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Reversible C ⇄ N Migration of the Ethoxycarbonyl Group in the Reactions of Pyridinium and Isoquinolinium Ylides Derived from Malonic Ester with Isocyanates

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ABSTRACT: *Pyridinium and isoquinolinium ylides (***7** *and* **12***) derived from malonic ester react in an unusual manner with isocyanates giving the new pyridinium ylide (***9***) and the new isoquinolinium ylide (***14***). C → N Migration of the COOEt group takes place at room temperature, but, at an elevated temperature, reverse N → C migration of the COOEt group proceeds and ylides* **9** *and* **14** *are reconverted into the starting ylides* **7** *and* **12***, respectively.*
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INTRODUCTION

Although the reactions of carbanions with isocyanates have been known for many years as a route to monosubstituted amides [1], the carbanionic species **1** can behave in a novel way leading to the formation of the carbamate **3** via rearrangement of the initially formed nitrogen anion **2** [2–6] (Scheme 1).

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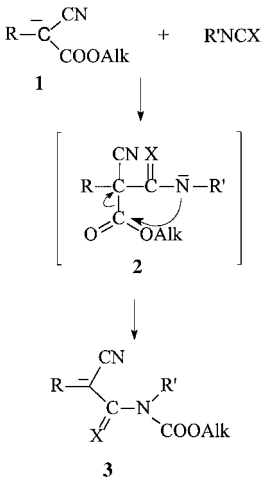
This type of behavior can be regarded as a general method for the apparent insertion of RNCX into a carbon–carbon bond and appears to have wide applicability. Such behavior is, however, limited to anions that do not contain other acidic protons, because, if these are present, self-protonation of the intermediate N-anion can occur leading to the formation of an N-monosubstituted amide.

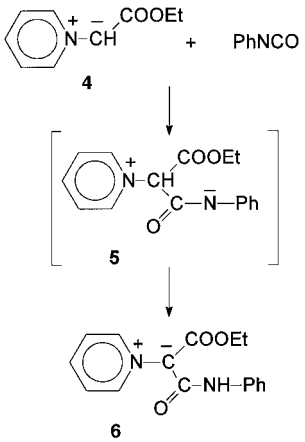
It was shown, for example, that pyridinium ylide (**4**) reacts with phenyl isocyanate to give the monosubstituted amide **6**, via self-protonation of the intermediated N-anion **5** [7] (Scheme 2).

RESULTS AND DISCUSSION

It was established by us that *N*-ylide **7**, derived from malonic ester [8,9], reacts with isocyanates in an unexpected way. Because of the lack of a mobile hydrogen, intermediate **8** was transformed (via C → N migration of COOEt) into the new *N*-ylide **9**. This rearrangement in the reaction of the pyridinium ylide (**7**) with each isocyanate occurs in CH_2Cl_2 solution, at room temperature, to give the corresponding carbamate (Scheme 3), which was either obtained as a pure compound (**9b,c,f**) or else its formation was detected in the reaction mixture by ^{1}H NMR spectroscopy (**9a,e,g**). Crude **9d** was transformed into the corresponding salt **10** with $MeSO_2OH$ (Scheme 4).



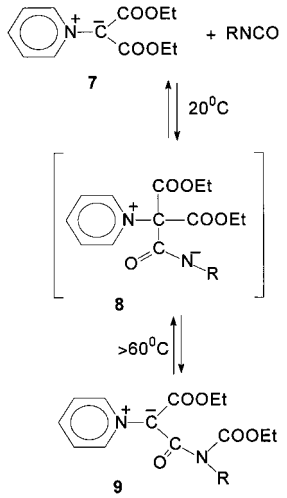
SCHEME 1 R = $Pr_3^iP^+CH_2$, Ph; Alk=Me, Et; X=O, S; R′ = Me or Ar = Ph, *m*-Tol, 1-naphthyl, p-ClC_6H_5, *m,p*-$Cl_2C_6H_3$, C_6H_5—NO_2-p.



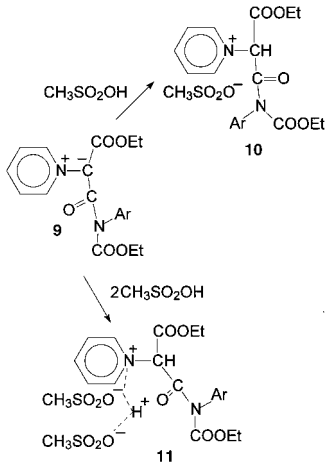
SCHEME 2

The degree of the rearrangement can easily be followed by ^{1}H NMR spectroscopy. Protons of the pyridinium ring in the starting ylide **7** and the ylides **9** have differences in their chemical shifts. Groups C_2H_5 in carbamates **9** are not equal in contrast to the protons of the C_2H_5 groups in the starting ylide **7**. For instance, the relationships of the ylides **7** and **9f** in the respective reaction mixtures were established by a comparison between the intensities of the α-H signals of the pyridinium rings and the protons of the CH_3CH_2 groups which belong to the ylide **7** (23–25%) and **9f** (75–77%) (Fig. 1).

According to the IR spectroscopic data, the negative charge in *N*-ylide **7** is delocalized with the participation of both COOEt groups ($\upsilon_{C=O}$ = 1658 cm^{-1}) but in the *N*-ylide **9f** only one COOEt group is conjugated with the anionic charge ($\upsilon_{C=O}$ = 1591 cm^{-1}).



