Tetrahedron. Vol. 31, pp. 1123 to 1128. Pergamon Press 1975. Printed in Great Britain

PHOTOREACTIONS OF NITROSO COMPOUNDS IN SOLUTION—XXVIII

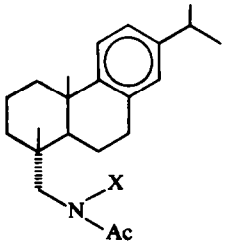
APPLICATIONS OF NON-OXIDATIVE AND OXIDATIVE PHOTOREACTIONS OF NITROSAMIDES[a]

J. N. S. TAM, T. MOJELSKY, K. HANAYA and Y. L. CHOW*
Department of Chemistry Simon Fraser University, Burnaby 2, British Columbia, Canada V5A 1S6

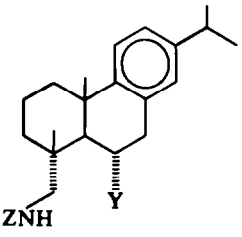
(*Received USA* 31 *May* 1974; *Received UK for publication* 18 *June* 1974)

Abstract—Two model nitrosamides were used to illustrate the application of oxidative and non-oxidative nitrosamide photorearrangements. N-nitroso-N-acetyldehydroabietylamine photolytically rearranges to give stable 6α-nitroso and 6α-nitrato derivatives respectively. Similar photorearrangement of N-nitroso-N-methyl-*o*-toluamide gave good yields of the corresponding oximino and nitrate esters; they, however underwent facile photolytic and thermal reactions to give various products.

Photolysis of a N-nitrosamide under an inert atmosphere[2-5] and in the presence of oxygen[2] has been demonstrated to specifically functionalize the δ-position (with respect to the amide N atom) as the C-nitroso and C-nitrato group respectively. Applications of these non-oxidative and oxidative photolyses are described in this report using N-nitroso-N-acetyldehydroabietylamine (1) and N-nitroso-N-methyl-*o*-toluamide (7) as the model compounds.



1: X = NO
2: X = H



3: Z = Ac, Y = NO
4: Z = Ac, Y = ONO_2
5: Z = C_2H_5, Y = NH_2
6: Z = C_2H_5, Y = OH

RESULTS

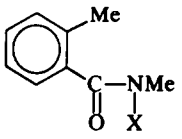
When a benzene solution of the nitroso derivative of N-acetyldehydrobietyamine (2) was irradiated under helium with a > 400 nm light source[2], the *anti*-dimer of 6α-nitroso-N-acetyldehydroabietylamine (3, 40%) deposited on the flask. The photolysate, after careful workup, contained the parent amide 2 and a small amount of N,N-diacetyldehydroabietylamine†. A similar photolysis in the presence ox oxygen in a Pyrex apparatus (the energy cut-off at 290 nm) gave 6α-nitrato-N-acetyldehydroabietylamine (4, 31%) in addition to 2 (45%) and the *anti*-dimer of 3 (6%). In the oxidative photolysis, the amount of the *anti*-dimer was much reduced when the oxygen supply was increased and was not formed when run under 100 mm/Hg pressure of oxygen. Due to its insolubility the dimer of 3 did not undergo further photolysis and was not readily isomerized to the corresponding oxime derivatives under acidic conditions.

The structures of the *anti*-dimer of 3 and nitrate ester 4 were determined by the analogous spectroscopic data with those of the known compounds.[2,3] The stereochemistry of the nitroso group in 3 was decided by the NMR decoupling experiments which demonstrated the axial orientation of H_6 with the coupling constants of 8, 8 and 2 Hz. Lithium aluminium hydride reduced the *anti*-dimer of 3 to the corresponding diamine 5 which gave the tribenzoyl derivative. By decoupling experiments, H_6 of nitrate 4 was shown to be axially oriented by the coupling constants of 8, 8 and 2 Hz with H_5, H_{7ax} and H_{7eq} respectively; the nitrate group therefore has the α-orientation. Nitrate 4 when reduced with LAH followed by benzoylation afforded the N,O-dibenzoyl derivative of 6 as shown by the ir absorptions at 1710, 1630 and 1220 cm^{-1}.

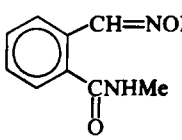
Irradiation of a benzene solution of nitrosamide 7 under nitrogen with a > 400 nm light source deposited a white solid of oxime 9 in 77% yield. The residue from the photolysate consisted of oxime 9 and other unknown products, and became a more complex mixture on attempted recrystallization and chromatography. When a similar photolysis was carried out through a Pyrex filter the amount of the byproducts increased drastically at the cost of the yield of oxime 9. After considerable difficulties, phthalic anhydride, phthalimide, N-methylphthalimide and a mixture of cyano derivatives in addition to 20 ~ 30% oxime 9 were obtained from the photolysate. The purification was frustrated by ubiquitous chemical transformations occurring during purification processes.

