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1,3-DIPOLAR CYCLOADDITION REACTION WITH 1-METHYLBENZIMIDAZOLE 3-OXIDE

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RECENTLY, 1,3-dipolar cycloaddition reaction has been developed extensively by Huisgen and co-workers (1). A number of 1,3-dipolar systems has been revealed and heteroaromatic N-oxides are regarded as a potential 1,3-dipolar system. The first example of 1,3-dipolar cycloaddition in heteroaromatic N-oxide series was shown by Hayashi (1961)(2), who obtained 6-anilinophenanthridine by the reaction of phenanthridine N-oxide with phenylisocyanate. A few of additional examples, which involve reactions of isoquinoline N-oxide and pyridine N-oxide with some dipolarophiles, has been described in the recent review (1).

In the course of studies on benzimidazole N-oxide, the present investigation was undertaken to see if a five-membered heteroaromatic N-oxide, 1-methylbenzimidazole 3-oxide (I)(3), could behave as a 1,3-dipole.

1-Methylbenzimidazole 3-oxide reacted with such dipolarophiles as phenylisocyanate, phenylisothiocyanate, carbon disulfide, methyl propiolate, dimethyl acetylenedicarboxylate at ordinary temperature, and as benzonitrile and phenyl isocyanide on heating.

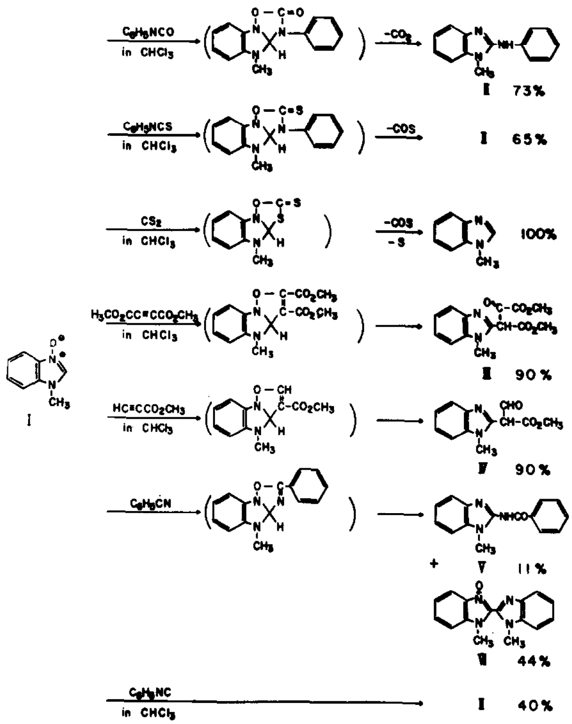
The reaction solvents, reaction products, and yields are shown in the accompanying Chart, and melting points and analyses of the products are listed in the accompanying Table.

As in the examples already reported, any incipient cycloadducts could not be isolated in these reactions. However, the products formed can be reasonably interpreted by initial formation of cycloadducts, followed by the ring opening to stable products.

The structures of II and V were confirmed by comparison with the samples prepared by authentic methods; II was synthesized from 2-chloro-1-methylbenzimidazole and aniline and V from 2-amino-1-methylbenzimidazole and benzoyl chloride.

The structures of III and IV were confirmed by the following methods. The presence of an enolizable carbonyl group in III and IV was deduced by the positive color reaction with ferric chloride.

On hydrolysis, both compounds III and IV gave 1-methyl-2-benzimidazolylacetic acid, m.p. 75° dec. (Found: C, 63.10; H, 5.18; N, 15.00. $C_{10}H_{10}N_2O_2$ requires: C, 63.15; H, 5.30; N, 14.73%), which was easily decarboxylated to 1,2-dimethylbenzimidazole (4), and by action of hydroxylamine, they afforded methyl 1-methyl-2-benzimidazolylacetate, m.p. 66-68°. (Found: C, 64.87; H, 6.03; N, 13.53. $C_{11}H_{12}N_2O_2$ requires: C, 64.69; H, 5.92; N, 13.72%). Reaction of the above ester with dimethyl oxalate in the presence of sodium methoxide in ether


I
C6H5NCO
in CHCl3
-CO2
II 73%
C6H5NCS
in CHCl3
-COS
II 65%
CS2
in CHCl3
-COS
-S
100%
H3CO2CC≡CCO2CH3
in CHCl3
III 90%
HC≡CCO2CH3
in CHCl3
IV 90%
C6H5CN
V 11%
VI 44%
C6H5NC
in CHCl3
II 40%

CHART

TABLE

Compound	M. p. *	Formula	Analysis	
			Required %	Found %
2-Anilino-1-methylbenzimidazole (II)	201-202°	$C_{14}H_{13}N_3$	C, 75.31 H, 5.87 N, 18.82	C, 75.10 H, 5.73 N, 18.57
Dimethyl 1-methyl-2-benzimidazolyloxalacetate (III)	185° (dec.)	$C_{14}H_{14}N_2O_5$	C, 57.93 H, 4.86 N, 9.65	C, 58.15 H, 5.03 N, 9.59
Methyl α-formyl-(1-methyl-2-benzimidazolyl)-acetate (IV)	183° (dec.)	$C_{12}H_{12}N_2O_3$	C, 62.06 H, 5.21 N, 12.06	C, 62.13 H, 5.31 N, 11.83
2-Benzamido-1-methylbenzimidazole (V)	161-162°	$C_{15}H_{13}N_3O$	C, 71.69 H, 5.21 N, 16.72	C, 71.77 H, 5.43 N, 16.69
1, 1'-Dimethyl-2, 2'-bibenzimidazole 3-oxide (VI) (hydrate)	120-130° (hydrate) 215° (dec.) (anhydrous crystals)	$C_{16}H_{14}N_4O \cdot H_2O$	C, 64.85 H, 5.44 N, 18.91 H_2O, 6.08	C, 65.13 H, 5.55 N, 18.59 H_2O, 6.11

* All m.p.s were taken on a Kofler hot-stage and are uncorrected.

reproduced III.

The by-product VI was reduced catalytically over Raney Ni to 1, 1'-dimethyl-2, 2'-bibenzimidazole, which was identified with a sample prepared by methylation of 2, 2'-bibenzimidazole (5).

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REFERENCES

1. R. Huisgen, Angew. Chem. 75, 604 (1963).
2. E. Hayashi, Yakugaku Zasshi, 81, 1030 (1961).
3. S. Takahashi and H. Kanō, submitted for publication.
4. M. A. Phillips, J. Chem. Soc. 2820 (1929).
5. H. Hübner, Ann. 209, 339 (1881).