SCHEME 3 R = cyclohexyl (**a**), Ph (**b**), 2-Tolyl (**c**), 3,4-dichlophenyl (**d**), 2-nitrophenyl (**e**), 4-nitrophenyl (**f**) and 1-naphthyl (**g**).



SCHEME 4 Ar = Ph (**10b**), 3,4-Cl_2-phenyl (**10d**), p—NO_2—C_6H_4 (**10f, 11f**).

The $\upsilon_{C=O}$ signal of another COOEt group at nitrogen is found at 1720 cm^{-1} (Fig. 2).

Initially, adduct **8** seems to be formed. Since the N-anionic intermediate **8** does not contain sufficiently active hydrogen atoms that would be able to protonate its N-anionic center, but does contain an ethoxycarbonyl group, intramolecular transformations as depicted in Scheme 3 become possible. This process is unusual, because a carbanion rather than an ethoxy anion (as in the case of aminolysis of esters) acts as the leaving group upon nucleophilic attack by nitrogen on the carbonyl group. Perhaps this unique situation in which cleavage of a C—C bond is preferred over cleavage of a C—O bond is due to

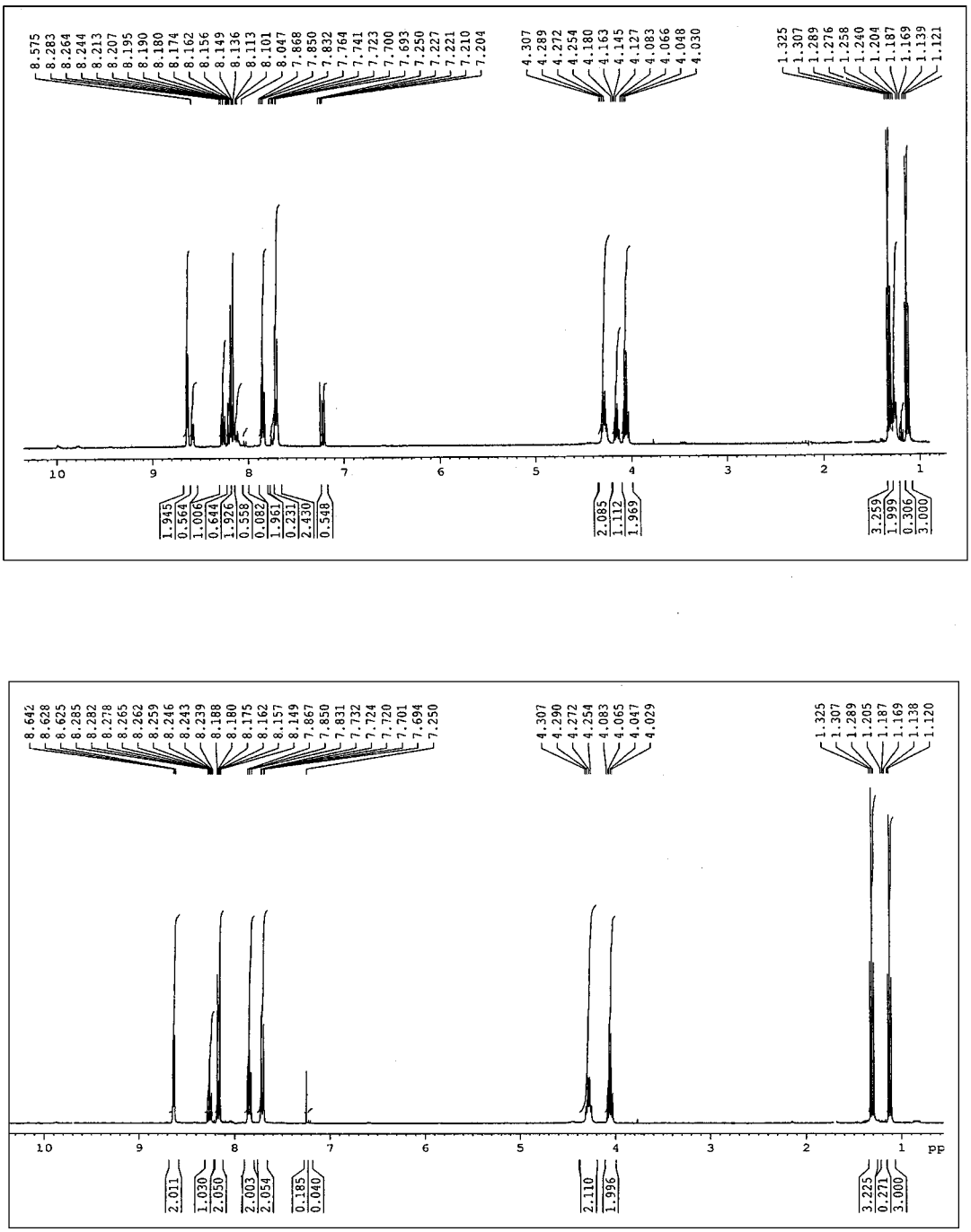


FIGURE 1 ^{1}H NMR spectrum of the reaction mixture of ylide **7** (upper picture) and the ylide **9f**.

the efficient delocalization of the negative charge in the resulting carbanions **9**. The latter is indicated by the data of IR spectroscopy; a change occurs in the intensity and the position of the absorption bands for the carbonyl group at the carbanion center in the ylide **9f** as compared with the absorption bands for the carbonyl group at the carbanion center in ylide **7** (Fig. 2).

