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SYNTHESIS OF SOME FUSED PYRIDINE- AND OXAZOLE-POLYCYCLIC SYSTEMS FROM 10-(METHOXYIMINO)PHENANTHREN-9-ONE

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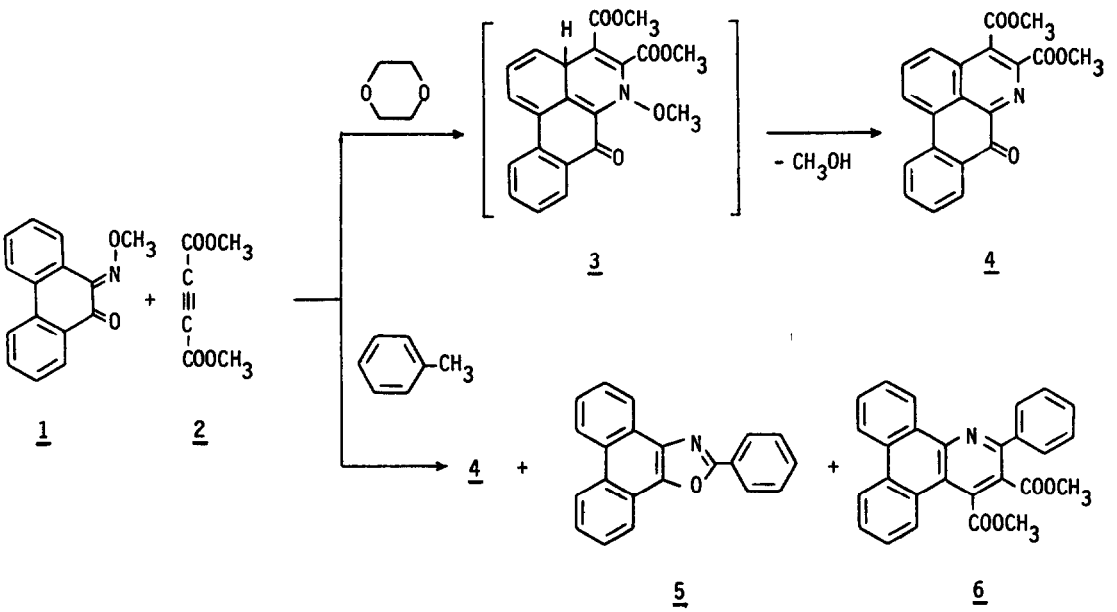
Abstract. 10-(Methoxyimino)phenanthren-9-one (1) reacts with DMAD (2) in dioxane to give dimethyl 7-oxo-7H-dibenzo[de,g]quinoline-4,5-dicarboxylate 4, whereas from the reaction of 1 with 2 in toluene besides 4, the oxazole 5 and also dimethyl 2-phenyldibenzo[f,h]-quinoline-3,4-dicarboxylate 6 are obtained. Reaction of 1 with methylsubstituted aromatic compounds furnishes oxazoles 5, 11(a-e) and 12. Oxazole 5 is also formed from the reaction of 1 with benzyl bromide. Treatment of tetrabromomonoxime 13 with phosphorus ylide 16 results to the formation of oxazole 14.

McKillop and Sayer[1] reported that monoximes of benzoquinones and 1,2-naphthoquinones, as well as their methyl ethers failed to react with dimethylacetylenedicarboxylate (DMAD), even after prolonged reaction times. However, when the bis copper (II) complexes of the above oximes were used the expected 1,4-benzoxazines were obtained, in high yields, through a [4+2] cycloaddition of DMAD to the heterodiene. The role of the copper ion is to polarize electron density toward the termini of the heterodiene system and also to create a "coordinative template" for reaction. Recently Elferink and Bos[2] reported that "cisoid" methyl ethers of some o-quinone monoximes react with N,N-diethyl-phenylethylamine to give through a [2+2] cycloaddition γ-methoxyimino-α,β-unsaturated carboxamides, which can be converted into fused quinoline carboxamides. In contrast to the monoximes, o-quinone monoimides react with electron-rich alkenes and with 1-(diethylamino)propyne to give through 1,4-cycloaddition reactions 1,4-benzoxazine derivatives[3]. o-Quninone monoimides also add across one of the double bonds of various conjugated dienes in an inverse electron demand Diels-Alder reaction[4] whereas with electron rich aromatic reagents they afford either o-hydroxy-N-substituted-derivatives[5,6] or benzoxazine cycloadducts[6]. By treatment with triphenylphosphine o-quinone monoimides are converted into benzoxazoles[7]. Photolysis of phenanthraquinone monoimine, in the presence of substituted toluenes, gives phenanthroxazoles[8] It is believed that intermediates arising from homolytic scission of the aryl C-H bond are involved in this remarkable transformation[9].

