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Studies on Heteroaromatic N-Oxides. XI.[1] Aminolysis of Esters of Benzazole N-Oxides and Related Quaternary Salts

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In connection with the abnormal reaction of ethyl 1-methyl-2-benzimidazolecarboxylate 3-oxide (**1**) with piperidine, aminolyses of several related esters were investigated. The esters: **1**, 2-ethoxycarbonyl-1,3-dimethylbenzimidazolium iodide (**11**), 2-methoxycarbonylmethyl-1,3-dimethylbenzimidazolium iodide (**17**), ethyl 2-benzothiazolecarboxylate 3-oxide (**26**) and 2-ethoxycarbonyl-3-methylbenzothiazolium perchlorate (**34**) under went abnormal aminolysis partly or predominantly, not only with secondary amine (piperidine) but also with some primary amines, to give the corresponding carbamates. Ethyl tribromoacetate (**57**) also underwent abnormal cleavage with some primary amines.

On the other hand, ethyl 1-methyl-2-benzimidazolecarboxylate (**21**), ethyl 2-benzothiazolecarboxylate (**37**), ethyl 2- and 4-pyridinecarboxylate N-oxide (**44**, **45**) 4-ethoxycarbonyl-1-methylpyridinium iodide (**55**) reacted with both primary and secondary amines to yield only normal products, amides.

Mechanisms accounting for the different behavior of the esters towards amines have been discussed from electronic and steric points of view.

In Part VIII of this series,[3] we reported that the reaction of ethyl 1-methyl-2-benzimidazolecarboxylate 3-oxide (**1**) with piperidine did not give the anticipated amide (**2**) but a mixture of 1-methylbenzimidazole 3-oxide (**3**) and ethyl piperidinocarboxylate (**4**), while the reaction with ammonia or methylamine gave the normal product, amide. A very similar type of reaction of ethyl trichloroacetate was reported by Joullié and co-workers[4]; treatment of the ester with secondary amines gave predominantly chloroform and the corresponding carbamates, while treatment with primary amines gave the normal products, amides. They postulated that the difference in behavior between primary and secondary amines might be due to the relative acidities (tendency for proton transfer) of the N–H bonds in the intermediate complexes.

The present work was undertaken to see whether any other esters of heteroaromatic carboxylic acids undergo abnormal aminolysis and to shed light on the reaction mechanism.

Esters of 1-methyl-2-benzimidazolecarboxylic acid 3-oxide, 2-benzothiazolecarboxylic acid 3-oxide, pyridinecarboxylic acid N-oxides, and related quaternary salts were treated with various amines (ammonia, butylamine, isopropylamine, *tert*-butylamine, and piperidine). Esters of the corresponding parent compounds and ethyl tribromoacetate were also treated with the amines for comparison.

Reactions of 1-Methylbenzimidazole Derivatives

Whereas reactions of the N-oxide **1** with primary amines such as ammonia, butylamine and isopropylamine gave the corresponding amides (**5**—**7**) exclusively, the reaction with *tert*-butylamine gave the corresponding carbamates (**9**) and **3**, in addition to the amide (**8**) and 2-*tert*-butylamino-1-methylbenzimidazole (**10**).

1) Part X: S. Takahashi, S. Hashimoto, and H. Kanō, *Chem. Phamr. Bull.* (Tokyo), **18**, 1176 (1970).
2) Location: *Fukushima-ku, Osaka, 553, Japan.*
3) S. Takahashi and H. Kanō, *Chem. Pharm. Bull.* (Tokyo), **16**, 527 (1968).
4) *a*) M.M. Joullié and A.R. Day, *J. Am. Chem. Soc.*, **76**, 2990 (1954); *b*) M.M. Joullié, *ibid.*, **77**, 6662 (1955); *c*) A.C. Pierce and M.M. Joullié, *J. Org. Chem.*, **28**, 658 (1963).

The reaction of 2-ethoxycarbonyl-1,3-dimethylbenzimidazolium iodide (**11**) gave the corresponding carbamates (**13**—**15**, **9**, **4**) and 1,3-dimethylbenzimidazolium iodide (**12**),[5] not only with piperidine but also with all the primary amines even at room temperature (for 2—4 days). A ring expanded product, 1,4-dimethyl-2,3-quinoxalinedione (**16**)[6] was also obtained as a by-product of the reaction with *tert*-butylamine.

2-Methoxycarbonylmethyl-1,3-dimethylbenzimidazolium iodide (**17**), in which the ester portion is separated from the hetero ring by a methylene group, underwent abnormal cleavage on reaction with ammonia, butylamine, and piperidine at 100° to yield 1,2,3-trimethylbenzimidazolium iodide (**18**)[7] and the corresponding carbamates (**14'**, **15'**, **4'**; except with ammonia). The reactions with butylamine and isopropylamine gave amides (**19**, **20**) in addition to the carbamates **14** and **15**. The quaternary salt, **17**, however, did not react with *tert*-butylamine.

