced by a chlorine atom.

TABLE 2

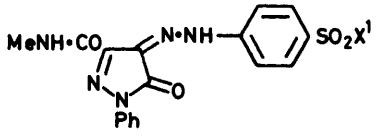
Chlorosulphonyl-containing naphthol azo-dyes prepared with $POCl_3$–DMA [a]



Compd.	R^5	Yield (%)	M.p. (°C)
(8b)	Me	91	248 (decomp.)
(9b)	Cyclohexyl	99	239 (decomp.)
(10b)	Cyclopentyl	94	251—252 (decomp.)

[a] The reaction conditions were the same as described in Table 1.

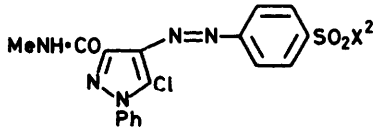
Chlorination of (2a) with $POCl_3$–DMF afforded another by-product (12) having the molecular formula $C_{18}H_{13}Cl_2N_5O_4S$ (*m/e* 465). Its absorption band ($\lambda_{max.}$ 346 nm) indicated that the compound had a similar chromophore to that of (11). A ^1H n.m.r. signal at δ 9.07 could be ascribed to a formyl proton. A peak at *m/e* 408 (M^+ —



(2)

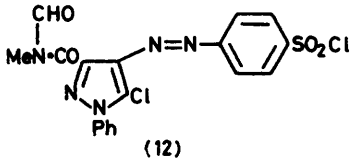
a; X^1 = ONa

b; X^1 = Cl



(11) X^2 = Cl

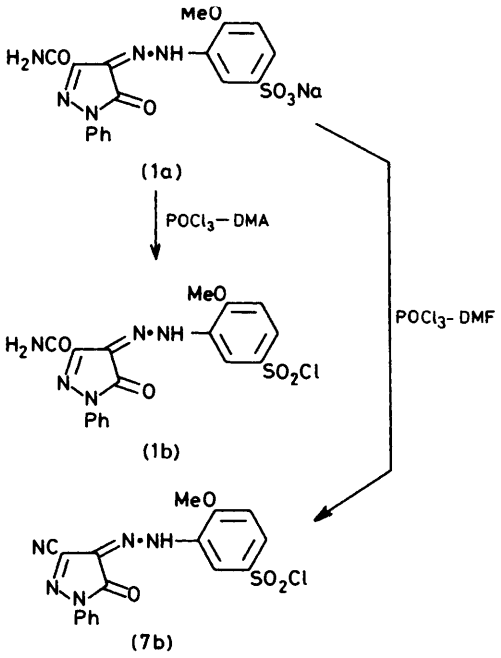
(12) X^2 = NH_2



(12)

MeNCO) was considered to be derived by a cyclic carbonyl fragmentation, which indicated the presence of a Me(HCO)NCO group. Moreover, ammonolysis of the by-product (12) gave the same sulphonamide (13) as that of (11). These facts indicated that the by-product had structure (12) which came from the undesired formylation of the amide group and chlorination of the pyrazolone enol group of (2a). Chlorination of (2a) with $SOCl_2$–DMF yielded a complex mixture of (2b), (11), 12), and an unidentified product.

The difference between the action of $POCl_3$–DMA and that of $POCl_3$–DMF was more clearly illustrated in the case of the chlorination of (1a). The $POCl_3$–DMA reagent gave exclusively the corresponding sulphonyl chloride (1b), in which the carbamoyl group remained



(1a)

(1b)

(7b)

unchanged. On the other hand, $POCl_3$–DMF chlorination of (1a) has been reported to afford another product (7b) which has a cyano-group resulted from dehydration of the carbamoyl function.[8]

EXPERIMENTAL

^1H N.m.r. spectra were determined on a Varian EM-390 90 MHz n.m.r. spectrometer at 90 MHz at room temperature with [$^2H_6$]dimethyl sulphoxide as a solvent. Mass spectra (m.s.) and field desorption mass spectra (f.d.m.s.) were determined on a JEOL-O1SG-2 mass spectrometer. I.r. spectra were measured with a JASCO IRA-2 diffraction grating i.r. spectrophotometer. Visible spectra (v.s.) were obtained using a Hitachi 323 spectrophotometer. Melting points are uncorrected.