The work detailed here involves the interaction of 10-(methoxyimino)phenanthren-9-one 1 with DMAD in the presence or absence of toluene and also some reactions of 1 with methyl-substituted aromatic systems and benzyl bromide leading to the formation of phenanthroxazoles 11 as it is depicted in Schemes 1 and 3.

RESULTS AND DISCUSSION

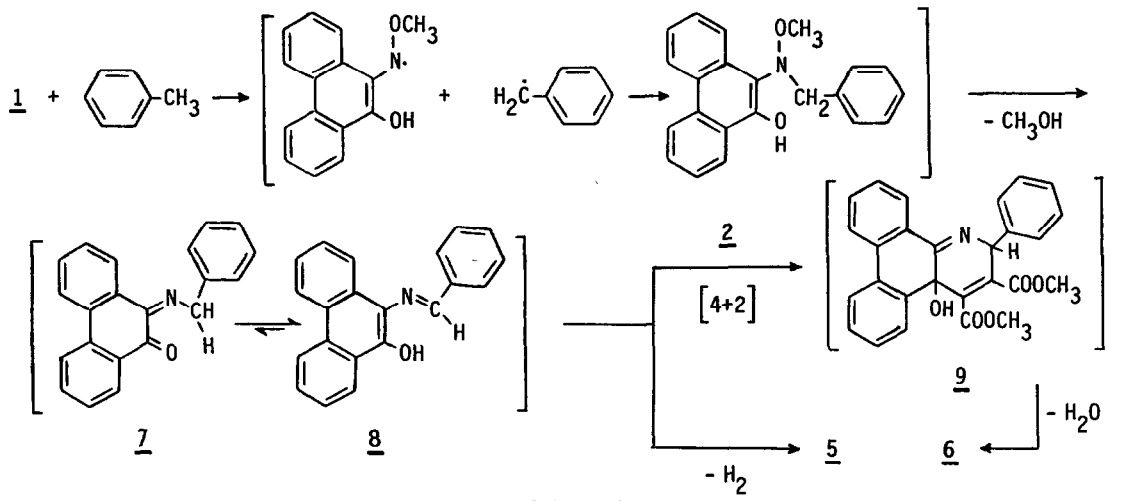
When oxime 1 and two equivalents of DMAD (2) were heated in toluene at reflux for 10 days and then the reaction mixture was allowed to stand at room temperature yellow crystals of dimethyl 7-oxo-7H-dibenzo[de,g]quinoline-4,5-dicarboxylate (4) were precipitated. By subsequent preparative t.l.c. of the filtrate besides 4 (total yield 27%) the known[8] 2-phenylphenanthro[9,10-d]oxazole (5) and also the dimethyl 2-phenyldibenzo[f,h]quinoline-3,4-dicarboxylate (6) were isolated in 27% and 17% yield respectively (Scheme 1). Compound 4 can be formed by direct condensation of oxime 1 with the dienophile 2, whereas for the formation of the unexpected products 5 and 6 also participation of the solvent toluene must be involved. This was proved by treatment of 1 with two equivalents of 2 in boiling dioxane for 5 days whereupon only the cycloadduct 4 was isolated in 25% yield, and also by refluxing a solution of 1 in toluene for 3 days. From the latter reaction only compound 5 was obtained in 37% yield. The proposed structures of 4 and 6 were confirmed by elemental



Scheme 1

analysis and spectral data. For the formation of compound 4 an unusual [4+2] cycloaddition of DMAD across the heterodiene system -C=C-C=N-OCH_3, extended from the exocyclic imino bond to the aromatic system, leading to the formation of the intermediate 3 can be proposed. By elimination of methanol and rearomatization of the system the isolated cycloadduct 4 can be formed (Scheme 1).

