

Contribution from the Organic Chemical Research Section,
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N,N'-Carbonyldiimidazole as a Reagent for the Preparation of Five-membered Heterocycles

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Derivatives of 2-benzimidazolinone, 2-imidazolidinone, and 2-oxazolidinone are obtained in good to excellent yield when the appropriate diamine or aminoalcohol is allowed to react with N,N'-carbonyldiimidazole.

N,N'-Carbonyldiimidazole (I), first described by Staab (1) in 1957, is a versatile reagent for the synthesis of many classes of organic compounds, including amides, anhydrides, esters, hydrazides, hydroxamic acids, peptides, ureas, urethanes, etc. (2). It is an excellent reagent for small-scale laboratory preparations, as it is a non-toxic, stable solid which can be easily and accurately measured and often leads to nearly quantitative yields of easily purified products.

The use of N,N'-carbonyldiimidazole as a means of introducing the carbonyl group in the preparation of five-membered heterocyclic systems has ap-

parently not been described in the literature. We have now studied the reaction of this reagent with derivatives of *o*-phenylenediamine (II), ethylenediamine (III) and 2-anilinoethanol (IV) in tetrahydrofuran or tetrahydrofuran and benzene at 25-65°. The high temperature often required in cyclization procedures (3,4,5) and the danger inherent in the use of phosgene were avoided by this procedure. The expected 2-benzimidazolinones (V), 2-imidazolidinones (VI) and 2-oxazolidinones (VII) were obtained in good to excellent yields (Tables I and II), and the crude products were generally light colored and analytically pure without recrystallization or further purification.

CHART I

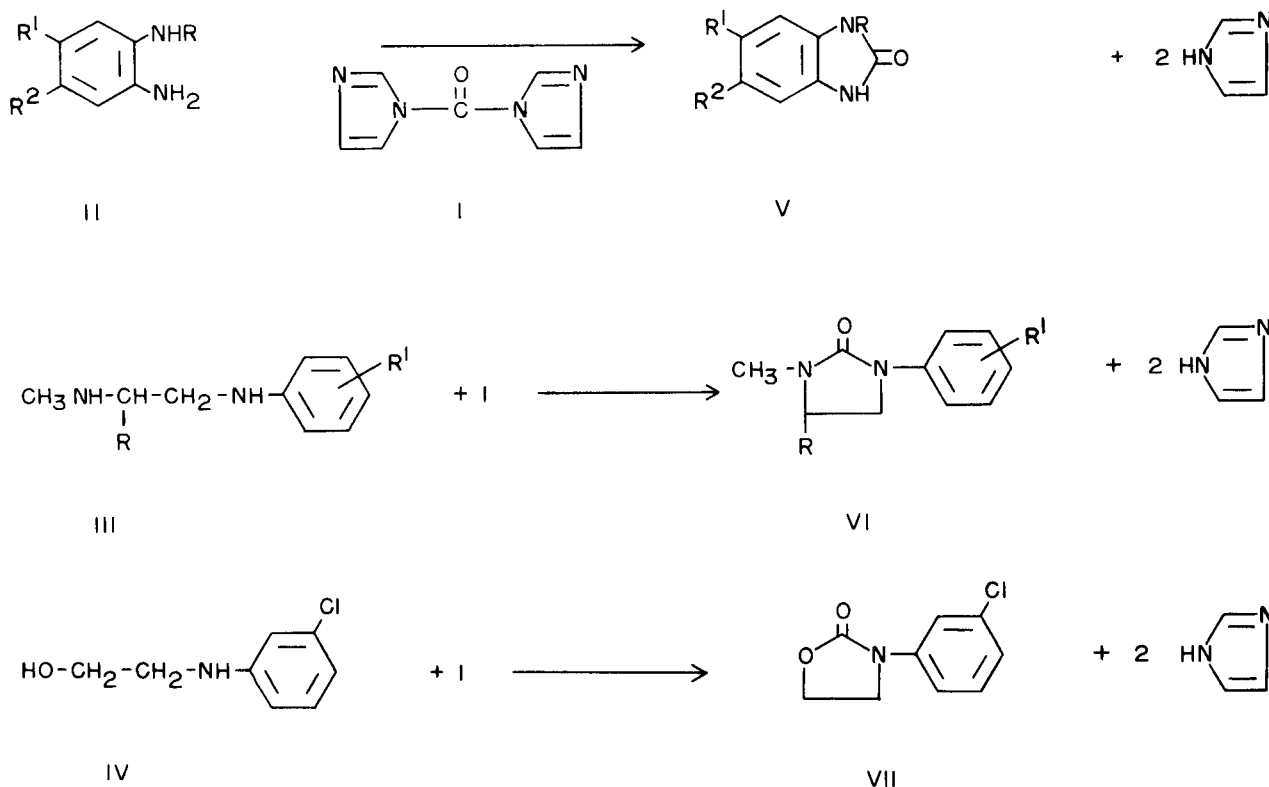
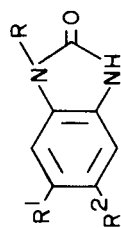