Oxidative photolysis of nitrosamide 7 in benzene gave the expected nitrate ester 10 (1640, 1290 and

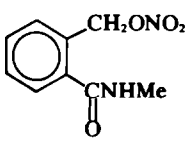
[a]For part XXVII see Ref. 1.
*To whom any enquiry should be directed.
†This diacetyl compound was isolated in every experiment and was believed to be formed during the nitrosation in a mixture of acetic anhydride-acetic acid.



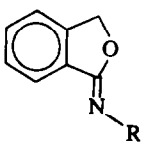
7: X = NO
8: X = Br



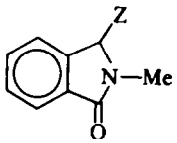
9



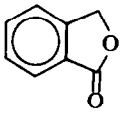
10



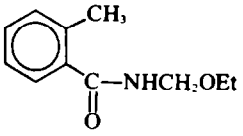
11: R = Me
12: R = CMe$_3$



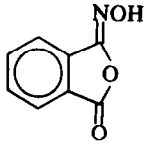
13: Z = OEt
14: Z = OH



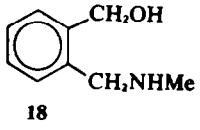
15



16



17



18

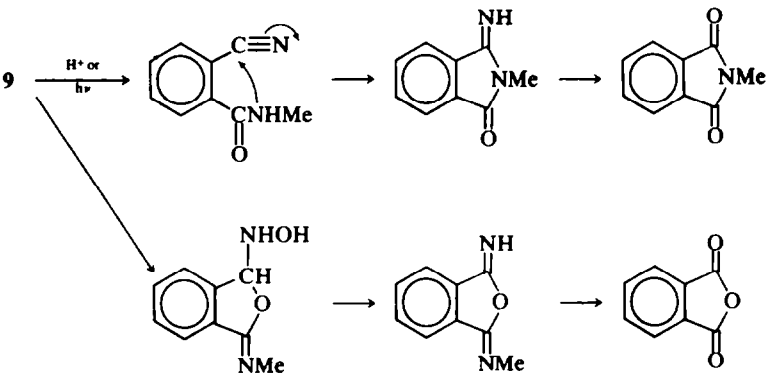
850 cm^{-1}) contaminated by small amounts of other products as shown by the IR spectrum of the crude product. However, nitrate ester **10** rearranged gradually to the crystalline nitrate salt of N-methyliminopthalide **11**. The nitrate salt could be recrystallized but was accompanied by decompositions. On chromatography of the residue on silicic acid, it gave N-methylphthalimide, phthalide (**15**), 3-ethoxy-N-methylphthalimidine (**13**), phthalimide, N-ethoxymethyl-*o*-toluamide (**16**), phthaloxime (**17**), 3-hydroxy-N-methylphthalimidine (**14**) in addition to two unknowns and the nitrate salt of **11**. The total isolated yield of the nitrate salt of **11** was 42%. The structures of the minor compounds **13**, **14**, and **16** were determined by their spectroscopic and analytical data.

Nitrate ester **10** was also prepared from the nitration of *o*-hydroxymethyl-N-methylbenzamide and was shown to rearrange gradually to the nitrate salt of **11**. Free iminophthalide **11**, obtained as an oil, and its nitrate salt both showed the indistinguishable mass spectral pattern with that of N-methyl-phthalimidine. Mild hydroylsis of **11** gave phthalide **15** and LAH reduction of the nitrate of **11** followed by benzoylation gave the N,O-dibenzoyl derivative of **18**; these observations ruled out the possibility that the compound is N-methylphthalimidine and supported the assignment of N-methyliminophthalide. In order to ascertain the structure unambiguously, the hydrobromide of **11** was also independently synthesized by the photolysis of N-bromo-N-methyl-*o*-toluamide (**8**) in a one step operation;[6,7] treatment of the photolysate with sodium carbonate gave **11** identical in all respects with that obtained from the nitrosamide photolysis. The photorearrangement of bromamides is a general method as shown previously.[6,7] Similar photolysis of N-bromo-N-tert-butyl-*o*-toluamide gave the corresponding hydrobromide of N-t-butyliminophthalide (**12**); the free base **12** was a stable compound.

DISCUSSION

The mechanisms of non-oxidative and oxidative photochemical decompositions of nitrosamides have been discussed previously.[2-5] Under an inert atmosphere, the photolysis yields the corresponding C-nitroso compound which is generally isolated as its *anti*-dimer as in **3** or as its oxime as in **9**. In the presence of oxygen, nitric oxide is quickly oxidized to $\cdot NO_3$ and the reaction leads to a clean formation of the corresponding nitrate esters (*eg.* **4** and **10**) as demonstrated before.[2] The wavelength dependency of nitrosamide photolysis has also been discussed in the previous report.[2,8] The non-oxidative and oxidative photolysis operate cleanly under ordinary conditions[2,3] in the case of nitrosamide **1**. However it has been noted that if the non-oxidative photolysis of **1** is carried out in a Pyrex apparatus, a complex mixture is obtained due to disproportionation reaction of nitric oxide[2]. In the oxidative photolysis of **1**, a higher oxygen concentration in solution is necessary to ensure a complete oxidation of nitric oxide since only under 100 mm/Hg of the oxygen pressure the formation of **2** can be completely eliminated.