Ethyl 1-methyl-2-benzimidazolecarboxylate (**21**),[8] underwent reaction with the amines (except *tert*-butylamine, with which no reaction occurred) to yield the corresponding amides (**22**—**25**) exclusively.

Reactions of Benzothiazole Derivatives

Reactions of ethyl 2-benzothiazolecarboxylate 3-oxide (**26**)[1] with ammonia, isopropylamine, *tert*-butylamine, and piperidine at 60—100° gave predominantly the corresponding amides (**27**—**30**), although small amounts of carbamates (**9**, **4**) were detected in the reactions with *tert*-butylamine and with piperidine. The reaction of **26** with butylamine gave N,N'-dibutyloxalamide (**31**)[9] as the sole product and the reaction with *tert*-butylamine gave N,N'-di-*tert*-butyloxalamide (**32**)[10] as a by-product.

On reaction with piperidine, 2-piperidinobenzothiazole 3-oxide (**33**) was obtained as a by-product.

Formation of **33** can be explained by a mechanism involving initial abnormal aminolysis of **26** followed by nucleophilic attack of piperidine on the initially formed benzothiazole N-oxide, although no hydrogen acceptor could not be detected in the latter step. The compound **33** was actually found to be obtained by the reaction of benzothiazole N-oxide with piperidine. A reaction of this type with quinoline N-oxide was reported by Kato, *et al.*[11]; who have disclosed that 2-phenylquinoline N-oxide was obtained on treatment with phenylmagnesium bromide.

Reactions of 2-ethoxycarbonyl-3-methylbenzothiazolium perchlorate (**34**) with the amines, unlike those of the corresponding benzimidazolium salt, gave the ring opened product, 2,2'-dithio-bis(N-methylaniline) (**35**)[12] as the major product. Small amounts of carbamates (**15**, **4**) were obtained from the reactions with isopropylamine and piperidine. Reactions with butylamine, isopropylamine, and *tert*-butylamine gave the corresponding oxaldiamides (**31**,[9] **36**,[13] **32**[10]) as by-product.

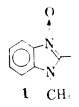
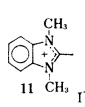
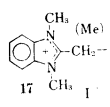
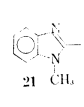
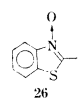
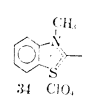
Reactions of ethyl 2-benzothiazolecarboxylate (**37**) with the amines gave the corresponding amides (**38**—**42**) almost exclusively. In the reactions with butylamine, isopropylamine, and *tert*-butylamine, a minute amount of benzothiazole (**43**) was detected; however, the formation of **43** may involve hydrolysis of ester and successive decarboxylation because the corresponding carbamates could not be detected.

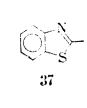
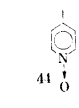
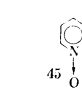
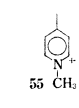
5) Cf. E. Hayashi, T. Ishikawa, and M. Inaoka, *Yakugaku Zasshi*, **80**, 838 (1960).
6) G.T. Newbold and F.S. Spring, *J. Chem. Soc.*, **1948**, 519.
7) R.N. Shriner and P.G. Bōermans, *J. Am. Chem. Soc.*, **66**, 1810 (1944).
8) S. Takahashi and H. Kanō, *Chem. Pharm. Bull.* (Tokyo), **12**, 1290 (1964).
9) L.M. Rice, C.H. Grogan, and E.E. Reid, *J. Am. Chem. Soc.*, **75**, 242 (1953).
10) M. Brander, *Rec. Trav. Chim.*, **37**, 67 (1917) [*C.A.*, **12**, 1467 (1918)].
11) T. Kato and H. Yamanaka, *J. Org. Chem.*, **30**, 910 (1965).
12) A.I. Kiprianov and Z.N. Pazenko, *Z. Obshch. Khim.*, **19**, 1923 (1949) [*C.A.*, **44**, 3488 (1950)].
13) C. Dermer and J.W. Hutchson, *Proc. Oklahoma Acad. Sci.*, **23**, 60 (1943) [*C.A.*, **38**, 2006 (1944)].

