Tetrahedron Vol. 38, No. 12, pp. 1793 to 1796, 1982
Printed in Great Britain.

0040-4020/82/121793-04$03.00/0

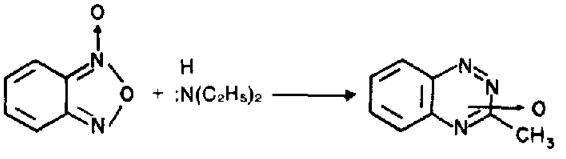
OXIDES OF 3-METHYL-1,2,4-BENZOTRIAZINE

RAJA H. ATALLAH and MUSA Z. NAZER
University of Jordan, Amman, Jordan

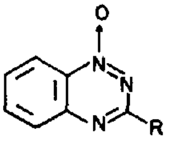
(*Received in UK* 14 *September* 1981)

Abstract—The previously prepared 3-methyl-1,2,4-benzotriazine oxide[1] is shown to be the 4-oxide **5**. Synthesis and structures of other isomeric and related oxides are described. A modification of a previously described synthesis of 1,2,4-benzotriazines produces purer products in higher yields.

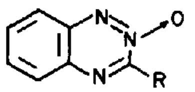
The reaction of benzofurazan oxide **1** with diethylamine **2** was shown to produce, among other products, a 3-methyl-1,2,4-benzotriazine oxide[1](**0–130**), of melting point 130°. Preliminary spectral data suggested a 4-oxide structure **5**. However, owing to the unavailability of other isomeric monoxides of established structures[2] and the uncertainties encountered in assigning the position of oxygen in most benzotriazine monoxides,[3–5] further evidence in support of the above structural assignment became necessary. This is provided in the present work through a comparative study of the three possible isomeric monoxides (**3–5**) and related compounds.



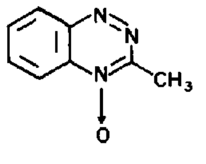
1 2 0–130



3
a: R = CH₃
b: R = H

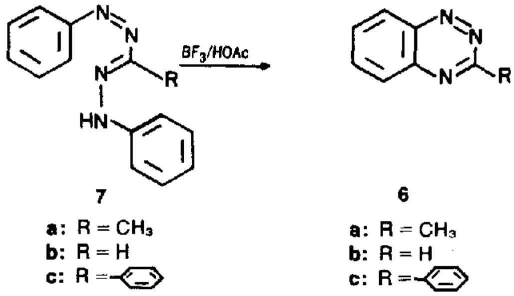


4
a: R = CH₃
b: R = H



5

A possible route to some of the desired oxides involves peracid N-oxidation[3,6] of the corresponding 1,2,4-benzotriazines **6**. Attempts to prepare 3-methyl-1,2,4-benzotriazine **6a** according to reported syntheses[7] yielded insufficient quantities for further work. However, good yields of this and other 3-substituted triazines (**6b**, **c**) were realized by a modification of the Bamberger synthesis.[8] It was found that use of BF_3/AcOH in place of conc H_2SO_4 resulted in a more effective cyclization of the formazan precursore **7**.[9–11]

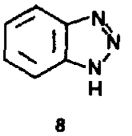


3-Methyl-1,2,4-benzotriazine **6a** was treated with H_2O_2/HOAc at room temperature for four days, after which the following five products were isolated (repeated column chromatography):

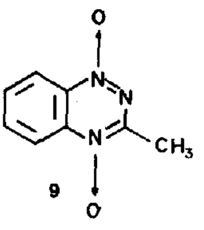
two monoxides of 3-methyl-1,2,4-benzotriazine
(**0–100**, m.p. 100–102° and **0–140**, m.p. 140–142°);
a dioxide (**D-186**, m.p. 186–188°);
benzotriazole (**8**, m.p. 96–98°);[12] and
2-methylbenzimidazole (**10**, m.p. 173–175°).[13]

Oxidation of the triazine using *m*-chloroperbenzoic acid[6] in benzene also gave the same two monoxides and the same dioxide. The latter oxidation produced relatively more of monoxide **0–140**. None of monoxide **0–130** however, could be isolated from either oxidation.

