Nucleophilic Substitution in Carbonic Acid Derivatives. Part II.[1] Kinetics and Mechanism of the Solvolyses of NN-Dialkylcarbamoyl Chlorides

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The effects of structural changes in NN-dialkylcarbamoyl chlorides and in some hydroxylic compounds as solvolytic agents. of solvent polarity. and of the kinetic mass-law, on the rates of solvolyses have been studied. The pseudo-unimolecular constants are enhanced by the increase of the electron-releasing effects of N-alkyl groups as well as by increasing solvent polarity. and are sensitive to the presence of chloride ions. These results are in agreement with the assumption of the unimolecular mechanism in all cases. The isokinetic relationships suggest two interaction mechanisms by solvation of the transition states.

CARBONIC ACID CHLORIDES, as a particular kind of acyl chlorides, show interesting features in nucleophilic substitution mechanisms, e.g. the reactions of ethyl chloroformate with substituted anilines [1] and hydrolyses of substituted aryl chloroformates.[2] Although the solvolysis of alkyl chloroformates has been widely investigated, only a few studies of the reactions of NN-dialkylcarbamoyl chlorides have been reported. Hall [3,4] has demonstrated the unimolecular mechanism of hydrolysis of NN-dimethylcarbamoyl chloride in water–dioxan (86·1% v/v) on the basis of the kinetic mass-law effect of the chloride ion, the insensivity of the reaction rate to strong nucleophiles (such as the hydroxide ion, pyrrolidine, or hydroxylamine), the activation parameters, and the catalytic action of Hg^{++} ions. This mechanism has been confirmed for the hydrolysis of NN-di-isopropylcarbamoyl and NN-pentamethylene-carbamoyl chlorides in water–acetone (10·9% v/v) [5] and for NN-dimethylcarbamoyl chloride in water.[6]

Hall has suggested a bimolecular mechanism for the reactions of NN-dimethylcarbamoyl chloride with aliphatic amines.[7]

RESULTS

Kinetics were followed by direct conductometric measurements. The pseudo-first-order rate constants for the
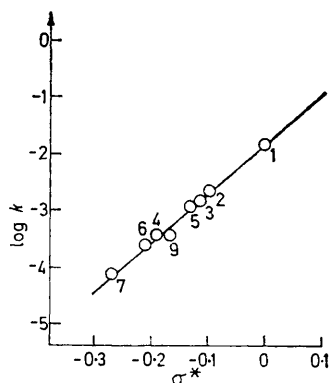

FIGURE 1   Plot of log k against σ* for the solvolyses of NN-dimethylcarbamoyl chloride at 80 °C; alcohols are numbered as in Table 1

solvolysis of NN-dimethylcarbamoyl chloride in alcohols and formic acid, as well as the activation parameters, are

in Table 1. Figure 1 shows the plot of logarithm of rate constants against σ* [8] for the alcoholysis of NN-dimethyl-carbamoyl chloride at 80 °C, from which log $k = -1·855 + 8·60σ*$ ($r = 0·999$). The unexpectedly good correlation of
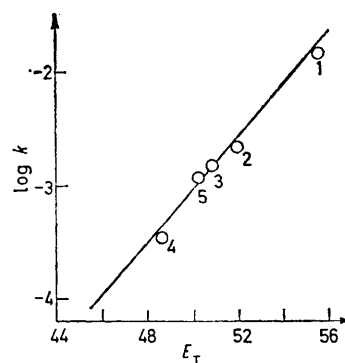

FIGURE 2   Plot of log k against E_T parameters [9] for solvolyses of NN-dimethylcarbamoyl chloride at 80 °C. Alcohols are numbered as in Table 1
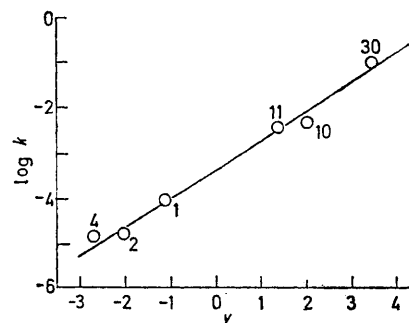
FIGURE 3   Plots of log k against Y parameters [10] for the solvolyses of NN-dimethylcarbamoyl chloride at 30 °C; numbered as in Tables 1 and 2; number 30 is for water (data from ref. 6)

rate data with σ* demonstrates that in these cases the alkyl groups of the alcohols exert only a polar effect in the