The rate of formation of the ylides **9** depends on electronic and spatial characteristics of the isocyanates. The first step of the reaction (Scheme 3) involves the nucleophilic attack of the carbanion at the carbon of the isocyanate group and the rate of this step is dictated by electronic factors mainly (cf. [10]). The rate of the second stage should be particularly sensitive to the electronic and also,

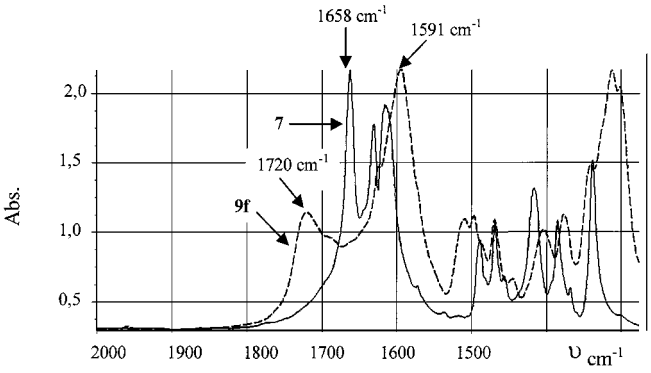


FIGURE 2 IR spectrum of the starting ylide **7** and ylide **9f** in the $\upsilon_{C=O}$ region.

especially, to the spatial effects of the substitutents in the nucleus of ArNCO [11]. Actually, the cyclohexyl isocyanate (fivefold excess) reacts with the ylide **7** very slowly, and within 1 month only 64% of the compound **9a** was revealed in the reaction mixture by ^{1}H NMR spectroscopy. Moreover, the ylide **7** reacts with phenyl or 4-nitrophenyl isocyanates (70% excess) in CH_2Cl_2 during 24 h, being transformed completely into carbamates **9b** and **9f**, respectively.

Steric effects of the substituents in the ortho position of ArNCO, whether of the donor or acceptor type, decrease the rate of formation of the ylides **9**. For example, ylide **7** reacts with *o*-tolyl isocyanate (fivefold excess) in CH_2Cl_2, and after 2 weeks at room temperature, the reaction mixture consists of the starting ylide **7** (7%) and carbamate **9c** (93%). In a similar manner, ylide **7** reacts with *o*-nitrophenyl isocyanate (twofold excess). In this instance, after 2 weeks at room temperature, the reaction mixture contains two main compounds: carbamate **9e** (85%) and ylide **7** (15%).

Rearrangement as depicted in Scheme 3 is reversible. While stable in the crystal state at room temperature, ylides **9** transform back into ylide **7** and an isocyanate polymer at elevated temperatures or after several weeks at room temperature in $CDCl_3$ or acetone. For example, crystalline **9f** is transformed in solution in $CDCl_3$ to the starting ylide **7** in 28% yield in 2 days and in 35% yield in a week (^{1}H NMR data). In a similar manner, ylide **9c** is transformed into the starting ylide **7** in 8% yield in a day and in 50% yield in 16 days in a solution in $CDCl_3$. The reversible equilibrium situation is reached after 3 weeks: 70% of the ylide **7** and 30% of the ylide **9c**.

The yellow compounds **9** react in CH_2Cl_2 with $MeSO_2OH$ to form the corresponding stable salts **10** (Scheme 4).

It is interesting to note that the reaction of the ylide **9f** with one equivalent of $MeSO_2OH$ leads to the mono-salt **10f**, but introduction of the ylide **9f** into reaction with two equivalents of the same acid brings about formation of the salt **11f**, which contains two equivalents of $MeSO_2OH$. A special problem is the structure of this double-salt **11f**. Literature data [12] regarding the protonation of bis-substituted amides show that the place of the protonation is oxygen, not nitrogen. As support for this statement the data of the IR spectroscopy [13] can be cited, because the protonation of the C=O group leads to a change in its intensity and the position of the $\upsilon_{C=O}$ band. In our case, IR spectra of the mono- **10f** and double- **11f** salts show no principal differences (Fig. 3).

However, it is interesting to note that all signals in the ^{1}H NMR spectra of the double salt **11f** exhibit higher field shifts compared with the corresponding signals of the mono-salt **10f** (Table 1).

In the case of the protonation of any one of the atoms of compound **10f**, one would expect that all the protons in the ^{1}H NMR spectra of the bis-salt **11f** should undergo a downfield shift. From the results obtained it may be concluded that **11f** is an adduct of the salt **10f** and $MeSO_2OH$, in which a proton of the latter is not located in the cationic part of **11f** but is rather connected with both $MeSO_2O^-$ anions. Also, the distance between the positive charge of the pyridinium ring and the anion center of **11f** is evidently very short because the signal of the proton in N^+—CH in **11f** has a high field shift compared with that of the mono-salt **10f**.

An isoquinolinium ylide derived from malonic ester (**12**) [8] reacts with aryl isocyanates similarly to the pyridinium ylide (**7**) (Scheme 5). Starting ylide **12** enters into reaction with 4-nitrophenyl isocyanate (twofold excess) completely during 24 h with the formation of the new ylide **14a**.