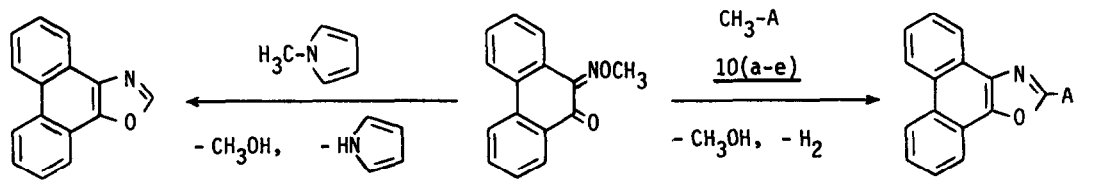
Formation of products 5 and 6 may be rationalized mechanistically as shown in Scheme 2.

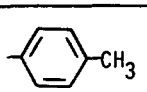
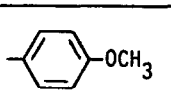
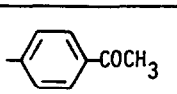
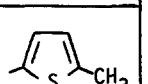


Scheme 2

It is believed that a homolytic methanol elimination between 1 and toluene leads originally to the formation of the intermediate o-quinone-imine derivative 7 which tautomerizes to the hydroxy-form 8. Dehydration of 8 gives the oxazole 5, while [4+2] cycloaddition of DMAD to the heterodiene system of 8 furnishes the intermediate 9 from which compound 6 can be formed by dehydration and rearomatization.

The unexpected formation of oxazole 5 prompted us to study the reactions of oxime 1 with several methylsubstituted aromatic systems. The reactions studied and the products obtained are depicted in Scheme 3.



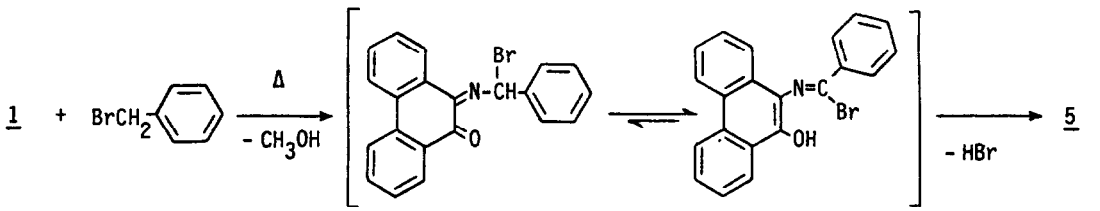
10,11	a	b	c	d	e
-A					

Scheme 3

All reactions were carried out by boiling solutions of 1 into the aromatic methyl system 10, used also as solvent. The yields of the oxazoles 11 were satisfactory (23-58%) with exception of 11d, which under the conditions studied was obtained in 9% yield. No effords to optimize yields were made. It should also be noticed that from the reactions with the dimethyl-aromatics, 10a and 10e, only mono-derivatives namely the oxazoles 11a and 11e were obtained. The mono-derivative 11a was again isolated even when the reaction with p-xylene (10a) was carried out with two equivalents of 1 in boiling dioxane for 4 days. In addition, no reaction was observed by refluxing equimolar amounts of the oxazole 11a and the oxime 1 in dioxane.