Chlorination of the Sodium Salts of the Sulphonic Acid Dyes (1a)—(10a) *with* $POCl_3$–DMA.—*A Representative procedure* (*A*). To a stirred suspension of 3-(*N*-methylcarbamoyl)-1-phenyl-4-(4-sulphophenylhydrazono)pyrazol-5-one sodium salt (2a) (4.23 g, 0.01 mol) in acetonitrile (20 ml) and DMA (3.6 ml) was added dropwise phosphoryl chloride (3.6 ml, 0.039 mol) during 10 min below 40 °C. The reaction mixture was stirred at 50—55 °C for 1.5 h, cooled to room temperature and, then, poured into ice–water (150 ml). The crystals precipitated were filtered off,

washed with water, and air-dried. The corresponding sulphonyl chloride (2b) was obtained in a 94% yield (3.96 g). Recrystallization from acetonitrile gave an analytically pure sample, m.p. 244—245 °C (decomp.) (Found: C, 48.55; H, 3.15; N, 16.75%. Calc. for $C_{17}H_{14}ClN_5O_4S$: C,48.64; H, 3.36; N, 16.68%), (*m/e*) 419 (M^+), 401 ($M^+ - H_2O$), 388 ($M^+ - MeNH_2$), 384 ($M^+ - Cl$), 320 ($M^+ - SO_2Cl$), 244 ($M^+ - C_6H_4SO_2Cl$); $\lambda_{max.}$ (Me_2CO) 405 nm (ε 28 300); $\nu_{max.}$ (KBr) 3 380, 1 715, and 1 652 cm^{-1}; δ_H 9.17br (1 H, MeN*H*), 8.06 (2 H, d, *J* 9 Hz, ArH), 7.75 (2 H, d, *J* 9 Hz ArH), 7.6—7.2 (5 H, m, Ph), and 2.88 (3 H, m, CH_3N).

Other chlorosulphonyl dyes were obtained by similar methods as shown in Tables 1 and 2.

3-*Carbamoyl*-4-(5-*chlorosulphonyl*-2-*methoxyphenylhydrazono*)-1-*phenylpyrazol*-5-*one* (1b). This compound had m.p. 226—227 °C (decomp.) (Found: C, 47.0, H, 3.2; N, 15.55; Calc. for $C_{17}H_{14}ClN_5O_5S$: C, 46.85; H, 3.24; N, 16.07%), *m/e* 435 (M^+), 417 ($M^+ - H_2O$), 336 ($M^+ - SO_2Cl$), 230 ($M^+ - MeOC_6H_3SO_2Cl$); $\lambda_{max.}$ (Me_2CO) 432 nm (ε 19 900); $\lambda_{max.}$ (KBr) 1 705 and 1 660 cm^{-1}; δ_H 8.56, 8.40br (2 H, NH_2), 8.2—8.0 (3 H, m, ArH), 7.7—7.1 (5 H, m, Ph), and 3.96 (3 H, s, CH_3O).

4-(5-*Chlorosulphonyl*-2-*methoxyphenylhydrazono*)-3-(N-*methylcarbamoyl*)-1-*phenylpyrazol*-5-*one* (3b). This compound had m.p. 227—228 °C (decomp), (Found: C, 48.25; H, 3.6; N, 16.0. Calc for $C_{18}H_{16}ClN_5O_5S$: C, 48.06, H, 3.59, N, 15.57%), *m/e* 449 (M^+), 431 ($M^+ - H_2O$), 414 ($M^+ - Cl$), 244 ($M^+ - MeOC_6H_3SO_2Cl$); $\lambda_{max.}$ (Me_2CO) 421 nm (ε 18 900); $\nu_{max.}$ (KBr): 3 410, 1 712, and 1 656 cm^{-1}; δ_H 9.14br (1 H, MeN*H*), 8.2—7.8 (3 H, m, ArH), 7.7—7.1 (5 H, m, Ph), 4.02 (3 H, s, CH_3O), and 2.95 (3 H, m, CH_3N).