Oxime **9** is shown to undergo extensive secondary reactions, both photolytic and thermal, leading to a complex mixture when the photolysis is carried out in a Pyrex apparatus or when the crude product is heated in solution. Apparently one of these side reactions is the dehydration of the oximino group to form a cyano group containing compounds which could not be obtained in pure forms. It is assumed that at various stages of intermediacy neighboring group participated reactions, mechanistically similar to the intramolecularly catalysed hydrolysis of phthalamic acid,[9] occur extensively leading to the observed final products. One formal pathway, among other possible, of representing the reaction is given below. As oxime **9** can be precipitated out of the reaction system, a good yield of **9** can be obtained under carefully controlled conditions.

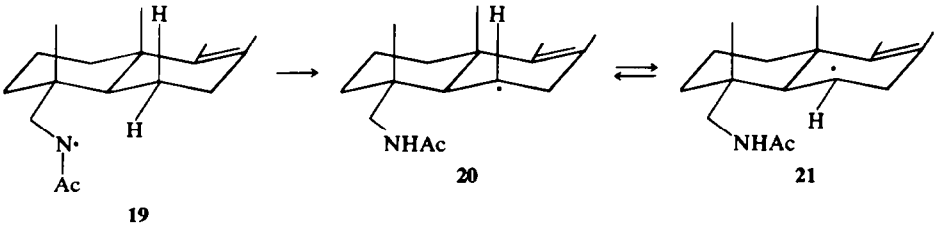


In the oxidative photorearrangment of **7**, nitrate ester **10** has been formed in an excellent yield but undergoes both intramolecular nucleophillic substitution to form the nitrate salt of **11** and the elimination of nitrous acid to form *o*-formyl-N-methylbenzamide. Both types of decomposition processes are known to occur with nitrate esters.[2,8] These two intermediates no doubt can account for the formation of **13**, **14** and **15**. However it is not clear at what stage and how oxidation occurs to form the minor amounts of phthalimide, phthalic acid and phthaloxime **17**. It is possible that oxidation of the benzyl position has occurred during photolysis but the extent must be minimal judging from the ir spectrum of the crude product. Since both nitric and nitrous acids are known oxidizing agents, the oxidation may have taken place during isolation.

The independent synthesis of **11** through the photolysis N-bromamide **8** has proven the structure **11**; this compound and its salts exhibit the unusually deshielded methylene chemical shifts and the C=N bond stretching at the markedly high wave numbers (Experimental). While the salt of **11** is reasonably stable under recrystallization conditions, free base **11** is rapidly hydrolysed to phthalide in solution.

It is believed that the 6α-hydrogen is abstracted during the rearrangement of the amido radical **19** generated from **1**. The specific functionalization at the 6α-position observed in **3** may be ascribed to the fast nitric oxide capture process that occurs before **20** undergoes the radical inversion to form **21** in analogy to our previous proposal.[2] Alternatively, since the nitric oxide approach from the α-side is obviously favoured due to the severe steric hindrance of 10β-Me group, the stereospecificity observed in **3** can be ascribed purely to the steric reason. The stereospecific formation of 6α-nitrate in **4** is no doubt due to the latter reason since a recombination process of a C-radical with $\cdot NO_3$ has been shown to be slower than a cyclohexyl radical inversion process.[2]

We have shown two extreme cases of the application of nitrosamide photolysis under non-oxidative and oxidative conditions; one in which the primary products are very stable and the other very sensitive to photolytic and thermal decompositions. The majority of the primary products obtained in other studies[10] have intermediate reactivities and can be isolated in fairly good yields with some modification of the reaction conditions.



19 20 21

EXPERIMENTAL

General. All NMR spectra were measured with a Varian A-56/60 spectrometer and the decoupling experiments were run by Dr. T. S. Sorensen,* University of Calgary, Alberta using HA-100 spectrometer. Chemical shifts were expressed on the τ scale. IR spectra were recorded with a Perkin-Elmer Model 457 spectrophotometer and UV spectra with a Unicam Model SP 800 Spectrophotometer. Mass spectra were taken with a Hitachi-Perkin-Elmer RMU-6D instrument at 80 eV with a heated inlet. Melting points were determined on a Fisher-Johns hot-stage and were uncorrected. The microanalyses were performed by Dr. A. Bernhardt, Elbach uber Engelskirchen, West Germany.

Photolysis. For the photolysis apparatus, filter solns and conditions see our previous publication.[2] Nitrosamides **1** and **7** were prepared according to the procedure described by White.[11] Compound **1** exhibited the following physical constants; IR 1735 and 1520 cm^{-1}; UV (benzene) λ_{max} 427 nm (e, 77), 408 (76) and 392 (50); NMR τ 7·33 (s, 3H) and 6·32 (2H). N-nitroso-N-methyltoluamide has IR 1725 and 1505 cm^{-1}; UV benzene) λ_{max} 429 nm (e, 133); 410 (123) and 394 (72); NMR τ 6·84 (s, 2H).