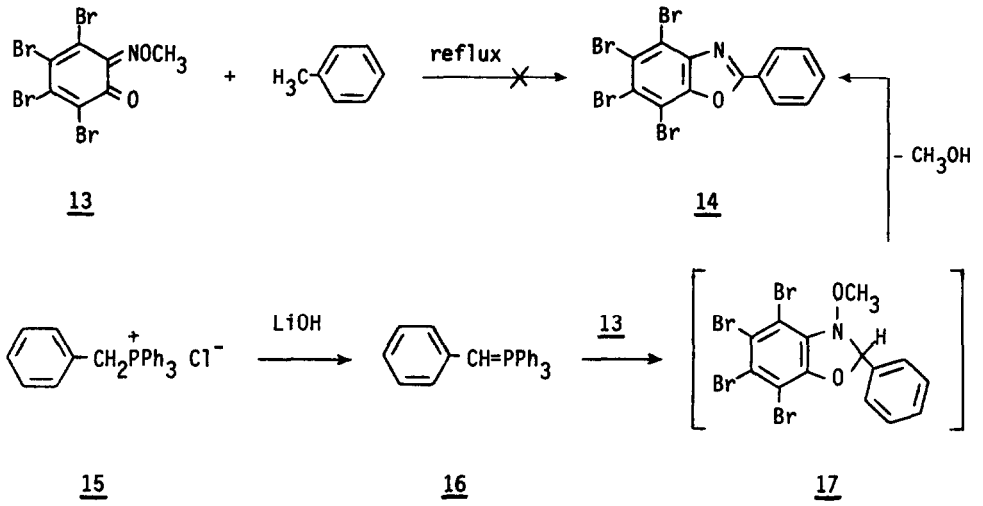
The formation of the unsubstituted oxazole 12 (Scheme 3) from the reaction between 1 and N-methylpyrrole can be considered of a particular interest because in this case elimination of pyrrole, instead of hydrogen takes place. This result could be used as evidence, for a polar mechanism, at least in this case, for the final step of the oxazole formation, due to the stronger aromatic character of the eliminated pyrrole-anion.

Preparation of oxazoles can also be achieved by the reaction of oxime 1 with bromomethylsubstituted aromatics. So, in a preliminary experiment the oxazole 5 was prepared in 37% yield by refluxing a solution of 1 in benzyl bromide for 3 h (Scheme 4).



Scheme 4

In contrast to oxime 1 the tetrabromo-oxime 13 doesn't react with methyl-substituted aromatics. When a solution of 13 was refluxed in toluene for 24 h only a gradual transformation to the corresponding quinone was observed, as indicated by t.l.c. However, the expected oxazole 14 was prepared by treatment of 13 with phosphorus ylide 16, prepared in situ from the phosphonium ylide 15, under phase transfer catalysis conditions. The mechanism proposed in Scheme 5 can account for the formation of oxazole 14. It is believed that the intermediate 17 is originally formed from which by further elimination of methanol the oxazole 14 is obtained. This reaction is analogous with the reactions of tetrahalo-o-benzoquinones with phosphorus ylides,[10,11] from which benzodioxoles were isolated.



Scheme 5

Although benzoxazoles and other condensed oxazoles are prepared by several other methods, mainly from N-substituted o-amino-phenol derivatives[12,13] and also recently by ring contraction of 1,2,4-benzoxadiazines[14], the method reported in this paper is believed to be of considerable interest for its simplicity and for the use of convenient starting materials.

EXPERIMENTAL

M.p.s. are uncorrected and were determined on a Kofler hot-stage apparatus. IR spectra were obtained with a Perkin-Elmer 297 spectrophotometer as films or Nujol mulls. ^1H NMR spectra were recorded with deuteriochloroform as a solvent on a Varian A60-A (60 MHz) spectrometer or on a Bruker Model AW 80 (80 MHz) spectrometer with tetramethylsilane as the internal standard. Mass spectra were determined on a Hitachi Perkin-Elmer RMU-6L mass spectrometer. The ionisation energy was maintained at 70 eV. Light petroleum refers to the fraction of 40-60 °C.