Monoxides **0–100**, **0–130**, and **0–140** were shown to be isomeric by elemental analyses, parent mass ion *m/e* 161 for $C_8H_7N_3O$, and subsequent reduction with sodium dithionite[14] to the parent 3-methyl-1,2,4-benzotriazine (**6a**).



8



9

The relationship between monoxides **0–100** and **0–130** was further revealed by their transformation to dioxide **D-186** upon treatment with *m*-chloroperbenzoic acid in benzene. Monoxide **0–140** resisted oxidation. Upon treatment with sodium dithionite dioxide **D-186** was completely deoxygenated to 3-methyl-1,2,4-benzotriazine **6a**. However, it was partially deoxygenated to monoxide **0–100** by trimethylphosphite in refluxing propanol.[15]

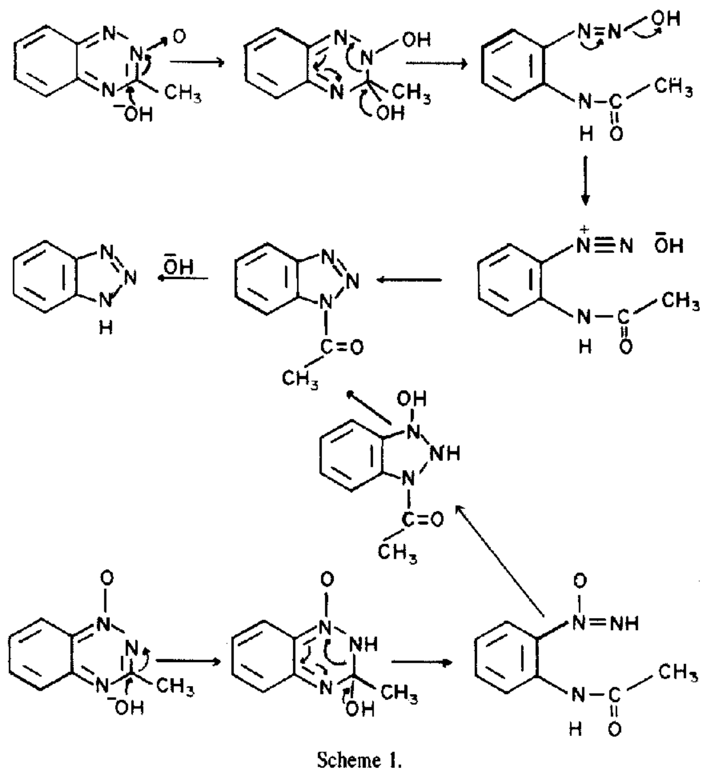
In view of the fact that **0–130** is obtained from benzofurazan oxide **1** it must have either the 1-oxide structure **3a** or the 4-oxide structure **5**. Since either **0–130** or **0–100** could be oxidized to dioxide **D-186**, monoxide **0–100** can also possess either structure **3a** or **5**. Consequently, oxide **0–140** would have the 2-oxide structure **4a**. Such structural assignments have been further supported by chemical transformations and spectroscopic properties of these oxides. The formation of benzotriazole **8** from $H_2O_2/HOAc$ oxidation of 3-methyl-1,2,4-benzotriazine **6a** suggests the possibility of hydrolysis of some oxidation products. Lability to hydrolysis was indicated by the effect of base on the UV spectra of the various oxides of 3-methyl-1,2,4-benzotriazine. An immediate change in the spectrum of monoxide **0–140** is observed upon addition of few drops of potassium hydroxide solution. A change in the spectrum of **0–100** is observed only after refluxing for 30 min. The spectrum of **0–130**, however, remains unaffected at room temperature or after brief heating (10 min.). Guided by these observations, we studied the base hydrolysis of all three monoxides and found that monoxide **0–140** gave benzotriazole at room temperature within 30 minutes, whereas **0–100** required heating. In contrast, **0–130** was recovered practically unchanged after 10 minutes except for a trace of deoxygenation to the parent, triazine. This behavior towards base is best explained if monoxide **0–100** is assigned the 1-oxide structure **3a** and **0–140** the 2-oxide structure **4a**. Consequently **0–130** is the 4-oxide **5** and **D-186** is the 1,4-dioxide **9**. Apparently the presence of $-N{=}\overset{O}{N}-$, as in the 1-oxide or the 2-oxide, is necessary for the generation of intermediates that lead to the formation of benzotriazole (Scheme 1). Since the hydrolysis involves nucleophilic attack by ^{-}OH on C_3, a 2-oxide function renders this position more susceptible to attack than would a 1-oxide. Consequently, it would be expected that **0–140**, the 2-oxide, would react fastest with base, as was found to be the case. These results are in agreement with those obtained by Carbon[16] on the hydrolysis of some 3-amino-1,2,4-benzotriazine oxides.