TABLE I. Products of Aminolysis of the Esters

$$RCO_2Et \xrightarrow{\text{Amine}} \text{Amide (A) and/or RH+Carbamate (C)}$$

A (%), RH (%), C (%), Others (%)

Amine	R-CO_2Et (R-)					
	 1	 11	 17	 21	 26	 34
NH_3	**5** (100)	(0)	(0)	**22** (90)	**27** (92)	(0)
	(0)	**12** (100)	**18** (95)	(0)	(0)	(0)
	(0)	**13** (68)	(0)	(0)	(0)	(0)
	—	—	—	—	—	**35** (84)
$BuNH_2$	**6** (90)	(0)	**19** (47)	**23** (90)	(0)	(0)
	(0)	**12** (100)	**18** (37)	(0)	(0)	(0)
	(0)	**14** (42)	**14'**(4)	(0)	(0)	(0)
	—	—	—	—	**31** (70)	**31** (87), **35** (40)
iso-$PrNH_2$	**7** (82)	(0)	**20** (40)	**24** (85)	**28** (63)	(0)
	(0)	**12** (100)	**18** (45)	(0)	(0)	(0)
	(0)	**15** (50)	**15'**(17)	(0)	(0)	**15** (3)
	—	—	—	—	—	**35** (28), **36** (93)
tert-$BuNH_2$	**8** (16)	(0)	no reaction	no reaction	**29** (83)	(0)
	3 (54)	**12** (72)			(0)	(0)
	9 (<10)	**9** (<10)			**9** (<10)	(0)
	10 (19)	**16** (27)			**32** (6)	**32** (80), **35** (46)
	**2** (0)	(0)	(0)	**25** (80)	**30** (78)	(0)
	3 (100)	**12** (100)	**18** (100)	(0)	(0)	(0)
	4 (45)	**4** (36)	**4'**(100)	(0)	**4** (10—20)	**4** (25)
	—	—	—	—	**33** (7)	**35** (35)

Amine	R-CO_2Et (R-)				Br_3C- **57**	Cl_3C- **62**
	 37	 41	 45	 55		
NH_3	**38** (100)	**46** (100)	**50** (85)	**56** (100)	**58** (85)	(81)[4a]
	(0)	(0)	(0)	(0)	(0)	(0)
	(0)	(0)	(0)	(0)	(0)	(0)
	—	—	—	—	—	—
$BuNH_2$	**39** (95)	**47** (86)	**51** (90)	tar	**59** (5)	(92)[4c]
	43 (~1)	(0)	(0)		**61** (35)	(8)
	(0)	(0)	(0)		**14** (90)	(8)
	—	—	—		—	—
iso-$PrNH_2$	**40** (90)	**48** (90)	**52** (100)	tar	**60** (15)	(83)[4a]
	43 (~1)	(0)	(0)		**61** (20)	(0)
	(0)	(0)	(0)		**15** (75)	(0)
	—	—	—		—	—
tert-$BuNH_2$	**41** (75)	no reaction	**53** (75)	tar	tar	(54)[4a]
	43 (~1)		(0)			(0)
	(0)		(0)			(0)
	—		—			—
	**42** (90)	**49** (60)	**54** (70)	tar	tar	(8)[4c]
	(0)	(0)	(0)			(92)
	(0)	(0)	(0)			(92)
	—	—	—			—

Reaction of Pyridine Derivatives and of Tribromoacetate

Reaction of ethyl 4- and 2-pyridinecarboxylate 1-oxides (**44**, **45**) with the amines gave the corresponding amides (**46**—**49**; **50**—**54**) except the reaction with *tert*-butylamine, in which the ester was recovered.

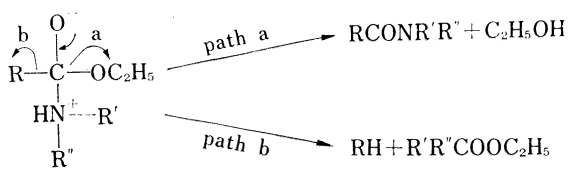
Reaction of 4-ethoxycarbonyl-1-methylpyridinium iodide (**55**) with ammonia gave the amide (**56**) quantitatively. The reactions with the other amines gave only tarry products, and the reactions with *tert*-butylamine and piperidine gave the corresponding amine hydroiodides accompanied with tar.

Ethyl tribromoacetate (**57**) underwent abnormal aminolysis more readily than trichloroacetate; reactions with butylamine and isopropylamine at room temperature gave the corresponding carbamates (**14**,**15**) as the major products, and the amides (**59**, **60**) as minor products. The reactions with *tert*-butylamine and piperidine gave tarry products, from which the corresponding amine hydrobromides were isolated.

All the products thus obtained and also those from ethyl trichloroacetate (**62**) are shown in Table I.

Discussion

Reactions of esters with amines are generally assumed to proceed *via* tetrahedral transition complexes (**63**), which undergo C–OC_2H_5 cleavage (path a) to yield amides with alcohol as the leaving group. On the other hand, the abnormal R–C cleavage (path b) gives RH and carbamates.