Reaction of 10-(Methoxyimino)phenanthren-9-one (1) with DMAD. Preparation of compounds (4), (5) and (6). A solution of 1 (0.237 g, 1 mmol) and DMAD (0.284 g, 2 mmol) in toluene (35 ml) was refluxed for 10 days and then set aside overnight during which time yellow crystals separated. This crystalline solid was filtered off and was further purified by recrystallization from dichloromethane to give dimethyl 7-oxo-7H-dibenzo[de,g]quinoline-4,5-dicarboxylate (4) (0.071 g, 20%), m.p. 268-272 °C; ν_{max} 1732, 1712, 1665 cm^{-1};

^{1}H NMR (60 MHz) δ 4.10 (s, 3H), 4.15 (s, 3H), 7.58-8.68 (m, 7H). Mass spectrum:m/z 347 (M^+, 29%), 316 (17), 231 (100), 173.5 (M/2, 1). (Found: C, 68.88; H, 3.88; N, 3.83. $C_{20}H_{13}NO_5$ requires: C, 69.16; H, 3.77; N, 4.03). The toluene mother liquors were concentrated under reduced pressure. Preparative t.l.c. of the residue on silica gel (light petroleum-ethyl acetate 7:1) gave 2-phenylphenanthro[9,10-d]oxazole (5) (0.071 g, 27%), m.p. 204-205 °C (from dichloromethane-light petroleum)(lit.[8] m.p. 205-206 °C); dimethyl 2-phenyldibenzo[f,h]quinoline-3,4-dicarboxylate (6) (0.072 g, 17%), m.p. 243-245 °C (from dichloromethane-light petroleum); ν_{max} 1740, 1705 cm^{-1}; ^{1}H NMR (60 MHz) δ 3.56 (s, 3H), 4.06 (s, 3H), 6.23-6.55 (m, 2H), 6.55-6.92 (m, 3H), 7.53-7.90 (m, 4H) and 7.90-9.02 (m, 4H). Mass spectrum: m/z 421 (M^+, 100%), 390 (16), 359 (37), 332 (29), 305 (26), 302 (34), 165.5 (M/2, 7). (Found: C, 77.13; H, 4.69; N, 3.23. $C_{27}H_{19}NO_4$ requires: C, 76.95; H, 4.54; N, 3.32) and 4 (0.024 g, 7%; total yield of 4 27%).

When the above reaction was repeated by refluxing a solution of 1 (0.237 g, 1 mmol) and DMAD (0.284 g, 2 mmol) in dioxane (35 mL) for 5 days only compound 4 was separated by preparative t.l.c. on silica gel (light petroleum-ethyl acetate 7:1) (0.087, 25%).

Reaction of 10-(Methoxyimino)phenanthren-9-one (1) with Toluene. Preparation of 2-Phenylphenanthro[9,10-d] oxazole (5). A solution of 1 (0.1 g, 0.42 mmol) in toluene (2 mL) was refluxed for 3 days. The solvent was evaporated and the residue was separated by preparative t.l.c. on silica gel (light petroleum- ethyl acetate 7:1) to give compound 5 (0.045 g, 37%), m.p. 204-205 °C (from dichloromethane-light petroleum) (lit.[8] m.p. 205-206 °C).

Reaction of compound 1 with p-Xylene. Preparation of 2-(p-Tolyl)-phenanthro[9,10-d]-oxazole (11a). A solution of 1 (0.1 g, 0.42 mmol) in p-xylene (2 mL) was refluxed for 2 days. The solvent was evaporated under reduced pressure and by addition of dichloromethane-light petroleum to the residue the product 11a was precipitated (0.055 g, 42%), m.p. 244-246 °C (from dichloromethane-light petroleum) (lit.[8] m.p. 246-248 °C).

Reaction of compound 1 with p-Methoxytoluene. Preparation of 2-(4-Methoxyphenyl)-phenanthro[9,10-d]oxazole (11b). A solution of 1 (0.2 g, 0.84 mmol) in p-methoxytoluene (2 mL) was refluxed for 1.5 h. By cooling the reaction mixture at room temperature the product 11b was precipitated (0.160 g, 58%), m.p. 220-222 °C (from dichloromethane-light petroleum) (lit.[8] m.p. 222-223 °C).