[1] Part I, G. Ostrogovich, C. Csunderlik, and R. Bacaloglu, J. Chem. Soc. (B), 1971, 18.
[2] G. Ostrogovich, C. Csunderlik, and R. Bacaloglu, unpublished results.
[3] H. K. Hall, jun., J. Amer. Chem. Soc., 1955, 77, 5993.
[4] H. K. Hall, jun., and C. H. Luek, J. Org. Chem., 1963, 28, 2818.
[5] I. Ugi and F. Beck, Chem. Ber., 1961, 94, 1839.
[6] A. Queen, Canad. J. Chem., 1967, 45, 1619.
[7] H. K. Hall, J. Org. Chem., 1964, 29, 3539.
[8] J. E. Leffler and E. Grunwald, ' Rates and Equilibria of Organic Reactions,' Wiley, New York, 1963, p. 222.

TABLE 1

Rate constants and activation parameters for the solvolyses of NN-dimethylcarbamoyl chloride

No.	Hydroxylic compound	σ*[a]	E_T[b]	10^2[Me$_2$N·COCl]/M	T/°C	n[c]	Conversion (%)[d]	$10^5(k \pm p)$/s^{-1}[e]	ΔH‡ kcal mol^{-1}	ΔS‡ cal mol^{-1} K^{-1}
1	MeOH	0.00	55.5	1.34	20.4	25	50	2.95 ± 0.01		
				1.10	30.0	20	93	9.10 ± 0.06		
				1.09	39.5	20	95	27.50 ± 0.06		
					80.0			1400 [f]	19.9	−8.0
2	EtOH	−0.100	51.9		30.0			1.35 [f]		
				1.23	40.0	25	80	5.05 ± 0.02		
				1.13	50.0	20	90	14.75 ± 0.05		
				1.28	60.0	15	90	35.60 ± 0.15		
				1.45	60.0	20	90	36.30 ± 0.30		
					80.0			214.0 [f]	20.0	−14.3
3	Pr^{n}OH	−0.115	50.7	1.07	60.0	20	85	21.4 ± 0.1		
				1.10	70.0	20	95	57.0 ± 0.4		
				1.33	80.0	20	90	149.0 ± 0.9	22.7	−7.6
4	Pr^{i}OH	−0.190	48.6		30.0			1.49 [f]		
				1.40	50.0	20	79	6.08 ± 0.03		
				1.28	60.0	20	86	11.2 ± 0.2		
				1.39	70.0	15	94	20.5 ± 0.2		
					80.0			34.5 [f]	12.8	−38.4
5	Bu^{n}OH	−0.130	50.2	1.43	60.0	15	90	21.6 ± 0.1		
				1.26	70.0	15	90	52.5 ± 0.2		
				1.26	80.0	15	90	117.0 ± 0.2	19.5	−16.7
6	Bu^{s}OH	−0.210		1.43	70.0	20	90	11.6 ± 0.1		
				1.37	80.0	20	90	28.2 ± 0.3		
				1.31	90.0	20	90	58.4 ± 0.2	17.9	−24.6
7	n-C$_6$H$_{13}$·CHMe·OH	−0.270 [g]			80.0			7.01		
				1.47	90.0	13	65	17.0 ± 0.2		
				1.50	100.0	15	74	32.9 ± 0.2		
				1.72	110.0	10	75	61.7 ± 0.5	16.4	−30.7
8	HO·CH$_2$·CH$_2$·OH	+0.250 [h]	56.3	1.62	30.0	15	85	41.0 ± 0.2		
				1.65	40.0	20	80	132.0 ± 0.4		
				1.07	45.0	20	90	298.0 ± 1.2		
				1.65	50.0	10	90	380.0 ± 4.7		
					80.0			25,800	21.1	−4.5
9	cyclo-C$_6$H$_{11}$·OH	−0.170		1.39	70.0	20	90	14.75 ± 0.05		
				1.35	80.0	20	90	32.2 ± 0.1		
				1.24	90.0	20	90	68.8 ± 0.1	18.5	−22.1
10	HCO$_2$H (99.0%)			1.10	25.0	15	90	235 ± 0.5		
				1.56	30.0	10	95	370 ± 4		
				1.08	35.0	10	84	579 ± 1	15.3	−19.1