TABLE I

2-Benzimidazolinone Derivatives

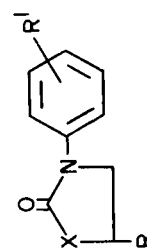


R	R ¹	R ²	Procedure	Yield, %	M. p., °C (a)	Literature M. p., °C	Formula	% Carbon		% Hydrogen		% Chlorine		% Nitrogen	
								Calcd.	Found	Calcd.	Found	Calcd.	Found	Calcd.	Found
H	Cl	H	A	86 (b)	324-326	>270 (c)	C ₇ H ₅ ClN ₂ O	49.9	50.1	3.0	3.3	21.0	20.8	16.6	16.3
H	CH ₃ O	H	B	75 (b)	256-257	256-257 (d)	C ₈ H ₈ N ₂ O ₂	58.5	58.7	4.9	5.1			17.1	17.4
H	Cl	Cl	A	92 (b)	>400	345 (d)	C ₇ H ₄ Cl ₂ N ₂ O	41.4	41.7	2.0	2.2	34.9	34.3	13.8	13.9
H	CH ₃	CH ₃	B	67 (b)	384-386	>345 (d)	C ₉ H ₁₀ N ₂ O	66.7	66.8	6.2	6.4			17.3	17.0
C ₂ H ₅	Cl	H	C	67 (e)	190-191	185-186 (f)	C ₉ H ₉ ClN ₂ O	55.0	54.7	4.6	4.6	18.0	18.1	14.2	14.4

(a) Melting points are uncorrected. (b) Analysis and melting point as reported without recrystallization. (c) Reference 7. (d) Reference 4. (e) Prepared from crude 2-amino-5-chloro-N-ethylaniline and recrystallized from ethyl acetate. (f) Reference 3.

TABLE II

2-Oxazolidinones and 2-Imidazolidinones



X	R	R ¹	Procedure	Yield, %	M. p., °C (a)	Literature M. p., °C	Formula	% Carbon		% Hydrogen		% Halogen		% Nitrogen	
								Calcd.	Found	Calcd.	Found	Calcd.	Found	Calcd.	Found
O	H	<i>m</i> -Cl	C (b)	50 (b)	52-53	53-53.5 (c)	C ₉ H ₉ ClNO ₂	54.7	55.1	4.1	4.1	17.9	17.9	7.1	6.9
CH ₃ N	CH ₃	H	D	83	48-49	48-49 (d)	C ₁₁ H ₁₄ N ₂ O	69.4	69.3	7.4	7.3			14.7	15.0
CH ₃ N	H	<i>m</i> -Cl	E	57	95-96	93-95 (d)	C ₁₀ H ₁₁ ClN ₂ O	57.0	56.8	5.3	5.4	16.8	17.0	13.3	13.7
CH ₃ N	H	<i>p</i> -CH ₃ O	E (e)	88	110-111	110-111 (f)	C ₁₁ H ₁₄ N ₂ O ₂	64.1	64.3	6.8	6.9			13.6	13.7