Additional support for the assignment of the 2-oxide structure for **0–140** was provided by the isolation of 2-methylbenzimidazole **10** from the peroxide oxidation ($H_2O_2/HOAc$) of 3-methyl-1,2,4-benzotriazine. Formation of **10** can be rationalized as shown in Scheme 2. When each of the three monoxides **0–100**, **0–130** and **0–140** was treated separately with $H_2O_2/HOAc$, only **0–140** gave 2-methylbenzimidazole together with benzotriazole. Both **0–100** and **0–130** gave the dioxide **D-186**.

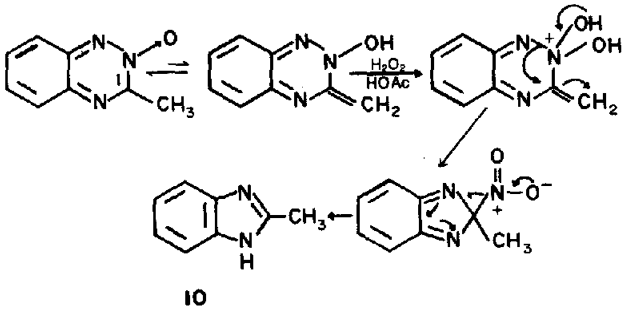
In a search to relate the above oxides to the oxides of the parent system, 1,2,4-benzotriazine **6b**, we found that only 1,2,4-benzotriazine-1-oxide **3b** was previously reported.[3] The UV and NMR (aromatic) spectra of an authentic sample of this oxide were identical with those of oxide **0–100**, thereby rendering further support for the assignment of the 1-oxide structure **3a** for **0–100**.

With no available information about the other possible N-oxides of the parent 1,2,4-benzotriazine, we treated **6b** with peracid ($H_2O_2/HOAc$) and isolated the known 1-oxide **3b** and benzotriazole **8**. In contrast, oxidation with *m*-chloroperbenzoic acid in benzene gave, in addition to the 1-oxide, an isomeric oxide (**0–86**, m.p. 86–88). The UV and NMR spectra of **0–86** were similar to those of 3-methyl-1,2,4-benzotriazine-2-oxide **4a**. In base, **0–86** is hydrolyzed faster than **4a**, a behavior consistent with increased susceptibility of position three toward nucleophilic attack when an H replaces a CH_3 on that position. Consequently, **0–86** is assigned the 2-oxide structure **4b**.

The present work represents the first study in which all the isomeric monoxides of 3-methyl-1,2,4-benzotriazine