[a] σ* constants from ref. 8.   [b] E_T constants from ref. 9.   [c] The number of constants determined.   [d] The conversion to which the reaction order was followed.   [e] $p = 0.675 \sqrt{[\Sigma(X^- - X_i)^2/n^2]}$.   [f] From Arrhenius equation.   [g] Calculated from the factor $f = 1.67$ ($f = $ σ* Pr^i/σ* Pr^n = 1.65; $f = $ σ* Bu^s/σ* Bu^n = 1.68) and the limit value σ* = −0.162 for large alkyl radicals.   [h] Calculated from the value σ* = +0.555 for CH$_2$·OH and 0.45 the relative attenuation coefficient of the inductive effect produced by a CH$_2$ group.[8]

TABLE 2

Rate constants and activation parameters for the hydrolyses in water–acetone (1 : 1 v/v) of NN-dialkylcarbamoyl chlorides

No.	R$_2$N·COCl	E_s[b]	σ*[a]	10^2[R$_2$N·COCl]/M	T/°C	n[c]	Conversion (%)[d]	$10^3(k \pm p)$/s^{-1}[e]	ΔH‡ kcal mol^{-1}	ΔS‡ cal mol^{-1} K^{-1}
11	Me$_2$	0.000	0.000	1.36	20.0	20	90	1.00 ± 0.03		
				1.16	25.0	17	90	1.80 ± 0.01		
				1.02	30.0	20	90	3.27 ± 0.01		
				0.87	50.0	18	95	28.5 ± 0.2	20.4	−2.6
12	Et$_2$	−0.07	−0.100	0.81	20.0	17	96	6.91 ± 0.02		
				0.77	30.0	12	96	25.4 ± 0.4		
				0.69	40.0	10	90	56.7 ± 0.2		
					50.0			146 [f]	18.3	−5.8
13	Pr$^n_2$	−0.36	−0.115	0.79	20.0	17	75	3.50 ± 0.02		
				0.66	30.0	20	96	11.2 ± 0.1		
				1.05	40.0	18	95	38.5 ± 0.3	21.2	+2.6
14	Pr$^i_2$	−0.47	−0.190	0.65	20.0	8	85	106 ± 2		
				0.66	25.0	12	90	127 ± 0.7		
				0.97	30.0	17	95	159 ± 0.7		
				1.05	35.0	9	90	200 ± 0.4	7.35	−37.8
15	Bu$^n_2$	−0.390	−0.130		20.0			2.25 [f]		
				0.74	30.0	13	90	6.26 ± 0.03		
				0.79	40.0	15	96	16.7 ± 0.1		
				0.64	50.0	10	94	50.2 ± 0.2	17.4	−11.2

Footnotes a—e as in Table 1.

transition state. The positive ρ^* values show that the rate depends on the acidity of the alcohol proton, *i.e.*, its specific capacity to solvate the reacting group. These features correspond to a unimolecular mechanism.

A marked steric effect due to the alkyl radical and Grunwald and Winstein's equation clearly shows that the ionizing power of the solvent is important, also supporting the unimolecular mechanism.

The rate data and activation parameters for hydrolyses in water–acetone (1 : 1 v/v) and for ethanolyses of various

TABLE 3

Rate constants and activation parameters for the ethanolyses of NN-dialkylcarbamoyl chlorides

