

## Aminimides IX (1). A General Synthesis of 1-Substituted-2-imidazolidinones (2)

David Aelony and William J. McKillip

Research Laboratories, Ashland Oil Co., Columbus, Ohio

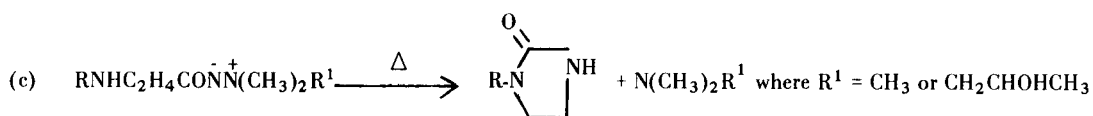
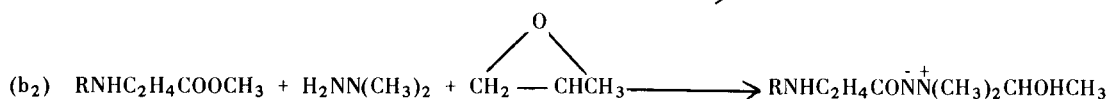
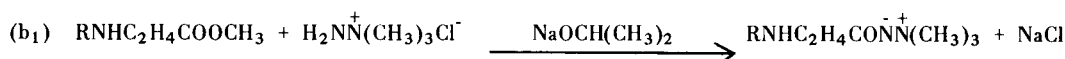
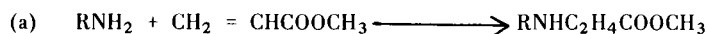
Received August 7, 1971

A general method for the preparation of 1-substituted-2-imidazolidinones has been developed. It consists of the addition of primary amines to acrylic esters, conversion of the esters to the corresponding aminimides and thermolysis of the aminimides to the 1-substituted imidazolidinones.

Substituted 2-imidazolidinones find actual and potential uses in bactericides, central nervous system depressants, plant growth promoters, female fly sterilants, adhesives, wrinkle resisting textiles and monomers for polymerization and copolymerization. Of particular interest is the use of 1-*m*-chlorophenyl-2-imidazolidinone as an intermediate in the synthesis of tranquilizers (3).

*N*-Substituted-2-imidazolidinones have been prepared by many different methods (4). We are proposing a new general synthesis of 1-substituted-2-imidazolidinones, based on the extension of aminimide chemistry, proved to be successful. Previous investigations conducted in this laboratory have shown the utility of aminimide to isocyanate conversion (1a,1b,1c). The thermally induced rearrangement of functionally substituted aminimides to isocyanates is of specific interest as a synthetic tool (1a). In this paper, the synthesis of functionally substituted aminimides is again described and a new synthetic method is proposed. The method consists of (a) addition of primary amines to acrylic esters, (b) conversion of the adduct to the aminimide, (c) thermolysis of the aminimide to the 1-substituted-2-imidazolidinone. In step (b), when weak aromatic primary amines are used, triethyl amine should be used as a catalyst. A combination of 1,1-dimethyl hydrazine with propylene oxide can be used instead of the *in situ* generated trimethylammonium imine.

The following equations illustrate the steps involved:



In general, addition yields are very good. Primary aliphatic amines are sufficiently strong bases and do not require base catalysts. *m*-Chloroaniline is considerably more sluggish than aniline, and although it gives low conversions the yields are quite acceptable. When methylamine is used, it is impossible to prevent the formation of large amounts of diadduct. In this case, the adducts can be separated by fractional distillation. A slight excess of acrylates prevents the formation of amide of the adduct.

The aminimides (procedure b<sub>1</sub>) are best prepared by dissolving sodium in boiling isopropanol (containing 4% methanol by volume to attain better solubility of the alkoxide), cooling the solution to 60° and adding trimethylhydrazinium chloride followed by the adduct. The mixture is agitated at 40-60° for several hours and allowed to stand overnight. The precipitated salt is filtered and the combined filtrates evaporated *in vacuo* below 60°. The residue is extracted with hot tetrahydrofuran or acetone which removes small amounts of unreacted trimethylhydrazinium chloride or sodium alkoxide. The total extract is evaporated *in vacuo* below 60° and the residue isolated and then recrystallized from suitable solvents.