63

The difference in behavior between primary and secondary amines towards most of the esters can be rationalized by the same mechanism as that postulated by Joullie, *et al.* in the aminolysis of ethyl trichloroacetate; the tendency for proton transfer from the complex **63** formed with primary amine (R′=H) might be greater than that from the complex formed with secondary amine (R′≠H, R″≠H), accordingly, the former complex would assist the C–OC_2H_5 cleavage by donating proton to the leaving $C_2H_5O^-$ group more effectively.

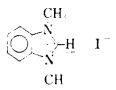
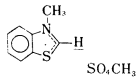
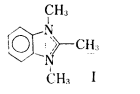
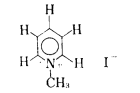
The products of the reactions of butylamine and isopropylamine with **17** and **57**, and those of the reactions of *tert*-butyl amine with **1** and **26**, contain both amides and carbamates. This suggests that two types of reaction can proceed competitively and that the bulkiness of the amides and the character of the R groups might influence the competing reactions.

For example, the distinct difference of the products of the reactions of *tert*-butylamine and isopropylamine with **1** can be explained by the steric factor; the complex (**63**) for *tert*-butylamine is more sterically crowded than that for isopropylamine and the strain in the former complex would be relieved by releasing the more bulky R group (compared with C_2H_5O group). In some cases, **17** and **21** for example, the *tert*-butyl group is too bulky to form the transition complex and no reaction occurs.

It is clear that the character of the R group influences the reaction mode most distinctly, and the tendency to cause R–C cleavage is in the following order: **11**>**57**≫**17**≫**1**>**26**≫ the other esters (see Table I).

The tendency to cause R–C cleavage may be related to that of forming the carbanion R^-. As an indicator of this tendency, the rates expressed as the half-life of hydrogen-deuterium exchange for some of the RH are listed in Table II. A rough relationship between the tendencies and the rates is noticed, except for compound (**17**).

Table II. Hydrogen-deuterium Exchange Rate (half life)

Compound	$\tau 1/2$	Compound	$\tau 1/2$
	<3 min (estimated)		*ca.* 130 min
	*ca.* 60 min		≫5 hr
	*ca.* 60 min		≫5 hr

Notes 1) The rate was determined by NMR in D_2O at 39°. 2) Both pD and ionic strength were not controlled. 3) 1-Methylbenzimidazole 3-oxide, benzothiazole 3-oxide, and 3-methylbenzothiazolium methosulfate were dissolved in D_2O in concentrations of *ca.* 0.5M; other compounds were in lower concentrations owing to their low solubility.

However, it is noticed that there is an intimate relationship between the ease of abnormal aminolysis of the esters and that of decarboxylation of the correspondihg acids; the carboxylic acids derived from the ester (**1**, **11**, **17**, **26**) are decarboxylated within a month even at room temperature. This result seems reasonable since a linear relationship between the relative rate of carbanion formation and the rate of decarboxylation of the corresponding acid was reported by Hine, *et al.*[14]

Experimental[15]

2-Ethoxycarbonyl-1,3-dimethylbenzimidazolium Iodide (**11**)——Ethyl 1-methyl-2-benzimidazolecarboxylate (2.0 g) was dissolved in methyl iodide (20 ml). After a few minutes, the clear solution became turbid and then an oily product precipitated, solidifying after *ca.* 1 hr. The solution was allowed to stand overnight at room temperature and the crystalline product was collected by filtration washed with AcOEt. Recrystallization from CH_3CN–AcOEt at room temperature to give yellow needles, mp 148° (decomp.). *Anal.* Calcd. for $C_{12}H_{15}O_2N_2I$: C, 41.63; H, 4.38; N, 8.09. Found: C, 41.73; H, 4.42; N, 7.95.

When recrystallized from a hot solution, the salt decomposed to 1,3-dimethylbenzimidazolium iodide.

2-Methoxycarbonylmethyl-1,3-dimethylbenzimidazolium Iodide (**17**)——Methyl 1-methyl-2-benzimizazoleacetate[16] (300 mg) was dissolved in methyl iodide (6.0 ml). After *ca.* 0.5 hr, a crystalline product precipitated from the solution. The solution was allowed to stand overnight at room temperature and the product was collected (475 mg). Recrystallization from CH_3CN–AcOEt gave colorless prisms, mp 185° (decomp.). *Anal.* Calcd. for $C_{12}H_{15}O_2N_2I$: C, 41.63; H, 4.37; N, 8.09. Found: C, 41.71; H, 4.39; N, 7.89.