No.	$R_2N{\cdot}COCl$	$E_s{}^b$	$\sigma^{*\ a}$	$10^2[R_2N{\cdot}COCl]/M$	$T/°C$	n^e	Conversion (%)^d	$10^3(k \pm p)/s^{-1\ e}$	$\Delta H\ddagger$ kcal mol^{-1}	$\Delta S\ddagger$ cal mol^{-1} K^{-1}
18	Me$_2$	0·000	0·00	1·23	40·0	25	80	0·0505 ± 0·0002		
				1·13	50·0	20	90	0·1475 ± 0·0005		
				1·28	60·0	15	90	0·356 ± 0·002	20·0	−14·3
19	Et$_2$	−0·07	−0·100	1·61	50·0	20	89	0·666 ± 0·004		
				0·92	60·0	10	90	1·766 ± 0·04		
				1·08	65·0	10	90	2·78 ± 0·02	20·4	−10·1
20	Pr$^n_2$	−0·36	−0·115		40·0			0·145^f		
				1·03	50·0	14	84	0·447 ± 0·003		
				1·01	60·0	10	87	1·23 ± 0·01		
				1·24	65·0	10	85	2·15 ± 0·02	22·0	−5·8
21	Pr$^i_2$	−0·47	−0·190	1·05	20·0	15	95	2·02 ± 0·02		
				0·79	30·0	10	95	6·00 ± 0·05		
				0·95	40·0	10	95	15·1 ± 0·2		
					50·0			34·2^f	15·7	−16·8
22	Bu$^n_2$	−0·39	−0·130	0·90	50·0	12	75	0·420 ± 0·001		
				0·82	60·0	10	70	1·23 ± 0·006		
				0·75	65·0	10	82	1·94 ± 0·010	21·8	−6·7

Footnotes *a—e* as in Table 1.

TABLE 4

Rate constants and activation parameters for the solvolyses of piperidine and morpholine derivatives

No.	$R_2N{\cdot}COCl$	Solvent	$10^2[R_2N{\cdot}COCl]/M$	$T/°C$	n^e	Conversion (%)^d	$10^3(k \pm p)/s^{-1\ e}$	$\Delta H\ddagger$ kcal mol^{-1}	$\Delta S\ddagger$ cal mol^{-1} K^{-1}
16	·[CH$_2$]$_5$·	Water–acetone (1 : 1 v/v)	1·53	20·0	17	97	0·98 ± 0·01		
			0·98	25·0	19	90	2·20 ± 0·01		
			0·78		16	95	2·43 ± 0·01		
			1·04	30·0	13	97	3·78 ± 0·05		
			1·14		13	93	3·55 ± 0·04		
			0·87	40·0	11	97	13·0 ± 0·2		
			0·80		13	92	15·1 ± 0·02	24·4	+15·5
17	·[CH$_2$]$_2$·O·[CH$_2$]$_2$·	Water–acetone (1 : 1 v/v)	1·37	20·0	16	92	3·57 ± 0·01		
			1·21	30·0	10	90	11·7 ± 0·1		
			1·70	40·0	15	90	37·2 ± 0·1	20·8	+1·4
23	·[CH$_2$]$_5$·	EtOH	1·35	50·0	16	90	1·234 ± 0·005		
			1·33	60·0	13	90	3·11 ± 0·01		
			1·15	65·0	10	98	4·45 ± 0·05	18·1	−15·9
24	·[CH$_2$]$_5$·O·[CH$_2$]$_2$·	EtOH	1·72	50·0	12	67	0·088 ± 0·005		
			1·48	60·0	14	88	0·238 ± 0·003		
			1·52	65·0	15	90	0·409 ± 0·005	21·7	−10·2
	·[CH$_2$]$_5$·	cyclo-C$_6$H$_{11}$·OH	1·05	90·0	21	90	3·45 ± 0·08		
	·[CH$_2$]$_2$·O·[CH$_2$]$_2$·	cyclo-C$_6$H$_{11}$·OH	1·27	90·0	16	98	0·410 ± 0·009		

Footnotes *c—e* as in Table 1.

negative ρ^* values would be expected for a bimolecular mechanism. The validity of this hypothesis is demonstrated by the good correlation of the logarithm of these rate constants with the empirical solvent parameters E_T [9] (Figure 2) and Grunwald and Winstein's parameter Y [10] (Figure 3) [equations (1) and (2)]. The correlation in

$$\log k = -14\cdot64 + 0\cdot232 E_T \quad (r = 0\cdot885) \quad (1)$$

$$\log k = -3\cdot42 + 0\cdot620 Y \quad (r = 0\cdot992) \quad (2)$$

NN-dialkylcarbamoyl chlorides are in Tables 2 and 3. The Taft-type plots (3) are in Figure 4. The parameters

$$\frac{1}{2E_s} \cdot \log\frac{k}{k_0} = s + \rho^* \frac{\sigma^*}{E_s} \quad (3)$$

for hydrolyses at 50 °C are $\rho^* = -4\cdot11$ ($r = 0\cdot992$) and $s = +0\cdot80$, and for ethanolyses at 50 °C are $\rho^* = -3\cdot70$ ($r = 0\cdot956$) and $s = +0\cdot62$. The negative values of ρ^* from the Taft plots indicate formation of a partial cationic

[9] Ch. Reinhard and K. Dimroth, *Fortschr. Chem. Forsch.*, 1968, **11**, 1.