(a) Melting points are uncorrected. (b) Product was extracted into ether and distilled, b.p. 144-150°/0.1 mm. Crude yield before distillation was about 95%. (c) Reference 8. (d) Reference 5. (e) Prepared from *N*-(*p*-methoxyphenyl)-*N'*-methylethylenediamine monohydrochloride. (f) Reference 5 reported m.p. 100-110° through a typographical error.

EXPERIMENTAL (6)

Procedure A. 5-Chloro-2-benzimidazolinone.

A solution of 7.1 g. (0.05 mole) of 4-chloro-*o*-phenylenediamine in 50 ml. of dry tetrahydrofuran was cooled and a solution of 8.5 g. (0.052 mole) of N,N'-carbonyldiimidazole in 60 ml. of dry tetrahydrofuran was added rapidly with stirring. The cooling bath was removed and stirring was continued for 3 hours. Precipitation began within 5 minutes. The reaction mixture was diluted with 400 ml. of water, and the precipitate was filtered, washed with water, benzene and ether and dried in the oven at a temperature of 60°.

Procedure B. 5-Methoxy-2-benzimidazolinone.

A solution of 13.8 g. (0.1 mole) of 4-methoxy-*o*-phenylenediamine in 150 ml. of benzene was distilled until the distillate was clear in order to remove traces of moisture from the reagents. The reaction mixture was cooled and a solution of 16.2 g. (0.1 mole) of N,N'-carbonyldiimidazole in 100 ml. of dry tetrahydrofuran was added rapidly with stirring. The mixture was stirred at room temperature for 4 hours. The precipitate which separated was filtered, washed with tetrahydrofuran, benzene and ether and dried at a temperature of 60°.

Procedure C. 5-Chloro-3-ethyl-2-benzimidazolinone.

A solution of 2.0 g. of N,N'-carbonyldiimidazole in 20 ml. of dry tetrahydrofuran was added to a solution of 2.0 g. of crude 2-amino-5-chloro-N-ethylaniline (3) in 20 ml. of dry benzene. The solution was allowed to stand at room temperature for 18 hours and then heated on the steam bath for 3 hours. The reaction mixture was diluted with 40 ml. of water and concentrated to remove the organic solvents. The crystalline product was filtered, washed with water, dried and recrystallized from ethyl acetate.

Procedure D. 3,4-Dimethyl-1-phenyl-2-imidazolidinone.

A solution of 0.82 g. (0.005 mole) of N²-methyl-N¹-phenyl-1,2-propanediamine in 10 ml. of dry tetrahydrofuran was mixed with 1.05 g. (0.005 mole) of 77% N,N'-carbonyldiimidazole and the solution was

allowed to stand at room temperature for 7 days. The reaction mixture was concentrated to remove the solvent and the residue was extracted with ether. The ether layer was washed with water, dried over magnesium sulfate, and concentrated. The residue was triturated with petroleum ether and the product was filtered.

Procedure E. 1-(*m*-Chlorophenyl)-3-methyl-2-imidazolidinone.

A mixture of 1.10 g. (0.0032 mole) of N-(*m*-chlorophenyl)-N'-methyl-ethylenediamine dihydrochloride and 0.54 g. (0.0033 mole) of N,N'-carbonyldiimidazole in 30 ml. of dry tetrahydrofuran was heated on the steam bath for 2 hours and diluted with 10 ml. of water. The reaction mixture was concentrated to remove the tetrahydrofuran, and the product was extracted into benzene. The benzene layer was washed with water, dried over magnesium sulfate and concentrated to remove the solvent. The crystalline product was warmed with a little hexane, cooled and filtered.

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