Photolysis of N-*nitroso*-N-*acetyldehydroabietylamine* (**1**)

A soln of **1** (6·2 g, 17·4 mmoles) in benzene (50 ml) was photolyzed under helium for 1 1/2 h. A white solid of the

*We are grateful to Professor Sorensen for the decoupling experiments.

anti dimer of 6α-nitroso-N-acetyldehydroabietylamine (2·48 g, 40%) was precipitated and was recrystallized from isopropanol; mp 159–160°; IR (nujol) 3340, 1650, 1560, 1295 and 1220 cm^{-1}; NMR (CF_3CO_2H) τ 8·80 (s, C-CH_3), 8·63 (s, C-CH_3), 8·65 (d, J = 6 Hz, 6H, CH-CH_3), 7·62 (s, $COCH_3$), 4·39 (t, J = 8, 8 and 2 Hz, H_6), 6·7 (H_{6eq}), 7·6 (H_{6ax}), 7·56 (d, J = 8 Hz, H_5) and 6·54 and 7·38 (H_{13}, AB quartet, J = 17 Hz); ms *m/e* (%) 356 (48, monomer), 340 (40), 325 (29), 308 (22), 295 (31), 284 (69), 264 (53), 200 (100) and 43 (100). The decoupling experiment at 100 Mc is described in the thesis.[10]

The filtrate was evaporated to give an oil (1·87 g) which was chromatographed on a silicic acid column to give two components. The first component was recrystallized from isopropanol to give N,N-diacetyl-dehydroabietylamine (485 mg, 8%); mp 95·5–96·5°; IR (nujol) 1705, 1695 cm^{-1}; NMR τ 9·19 (2, C-CH_3), 8·80 (s, C-CH_3), 8·80 (d, J = 7 Hz, 6H, CH-CH_3), 7·69 (s, 6H, $COCH_3$) and 6·30 (s, CH_2N); ms *m/e* (%) 369 (M^+, 11), 354 (5), 326 (1), 256 (20), 254 (10), 186 (23), 173 (100), 155 (23). (Found: C, 78·00, H, 9·55; N, 3·79. Calcd. for $C_{23}H_{35}NO_2$: C, 78·22, H, 9·38; N, 3·95).

The second component was eluted with a mixture of chloroform–methanol (98:2) to give parent amide **2** (2·98 g, 52%).

Lithium aluminium hydride reduction of the dimer of **3** *and benzoylation of the product*

A soln of the dimer **3** (302 mg) and LAH (1·0 g) in anhyd ether (50 ml) was refluxed at 40° for 12 h. Excess LAH and the complex were decomposed by 15% NaOH aq (6 ml) and water (1·5 ml). The ether soln was dried ($MgSO_4$) and the solvent was removed to give an oil (198 mg).

This crude oil was dissolved in a mixture of benzene (15 ml) and pyridine (10 ml). Benzoyl chloride (1·5 g) was added and the mixture was refluxed for 2 h. The soln was poured into cold water (100 ml) and the organic layer was separated. The aqueous layer was extracted with benzene (25 ml × 2). The combined organic later was washed with water (20 ml × 2), Na_2CO_3 aq (10 ml) and again with water (20 ml × 2) and finally dried with $MgSO_4$. The residue obtained after evaporating off the solvent was taken up in light petroleum and chromatographed on a basic alumina column to give an oil (286 mg). This oil was rechromatographed on a a silicic acid column to afford the oily tribenzoyl derivative of **5** (259 mg); IR ($CHCl_3$) 1710 and 1630 cm^{-1}; NMR (HA-100) τ 9·2 (t, Ch_2CH_3), 8·8 (s, C-CH_3), 8·4 (s, C-CH_3), 8·8 (d, J = 7 Hz, CH-CH_3) and 5·1 (broad s, CH-N).

Photolysis of **1** *under oxygen*

A soln of **1** (4·19 g, 11·8 mmoles) in benzene (100 ml) was irradiated for 2 h under oxygen pressure (70 mm above atmospheric). A white solid was separated and was filtered off. It was recrystallized from isopropanol to give the dimer of **3** (260 mg, 6%). The filtrate was evaporated to give an oil (5·62 g). This oil was chromatographed on a silicic acid column to afford (i) dehydroabietyl acetate (244 mg, 6%), (ii) N,N-diacetyldehydroabietylamine (441 mg, 10%), (iii) 6α-nitrato-N-acetyldehydroabietylamine **4** (1·40 g, 31%) and (iv) the parent amide **2** (1·75 g, 45%).

The nitrate ester **4** showed the following physical constant: IR (film) 3320, 1660, 1560, 1300, 1630, 1280 and 875 cm^{-1}; NMR ($CDCl_3/D_2O$) τ 8·87 (s, C-CH_3), 8·78 (s, C-CH_3), 8·79 (d, 6H, CH-CH_3), 4·39 (d of d, H_5), 6·60 (d of t, H_{7ax}), 7·12 (d of d, H_{7eq}), 8·50 (d, H_5) and 6·50 and 7·46 (AB quartet, H_{13}). The decoupling experiments[10] showed that the coupling constants were J_{56}=8, J_{77}=19, J_{67ax} = 8, J_{67eq} = 2 and J_{1313}=14 Hz.