4-(4-*Chlorosulphonyl*-2-*methylphenylhydrazono*)-3-(N-*methylcarbamoyl*)-1-*phenylpyrazol*-5-*one* (4b). This compound had m.p. 217—218 °C (decomp.). (Found: C, 49.75; H, 3.5; N, 15.9. Calc. for $C_{18}H_{16}ClN_5O_4S$: C, 49.83; H, 3.72; N, 16.14%), *m/e* 433 (M^+) and 334 ($M^+ - SO_2Cl$); $\lambda_{max.}$ (Me_2CO) 411 nm (ε 26 800); $\nu_{max.}$ (KBr): 3 410, 1 716, and 1 655 cm^{-1}; δ_H 9.12br (1 H, MeN*H*), 8.2—7.1 (8 H, m, ArH), 2.86 (3 H, m, CH_3N), and 2.49 (CH_3, overlapped with Me_2SO).

4-(4-*Chlorosulphonyl*-3-*methylphenylhydrazono*)-3-(N-*methylcarbamoyl*)-1-*phenylpyrazol*-5-*one* (5b). This compound had m.p. 188—193 °C (decomp.) (Found: C, 49.7; H, 3.75; N, 15.4. Calc. for $C_{18}H_{16}ClN_5O_4S$: C, 49.83; H, 3.72; N, 16.14), *m/e* 433 (M^+), 415 ($M^+ - H_2O$), 334 ($M^+ - SO_2Cl$), and 244 ($M^+ - MeC_6H_3SO_2Cl$); $\lambda_{max.}$ (Me_2CO) 416 nm (ε 26 700); $\nu_{max.}$ (KBr) 3 390, 1 716, and 1 655 cm^{-1}; δ_H 9.21br (1 H, MeN*H*), 8.3—7.1 (8 H, m, ArH), 2.90 (3 H, m, CH_3N), and 2.63 (overlapped with Me_2SO, s, CH_3).

4-[3-*Chlorosulphonyl*-4-(2-*methoxyethoxy*)*phenylhydrazono*]-3-*cyano*-1-*phenylpyrazol*-5-*one* (6b). This compound had m.p. 182—183 °C (Found: C, 49.35; H, 3.3; N, 15.05. Calc. for $C_{19}H_{16}ClN_5O_5S$: C, 49.41; H, 3.49; N, 15.16%), *m/e* 461 (M^+), 426 ($M^+ - Cl$), 403 ($M^+ - MeOCH-CH_2$); $\lambda_{max.}$ (Me_2CO) 430 nm (ε 23 000); $\nu_{max.}$ (KBr) 2 230 and 1 665 cm^{-1} (CN); n.m.r. (partially decomposed on determination) δ_H 4.20 (m, OCH_2), 3.68 (m, CH_2OMe), and 3.36 (s, OCH_3).

4-(5-*Chlorosulphonyl*-2-*methoxyphenylhydrazono*)-3-*cyano*-1-*phenylpyrazol*-5-*one* (7b). This compound had m.p. 235—236 °C (decomp.) (Found: C, 48.8; H, 2.65; N, 16.6. Calc. for $C_{17}H_{12}ClN_5O_4S$: C, 48.87; H, 2.90; N, 16.76%), *m/e* 417 (M^+), 382 ($M^+ - Cl$), 318 ($M^+ - SO_2Cl$); $\lambda_{max.}$ (Me_2CO) 422 nm (ε 21 400); $\nu_{max.}$ (KBr) 2 240, 1 670 cm^{-1} (CN); δ_H 8.1—7.1 (m, ArH) and 4.00 (s, CH_3O).