The recommended procedure for method b<sub>2</sub> is to dissolve the adduct in an equal volume of 2-propanol. Molecular equivalents of freshly distilled 1,1-dimethylhydrazine and propylene oxide are added and the resulting solution is agitated at 80° until an infrared analysis shows no ester band in the 1740-1730 cm<sup>-1</sup> region. Two or three additions of small quantities of dimethyl hydrazine and propylene oxide are often necessary to compensate for possible losses due to volatility of these compounds. 2-Propanol is evaporated *in vacuo* below 60° and the residue is extracted with ether (most aminimides are quite insoluble

TABLE I  
 Summary of RNHC<sub>2</sub>H<sub>4</sub>COOCH<sub>3</sub> Preparations

R	Empirical Formulas	% Yield of Monoadduct	b.p. <sup>o</sup> (mm)	m.p. <sup>o</sup>	C	H	N	Cl	C	H	N	Cl
<i>n</i> -butyl allyl phenyl	C <sub>8</sub> H <sub>17</sub> NO <sub>2</sub> C <sub>7</sub> H <sub>13</sub> NO <sub>2</sub> C <sub>10</sub> H <sub>13</sub> NO <sub>2</sub>	70 84 87	37 (0.2) 40 (0.3) 112-120 (0.4-0.6)	37	58.74	9.09	9.79		58.67	9.07	9.65	
<i>m</i> -chloro-phenyl	C <sub>10</sub> H <sub>12</sub> ClNO <sub>2</sub> <i>m</i> -chloro-phenyl (a)	96	124-130 (0.35-0.4)		56.26	5.63	6.56	16.63	56.08	5.96	6.76	16.54
<i>m</i> -tolyl	C <sub>11</sub> H <sub>15</sub> NO <sub>2</sub>	80	121-127 (0.45)									
furfuryl	C <sub>9</sub> H <sub>13</sub> NO <sub>3</sub>	76	77-85 (0.23)		59.00	7.17	7.65		58.91	7.17	7.92	
3-picoyl	C <sub>10</sub> H <sub>14</sub> N <sub>2</sub> O <sub>2</sub>	76	122-126 (0.2)									
2-pyridino ethyl	C <sub>11</sub> H <sub>16</sub> N <sub>2</sub> O <sub>2</sub>	84	118-138 (0.3-0.4)		63.46	7.69			63.57	7.75		

(a) The yield was corrected for recovered, unreacted *m*-chloroaniline.

Notes

TABLE II

Summary of RNHC<sub>2</sub>H<sub>4</sub>CONN(CH<sub>3</sub>)<sub>2</sub>R<sup>1</sup> Synthesis

Empirical Formulas	R	R <sup>1</sup>	% Yield of Aminimide	m.p. <sup>o</sup>	C	H	N	Cl	C	H	N	Cl
C <sub>10</sub> H <sub>23</sub> N <sub>3</sub> O	<i>n</i> -butyl	CH <sub>3</sub>	85	34-38 (c)	59.65	11.54	20.87		59.64	11.23	20.61	
C <sub>9</sub> H <sub>19</sub> N <sub>3</sub> O	allyl	CH <sub>3</sub>	93	Liquid	58.38	10.27	22.70		58.00	10.00	22.97	
C <sub>12</sub> H <sub>19</sub> N <sub>3</sub> O	phenyl	CH <sub>3</sub>	83	125.5-126.5 (a)	65.16	8.60	19.00		65.06	8.40	19.25	
C <sub>14</sub> H <sub>23</sub> N <sub>3</sub> O <sub>2</sub>	phenyl	CH <sub>2</sub> CHOHCH <sub>3</sub>	85	103.5-107 (b)	63.40	8.68	15.85		63.21	8.74	15.56	
C <sub>12</sub> H <sub>18</sub> ClN <sub>3</sub> O	<i>m</i> -chloro-phenyl	CH <sub>3</sub>	84	98-99 (a)	56.36	7.15	16.43		56.71	7.13	16.59	
C <sub>14</sub> H <sub>22</sub> ClN <sub>3</sub> O <sub>2</sub>	<i>m</i> -chloro-phenyl	CH <sub>2</sub> CHOHCH <sub>3</sub>	87	103.5-104.5 (d)	56.09	7.35	14.02	11.85	56.14	7.46	13.95	11.52
C <sub>13</sub> H <sub>21</sub> N <sub>3</sub> O	<i>m</i> -tolyl	CH <sub>3</sub>	81	100.5-101.5 (b)	66.38	8.94	17.87		66.24	8.97	18.09	
C <sub>10</sub> H <sub>17</sub> N <sub>3</sub> O <sub>2</sub>	furfuryl	CH <sub>3</sub>	94	Liquid	58.67	8.44	18.67		58.35	8.35	18.46	
C <sub>12</sub> H <sub>20</sub> N <sub>4</sub> O	3-picoyl (c)	CH <sub>3</sub>	100	Liquid								
C <sub>13</sub> H <sub>22</sub> N <sub>4</sub> O	2-pyridino-ethyl	CH <sub>3</sub>	94	94-95 (b)	62.83	6.81	22.00		62.79	6.66	22.18	