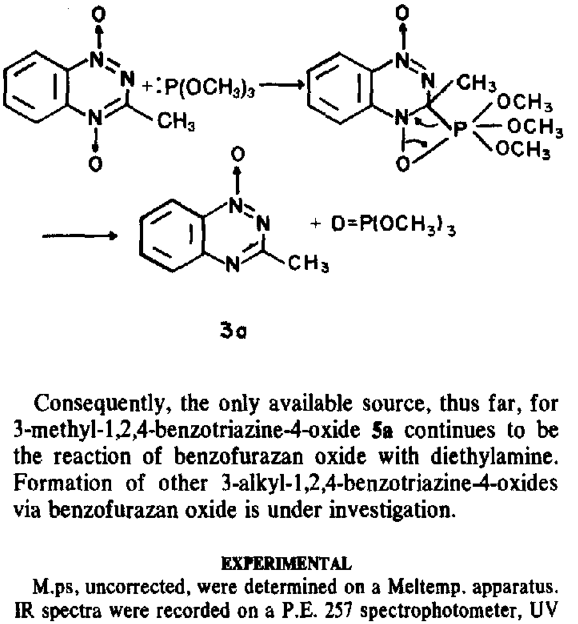


Scheme 1.



Scheme 2.

have been prepared and characterized. Of these, only the 1-and 2-oxides, but not the 4-oxide, are obtainable by peracid oxidation of the corresponding 3-methyl-1,2,4-benzotriazine. This also seems to be the case with other-1,2,4-benzotriazines.[3-5] The indirect path triazine → dioxide → monoxide did not produce the 4-oxide when applied to 3-methyl-1,2,4-benzotriazine. Reduction of the dioxide **9** with sodium dithionite[14] regenerated the corresponding triazine **6a**. Use of the selective deoxygenating agent,[15] trimethylphosphite, on the other hand, reduced the dioxide to the 1-oxide **3a**. Such selectivity is consistent with the following mechanism:



Consequently, the only available source, thus far, for 3-methyl-1,2,4-benzotriazine-4-oxide **5a** continues to be the reaction of benzofurazan oxide with diethylamine. Formation of other 3-alkyl-1,2,4-benzotriazine-4-oxides via benzofurazan oxide is under investigation.

EXPERIMENTAL

M.ps, uncorrected, were determined on a Meltemp. apparatus. IR spectra were recorded on a P.E. 257 spectrophotometer, UV spectra on a Carey-17B, NMR spectra on a Varian T-60 in $CDCl_3$ with TMS as an internal reference, and mass spectra on a Varian-Mat CH 5 at 70 ev, 100 uA, 200°. Elemental analyses were performed by Pascher Laboratories, Bonn, West Germany.

3-Methyl-1,2,4-benzotriazine **6a**. Benzenediazonium chloride soln, prepared from aniline (19 g, 0.2 mole), conc HCl (50 ml in 50 ml water), and $NaNO_2$ (14 g in 20 ml water), was added dropwise to a stirred soln of acetaldehyde phenylhydrazone in 350 ml pyridine. The mixture was stirred overnight at 0°. Addition of water and ice (300 g) resulted in the separation of crude 1,5-diphenyl-3-methylformazan which was washed several times with water. Crystallization from MeOH-water gave orange-red needles, 38 g., m.p. 120–122° (lit.[11]; 122°).

The formazan (4 g) was heated on a steam bath for 10 min with 20 ml BF_3/AcOH. The color of the soln changed from dark violet to dark brown. Water (50 ml) was added to destroy BF_3. The soln was extracted several times with benzene. The benzene soln was dried over Na_2SO_4 and evaporated. The residue was extracted with light petroleum ether leaving behind tarry black material. Evaporation of petroleum ether and repeated sublimation at 70° and reduced pressure afforded pure crystals of 3-methyl-1,2,4-benzotriazine (1.4 g., 60%) m.p. 94–96° (lit.[7]; 92–94) NMR: δ 3.00 (3H, s), 7.28–7.62 (3H, m), 7.98–8.18 (1H, m). Mass: 145 (M^+), 117 (M^+-N_2), 90 ($C_6H_4N^+$).

The residue from sublimation was found to contain as a major by-product phenazine, purified by column chromatography, 0.2 g., m.p. 177–179°.

3-Phenyl-1,2,4-benzotriazine **6c**. A mixture of 1,3,5-triphenyl formazan[7] (2 g) and BF_3 AcOH (5 ml) was heated on a steam bath for 5 min. Addition of water separated a solid which was extracted with ether. Evaporation of ether and crystallization of the resulting solid from EtOH yielded 1 gm (70%) of the triazine, m.p. 127–128° (lit.[7]; 126–127°).