4-(4-*Chlorosulphonylphenylazo*)-2-(N-*methylsulphamoyl*)-5-*methylsulphonylamino*-1-*naphthol* (8b). This compound had m.p. 248 °C (decomp.) (Found: C, 40.7; H, 3.05; N, 10.55%. Calc. for $C_{18}H_{17}ClN_4O_7S_3$: C, 40.56; H, 3.22; N, 10.51), *m/e* 532 (M^+), 453 ($M^+ - Ms$), 433 ($M^+ - SO_2Cl$), and 422 ($M^+ - Ms - MeNH_2$); $\lambda_{max.}$ (Me_2CO) 485 nm (ε 29 200); $\nu_{max.}$ (KBr): 3 360, 3 280, 1 638, and 1 586 cm^{-1}; δ_H 11.64 (1 H, s, MsN*H*), 8.80 (1 H, s, naphthalene 3-H), 8.1—7.2 (*ca.* 9 H, m, ArH, OH, and MeNH), 3.19 (3 H, s, CH_3SO_2), and 2.50 (overlapped with Me_2SO, CH-N).

4-(4-*Chlorosulphonylphenylazo*)-2-(N-*cyclohexylsulphamoyl*)-5-*methylsulphonylamino*-1-*naphthol* (9b). This compound had m.p. 239 °C (decomp.) (Found: C, 45.9; H, 4.0; N, 9.3. Calc. for $C_{23}H_{25}ClN_4O_7S_3$: C, 45.96; H, 4.19; N, 9.32%), *m/e* 600 (M^+), 521 ($M^+ - Ms$), 439 ($M^+ - Ms - C_6H_{10}$); $\lambda_{max.}$ (Me_2CO) 485 nm (ε 28 200); $\nu_{max.}$ (KBr) 3 280, 1 635, and 1 586 cm^{-1}; δ_H 11.54 (1 H, s, MsN*H*), 8.93 (1 H, s, naphthalene 3-H), 8.3—7.5 (*ca.* 7 H, ArH), *ca.* 6.1br (SO_2NH and OH), 3.25 (4 H, s + m, CH_3SO_2 and SO_2NHCH), and 1.9—0.9 [*ca.* 10 H, m, $(CH_2)_5$)].

4-(4-*Chlorosulphonylphenylazo*)-2-(N-*cyclopentylsulphamoyl*)-5-*methylsulphonylamino*-1-*naphthol* (10b). This compound had m.p. 251—252 °C (decomp.) (Found: C, 45.05; H, 3.8; N, 9.35. Calc. for $C_{22}H_{23}ClN_4O_7S_3$: C, 45.01; H, 3.95; N, 9.54%), *m/e* 586 (M^+), 507 ($M^+ - Ms$), 487 ($M^+ - SO_2Cl$), 439 ($M^+ - Ms - C_5H_8$), and 422 ($M^+ - Ms - C_5H_{11}N$); $\lambda_{max.}$ (Me_2CO) 485 nm (ε 29 000); $\nu_{max.}$ (KBr): 3 280, 1 635, and 1 586 cm^{-1}; δ_H 11.70 (1 H, s, MsN*H*), 8.94 (s, naphthalene 3-H), 9.5—8.5 (overlapped with a singlet at δ 8.94, broad, SO_2NH and OH), 8.3—7.6 (*ca.* 7 H, m, ArH), 3.63 (1 H, m, SO_2NHCH), 3.23 (3 H, s, CH_3SO_2), and 1.8—1.2 [*ca.* 8 H, m, $(CH_2)_4$].