(a) Recrystallized from acetone. (b) Recrystallized from benzene. (c) Benzene extract was evaporated *in vacuo* crystallized on standing. (d) Dissolved in methanol and precipitated with ether. (e) The compound decomposes slowly at room temperature and, therefore, it could not be properly analyzed.

TABLE III

Thermolysis of Aminimides to 1-Substituted-2-imidazolidinones

Empirical Formulas	R	% Yield of Imidazolidinone	m.p. <sup>o</sup>	b.p. <sup>o</sup> (mm)	Calculated %			Found %		
					C	H	N	C	H	N
C <sub>7</sub> H <sub>14</sub> N <sub>2</sub> O	<i>n</i> -butyl	88	36-39 (j)	102 (0.3)	59.11	9.94	19.70	58.98	9.97	19.58
C <sub>6</sub> H <sub>10</sub> N <sub>2</sub> O	allyl	82	56.5-58 (j)	95 (0.25)	57.12	8.00	22.21	57.38	7.98	21.90
C <sub>9</sub> H <sub>16</sub> N <sub>2</sub> O	cyclohexyl	82	167-167.5 (g)		64.72	9.60	16.65	64.83	9.51	16.77
C <sub>9</sub> H <sub>10</sub> N <sub>2</sub> O	phenyl (a)	90	162-162.5 (e)							
C <sub>9</sub> H <sub>10</sub> N <sub>2</sub> O	phenyl (b)	80	161-163 (e)							
C <sub>9</sub> H <sub>9</sub> ClN <sub>2</sub> O	<i>m</i> -chloro-phenyl	64	126-126.5 (h)		54.97	4.62	14.25	54.83	4.60	14.37
C <sub>9</sub> H <sub>9</sub> ClN <sub>2</sub> O	<i>m</i> -chloro-phenyl (b)	90	126-127							17.85
C <sub>10</sub> H <sub>12</sub> N <sub>2</sub> O	<i>m</i> -tolyl (c)	85	142.5-143 (e)							
C <sub>7</sub> H <sub>8</sub> N <sub>2</sub> O <sub>2</sub>	furfuryl	61	97.5 (d)	131-135 (0.3)	57.83	6.02	16.87	57.72	6.09	17.05
C <sub>9</sub> H <sub>11</sub> N <sub>3</sub> O	3-picolyl	31	92-93.5 (f)		61.02	6.21	23.73	61.30	6.42	23.62
C <sub>10</sub> H <sub>13</sub> N <sub>3</sub> O	2-pyridino-ethyl	35	93-94.5 (e)		62.83	6.81	22.00	62.79	6.66	22.18

(a) Thermolysis was carried out in boiling mesitylene in 5 hours instead of in xylene for 48 hours. It was prepared originally by H. E. Newman, *Ber.*, **24**, 2192 (1889). (b) Aminimide prepared by b<sub>2</sub> procedure was used. (c) Prepared previously by H. Najer, R. Giudicelli, J. Menin, and C. Morel. (d) Recrystallized from acetone. (e) Recrystallized from benzene. (f) Recrystallized from ethyl acetate. (g) Recrystallized from xylene. (h) Recrystallized from methanol. (i) Recrystallized from methanol-acetone mixture. (j) Distillates crystallized on standing.

in ether). Aminimides are generally quite hygroscopic, especially those made by the  $b_2$  method.