Reaction of compound 1 with p-Acetyltoluene. Preparation of 2-(4-Acetylphenyl)-phenanthro-[9,10-d]oxazole (11c). A solution of 1 (0.3 g, 1.3 mmol) in p-acetyltoluene (2 mL) was refluxed for 30 min. By addition of ether a solid precipitated which was purified by preparative t.l.c. on silica gel (light petroleum-ethyl acetate 5:1) to give 11c (0.125 g, 29%), m.p. 245-248 °C; ν_{max} 1675, 1600 cm^{-1}; Mass spectrum: m/z 337 (M^+, 100%), 322 (14), 294 (30). (Found: C, 81.80; H, 4.70; N, 3.95. $C_{23}H_{15}NO_2$ requires C, 81.88; H, 4.48; N, 4.15).

Reaction of 1 with 3-Methylthiophene. Preparation of 2-(3-Thienyl)-phenanthro[9,10-d]-oxazole (11d). A solution of 1 (0.3 g, 1.3 mmol) in 3-methylthiophene (1 mL) was refluxed for 6 h. The solvent was evaporated under reduced pressure and the residue was chromatographed on silica gel. Elution of the column with light petroleum-ethyl acetate 50:1 gave compound 11d (0.035 g, 9%), m.p. 258-260 °C (dichloromethane-light petroleum); ν_{max} 1595 cm^{-1}; ^1H NMR (80 MHz) δ 7.38-8.12 (m, 6H), 8.20-8.48 (m, 2H) and 8.50-8.98 (m, 3H). Mass spectrum: m/z 301 (M^+, 100), 272 (3), 206 (3), 164 (22), 150.5 (M/2, 5), 83 (9). (Found: C, 75.60; H, 3.86; N, 4.81. $C_{19}H_{11}NOS$ requires: C, 75.72; H, 3.68; N, 4.65).

Reaction of 1 with 2,5-Dimethylthiophene. Preparation of 2-(5-Methyl-2-thienyl)phenanthro [9,10-d]oxazole (11e). A solution of 1 (0.3 g, 1.3 mmol) in 2,5-dimethylthiophene (1 mL) was refluxed for 5 h. The solvent was evaporated under reduced pressure and the residue was separated by preparative t.l.c. on silica gel (light petroleum-ethyl acetate 20:1) to give 11e (0.090 g, 23%), m.p. 219-221 °C (from dichloromethane-light petroleum); ν_{max} 1590 cm^{-1}; ^1H NMR (80 MHz) δ 2.62 (s, 3H), 6.88 (br s, 1H), 7.45-7.90 (m, 5H), 8.18-8.44 (m, 1H) and 8.46-8.85 (m, 3H). Mass spectrum: m/z 315 (M^+, 100%), 300 (1), 286 (12), 272 (7), 233 (8), 219 (16), 164 (44), 157.5 (M/2, 25). (Found: C, 75.98; H, 3.98; N, 4.29. $C_{20}H_{13}NOS$ requires C, 76.16; H, 4.15; N, 4.44).

Reaction of 1 with N-Methylpyrrole. Preparation of Phenanthro[9,10-d]oxazole (12). A solution of 1 (0.2 g, 0.84 mmol) in N-methylpyrrole (2 mL) was refluxed for 1 h. The solvent was evaporated under reduced pressure and the residue was separated by preparative t.l.c. on silica gel (light petroleum-ethyl acetate 20:1) to give 12 (0.022 g, 12%) m.p. 143-145 °C (from dichloromethane-light petroleum) (lit.[16] m.p. 145 °C).

Reaction of 1 with Benzyl bromide. Preparation of 2-Phenylphenanthro[9,10-d]oxazole (5). A solution of 1 (0.119 g, 0.5 mmol) in benzyl bromide (2 mL) was refluxed for 2 h. The solvent was evaporated under reduced pressure and the residue was separated by preparative t.l.c. on silica gel (light petroleum-ethyl acetate 10:1) to give compound 5 (0.097 g, 37%), m.p. 204-205 °C (from dichloromethane-light petroleum) (lit.[8] m.p. 205-206 °C).