It is particularly remarkable that, in the ^{1}H NMR spectrum of the CH_2 groups, only those of the ylide **14b** reveals complex multiplets at room

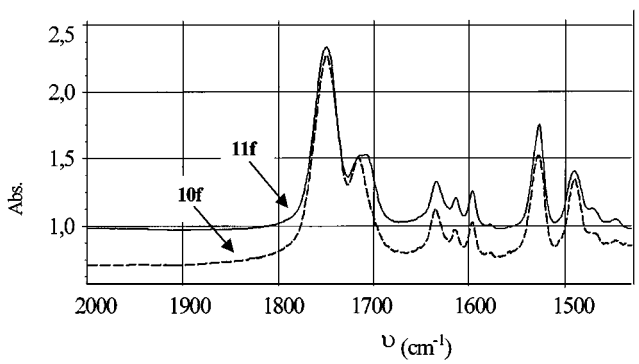
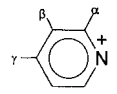
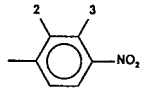
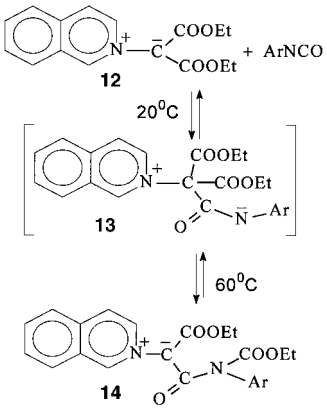


FIGURE 3 IR spectrum of the salts **10f** and **11f**.

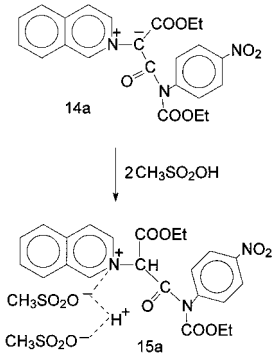
TABLE 1 Comparison ^{1}H NMR Data of Mono-Salt **10f** Bis-Salt **11f**

Compound		*CH—COOCH$_2$CH$_3$*	*N—COOCH$_2$CH$_3$*		*CH$_3$SO$_2$O$^-$*
10f	$\delta_{H\alpha} = 9.27$ $\delta_{H\beta} = 8.02$ $\delta_{H\gamma} = 8.52$	$\delta_H = 7.99$ δ_{CH_2} [a] $\delta_{CH_3} = 1.18$	δ_{CH_2} [a] $\delta_{CH_3} = 1.31$	$\delta_{H_2} = 7.68$ $\delta_{H_3} = 8.25$	$\delta_{CH_3} = 2.78$
11f	$\delta_{H\alpha} = 9.02$ ($\Delta\delta_{H\alpha} = 0.25$) $\delta_{H\beta} = 8.11$ ($\Delta\delta_{H\beta} = 0.09$) $\delta_{H\gamma} = 8.53$ ($\Delta\delta_H\gamma = 0.01$)	$\delta_H = 7.69$ ($\Delta\delta_H = 0.30$) δ_{CH_2} [a] $\delta_{CH_3} = 1.17$ ($\Delta\delta_{CH_3} = 0.01$)	δ_{CH_2} [a] $\delta_{CH_3} = 1.30$ ($\Delta\delta_{CH_3} = 0.01$)	$\delta_{H_2} = 7.58$ ($\Delta\delta_{H_2} = 0.10$) $\delta_{H_3} = 8.25$ $\Delta\delta_{H_3} = 0.00$	$\delta_{CH_3} = 2.88$ ($\Delta\delta_{CH_3} = 0.10$)

[a]m. 4.25–4.45 ppm.



SCHEME 5 Ar = 4-$O_2NC_6H_4$ (**a**), 1-naphthyl (**b**).



SCHEME 6

temperature. However, in contrast, at +55°C this unexpected effect disappears and the ^{1}H NMR spectra of the ylide **14b** shows no evidence of magnetic nonequivalence of the CH_2 protons. Perhaps this indicates that there is some unexpected asymmetry in the molecule **14b**, the effect of which is visible at room temperature. Asymmetry in the region of the nitrogen atom seems most likely, possibly owing to the strong impedance of rotation around the N—Ar bond. Apparently, this is an example of atropisomerism. A result of a similar nature was noted for the carbamate derived from 1-naphthyl isocyanate and a phosphorus containing zwitter ion [5].

Isoquinolinium carbamate (**14a**) is transformed into the corresponding double salt **15a** by action of two equivalents of $MeSO_2OH$ (Scheme 6).

EXPERIMENTAL

NMR spectra were recorded on a Bruker (AMX-400) spectrometer, ^{1}H (400.26 MHz), ^{13}C (100.68 MHz), (δ ppm, internal reference TMS and $CDCl_3$ for ^{1}H and ^{13}C spectra respectively). IR spectra were recorded on an IR-Fourier-spectrometer Magna-750 (KBr). The reactions were performed under a nitrogen or argon atmosphere.

Yields, analytical and spectral data (^{1}H NMR, IR) of products are given in Tables 2–5.