2-Ethoxycarbonyl-3-methylbenzothiazolium Methosulfate——A solution of ethyl 2-benzothiazolecarboxylate (4.5 g) and dimethyl sulfate (10 ml) in CH_2Cl_2 (20 ml) was refluxed for 3 hr, and then evaporated. The residue was triturated with ether and the insoluble material was recrystallized from EtOH–AcOEt to give colorless prisms, mp 144—146°. *Anal.* Calcd. for $C_{12}H_{15}O_6NS_2$: C, 43.25; H, 4.54; N, 4.20. Found: C, 43.73; H, 4.50; N, 4.13.

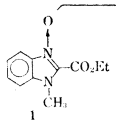
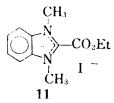
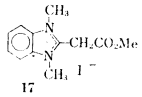
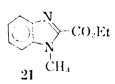
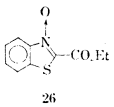
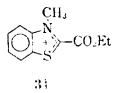
2-Ethoxycarbonyl-3-methylbenzothiazolium Perchlorate (**34**)——To a solution of the methosulfate obtained above (3.10 g) in H_2O (30 ml) was added $HClO_4$ (60%, 2.0 ml) dropwise with stirring. After a while, a crystalline product precipitated. After the mixture was allowed to stand at room temperature

14) J. Hine, N.W. Burske, M. Hine, and P.B. Langford, *J. Am. Chem. Soc.*, **79**, 1406 (1957).

15) All melting points were taken on a Kofler hot stage and are uncorrected. Solvents were removed under reduced pressure using a rotary evaporator. Gas–liquid chromatography analyses were carried out on a Varian Aerograph Model 1520-1B. Column: Stainless steel 5′×1/8″ OD, 5% liquid phase on chromosorb W (60—80 mesh). Temperature: injector 200°, detector (FID) 200°. Carrier gas: N_2 20 ml/min. Nuclear magnetic resonance (NMR) spectra were obtained on a Varian A-60 analytical NMR spectrometer.

16) S. Takahashi and H. Kanō, *Chem. Pharm. Bull.* (Tokyo), **12**, 1290 (1964).

Table III. Reaction Condition of the Aminolysis

Amine	Ester					
	 1	 11	 17	 21	 26	 34
NH_3	100° 1 hr	room temp. 2 days	100° 1 hr	100° 3 hr	reflux 10 min	90° 3 hr
$BuNH_2$	100° 1 hr	room temp. 2 days	100° 3 hr	100° 3 hr	95° 3 hr	100° 3 hr
iso-$PrNH_2$	100° 1 hr	room temp. 2 days	100° 3 hr	100° 3 hr	90° 2 hr	100° 3 hr
tert-$BuNH_2$	80° 3 hr	room temp. 4 days	100° 7 hr	100° 5 hr	100° 1 hr	100° 3 hr
	60° 2 hr	room temp. 2 days	100° 3 hr	100° 5 hr	60° 2 hr	90° 3 hr

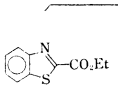
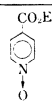
Amine	Ester				
	 37	 44	 45		Br_3CCO_2Et
NH_3	100° 3 hr	100° 3 hr	100° 1 hr	room temp. 3 hr	room temp. 12 hr
$BuNH_2$	100° 3 hr	95° 5 hr	100° 3 hr	room temp. 1 hr	room temp. 7 days
iso-$PrNH_2$	100° 3 hr	110° 24 hr	95° 5 hr	room temp. 1 hr	room temp. 10 days
tert-$BuNH_2$	120° 7 hr	110° 20 hr	100° 3 hr	room temp. 1 hr	room temp. 7 days
	95° 3 hr	110° 17 hr	100° 3 hr	room temp. 1 hr	room temp. 3 days

Table IV. Retention Time (adjusted) of the Carbamates

Carbamate	Liquid phase			
	XE-60 Column temp.		PDEAS Column temp.	
	100°	125°	100°	125°
H_2NCO_2Et (**13**)	—	0.75	—	0.50
$BuNHCO_2Et$ (**14**)	—	2.00	—	0.70
iso-$PrNHCO_2Et$ (**15**)	1.95	—	0.75	—
tert-$BuNHCO_2Et$ (**9**)	1.60	—	0.58	—
 NCO_2Et (**4**)	—	2.58	—	0.82
H_2NCO_2Me (**13′**)	—	0.57	—	0.44
$BuNHCO_2Me$ (**14′**)	—	1.57	—	0.62
iso-$PrNHCO_2Me$ (**15′**)	1.92	—	0.52	—
tert-$BuNHCO_2Me$ (**9′**)	1.17	—	0.40	—
 NCO_2Me (**4′**)	—	1.90	—	0.62

for 1 hr, and then chilled for 2 hr in an ice-water bath, the product was collected (2.70 g) and recrystallized from CH_3CN–AcOEt to give colorless prisms, mp 165°. *Anal.* Calcd. for $C_{11}H_{12}O_6NClS$: C, 41.06; H, 3.76; N, 4.35. Found: C, 41.35; H, 3.77; N, 4.33.