[10] E. Grunwald and S. Winstein, *J. Amer. Chem. Soc.*, 1948, **70**, 846.

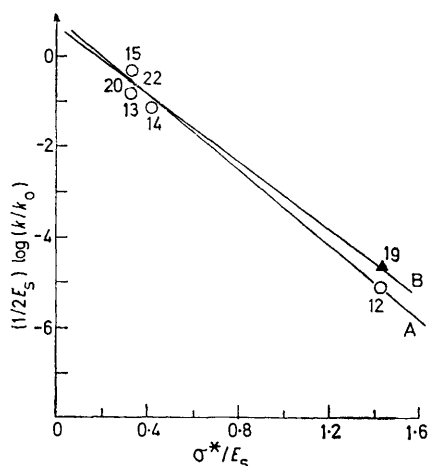charge on the carbon atom of the COCl group in the transition state, consistent with a unimolecular mechanism.

FIGURE 4 Plots for the hydrolyses, A, and for the enthanolyses, B, at 50 °C of NN-dialkylcarbamoyl chlorides, numbered as in Tables 2 and 3

This is also evident from comparison of rate constants for hydrolysis, ethanolysis, and cyclohexanolysis of piperidine and morpholine derivatives (Table 4). The morpholine

reactions ($s > 0$), the transition state must be more solvated than the initial carbamoyl chloride molecule.

The influence of decrease of solvent polarity and of chloride-ion concentration, through the kinetic mass-law effect, on reaction rates has been studied. Table 5 shows that the decrease of solvent polarity reduces the rate constants for ethylene glycolysis and ethanolysis. Table 6 shows that the kinetic mass-law effect of the chloride ion is important for the reaction in ethanol and formic acid. Both observations support the unimolecular mechanism.

There exist distinct isokinetic relationships, three for alcoholyses of NN-dimethylcarbamoyl chloride and two for hydrolyses and ethanolyses, of various NN-disubstituted carbamoyl chlorides. The isokinetic series have been identified by the methods of Petersen [11] (plots of $\log k/T$ against $1/T$) and Exner [12-14] (plots of $\log k$ against $1/T$ and $\log k_{T_1}$ against $\log k_{T_2}$). Good agreement of isokinetic temperatures has been obtained by the two methods.

DISCUSSION

In all solvolyses of carbamoyl chlorides with hydroxylic compounds studied by us, the unimolecular mechanism [(4) and (5)] has been demonstrated to be predominant.
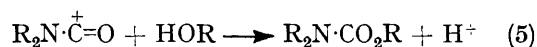
$$R_2N \cdot COCl \rightleftharpoons R_2N \cdot \overset{+}{C}{=}O + Cl^- \quad (4)$$

$$R_2N \cdot \overset{+}{C}{=}O + HOR \longrightarrow R_2N \cdot CO_2R + H^+ \quad (5)$$

TABLE 5

Rate constants and activation parameters for the solvolyses of NN-dimethylcarbamoyl chloride in mixed solvents

No.	Hydroxylic compound	Me$_2$CO (% v/v)	10^2[Me$_2$N·COCl]/M	$T/$°C	n [c]	Conversion (%) [d]	$10^5(k \pm p)/$s^{-1} [e]	$\Delta H^{\ddagger}$ kcal mol^{-1}	$\Delta S^{\ddagger}$ cal mol^{-1} K^{-1}
25	EtOH	10	1·29	40·0	20	79	3·80 ± 0·01		
		20	1·32	40·0	20	60	2·35 ± 0·02		
		30	0·96	40·0	20	68	2·32 ± 0·01		
26	HO·CH$_2$·CH$_2$·OH	12·5	1·12	45·0	15	90	168·0 ± 0·1		
		25	1·57	45·0	20	90	99·5 ± 0·2		
		25	1·43	40·0	20	90	53·8 ± 0·1		
		25	1·40	35·0	20	90	29·8 ± 0·1	22·3	—2·4

Footnotes c—e as in Table 1.