Lithium aluminium hydride reduction of **4** *and the benzoylation of the product*

A soln of **4** (770 mg) in anhyd ether (30 ml) was reduced by LAH (1·50 g) in 50 ml anhyd ether. The mixture was refluxed for 5 h. The excess LAH was decomposed by 15% NaOH aq (10 ml) and the complex by water (2 ml). The ether soln was separated, washed with water (5 ml × 2) and dried ($MgSO_4$). The solvent was expelled to leave a light yellow oil (443 mg). This oil was dissolved in a mixture of benzene (30 ml) and pyridine (10 ml). Benzoyl chloride (1·5 g) was added and the soln was refluxed for 2 h. Water (100 ml) was added and benzene layer was separated. The aqueous layer was extracted with benzene (30 ml × 2). The combined benzene soln was dried ($MgSO_4$) and evaporated to yield a light yellow oil (839 mg) which was chromatographed on a basic alumina column. With pure benzene, an oily N,O-dibenzoyl derivative of **6** (219 mg) was eluted; IR ($CHCl_3$) 1710, 1630, 1280 and 1220 cm^{-1}; NMR τ 4·15 (m, CH-O-COPh); ms *m/e* 432, 415, 400, 255, 177, 162, 105. Further purification of this benzamide by vacuum distillation (*ca* 200°) led to its decomposition and benzoic acid sublimed over.

Photolysis of N-*nitroso*-N-*methyl*-O-*toluamide* (**7**) *in benzene in the presence of oxygen*

A soln of **7** (3·83 g, 21·5 mmoles) in benzene (220 ml) was photolyzed with a 200 W Hanovia lamp for 1 1/2 h under O_2. Yellow solid was deposited at the bottom of the photolysis vessel. After the removal of the solvent, a thick oil (4·54 g) was left. The crude product showed characteristic absorption peaks of a nitrato compound at 1640, 1290 and 870 cm^{-1} in its IR spectrum. On standing overnight, the crude product solidified partially and the characteristic nirato absorption peaks disappeared. The crude product was recrystallized from chloroform (100 ml) to afford pale yellow crystals of the nitrate of **11** (1·28 g, 28·4%) which was further recrystallized from light petroleum and chloroform mixture to give white needles; mp 159–160°; IR (nujol) 2500–3300, 2900, 1695, 1410, 1385, 1340, 1315, 980 and 740 cm^{-1}; NMR ($CDCl_3$) τ 1·58 (broad multiplet, 1H D_2O exchangeable), 2·25 (broad multiplet, 4H), 4·10 (s, 2H) and 6·58 (s, 3H); ms *m/e* (%) 148 (10), 147 (100), 146 (71), 118 (51), 91 (29), and 77 (14). (Found: C, 51·60; H, 4·87; N, 13·13. Calcd. for $C_9H_{10}N_2O_4$: C, 51·43; H, 4·80; N, 13·33).

The mother liquor was evaporated to give an oil (2·93 g) which was chromatographed on a silicic acid column. With pure chloroform, the following fractions were obtained in order:

(i) An unidentified solid (54 mg) which was recrystallized from light petroleum benzene mixture to give pale yellow solid; mp 135–139°; IR (nujol) 1750, 1240 and 1010 cm^{-1}; NMR τ 7·38 (s, 3H), 2·75 (m, 4H) and 2·22 (m, 4H); ms *m/e* (%) 281 (1), 120 (10), 119 (100), 105 (12), 91 (29) and 65 (7). (Found: C, 68·08; H, 3·96; N, 5·00. Calcd. for $C_{16}H_{11}NO_4$: C, 68·33; H, 3·94; N, 4·98).

(ii) N-Methylphthalimide (282 mg, 8%) which was recrystallized from aqueous EtOH to give yellow needles; mp 130–132° (lit.[12] 133–134°); IR (nujol) 1710 and 1020 cm^{-1}; NMR τ 2·30 (m, 4H) and 6·87 (s, 3H); ms *m/e* (%) 162(10), 161 (M^+, 100), 160 (13), 133 (12), 132 (15), 177 (13), 105 (13), 104 (40), 77 (10), 76 (38), 66 (20), 52 (10) and 50 (18).

(iii) Phthalide (**15**, 46 mg, 2%); mp 73–74° (lit.[13] 75°), which was recrystallized from light petroleum to give pale yellow needles. This compound was identified by its superimposable IR and NMR spectra with those of an authentic sample.

(iv) 3-Ethoxy-N-methylphthalimidine (**13**, 368 mg, 9%) which was distilled twice at 50° (0·02 mm) to give a colorless oil; IR (film) 1700, 1440, 1400, 1110, 1080 and 1040 cm^{-1}; NMR τ 2·31 (m, 2H), 2·40 (m, 2H), 4·30 (s, 1H), 6·9 (q, J = 6·5 Hz, 2H), 6·93 (s, 3H) and 8·87 (t, J = 6·5 Hz, 3H); ms *m/e* (%) 191 (M^+, 4), 162 (5), 147 (15), 146 (100), 105 (5), 91 (13) and 77 (8).