Chlorination of Compound (2a) *with* $POCl_3$: *Isolation of the By-Product* 5-*Chloro*-4-(4-*chlorosulphonylphenylazo*)-3-(N-*methylcarbamoyl*)-1-*phenylpyrazole* (11). To a stirred mixture of compound (2a) (4.23 g, 0.01 mol), sulpholane (10 ml), and acetonitrile (10 ml) was added phosphoryl chloride (3.6 ml). T.l.c. of the reaction mixture [silica gel, ethyl acetate–benzene (1 : 2) as solvent] showed the formation of three components: an unknown compound (R_F 0.87), (2b) (R_F 0.55), and (11) (R_F 0.25). When the mixture was stirred at 70—75 °C for 8 h, compound (11) became a main product. The mixture was poured onto ice–water, and the resulting sticky oil was separated from the supernatant solution by decantation. Addition of acetonitrile resulted in crystallization of the oil. The crystals were filtered off and recrystallized from acetonitrile to afford compound (11) (1.70 g), m.p. 149—151 °C (Found: C, 46.65; H, 2.8; N, 15.7. Calc. for $C_{17}H_{13}Cl_2N_5O_3S$: C, 46.59; H, 2.99; N, 15.98%), *m/e* 437 (M^+), 419 ($M^+ - H_2O$), and 262 ($M^+ - C_6H_4SO_2Cl$); f.d.m.s. *m/e* 438 ($M + 1$); $\lambda_{max.}$ (Me_2CO) 346 nm (ε 21 300); $\nu_{max.}$ (KBr) 3 280 and 1 654 cm^{-1}; δ_H 8.62br (1 H, N*H*), 7.83 (5 H, s, Ph), 7.8—7.5 (4 H, m, C_6H_4), and 2.87 and 2.85 (3 H, CH_3N).

Chlorination of Compound (2a) *with* $POCl_3$–DMF. *Isolation of the By-Product* 5-*Chloro*-4-(4-*Chlorosulphonylphenylazo*)-3-(N-*formyl*-N-*methylcarbamoyl*)-1-*phenylpyrazole* (12).—To a stirred mixture of compound (2a) (4.23 g, 0.01 mol), acetonitrile (20 ml), and *N*,*N*-dimethylformamide (7.2 mol) was added dropwise phosphoryl chloride (7.2 ml) below 50 °C during 10 min. T.l.c. of the reaction mixture [silica gel, ethyl acetate–benzene (1 : 2)]

showed the formation of three components: an unknown compound (R_F 0.87), (12) (R_F 0.81), and (2b) (R_F 0.56). The reaction mixture was stirred at 50—55 °C for 1 h, cooled to room temperature, and then poured onto ice–water. The resulting oily product gradually crystallized with time. The crystals were filtered off and extracted with hot ligroin (300 ml). The ligroin extract was separated from insoluble material by filtration and gave yellow crystals overnight. Filtration and washing of the crystals with ligroin afforded compound (12) (0.7 g), m.p. 132—135 °C (Found: C, 46.2; H, 2.6; N, 14.8. Calc. for $C_{18}H_{13}Cl_2N_5O_4S$: C, 46.37; H, 2.81; N, 15.02%), *m/e* 465 (M^+), 430 (M^+ — Cl), 408 (M^+ — MeNCO), 230 (M^+ — $C_6H_4SO_2Cl$), and 262 (M^+ — N=N–$C_6H_4SO_2Cl$); $\lambda_{max.}$ (Me_2CO) 346 nm (ε 27 100); $\nu_{max.}$ (KBr): 1 728, and 1 660 cm^{-1}; δ_H 9.07 (1 H, s, CHO), 7.9—7.5 (9 H, m, ArH), and 3.20 (3 H, s, CH_3N).

Reaction of Compound (12) *with Ammonia.*—A 28% aqueous solution of ammonia (0.3 ml) was added to a solution of compound (12) (0.10 g) in acetone (10 ml). The reaction mixture was stirred at room temperature for 1 h, poured onto ice–water, and extracted with ethyl acetate. The extracts were dried over anhydrous sodium sulphate, filtered, and concentrated. The residue was triturated with acetonitrile to give yellow crystals of 5-chloro-3-(*N*-methylcarbamoyl)-1-phenyl-4-(4-sulphamoylphenylazo)pyrazole (13), m.p. 247—249 °C (Found: *M*, 418.0631. Calc. for $C_{17}H_{15}ClN_6O_3S$: *M*, 418.0619), $\lambda_{max.}$ (Me_2CO) 341 nm (ε 23 500).

Compound (13) was also obtained by the reaction of compound (11) with ammonia and identified with the above-described sample.

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