Pyridinium ylide (7) was prepared according to [8]. ^{13}C NMR δ: 14.22 ($OCH_2\underline{C}H_3$), 58.12 ($O\underline{C}H_2$ CH_3), 96.82 (C^-), 125.35 (C_β (Py)), 141.11 (C_γ (Py)), 149.41 (C_α (Py)), 164.18 ($\underline{C}$OOEt).

N-(Diethoxycarbonylmethyl)pyridinium Methosulfate

$MeSO_2OH$ (0.1 g, 1.05 mmol) was added dropwise to the ylide **7** (0.25 g, 1.05 mmol) in CH_2Cl_2 (10 ml). The colorless solution that formed was evaporated to dryness under reduced pressure. The residue was washed with ethyl ether, dried under reduced pressure, and recrystallized from acetone. White powder. Yield 67%, mp 103°C. ^{1}H NMR δ: 1.29 (t, 6H, $CH_2C\underline{H}_3$, J = 6.8 Hz), 2.70 (s, 3H, $C\underline{H}_3SO_2O^-$), 4.29

TABLE 2 Characterization Data of the Pyridinium Ylides and Their Salts

Compound	Molecular Formula	Molecular Weight	Yield (%)	mp (°C)	Elemental Analysis[a] (%)			
					C	H	N	S
7	$C_{12}H_{15}NO_4$	237.26	82	176	60.96 (60.75)	6.21 (6.37)	5.91 (5.90)	–
9b	$C_{19}H_{20}N_2O_5$	356.38	73	108–109[b]	63.84 (64.04)	5.69 (5.66)	7.72 (7.86)	–
10b	$C_{20}H_{24}N_2O_8S$	452.48	96	135–137	52.70 (53.09)	5.25 (5.35)	6.06 (6.19)	7.05 (7.09)
9c	$C_{20}H_{22}N_2O_5$	370.41	40	60–62[b]	65.11 (64.85)	5.86 (5.99)	7.61 (7.56)	–
9a	$C_{19}H_{26}N_2O_5$	362.43	57[c]	–	–	–	–	–
9d	$C_{19}H_{18}Cl_2N_2O_5$	425.27	86[c]	–	–	–	–	–
10d	$C_{20}H_{22}Cl_2N_2O_8S$	521.37	95	128–129	46.11 (46.07)	4.46 (4.25)	5.37 (5.37)	6.10 (6.15)
9e	$C_{19}H_{19}N_3O_7$	401.38	84[c]	–	–	–	–	–
9f	$C_{19}H_{19}N_3O_7$	401.38	62	58–60[b]	56.97 (56.86)	4.73 (4.77)	10.44 (10.47)	–
10f	$C_{20}H_{23}N_3O_{10}S$	497.48	70	120–122	47.47 (48.29)	4.72 (4.66)	7.93 (8.45)	6.64 (6.44)
11f	$C_{21}H_{27}N_3O_{13}S_2$	593.58	95	130–132	42.49 (42.63)	4.68 (4.58)	7.15 (7.08)	10.77 (10.80)
9g	$C_{23}H_{22}N_2O_5$	406.44	92[c]	–	–	–	–	–

[a]Values found are followed by the calculated values (in parentheses).
[b]Decomposition.
[c]^{1}H NMR Data.

(q, 2H, C$\underline{H}_2$CH$_3$, $J = 6.8$ Hz), 4.36 (q, 2H, C$\underline{H}_2$CH$_3$, $J = 6.8$ Hz), 7.28 (s, 1H, CH), 8.11 (t, 2H, H_β (Py), $J = 7.2$ Hz), 8.67 (t, 1H, H_γ (Py), $J = 7.6$ Hz), 9.32 (d, 2H, H_α (Py), $J = 5.6$ Hz). ^{13}C NMR δ: 13.36 (OCH$_2$C$\underline{H}_3$), 39.18 (CH$_3$S), 64.03 (O$\underline{C}$H$_2$CH$_3$), 71.48 (CH), 127.56 (C_β (Py)), 146.36 (C_γ (Py)), 147.72 (C_α (Py)), 162.18 ($\underline{C}$OOEt). IR (cm^{-1}) υ: 1751 (COOEt). Found: C, 46.73: H, 5.87; N, 4.19; S, 9.61. For $C_{13}H_{19}N_1O_7S$: C, 46.84; H, 5.74; N, 4.20; S, 9.62.

Reaction Between the Ylide **7** *and Cyclohexyl Isocyanate*

A solution of the ylide **7** (0.02 g, 0.08 mmol) in $CDCl_3$ was placed in a 5-mm NMR tube and treated at room temperature with cyclohexyl isocyanate (0.05 g, 0.42 mmol). After 25 days, the ^{1}H NMR spectrum showed the signals in the reaction mixture: 7.62 and 8.04 ppm (ylide **7**, H_β and H_γ (Py)); 7.69 and 8.11 ppm (**9a**, H_β and H_γ (Py)). There exist ylides **7** (38%) and **9a** (62%).