General Procedure for the Reaction of Ester and Amine——A mixture of the ester (1 mole) and the amine (1—3 mole), without solvent unless otherwise stated (in the case of ammonia, methanol solution was used), was submitted to the reaction conditions shown in Table III.

A small amount of the reaction mixture was analysed by gas–liquid chromatography (GLC) to determine the yield of carbamate; the retention times of the carbamates identified by GLC are listed in Table IV.

The other products were isolated by thin-layer chromatography (TLC) or recrystallization; the amides obtained are listed Table V.

TABLE V

Compound: Formula	Number	Recrystallization solvent	Crystal from	mp (°C)	Analyses calculated (Found): C	H	N
1-Methyl-2-benzimidazolecarboxamide 3-oxide ($C_9H_9O_2N_3$)	**5**	MeOH	colorless prisms or needles	251[3] (decomp.)			
N-Butyl-1-methyl-2-benzimidazolecarboxamide 3-oxide ($C_{13}H_{17}O_2N_3$)	**6**	ether–hexane	colorless needles	60— 61	63.14 (63.33)	6.93 (6.98)	16.99 (16.80)
N-Isopropyl-1-methyl-2-benzimidazolecarboxamide 3-oxide ($C_{12}H_{15}O_2N_3$)	**7**	AcOEt–hexane	colorless needles	152—153	61.78 (61.51)	6.48 (6.38)	18.02 (18.07)
N-*tert*-Butyl-1-methyl-2-benzimidazolecarboxamide 3-oxide ($C_{13}H_{17}O_2N_3$)	**8**	hexane	colorless plates	136—138	63.14 (63.39)	6.93 (7.13)	16.99 (16.99)
1-Methyl-2-benzimidazolecarboxamide ($C_9H_9ON_3$)	**22**	EtOH	colorless prisms	206—207[a]			
N-Butyl-1-methyl-2-benzimidazolecarboxamide ($C_{13}H_{17}ON_3$) (Picrate)	**23**	EtOH	yellow plates	142—144	49.59 (49.66)	4.38 (4.49)	18.26 (18.40)
N-Isopropyl-1-methyl-2-benzimidazolecarboxamide ($C_{12}H_{15}ON_3$)	**24**	hexane	colorless scales	129—130	66.34 (66.32)	6.96 (6.84)	19.34 (19.46)
2-(Piperidinocarbonyl)-1-methylbenzimidazole ($C_{14}H_{17}ON_3$)	**25**	hexane	colorless plates	123—124	69.11 (68.90)	7.04 (7.15)	17.27 (17.02)
2-(N-Butylcarbamoylmethyl)-1,3-dimethylbenzimidazolium iodide ($C_{15}H_{22}ON_3I$)	**19**	acetone–AcOEt	colorless plates	219—221	46.52 (46.00)	5.73 (5.40)	10.85 (10.56)
2-(N-Isopropylcarbamoylmethyl)-1,3-dimethylbenzimidazolium iodide ($C_{14}H_{20}ON_3I \cdot H_2O$)	**20**	acetone	colorless prisms	218—220	62.98 (62.90)	5.68 (5.29)	10.74 (10.69)
2-Benzothiazolecarboxamide 3-oxide ($C_8H_6O_2N_2S$)	**27**	EtOH	colorless scales	228—229[1]			
N-Isopropyl-2-benzothiazolecarboxamide 3-oxide ($C_{11}H_{12}O_2N_2S$)	**28**	hexane	colorless prisms	96— 97	55.93 (55.81)	5.12 (5.37)	11.86 (12.16)
N-*tert*-Butyl-2-benzothiazolecarboxamide 3-oxide ($C_{12}H_{14}O_2N_2S$)	**29**	hexane	colorless plates	87— 88	57.59 (57.70)	5.64 (5.61)	11.20 (11.33)
2-(Piperidinocarbonyl)-benzothiazole 3-oxide ($C_{13}H_{14}O_2N_2S$)	**30**	ether	colorless needles	97— 98	59.53 (59.69)	5.38 (5.50)	10.68 (10.70)
2-Benzothiazolecarboxamide ($C_8H_6ON_2S$)	**38**	EtOH	colorless plates	236—238[b]			
N-Butyl-2-benzothiazolecarboxamide ($C_{12}H_{14}ON_2S$)	**39**	pentane	colorless prisms	38— 39	61.52 (61.64)	6.02 (6.05)	11.96 (11.85)
N-Isopropyl-2-benzothiazolecarboxamide ($C_{11}H_{12}ON_2S$)	**40**	hexane	colorless plates	72— 74	59.99 (59.91)	5.49 (5.44)	12.72 (12.93)
N-*tert*-Butyl-2-benzothiazolecarboxamide ($C_{12}H_{14}ON_2S$)	**41**		oil		61.52 (61.61)	6.02 (5.98)	11.96 (11.69)
2-(Piperidinocarbonyl)-benzothiazole ($C_{13}H_{14}ON_2S$)	**42**	hexane	colorless prisms	87— 88	63.40 (63.81)	5.72 (5.45)	11.38 (11.20)
4-Carbamoyl-1-methylpyridinium iodide ($C_7H_9ON_2I$)	**56**	MeOH	yellow scales	267[c] (decomp.)			
Isonicotinamide N-oxide ($C_6H_6O_2N_2$)	**46**	H_2O	colorless prisms	305[d] (decomp.)			
N-Butyl-isonicotinamide 1-oxide ($C_{10}H_{14}O_2N_2$)	**47**	C_6H_6 or AcOEt	colorless scales	94— 96	61.83 (61.87)	7.27 (7.31)	14.42 (14.51)
N-Isopropyl-isonicotinamide 1-oxide ($C_9H_{12}O_2N_2$)	**48**	acetone	colorless plates	177—179	59.98 (60.20)	6.71 (6.75)	15.55 (11.29)