(v) Phthalimide (88 mg, 3%) which was recrystallized from chloroform–light petroleum mixture to give pale yellow crystals; mp 230–232° (lit.[13] 233°). This solid had its

IR and NMR spectroscopic data identical with those of an authentic sample.

(vi) N-Methyl-*o*-toluamide (318 mg, 10%) which was recrystallized from cyclohexane to give white needles; mp 74–75° (lit.[13] 75°). It was identified by its superimposable IR and NMR spectra with those of an authentic sample.

(vii) N-Ethoxymethyl-*o*-toluamide (**16**, 159 mg, 4%); IR (film) 3250, 1640, 1550, 1410, 1320 and 1160 cm^{-1}; NMR τ 2·75 (m, 4H), 3·72 (broad 2, 1H, D_2O exchangeable), 5·12 (d, J = 6·5 Hz, 2H, collapsed to a singlet on D_2O exchange), 6·36 (q, J = 6·6 Hz, 2H), 7·51 (s, 3H) and 8·77 (t, J = 6·5 Hz, 3H).

With 1% MeOH in chloroform, two fractions were eluted in the following order:

(i) phthaloxime (**17**, 64 mg) which was recrystallized from chloroform–light petroleum mixture to afford yellow crystals; mp 219–220° (d) (lit.[14] 220–226°, d); IR (nujol) 3150, 1780, 1720, 1700, 1190, 1140, 980 and 890 cm^{-1}; NMR (acetone-d_6) τ 2·08 (s, 1H, D_2O exchangeable) and 2·22 (s, 4H); ms *m/e* (%) 164 (13), 163 (M^+, 100), 147 (18), 133 (19), 132 (6), 105 (27), 104 (41), 77 (17), 76 (29), 66 (11), 52 (10) and 50 (8), (Found: C, 58·57; H, 3·14; N, 8·58. Calcd. for $C_8H_5NO_3$: C, 58·90; H, 3·09; N, 8·59).

(ii) 3-Hydroxy-N-methylphthalimidine (**14**, 297 mg, 9%) which was recrystallized from chloroform–light petroleum mixture to afford yellow crystals; mp 118–120°; IR (nujol) 3250, 1670 and 1060 cm^{-1}; NMR τ 2·58 (m, 4H), 4·53 (broad s, became sharp singlet on adding D_2O, 1H), 4·75 (broad s, D_2O exchangable, 1H) and 7·17 (s, 3H); ms *m/e* (%) 163 (M^+, 100), 162 (100), 146 (59), 135 (37), 133 (29), 119 (43), 118 (33), 105 (43), 91 (55) and 77 (29). (Found: C, 66·39; H, 5·56; N, 8·41. Calcd. for $C_9H_9NO_2$: C, 66·25; H, 5·56; H, 8·58).

With 5% MeOH in chloroform, an unknown solid was eluted. It was recrystallized from chloroform–light petroleum mixture to give yellow solid (112 mg); mp 131–133°; IR (nujol) 3000–26000 (broad), 1700, 1270 and 1060 cm^{-1}; NMR τ 1·65 (broad s, 1H), 2·45 (m, 4H), 4·37 (s, 2H) and 6·65 (s, 3H); ms *m/e* (%) 206 (< 1), 166 (6), 148 (20), 147 (100), 146 (70), 122 (26), 118 (53), 105 (30), 91 (30) and 77 (26).

With 10% MeOH in chloroform, the nitrate salt of **11** (544 mg, 13·8% total 42%) was obtained. This salt (80 mg) was dissolved in a mixture of a saturated soln of Na_2CO_3 (5 ml) and water (10 ml). After standing overnight, the soln was extracted under basic condition with dichloromethane (2 × 10 ml). The dichloromethane layer was washed with water and dried ($MgSO_4$). The solvent was evaporated to give a colorless oil of **11** (73·5 mg); IR (film) 3360, 1700, 1400, 1295, 1060 and 1000 cm^{-1}; NMR τ 2·50 (m, 4H), 4·75 (s, 2), 6·85 (s, 3H); ms the identical pattern as that of the salt of **11**.

Lithium aluminium hydride reduction of **11** *and benzoylation of the product*

A mixture of the salt of **11** (501 mg, 2·82 mmoles) and LAH (1·0 g, 29·4 mmoles) in ether (50 ml) was stirred under reflux overnight. 15% NaOH (8 ml) and water (2 ml) were added. The aluminium hydroxide was filtered off, washed with ether (2 × 25 ml) and the combined ethereal layer was dried ($MgSO_4$) and evaporated to give a colorless oil; IR (film) 3300, 1690, 1480, 1460, 1210, 1030, and 750 cm^{-1}; NMR τ 2·80 (m, 3H), 5·42 (s, 2H), 5·91 (s, 2H, D_2O exchangeable), 6·22 (s, 2H) and 7·61 (s, 3H). The product (214 mg) was benzoylated in pyridine (5 ml) and anhyd benzene (10 ml). The crude benzoylated product (554 mg) was purified by passing through a basic alumina column to afford thick colorless liquid of **18** (508 mg, 67%); IR (film) 1720, 1640 and 1275 cm^{-1}; NMR τ 7·22 (s, 3H), 5·20 (s, 2H), 4·67 (s, 2H) and 2·5 (m, 14H); ms *m/e* (%) 205 (5), 177 (2), 176 (2), 147 (100), 146 (47), 132 (52), 119 (44), 118 (45), 105 (9), 104 (14), 91 (47), 77 (11), 44 (28) and 32 (28). An attempt to purify this benzoylated product by recrystallization was unsuccessful. Distillation under reduced pressure (144°/0·02 mm) led to decomposition.