*Pyridinium (N-Ethoxycarbonyl-N-phenylcarbamoyl)ethoxycarbonylmethylide (***9b***)*

A mixture of the ylide **7** (2 g, 8.44 mmol) and PhNCO (1.5 g, 12.66 mmol) in $CHCl_3$ (25 ml) was left for 24 h at room temperature, and then the solvent was removed under reduced pressure without heating. The residue was dissolved in a minimum of acetone at room temperature and the solution was left to stand overnight at −20°C. Yellow crystals **9b** were filtered off. ^{13}C NMR δ: 10.66 (OCH$_2$C$\underline{H}_3$), 55.61 (O$\underline{C}$H$_2$CH$_3$), 57.60 (O$\underline{C}$H$_2$CH$_3$), 103.40 (C$^-$), 121.76–122.23 (Ph), 124.70 (C_β (Py)), 135.78 (N–C (Ph)), 138.49 (C_γ (Py)), 145.14 (C_α (Py)), 150.01 (C(O)N), 159.01 (N$\underline{C}$OOEt) 160.21 ($\underline{C}$OOEt).

*Pyridinium (N-Ethoxycarbonyl-N-2-tolylcarbamoyl)ethoxycarbonylmethylide (***9c***)*

A mixture of ylide **7** (0.5 g, 2.11 mmol) and 2-TolNCO (0.6 g, 4.88 mmol) in $CHCl_3$ (5 ml) was left for 17 days at room temperature Dry hexane (3 ml) was added to the reaction mixture; and precipitated powder (0.15 g, mp 170–174°C, starting ylide **7**) was filtered off. The filtrate was dried under reduced pressure without heating.

Reaction of Ylide **7** *with 3,4-Dichlorophenyl Isocyanate*

A mixture of ylide **7** (1 g, 4.20 mmol) and 3,4-dichlorophenyl isocyanate (1.2 g, 6.63 mmol) in $CHCl_3$ (25 ml) was left for 24 h at room temperature. The ^{1}H NMR spectrum showed the signals in