Preparation of 3,4,5,6-Tetrabromo-2-methoxyimino-1-benzoquinone (13). A solution of 3,4,5,6-tetrabromo-1,2-benzoquinone (8.5 g, 20 mmol) and methoxyamine hydrochloride (3.2 g, 38 mmol) was refluxed in methanol (100 mL) for 4 h. After evaporation of the solvent the residue was chromatographed on silica gel, using light petroleum-ethyl acetate (10:1) as eluant to give compound 13 (0.73 g, 9%), m.p. 123-125 °C (from dichloromethane-light petroleum); ν_{max} 1650 cm^{-1}; ^1H NMR (60 MHz) δ 4.47 (s, 3H). Mass spectrum: m/z 449/451/453/455/457 (M^+, 3%, 9, 12, 9, 3). (Found: C, 18.87; H, 0.78; N, 3.02. $C_7H_3Br_4NO_2$ requires C, 18.57; H, 0.67; N, 3.09).

Reaction of 13 with Benzyltriphenylphosphonium chloride (15). Preparation of 2-Phenyl-4,5,6,7-tetrabromobenzoxazole (14). To a solution of 13 (0.1 g, 0.22 mmol) in dichloromethane (5 ml) a water solution of 0.5 N LiOH (1.5 mL) and 15 (0.1 g, 0.26 mmol) was added and the reaction mixture was stirred vigorously for 6 h. The organic material was extracted with dichloromethane, washed with water, dried (Na_2SO_4), the solvent was evaporated and the residue was separated by preparative t.l.c. on silica gel (light petroleum-ethyl acetate 10:1) to give 14 (15 mg, 14%), m.p. 219-220 °C (from dichloromethane-light petroleum); ν_{max} 1605 cm^{-1}; ^1H NMR (80 MHz) 7.38-7.74 (m, 3H), 8.11-8.46 (m, 2H). Mass spectrum: m/z 507/509/511/513/515 (M^+, 0.4/1.4/2/1.4/0.4). (Found: C, 30.98; H, 2.76; N, 1.19. $C_{13}H_5Br_4NO$ requires C, 30.87; H, 2.74; N, 0.99.

REFERENCES

1. McKillop, A.; Sayer, T.S.B. J. Org. Chem. 1976, 41, 1079-1080.
2. Elferink, V.H.M.; Bos, H.J.T. J. Chem. Soc., Chem. Commun. 1985, 882-883.
3. Heine, H.W.; Barchiesi, B.J.; Williams, E.A. J. Org. Chem. 1984, 49, 2560-2565.
4. Heine, H.W.; Schairer, W.C.; Suriano, J.A.; Williams, E.A. Tetrahedron 1988, 3181-3186.
5. Heine, H.W.; Olsson, C.; Bergin, J.D.; Foresman, J.B.; Williams, E.A. J. Org. Chem. 1987, 52, 97-101.
6. Black, D.St.C.; Craig, D.C.; Heine, H.W.; Kumar, N.; Williams, E.A. Tetrahedron Lett. 1987, 28, 6691-6694.
7. Heine, H.W.; Empfield, J.R.; Golobish, T.D.; Williams, E.A.; Garbauskas, M.F. J. Org. Chem. 1986, 51, 829-833.
8. Pfundt, G.; Hardham, W.M. Tetrahedron Lett. 1965, 2411-2415.
9. Ranganathan, S.; Panda, C.S. Heterocycles 1977, 7, 529-545.
10. Bestmann, H.J.; Lang, H.J. Tetrahedron Lett. 1969, 2101-2106.
11. Nicolaides, D.N.; Litinas, K.E.; Argyropoulos, N.G. J. Chem. Soc. Perkin Trans I, 1986, 415-419.
12. Boyd, G.V. "Comprehensive Heterocyclic Chemistry" Vol. 6, Katritzky, A.R.; Rees, C.W. Eds, Pergamon Press, Oxford 1984, p. 216.
13. Abdelhamid, A.O.; Párkányi, C.; Rashid, S.M.K.; Lloyd, W.D. J. Heterocyclic Chem. 1983, 25, 403-405.
14. Gilchrist, T.L.; Harris, C.J.; King, F.D.; Peek, M.E.; Rees, C.W. J. Chem. Soc. Perkin Trans I 1988, 2169-2173.
15. Sahaino, S.Y. J. Chem. Soc. Jpn. 1976, 10, 1587.
16. Schönberg, A.; Awad W.I. J. Chem. Soc. 1947, 651-653.