1,2,4-Benzotriazine **6b**. 1,5-Diphenylformazan, prepared from malonic acid and benzene diazonium chloride,[11] was treated with BF_3/HOAc as previously described for 3-methyl-1,5-diphenylformazan. The sublimed product (at 60°) was 1,2,4-benzotriazine m.p. 74–76 (lit.[7]; 76–77). NMR: δ 7.8–8.3 (3H, m), 9.47–8.73 (1H, m), 9.97 (1H, s). Mass: 131 (M^+), 103 (M^+-N_2).

Oxidation of 3-methyl-1,2,4-benzotriazine **6a** *with peracetic acid.* 3-Methyl-1,2,4-benzotriazine (1.0 g) in 100 ml glacial AcOH and 12 ml 30% H_2O_2 was left at room temp for 4 days. The solvent was evaporated at reduced pressure, the residue extracted with benzene, the dried benzene extracts were concentrated to a small volume and column chromatographed. Fractions were further purified by thick layer chromatography and identified as (in order of elution from the column):

(a) *3-Methyl-1,2,4-benzotriazine-2-oxide* **4a**. Light yellow crystals from petroleum spirit (60–80), 0.1 g, m.p. 140–142°. (Found: C, 59.77; H, 4.40; N, 25.92. Calc. for: C, 59.62; H, 4.38; N, 26.07%). NMR: δ 2.73 (3H, s); 7.25–7.63 (4H, m) Mass: 161 (M^+), 131 (M^+-NO), 117 (M^+-N_2O), 90 $(C_6H_4N)^+$ UV: $\lambda_{max}^{H_2O}$ (E): 372 (6, 300), 270 (30,000).

(b) *3-Methyl-1,2,4-benzotriazine-1-oxide* (**3a**). Colorless crystals from benzene-light petroleum, 0.25 g, m.p. 101–102°. (Found: C, 59.77; H, 4.35; N, 26.10. Calc. for: C, 59.62; N, 26.07, H, 4.38%.) NMR: δ 2.65 (3H, s), 7.13–7.80 (3H, m), 7.95–8.21 (1H, m). Mass: 161 (M^+), 117 (M^+-N_2O), 90 ($C_6H_4N^+$) UV:$\lambda_{max}^{H_2O}$ (E): 355 (4,500), 268 (5,500), 245 (25,000).

(c) *Benzotriazole* **8**. Colorless crystals from EtOAc-petroleum ether, 0.05 g, m.p. 97–98°, identical with an authentic sample.[12] NMR: 7.27–7.53 (2H, m), 7.78–8.00 (2H, m).

(d) *3-Methyl-1,2,4-benzotriazine-1,4-dioxide* **9**. Yellow needles from EtOAc-light petroleum, 0.12 g, m.p. 184–186°. (Found: C, 54.33; H, 3.95; N, 23.35; Calc. for: C, 54.25; H, 3.95; N, 23.73%.) NMR: 2.63 (3H, s), 7.30–7.78 (2H, m), 7.97–8.17 (2H, m). Mass: 177 (M^+); 161 (M^+-O), 160 (M^+-OH), 136 (M^+-CH_3CN, BFO), 117 (M^+–O–N_2O), 90 ($C_6H_4N^+$). UV $\lambda_{max}^{H_2O}$ (E): 395.(8,500), 288 (7,000), 225 (15,500).

(e) 2-*Methylbenzimidazole*. Isolated from the benzene insoluble residue which upon extraction with MeOH, addition of ether and thick layer chromatography of the ppt gave 0.05 g of a crude product purified by repeated thick layer chromatography m.p. 173–175 (lit.[17]: 175–176). NMR: (CD_3OD): δ 2.20 (3H, s), 7.02–7.50 (4H, m) Mass: 132 (M^+). 131 (M^+–H), 104 ($C_6H_4N_2{}^+$), 90 ($C_6H_4N^+$).