Compound Formula	Number	Recrystallization solvent	Crystal form	mp (C°)	Analyses calculated (Found) C	H	N
4-(Piperidinocarbonyl)-pyridine 1-oxide ($C_{11}H_{14}O_2N_2$)	**49**	heptane	colorless prisms	140—141	64.06 (64.02)	6.84 (6.79)	13.58 (13.62)
Picolinamide 1-oxide ($C_6H_6O_2N_2$)	**50**	MeOH	colorless prisms	160—161[e]			
N-Butyl-picolinamide 1-oxide ($C_{10}H_{14}O_2N_2$)	**51**		oil	bp 0.1 150° (bath temp.)	61.83 (61.30)	7.27 (7.67)	14.42 (14.08)
N-Isopropyl-picolinamide 1-oxide ($C_9H_{12}O_2N_2$)	**52**	ether	colorless prisms	40— 42	59.98 (60.42)	6.71 (6.72)	15.55 (15.81)
N-*tert*-Butyl-picolinamide 1-oxide ($C_{10}H_{14}O_2N_2 \cdot H_2O$)	**53**	EtOH–AcOEt	colorless plates	172 (decomp.)	56.59 (56.70)	7.60 (7.62)	13.20 (13.04)
2-(Piperidinocarbonyl)-pyridine 1-oxide ($C_{11}H_{14}O_2N_2$)	**54**	AcOEt	colorless prisms	161—162	64.06 (64.09)	6.84 (6.91)	13.58 (13.62)
Tribromoacetamide ($C_2H_2ONBr_3$)	**58**	ether–pentane	colorless plates	122—123[f]			
N-Butyl-tribromoacetamide ($C_6H_{10}ONBr_3$)	**59**	pentane	colorless prisms	44.5—45.0	20.48 (20.66)	2.86 (3.13)	3.98 (3.77)
N-Isopropyl-tribromoacetamide ($C_5H_8ONBr_3$)	**60**	pentane	colorless prisms	86— 87[g]			

a) A.S. Petrov and I.N. Somin, *Khim Geterotsikl. Soedin., Akad. Nauk Latv. SSR*, **1966**, 472 [*C.A.*, **65**, 8894 (1966)]
b) A.I. Kiprianov and T.M. Verbovskaya, *J. Gen. Chem. USSR* (Eng. Transl.), **31**, 488 (1961)
c) J.W. Grochowski and J. Ambroziak, *Biul. Wajskowej Acad. Tech.*, **14**, 126 (1965) [*C.A.*, **64**, 17534 (1966)]
d) M. Shimizu, T. Naito, C. Ohta, T. Yoshikawa, and R. Dohmori, *Yakugaku Zasshi*, **72**, 1474 (1952)
e) G.T. Newbold and F.S. Spring, *J. Chem. Soc.*, **1949**, *suppl.*, **1**, 133
f) Broche, *J. Prakt. Chem.*, [2] **50**, 99 (1894) [*Beil.*, **2**, 221 (1920)]
g) R.A.Nyquist and R.D. McLachlan, U.S. Patent 3206509 (1965) [*C. A.*, **63**, 13090 (1965)]