Photolysis of **7** *under nitrogen*

A soln of **7** (1·90 g, 10·6 mmoles) in benzene (210 ml) was photolyzed with light > 400 nm for 1 1/2 h under N_2. White solid of **9** (1·46 g, 77%) was deposited and was recrystallized from chloroform–light petroleum mixture to yield white needles; mp 134–137°; IR (nujol) 3350, 1635, 1560 and 990 cm^{-1}; NMR τ 7·43 (d, 3, J = 4·5 Hz, collapsed to a singlet on D_2O exchange), 1·90 (broad s, D_2O exchangeable), 1·5 (complex multiplet), 0·83 (s, 1H) and − 1·07 (s, 1H, D_2O exchangeable); ms *m/e* 178 (M^+), 161, 160, 148, 130 and 118. (Found: C, 60·84; H, 5·66; N, 15·77. Calcd. for $C_9H_{10}N_2O_2$: C, 60·67; H, 5·66; N, 15·72).

The residue was recrystallized from chloroform–light petroleum mixture to afford white needles having an IR spectrum super imposable with that of **9**. The solvent in the filtrate was evaporated to give an oil (512 mg). Silicic acid column chromatography of this oil gave an unidentified solid (349 mg); mp 179–182°, IR (nujol) 2230, 1690, 1310, 1295, 1085 and 765 cm^{-1}.

Synthesis of N-methylphthalimidine

A soln of phthalide (2·00 g, 13·4 mmoles) in EtOH (30 ml) saturated with methylamine was heated in a bomb at 230° for 5 h. During the reaction, the pressure inside the bomb rose to 1000 psi. When the EtOH was completely removed, a brown oil (2·02 g) was left. This oil was chromatographed on a silicic acid column. With chloroform as eluant three fractions were obtained in the following order:

(i) N-Methylphthalimidine (1·40 g, 64%) which was recrystallized from light petroleum to give white crystals; mp 115–116·5° (lit.[15] 120°); IR (nujol) 1680, 1490, 1305, 1280, 1210 and 1060 cm^{-1}; NMR τ 2·5 (m, 4H) 5·73 (s, 2H) and 6·88 (s, 3H).

(ii) Unreacted phthalide (44 mg, 2%).

(iii) O-hydroxymethyl-N-methylbenzamide (769 mg, 31%) which was recrystallized from benzene to give white crystalline solids; mp 91–93° (lit. 122–123°)[15]; IR (nujol) 3300, 1640, 1560 and 1040 cm^{-1}; NMR τ 2·70 (m, 5H, one of which was D_2O exchangeable), 5·08 (s, 1H, D_2O exchangeable), 5·56 (s, 2H), 7·18 (d, 3H, J = 5 Hz, collapsed to a singlet when D_2O was added). (Found: C, 65·81; H, 6·77; N, 8·36. Calcd. for $C_9H_{11}NO_2$: C, 65·44; H, 6·71; N, 8·48).

Synthesis of α-nitrato-N-methyl -o-toluamide (**10**)

α-Nitrato-N-methyl-*o*-toluamide was prepared by Freeman's method.[16] Crystals of *o*-hydroxymethyl-N-methylbenzamide (80 mg, 0·49 mmole) were added slowly to a mixture of conc HNO_3 (10 ml) and conc HSO_4 (10 ml) in the presence of urea (30 mg) at 0°. The mixture was stirred for 1 h at room temp and was extracted with dichloromethane (2 × 20 ml). The dichloromethane layer was basified with a sat $NaHCO_3$ aq, washed with water (5 ml) and dried ($MgSO_4$). When all solvent had been removed, pale yellow solid (63 mg) of **10** was obtained; IR (nujol) 3280, 1630, 1560, 1280 and 870 cm^{-1}; NMR τ 2·15 (m, 4H), 3·50 (broad s, 1H, D_2O exchangeable), 4·33 (s, 2H) and 7·10 (d, 3H, J = 4·5 Hz, collapsed to a singlet on D_2O exchange).

The compound **10** prepared in the above synthesis was left at room temp overnight. The solid was then recrystallized from acetone–light petroleum mixture to give white needles having its IR spectrum superimposable with that of the nitrate salt of **11**.