TABLE 3 The ^{1}H NMR and IR Spectral Data of the Synthesized Compounds

Compound	*^{1}H NMR*	*IR (υ_{max} cm^{-1})*		
		C═O (C(O)OEt)	*C═O (─C(O)─N)*	*C═O (N─C(O)OEt)*
7	1.24 (t, 6H, $CH_2C\underline{H}_3$, $J = 7.1$ Hz), 4.14 (q, 4H, $C\underline{H}_2CH_3$, $J = 7.1$ Hz), 7.66 (t, 2H, H_β (Py), $J = 7.2$ Hz), 8.07 (t, 1H, H_γ (Py), $J = 7.6$ Hz), 8.53 (d, 2H, H_α (Py), $J = 5.6$ Hz) (cf. [6])	1658	–	–
9a	1.20 (t, 3H, $CH_2C\underline{H}_3$, $J = 7.2$ Hz), 1.27 (t, 3H, $CH_2C\underline{H}_3$, $J = 7.2$ Hz), 1.55–1.98 (m, 10H, C_6H_{11}), 3.86–3.92 (m, 1H, C_6H_{11}), 4.08 (q, 2H, $C\underline{H}_2CH_3$, $J = 7.2$ Hz), 4.15 (q, 2H, $C\underline{H}_2CH_3$, $J = 7.2$ Hz), 7.42 (t, 2H, H_β (Py), $J = 7.2$ Hz), 8.15 (t, 1H, H_γ (Py), $J = 8.0$ Hz), 8.57 (d, 2H, H_α (Py), $J = 5.2$ Hz)	–	–	–
9b	1.21 (t, 3H, $CH_2C\underline{H}_3$, $J = 7.2$ Hz), 1.26 (t, 3H, $CH_2C\underline{H}_3$, $J = 7.2$ Hz), 4.14 (q, 2H, $C\underline{H}_2CH_3$, $J = 7.2$ Hz), 4.22 (q, 2H, $C\underline{H}_2CH_3$, $J = 7.2$ Hz), 7.25–7.30 (m, 5H, Ph) 7.21 (t, 2H, H_β (Py), $J = 7.2$ Hz), 8.15 (t, 1H, H_γ (Py), $J = 7.6$ Hz), 8.56 (d, 2H, H_α (Py), $J = 5.6$ Hz)	1594	1594	1708
10b	1.15 (t, 3H, $CH_2C\underline{H}_3$, $J = 7.2$ Hz), 1.29 (t, 3H, $CH_2C\underline{H}_3$, $J = 7.2$ Hz), 2.77 (s, 3H,CH_3S), 4.20–4.40 (m, 4H, CH_2CH_3), 7.31–7.40 (m, 5H, Ph), 7.78 (s, 1H, CH), 7.95 (t, 2H, H_β (Py), $J = 7.6$ Hz), 8.43 (t, 1H, H_γ (Py), $J = 7.6$ Hz), 9.13 (d, 1H, H_α (Py), $J = 5.6$ Hz)	1748	1707	1748
9c	1.23 (t, 3H, $CH_2C\underline{H}_3$, $J = 7.2$ Hz), 1.26 (t, 3H, CH_2 $C\underline{H}_3$, $J = 7.2$ Hz), 2.34 (s, 3H, CH_3), 4.14–4.21 (m, 4H, $C\underline{H}_2CH_3$, 7.13–7.32 (m, 4H, Ar), 7.68 (t, 2H, H_β (Py), $J = 7.6$ Hz), 8.09 (t, 1H, H_γ (Py), $J = 8.0$ Hz), 8.64 (d, 2H, H_α (Py), $J = 5.6$ Hz)	1586	1586	1712
10c	1.17 (t, 3H, $CH_2C\underline{H}_3$, $J = 7.2$ Hz), 1.29 (t, 3H, $CH_2C\underline{H}_3$, $J = 7.2$ Hz), 2.23 (s, 3H, CH_3), 2.76 (s, 3H, CH_3S), 4.20–4.40 (m, 4H, $C\underline{H}_2CH_3$), 7.18–7.27 (m, 3H, Ar), 7.53 (d, 1H, Ar, $J = 7.6$ Hz), 7.78 (s, 1H, CH), 7.97 (t, 2H, H_β (Py), $J = 7.2$ Hz), 8.45 (t, 1H, H_γ (Py), $J = 7.6$ Hz), 9.22 (d, 2H, H_α (Py), $J = 6.4$ Hz)	–	–	–
9d	1.10 (t, 3H, $CH_2C\underline{H}_3$, $J = 7.2$ Hz), 1.18 (t, 3H, $CH_2C\underline{H}_3$, $J = 7.2$ Hz), 4.02 (q, 2H, $C\underline{H}_2$ CH_3, $J = 7.2$ Hz), 4.13 (q, 2H, $C\underline{H}_2CH_3$, $J = 7.2$ Hz), 7.28–7.29 (m, 2H, Ar), 7.54 (bs, 1H, Ar), 7.68 (t, 2H, H_β (Py), $J = 7.2$ Hz), 8.10 (t, 1H, H_γ (Py), $J = 8.0$ Hz), 8.50 (d, 2H, H_α (Py), $J = 5.6$ Hz)	–	–	–
10d	1.20 (t, 3H, $CH_2C\underline{H}_3$, $J = 7.2$ Hz), 1.29 (t, 3H, $CH_2C\underline{H}_3$, $J = 7.2$ Hz), 2.74 (s, 3H, CH_3S), 4.23–4.43 (m, 4H, $C\underline{H}_2CH_3$), 7.36 (m, 2H, $H_{2,6}$ (Ar)), 7.45 (d, 1H, H_5 (Ar), $J = 8.4$ Hz), 7.88 (s, 1H, CH), 7.99 (t, 2H, H_β (Py), $J = 6.8$ Hz), 8.50 (t, 1H, H_γ (Py), $J = 7.6$ Hz), 9.22 (d, 2H, H_α (Py), $J = 4.0$ Hz)	1746	1704	1746
9e	1.15 (t, 3H, $CH_2C\underline{H}_3$, $J = 7.2$ Hz), 1.17 (t, 3H, $CH_2C\underline{H}_3$, $J = 7.2$ Hz), 4.08 (q, 2H, $C\underline{H}_2CH_3$, $J = 7.2$ Hz), 4.13 (q, 2H, $C\underline{H}_2CH_3$, $J = 7.2$ Hz), 7.36 (t, 1H, Ar, $J = 8.0$ Hz), 7.50 (t, 1H, Ar, $J = 8.0$ Hz), 7.70 (t, 2H, H_β (Py), $J = 7.2$ Hz), 7.87 (d, 1H, Ar, $J = 8.0$ Hz), 8.05 (d, 1H, Ar, $J = 8.0$ Hz), 8.13 (t, 1H, H_γ (Py), $J = 7.6$ Hz), 8.53 (d, 2H, H_α (Py), $J = 5.6$ Hz)	–	–	–
9f	1.12 (t, 3H, $CH_2C\underline{H}_3$, $J = 7.2$ Hz), 1.30 (t, 3H, $CH_2C\underline{H}_3$, $J = 7.2$ Hz), 4.05 (q, 2H, $C\underline{H}_2CH_3$, $J = 7.2$ Hz), 4.28 (q, 2H, $C\underline{H}_2CH_3$, $J = 7.2$ Hz), 7.71 (d, 2H, Ar, $J = 9.2$ Hz), 7.85 (t, 2H, H_β (Py), $J = 7.6$ Hz), 8.17 (d, 2H, Ar, $J = 9.2$ Hz), 8.26 (t, 1H, H_γ (Py), $J = 8.0$ Hz), 8.63 (d, 2H, H_α (Py), $J = 5.6$ Hz)	1591	1591	1720
10f	1.18 (t, 3H, $CH_2C\underline{H}_3$, $J = 7.2$ Hz), 1.31 (t, 3H, $CH_2C\underline{H}_3$, $J = 7.2$ Hz), 2.78 (s, 3H, CH_3S), 4.25–4.45 (m, 4H, $C\underline{H}_2CH_3$), 7.68 (d, 2H, Ar, $J = 8.8$ Hz), 7.99 (s, 1H, CH), 8.02 (t, 2H, H_β (Py), $J = 7.2$ Hz), 8.25 (d, 2H, Ar, $J = 8.8$ Hz), 8.52 (t, 1H, H_γ (Py), $J = 7.6$ Hz), 9.27 (d, 2H, H_α (Py), $J = 6.0$ Hz)	1750	1711	1750

(Continued)