Oxidation of 3-*methyl*-1,2,4-*benzotriazine with* m-*chloroperbenzoic acid*. *m*-Chloroperbenzoic acid (0.5 g in 25 ml of benzene) and 3-methyl-1,2,4-benzotriazine (0.8 g in 25 ml benzene) were mixed and left at room temp for 4 days. The mixture was divided into two portions. The first portion was extracted once with $Na_2S_2O_3$ aq (0.1 g in 10 ml water) and several times with 2% Na_2CO_3 aq (total volume of 50 ml). The benzene extracts were washed with water, dried over Na_2SO_4, concentrated to a small volume and chromatographed over silica gel. The compounds obtained, in order of their elution from the column were: **4a** (0.1 g), **3a** (0.01 g), **6a** (0.05 g) and **9** (0.03 g).

The second portion was concentrated to a small volume and chromatographed over silica gel. The following were obtained in order of elution: *m*-Chloroperbenzoic acid, 3-Methyl-1,2,4-benzotriazine-2-oxide (0.1 g), 3-Methyl-1,2,4-benzotriazine-1-oxide (0.01 g), Unreacted 3-methyl-1,2,4-benzotriazine (0.05 g), *m*-Chlorobenzoic acid and 3-Methyl-1,2,4-benzotriazine-1,4-dioxide (0.05 g).

Oxidation of 1,2,4-*benzotriazine* **6b**

(a) *With peracetic acid*. A mixture of 1,2,4-benzotriazine (0.5 g), AcOH (50 ml), and 30% H_2O_2 (6 ml), was kept at room temp for 4 days. The soln was evaporated to dryness under reduced pressure, the residue extracted with benzene, the dried benzene extracts concentrated to a small volume and chromatographed over silica gel. The following compounds were eluted off the column:

(i) 1,2,4-*Benzotriazine*-1-*oxide*. Colorless crystals (0.15 g), m.p. 138–140° from light petroleum, (lit.[3]: 138–140°). NMR: δ 7.68–8.13 (3H, m), 8.43–8.56 (1H, m), 9.03 (1H, s) UV: $\lambda_{max}^{H_2O}$ (E); 345 (3500), 275 (6500), 238 (17000).

(ii) *Benzotriazole* (0.05 g), m.p. 94–96°.

(b) *With* m-*chloroperbenzoic acid*. A mixture of 1,2,4-benzotriazine (0.5 g), *m*-chloroperbenzoic acid (0.8 g), and benzene (50 ml) was left at room temp for 4 days. It was then extracted once with $Na_2S_2O_3$ (0.1 g in 10 ml water) and several times with $NaHCO_3$ aq (2%, total of 50 ml). The dried benzene soln was concentrated to a small volume and chromatographed on preparative thick layer plate using benzene-EtOAc (4:1) to give:

(i) 1,2,4-*Benzotriazine*-2-*oxide* (0.03 g), m.p. 86–88° from light petroleum ether. NMR: δ 7.63–8.03 (4H, m), 8.87 (1H, s) Mass: 147 (M^+), 131 (M^+–O), 117 (M^+–NO), 103 (M^+–N_2O), 90 ($C_6H_4N^+$). UV: $\lambda_{max}^{H_2O}$ (E) 373 (5600), 265 (21000).

(ii) 1,2,4-*Benzotriazine*-1-*oxide* (0.07 gm), m.p. 138–140°.

Reduction of 3-*methyl*-1,2,4-*benzotriazine*-1,4-*dioxide* **9**

(a) *With sodium dithionite*. To a magnetically stirred refluxing soln of the dioxide (0.2 g in 10 ml water) was added sodium dithionite (0.8 g in 10 ml water) in portions. Refluxing was continued for 4 more hr. Extraction with benzene afforded 3-methyl-1,2,4-benzotriazine (0.12 g), m.p. 94–96 (from hexane).