Thermolysis of aminimides is best conducted in dilute solutions in dry solvents, such as, mesitylene, xylenes, and diethyl benzenes. Thermolyses are run at reflux until the disappearance of the aminimide peak at  $1590\text{--}1560\text{ cm}^{-1}$ . The solution after it is filtered hot, is either allowed to crystallize or is evaporated and the residue recrystallized from a suitable solvent. In most cases, when mesitylene is used as a solvent, thermolysis is complete in 2-4 hours.

Results of primary amine to acrylate addition are summarized in Table I.

Aminimide preparations are given in Table II.

Results of thermolyses of the aminimides in boiling xylene (1:10 ratio) are given in Table III.

#### EXPERIMENTAL

Each reaction step is illustrated by a single example.

##### Addition of Allylamine to Methyl Acrylate.

Methyl acrylate (176 g., 2.04 moles) was added at once to a solution of 114 g. (2 moles) of allylamine in 200 ml. of methanol. The reaction was highly exothermic. The solution was cooled and allowed to stand over a period of two days. The product was evaporated in a rotary evaporator at  $55^\circ$  and 10 mm. The residue was fractionated in high vacuum through a pear topped by a 1' Vigreux column;  $\text{ir } 3340\text{ cm}^{-1}$  (N-H),  $3080\text{ cm}^{-1}$  (CH=CH),  $1730\text{ cm}^{-1}$  (C=O).

Fraction No. 1	b0.25	$40^\circ$	weighed	219.6 g.
Fraction No. 2	b0.25	$40\text{--}90^\circ$	weighed	3 g. (the column was removed)
Fraction No. 3	b0.25	$90\text{--}100^\circ$	weighed	37 g. (diadduct)
Residue				0.8 g.

*Anal.* Calcd. for  $\text{C}_7\text{H}_{13}\text{NO}_2$ : C, 58.74; H, 9.09; N, 9.79. Found: C, 58.67; H, 9.07; N, 9.65.

##### Trimethylammonium-*N*-( $\beta$ -butylpropionyl)imine.

Sodium metal (9.9 g., 0.43 mole) was dissolved in a refluxing mixture of 500 ml. of 2-propanol and 20 ml. of methanol. The solution was cooled to  $60^\circ$ . Trimethylhydrazinium chloride (47.5 g.) was added in one portion and was followed by methyl *N*-butyl- $\beta$ -amino propionate (68.4 g.). The mixture was agitated for 5 hours at  $55^\circ$  and was allowed to stand overnight. The product was filtered and the salt was extracted with boiling 2-propanol. The combined filtrates were evaporated *in vacuo* at  $60^\circ$ . The residue weighed 73.7 g. (85.2% theory). It was a nearly colorless liquid which suddenly crystallized with a considerable amount of heat. The solid, which was very hygroscopic, melted at  $34\text{--}38^\circ$ ;  $\text{ir } 3298\text{ cm}^{-1}$  (N-H),  $1585\text{ cm}^{-1}$  (C=O of aminimide).

*Anal.* Calcd. for  $\text{C}_{10}\text{H}_{23}\text{N}_3\text{O}$ : C, 59.65; H, 11.54; N, 20.87. Found: C, 59.64; H, 11.23; N, 20.61.