Reaction of 11 with *tert*-Butylamine——A mixture of **11** (200 mg) and *tert*-$BuNH_2$ (3.0 ml) was allowed to stand at room temperature for 10 days with occasional shaking. To the resulting nearly colorless mixture was added AcOEt (10 ml) to give a colorless crystalline product which was proved to be 1,3-dimethylbenzimidazolium iodide (**12**) (115 mg, mp 195—196°).[5] The mother liquor was concentrated (below 10°) and hexane was added. A sample of the hexane solution was analysed by GLC to determine the yield of carbamate. The insoluble material was collected and chromatographed (Al_2O_3) with CH_2Cl_2 and then recrystallized from EtOH to give colorless prisms (30 mg), mp 259—260°, which were proved to be 1,4-dimethyl-1,2,3,4-tetrahydro-2,3-quinoxalinedione (**16**).[6]

Reaction of 1 with *tert*-Butylamine——A mixture of **1** (300 mg) and *tert*-$BuNH_2$ (1.5 ml) was heated in a sealed tube at 80° for 3 hr. After cooling, the precipitated product (178 mg) was collected by filtration, washed with ether and recrystallized from acetone to give white prisms, mp 60—62°, which were proved to be 1-methylbenzimidazole 3-oxide (**3**).[17] The mother liquor was evaporated and the residue was chromatographed (Al_2O_3) with AcOEt to give colorless needles (60 mg) and colorless prisms (120 mg), both crystals were recrystallized from hexane. The former crystals, mp 150.0—150.5°, were shown to be 2-*tert*-butylamino-1-methylbenzimidazole (**10**). *Anal.* Calcd. for $C_{12}H_{17}N_3$: C, 70.90; H, 8.43; N, 20.67. Found: C, 71.13; H, 8.64; N, 20.65. The latter crystals, mp 136—138°, were shown to be N-*tert*-butylamino-1-methyl-2-benzimidazolecarboxamide 3-oxide (**8**).

Reaction of 26 with Butylamine——A solution of **26** (100 mg) in $BuNH_2$ (1.0 ml) was heated at 95° in a seled tube for 2 hr and then evaporated. The residue was separated by preparative TLC (Al_2O_3, $CHCl_3$) to give a crystalline product (30 mg). Recrystallization from EtOH gave colorless needles, mp 149—150°, shown to be N,N′-di-butyloxalamide (**31**).

Reaction of 26 and Piperidine——A solution of **26** (1.00 g) and piperidine (0.50 ml) in EtOH (7.5 ml) was heated in a sealed tube at 60° for 2 hr and then evaporated. The residue was separated by preparative TLC (Al_2O_3, $CHCl_3$–EtOH (30:1)) to give two products, *Rf* 0.30 (0.08 g) and 0.70 (0.92 g). The picrate of the product of *Rf* 0.30 was recrystallized from MeOH to give yellow prisms, mp 136—138°. *Anal.* Calcd. for $C_{12}H_{14}ON_2S$–$C_6H_3O_7N_3$ (2-piperidinobenzothiazole 3-oxide (**33**), picrate): C, 46.65; H, 3.70; N, 15.12. Found: C, 46.53; H, 3.72; N, 15.06.

Deoxygenation of **33** over Raney Ni gave 2-piperidinobenzothiazole, mp 90—91°.[18]

17) S. Takahashi and H. Kanō, *Chem. Pharm. Bull.* (Tokyo), **11**, 1375 (1963).
18) M. Colonna, *Pubbl. ist. chim. univ. Bologna*, **1943**, No. 5, 3 [*C.A.*, **41**, 754 (1947)].

The product of *Rf* 0.70 was recrystallized from ether to give colorless needles, mp 97—98°, shown to be 2-(piperidinocarbonyl)-benzothiazole 3-oxide (**27**).

Reaction of 34 with Ammonia——**34** (200 mg) was added to NH_3-MeOH (satd. at 0°, 3 ml) and the solution was heated at 90° in a sealed tube for 3 hr and then evaporated. The residue was extracted with ether and removal of the solvent gave a yellow crystalline product (72 mg) which was recrystallized from hexane to give yellow plates, mp 60—62°. This compound was proved to be 2,2′-dithio-bis(N-methylaniline) (**35**) and was identified with an authentic specimen.[12]

Reaction of Benzothiazole N-Oxide and Piperidine——A solution of benzothiazole N-oxide[1] (180 mg) and piperidine (0.16 ml) in EtOH (1.5 ml) was heated at 60° in a sealed tube for 4 hr and then evaporated. The residue was separated by preparative TLC (Al_2O_3, AcOEt) to give two colorless oily products (13 mg and 125 mg). The former was proved to be benzothiazole by GLC (the same conditions as used for the carbamate mentioned above, retention time, 1.82 min (SE-30, column temperature 125°)). The latter product was analysed as its picrate. Recrystallization from MeOH gave yellow prisms, mp 136—138°, shown to be 2-piperidinobenzothiazole 3-oxide and identified with **33** obtained by the reaction of **26** and piperidine.

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