(b) *With trimethyl phosphite*. A soln of the dioxide (0.2 g) in propanol (15 ml) and trimethyl phosphite (0.3 g) was refluxed for 4 hr. Evaporation to a solid residue and extraction with benzene afforded 3-methyl-1,2,4-benzotriazine-1-oxide (0.12 g) m.p. 98–100°.

Hydrolysis with sodium hydroxide

(a) 3-*Methyl*-1,2,4-*benzotriazine*-1-*oxide*. The oxide (0.2 g) and 10 ml 2% NaOH aq when left at room temp for several hr remained unchanged (examined by TLC).

The above mixture was then refluxed for 30 min, neutralized with HCl and evaporated to dryness (at room temp). The dry solid was extracted with hot benzene. Evaporation of the extracts yielded benzotriazole (0.06 g), m.p. 94–96 (from benzene–petroleum ether).

(b) 3-*Methyl*-1,2,4-*benzotriazine*-2-*oxide*. The oxide (0.2 g), 2% NaOH aq (15 ml), if kept at room temp for 5 hr or refluxed for only 10 min gives after work up 0.03 g benzotriazole, m.p. 94–96°.

(c) 3-*Methyl*-1,2,4-*benzotriazine*-4-*oxide*. Refluxing the oxide with 2% NaOH for periods of 30 min to 5 hr gave a complex mixture from which 3-methyl-1,2,4-benzotriazine could be isolated (thick layer chromatography) but no benzotriazole is detected in the mixture.

(d) 1,2,4-*Benzotriazine*-2-*oxide*. A few crystals of the oxide were treated with NaOH aq at room temp. Examination of the mixture by tlc revealed the disappearance of the oxide after 5 min. Benzotriazole is shown to be formed by comparison on tlc.

Acknowledgements—We wish to thank Prof. Costas H. Issidoridis and Prof. Maklouf J. Haddadin of the American University of Beirut for their help throughout this work. Also we are grateful to the University of Jordan Research Council for financial support.

REFERENCES

[1] M. Z. Nazer, C. H. Issidoridis and M. J. Haddadin, *Tetrahedron* **35**, 681 (1979).

[2] H. Igeta, T. Nakai and T. Tsuchiya, *J. Chem. Soc.* Chem. Comm. 622 (1973).

[3] R. F. Robbins and K. Schofield, *Ibid.* 3186 (1957).

[4] J. C. Mason and G. Tennant, *Ibid.* (B) 911 (1970).

[5] F. J. Wolf, K. Pfister, R. M. Wilson and C. A. Robinson, *J. Am. Chem. Soc.* **76**, 3551 (1974).

[6] A. R. Katritzky and J. M. Logowski, *Chemistry of Heterocyclic N-oxides*, pp. 22–58. Academic press, New York (1977).

[7] R. A. Abramovitch and K. Schofield, *J. Chem. Soc.* 2326 (1955).

[8] E. Bamberger and E. Wheelwright, *Ber. Dtsch. Chem. Ges.* **25**, 3201 (1892).

[9] J. N. Ashley, B. M. Davis, A. W. Nineham and R. Slaok, *J. Chem. Soc.* 3881 (1953).

[10] D. Dale, *Ibid* (*A*) 279 (1967).

[11] H. V. Pechman, *Ber. Dtsch. Chem. Ges.* **25**, 3186 (1892).

[12] E. C. Horning, *Organic Syntheses*, Coll. Vol. III, 106 (1964).

[13] 2-Methylbenzimidazole obtained from the column is contaminated with a tenaciously held unidentified byproduct (m.p. 200–202). Purification required repeated thick layer chromatography.

[14] M. J. Haddadin, G. E. Zahr, T. N. Rawdah, N. C. Chelhot and C. H. Issidorides, *Tetrahedron* **30**, 659 (1974).

[15] J. Dirlam and J. W. McFarland, *J. Org. Chem.* **42**, 130 (1977).

[16] J. A. Carbon. *Ibid.* **27**, 185 (1962).

[17] J. Grasselli and W. M. Ritchey, *Atlas of Spectral Data and Physical Constants* (2nd Ed.) Vol. II, p. 370, CRC Press.