##### 1,1-Dimethyl-1-(2-hydroxypropyl)ammonium-(*N*-phenyl- $\beta$ -aminopropionyl)imine.

Methyl *N*-phenyl- $\beta$ -aminopropionate (0.25 mole) was dissolved in 45 ml. of 2-propanol. Freshly distilled 1,1-dimethylhydrazine (16 g.) and propylene oxide (15 g.) were added. An increase in

temperature to  $45^\circ$  was observed. The reaction was allowed to agitate overnight at this temperature. Infrared analysis indicated a shoulder at  $1740\text{ cm}^{-1}$  which persisted even after additional agitating and heating for 2 hours at  $80^\circ$ . Two g. each of 1,1-dimethylhydrazine and propylene oxide were added and the agitation at  $80^\circ$  continued for several additional hours after which the  $1740\text{ cm}^{-1}$  shoulder disappeared completely. The product was evaporated *in vacuo* below  $80^\circ$ . The residue was dissolved in 350 ml. of boiling benzene, allowed to cool to room temperature, filtered, washed with ether, and dried. The first crop weighed 56.1 g., m.p.  $98\text{--}104^\circ$  (very hygroscopic);  $\text{ir } 3240\text{ cm}^{-1}$  (N-H), 1600 (C-H aromatic), 1580 (C=O of aminimide). The mother liquors were evaporated to 40 ml., cooled, filtered, washed with ether, and dried *in vacuo*. The second crop weighed 7.2 g., m.p.  $98\text{--}104^\circ$ .

*Anal.* Calcd. for  $\text{C}_{14}\text{H}_{23}\text{N}_3\text{O}_2$ : C, 63.40; H, 8.68; N, 15.85. Found: C, 63.21; H, 8.74; N, 15.56.

##### Thermolysis of Trimethylammonium-*N*-(phenyl- $\beta$ -aminopropionyl)imine.

Trimethylammonium-*N*-(phenyl- $\beta$ -aminopropionyl)imine (20.1 g.) was thermolyzed in 200 ml. of dry mesitylene under reflux for 5 hours. The solution was filtered hot. Precipitation of the filtrate began at  $100^\circ$ . The precipitate was filtered at room temperature, washed with ether and dried. The beautiful long needles weighed 13.2 g. (90% of theory) and melted at  $162\text{--}162.5^\circ$ . The mother liquor was evaporated to 35 ml. yielding 0.4 g. needles, m.p.  $142\text{--}160^\circ$ . The evaporated mother liquor, which was a viscous liquid, weighed 1 g.

#### REFERENCES

- (1a) W. J. McKillip, L. M. Clemens, and R. Haugland, *Can. J. Chem.*, **45**, 2613 (1967); (b) W. J. McKillip and R. C. Slagel, *ibid.*, **45**, 2619 (1967); (c) R. C. Slagel and A. E. Blomquist, *ibid.*, **45**, 2625 (1967); (d) B. M. Culbertson and R. C. Slagel, *J. Polymer Sci. Part A-1*, **6**, 363 (1968); (e) B. M. Culbertson, E. A. Sedor, S. Dietz, and R. E. Freis, *ibid.*, Part A-1, **6**, 2197 (1968); (f) R. C. Slagel, *J. Org. Chem.*, **33**, 1374 (1968); (g) B. M. Culbertson, E. A. Sedor, and R. C. Slagel, *Macromolecules*, **1**, 254 (1968); (h) B. M. Culbertson and R. E. Freis, *ibid.*, **3**, 715 (1970).
- (2) The bulk of the paper was presented at the Second Regional ACS Meeting at Ohio State University, Columbus, June 3-6 (1970).
- (3) W. B. Wright, Jr., H. J. Brabander, R. A. Hardy, Jr., and A. C. Osterberg, *J. Med. Chem.*, **9**, 852 (1966); W. B. Wright, Jr., H. J. Brabander, and R. A. Hardy, Jr., *ibid.*, **9**, 858 (1966).
- (4) F. Baiocchi, R. A. Franz, and L. Horwitz, *J. Org. Chem.*, **21**, 1546 (1956); R. Duschinsky and L. A. Nolan, *J. Am. Chem. Soc.*, **68**, 2350 (1946); C. J. M. Stirling, *J. Chem. Soc.*, 4531 (1958); H. Najer, R. Giudicelli, J. Menin and C. Morel, *Bull. Soc. Chim. France*, 323 (1963); B. Abramoritch, U. S. Patent, 2,518,264; E. Gulbins, R. Morlock, and K. Hamann, *Am.*, **698**, 180-5; W. B. Wright, Jr., H. J. Brabander, R. A. Hardy, Jr., *J. Med. Chem.*, **9**, 858 (1966).