Photolysis of **7** *under air*

A soln of **7** (1·01 g, 5·7 mmoles) in benzene (100 ml) was photolysed in the presence of a slow stream of air for 1·5 h. From the ppt oxime **9** (286 mg, 25%) and phthaloxime **17** (168 mg, 18%) were obtained. The photolysate was worked up in the usual manner to afford the nitrate salt of **11** (165 mg, 17%), the parent amide (47 mg, 5%) and the unidentified solid with mp 179–182°.

Photolysis of N-*bromo*-N-*t*-*butyltouamide*

Crystaline N-t-butyltoluamide (mp 74–75°) was prepared from *o*-toluic acid. The toluamide (224 mg) was treated with t-butyl-hypobromite at 0° to give the crude N-bromamide (331 mg); ir 3030, 1660, 1600, 1550, 1480, 1280, 980 and 655 cm^{-1}; UV (CCl_4) absorption tailed to 350 nm.

The bromamide in benzene (120 ml) was irradiated in a pyrex apparatus with a 200 Watt Hanovia lamp for 1 h. The residue from the photolysis was recrystallized from acetone–chloroform (3:1) to give hydrobromide of N-t-butyliminophthalide (**12**, 164 mg): mp 110–111°; IR 3400 ~ 3200, 1675, 1205, 925 and 665 cm^{-1}; NMR τ 2·50 (m, 4H), 4·1 (s, 2H) and 8·25 (s, 9H). The free base **12** was liberated by a treatment with Na_2CO_3 aq; IR (CCl_4) 3040, 1700, 1290 and 670 cm^{-1}; NMR τ 2·2 (m, 1H), 2·4 (m, 3H), 4·75 (s, 2H), 8·6 (s, 9H); ms *m/e* (%) 189 (12), 174 (100), 134 (71), 132 (27), 116 (40), 104 (24), 90 (36) and 89 (35).

The free base **12** is stable when refluxed in ether with lithium aluminium reduction for 12 h and when treated with dilute acid. Treatment of **12** in 20% H_2SO_4 for 3 h on a water bath gave a quantitative yield of phthalide **15**.

Photolysis of N-*bromo*-N-*methyltoluamide* **8**

Bromamide **8** (570 mg) was prepared as described above and its crude product was photolysed in benzene (120 ml) for 1 h. The product was recrystallized to give the hydrobromide of **11** (212 mg); mp 205–206°; IR ($CHCl_3$) 3460, 1700, 1605, 1470, 1125 and 975 cm^{-1}; NMR (D_2O) τ 2·1 (m, 4H) 4·0 (s, 2H) and 6·6 (s, 3h). (Found: C, 47·47; H, 4·51; N, 6·25. Calcd. for $C_9H_{10}NOBr$: C, 47·39; H, 4·42; N, 6·14).

The hydrobromide was treated with sat Na_2CO_3 aq to give free base **11** (113 mg) which exhibited the identical IR, MNR and MS spectra with those of the sample obtained in the nitrosamide photolysis. On chromatography of this sample on a neutral alumina column a quantitative yield of phthalide was recovered.

Acknowledgement—The authors are grateful to the National Research Council of Canada and the Defense Research Board, Ottawa for the financial support of this research.

REFERENCES

[1]T. Mojelsky and Y. L. Chow, *J. Am. Chem. Soc.* **96**, 0000 (1974)
[2]Y. L. Chow, J. N. S. Tam, C. J. Colon and K. S. Pillay, *Canad J. Chem.* **51**, 2469 (1973)
[3]Y. L. Chow, J. N. S. Tam and A. C. H. Lee, *Ibid.* **47**, 1065 (1969)
[4]O. E. Edwards and R. S. Rosich, *Ibid.* **45**, 1287 (1965)
[5]L. P. Kuhn, G. G. Kleinspehn and A. C. Duckworth, *J. Am. Chem. Soc.* **89**, 3858 (1967)
[6]R. S. Neale, N. L. Marcus and R. G. Schepers, *Ibid.* **88**, 3051 (1966)
[7]Y. L. Chow, T. C. Joseph, *J. Chem. Soc., Chem. Commun.* 490 (1969)
[8]Y. L. Chow, J. N. S. Tam and K. S. Pillay, *Canad. J. Chem.* **51**, 2477 (1973)
[9]M. L. Bender, Y. L. Chow and F. Chloupek, *J. Am. Chem. Soc.* **80**, 5380 (1958)
[10]J. N. S. Tam, Ph. D. Thesis, Simon Fraser University, Burnaby, British Columbia (1970)
[11]E. H. White, *J. Am. Chem. Soc.* **77**, 6008, 6011, 6014 (1955)
[12]J. Breslauer and A. Pictet, *Ber. Dtsch. Chem. bis* **40**, 3784 (1907)
[13]*Dictionary of Organic Compounds* (Edited by J. R. A. Pollock and R. Stevens) Vol. 5, 2741. Eyre and Spottiswoode, London (1965)
[14]O. L. Brady, L. C. Baker, R. F. Goldstein and S. Harris, *J. Chem. Soc.* 529 (1928)
[15]W. Theilacker and H. Kalenda *Liebigs Ann.* **584**, 87 (1953)
[16]J. P. Freeman and J. G. Shepard, *Org. Syn.* **44**, 83 (1963)