TABLE 6

Rate constants for the solvolyses of NN-dimethylcarbamoyl chloride in the presence of LiCl

No.	Hydroxylic compound	10^2[LiCl]/M	10^2[Me$_2$N·COCl]/M	$T/$°C	n [c]	Conversion (%) [d]	$10^5(k \pm p)/$s^{-1} [e]
27	EtOH	2·41	1·41	60·0	15	85	27·8 ± 0·3
		5·75	1·20	60·0	20	80	23·2 ± 0·6
28	HO·CH$_2$·CH$_2$·OH	4·41	1·65	45·0	15	90	327 ± 1·3
		8·23	1·09	45·0	15	90	324 ± 1·0
29	HCO$_2$H (99·7%)	0·00	1·25	25·0	16	90	300 ± 2
		6·21	1·37	25·0	10	90	254 ± 2
		11·1	1·49	25·0	20	86	231 ± 4

Footnotes c—e as in Table 1.

derivative reacts about ten times more slowly than piperidine in all three solvolyses because of the electron-withdrawing effect of the oxygen atom. As the steric effect of the alkyl group at the nitrogen atom retards the

It is evident that the powerful mesomeric electron donation of the dialkylamino-group strongly stabilizes the acylium ion and in this way favours the ionization mechanism.

[11] R. C. Petersen, *J. Org. Chem.*, 1964, **29**, 3133.
[12] O. Exner, *Ind. chim. belge*, 1968, **33**, 343.

[13] O. Exner, *Nature*, 1970, **227**, 366.
[14] O. Exner, *Nature*, 1970, **227**, 315.

The solvation of the transition state must play a prominent part in the ionization process as is apparent from the steric effects of N-alkyl groups and the effect of solvent polarity on the reaction rates.

The different isokinetic series suggest that the interaction between carbamoyl chlorides and solvents in the transition state of the ionization process is more complicated than expected. In our case the isokinetic relationship seems to depend not only on the major features of the mechanism, but also on finer aspects such as the solvation type of the transition state. It is possible that two interaction mechanisms [15,16] could, by solvation of the transition states, lead to two or three isokinetic series for each case.

It is remarkable that some of the reactions studied are characterized by a very low activation entropy although the mechanism is unimolecular. This demonstrates that the entropy criterion of mechanism must be used very carefully and in connection with other arguments.

A marked kinetic mass-law effect of the chloride ion for the reaction in ethanol and formic acid suggests that solvent molecules are competing with the chloride ion for the carbonium ions formed in the initial ionization step. This can be a new argument for the relative stability of the intermediate carbonium ions, at least in these conditions. This effect was not noticed in the case of ethylene glycol.

EXPERIMENTAL

The preparation, purification, and characterization of the NN-dialkylcarbamoyl chlorides have been described.[17] The alcohols (commercial samples) were refluxed for 24 h

[15] O. Exner, *Nature*, 1970, **227**, 145.
[16] J. L. Leffler, *J. Org. Chem.*, 1966, **31**, 533.
[17] C. Dăescu, *Bul. Inst. Politehn. Timişoara*, in the press.

over CaO, and distilled. Cyclohexanol was distilled and octan-2-ol and ethylene glycol were distilled at reduced pressure. Acetone was purified as described.[1] Lithium chloride was dried for 2 h at 500 °C.

TABLE 7

Rate constants for hydrolysis of NN-dimethylcarbamoyl chloride in water–acetone (1 : 1 v/v) at 30 °C; $[Me_2N \cdot COCl] = 1 \cdot 02 \times 10^{-2}$M

t/s	$10^6 \Lambda_t / \Omega^{-1}$ [a]	$10^3 k / s^{-1}$ [b]
90	270	3·21
120	365	3·31
150	450	3·36
180	515	3·30
210	585	3·33
240	640	3·30
270	695	3·30
300	740	3·27
330	780	3·25
360	820	3·25
390	855	3·25
420	895	3·29
450	925	3·29
480	945	3·24
510	970	3·24
540	995	3·27
570	1015	3·27
600	1030	3·23
660	1065	3·27
720	1087	3·22
∞	1210	—

Average rate constant 3·27 ± 0·01.

[a] Conductivity at time t. [b] Pseudo-unimolecular rate constants.

Kinetic procedures were as before. A typical example for a rate-constant determination is in Table 7.