TABLE 3 Continued

Compound	^1H NMR	IR (υ_{max} cm^{-1}) C=O (C(O)OEt)	C=O (—C(O)—N)	C=O (N—C(O)OEt)
11f	1.17 (t, 3H, $CH_2C\underline{H}_3$, $J = 7.2$ Hz), 1.30 (t, 3H, $CH_2C\underline{H}_3$, $J = 7.2$ Hz), 2.88 (s, 6H, CH_3S) 4.27–4.42 (m, 4H, $C\underline{H}_2CH_3$), 7.58 (d, 2H, Ar, $J = 6.8$ Hz), 7.69 (s, 1H, CH), 8.11 (bs, 2H, H_β (Py)), 8.25 (d, 2H, Ar, $J = 7.2$ Hz), 8.53 (bs, 1H, H_γ (Py)), 9.02 (bs, 2H, H_α (Py)), 13.34 (bs, 1H, H^+)	1750	1711	1750
9g	1.17 (t, 3H, $CH_2C\underline{H}_3$, $J = 6.8$ Hz), 1.29 (t, 3H, $CH_2C\underline{H}_3$, $J = 7.2$ Hz), 4.17 (q, 2H, $C\underline{H}_2CH_3$, $J = 6.8$ Hz), 4.25 (q, 2H, $C\underline{H}_2CH_3$, $J = 7.2$ Hz), 7.40–7.48 (m, 3H, Nf), 7.53–7.58 (m, 3H, Nf) 7.78 (t, 2H, H_β (Py), $J = 8.6$ Hz), 7.93 (t, 1H, Nf, $J = 8.0$ Hz), 8.25 (bs, 1H, H_γ (Py)), 8.55 (d, 2H, H_α (Py), $J = 6.0$ Hz)	–	–	–

the reaction mixture: 7.61 and 8.02 ppm (ylide 7, H_β and H_γ (Py)), 7.70 and 8.13 ppm (**9d**, H_β and H_γ (Py)). This corresponds to ylides **7** (15%) and **9d** (85%).

Reaction of Ylide **7** *with 2-Nitrophenyl Isocyanate*

A mixture of ylide **7** (0.5 g, 2.11 mmol) and 2-nitrophenyl isocyanate (1 g, 6.04 mmol) in CH_2Cl_2 (10 ml) was left for 16 days at room temperature. The ^1H NMR spectrum showed the signals in the reaction mixture: 8.49 ppm (ylide **7**, H_α (Py)), 8.53 ppm (**9e**, H_α (Py)). These correspond to ylides **7** (25%) and **9e** (75%).

*Pyridinium (N-Ethoxycarbonyl-N-4-nitrophenylcarbamoyl)ethoxycarbonylmethylide (***9f***)*

Compound **9f** was prepared similarly to **9b**. ^{13}C NMR δ: 14.29 ($OCH_2\underline{C}H_3$), 59.63 ($O\underline{C}H_2CH_3$), 62.01 ($O\underline{C}H_2CH_3$), 107.34 (C^-), 122.59 ($C_{2,6}$ (Ar)), 123.93 ($C_{3,5}$ (Ar)), 126.29 (C_β (Py)), 142.66 (C_γ (Py)), 143.45 (C—NO_2), 145.58 (N—C (Ar)), 148.88 (C_α (Py)), 152.77 (C(O)N), 161.28 (N$\underline{C}$OOEt) 163.41 ($\underline{C}$OOEt).

Reaction of Ylide **7** *with 1-Naphthyl Isocyanate*

A mixture of ylide **7** (0.4 g, 1.69 mmol) and 1-naphthyl isocyanate (0.7 g, 4.14 mmol) in CH_2Cl_2 (5 ml) was left for 13 days at room temperature. The ^1H NMR spectrum of the reaction mixture showed the signals in the reaction mixture: 8.50 ppm (ylide **7**, H_α (Py)), 8.55 ppm (**9g**, H_α (Py)). These correspond to ylides **7** (8%) and **9g** (82%).

*N-[(N-Ethoxycarbonyl-N-phenylcarbamoyl) ethoxycarbonylmethyl]pyridinium Methosulfate (***10b***)*

$MeSO_2OH$ (0.135 g, 1.40 mmol) was added dropwise to a stirred yellow solution of the crude **9b** (0.5 g, 1.40 mmol) in CH_2Cl_2 (2 ml). A colorless solution that formed was evaporated to dryness under reduced pressure, and the residue was recrystallized (acetonitrile/hexane) to obtain white crystals.

TABLE 4 Characterization Data of Isoquinolinium Ylides and Bis-Salt **15a**

Compound	Molecular Formula	Molecular Weight	Yield (%)	mp (°C)	Elemental Analysis[a] (%) C	H	N	S
12	$C_{16}H_{17}NO_4$	287.32	70	191–193	–	–	–	–
14a	$C_{23}H_{21}N_3O_7$	451.44	68	90–91[b]	60.99 (61.19)	4.48 (4.69)	9.48 (9.31)	–
15a	$C_{25}H_{29}N_3O_{13}S_2$	643.64	93	134–136	47.42 (46.65)	4.54 (4.69)	6.56 (6.53)	10.07 (9.96)
14b	$C_{27}H_{24}N_2O_5$	456.50	81	79–80[b]	70.75 (71.04)	5.49 (5.30)	5.83 (6.14)	–

[a] Values found are followed by the calculated values (in parentheses).
[b] Decomposition.

TABLE 5 The ^{1}H NMR and IR Spectral Data of the Synthesized Compounds

Compound	^{1}H NMR	IR (υ_{max} cm^{-1}) C=O (C(O)OEt)	C=O (—C(O)—N)	C=O (N—C(O)OEt)
12	1.29 (t, 6H, $CH_2C\underline{H}_3$, $J = 7.2$ Hz), 4.19 (q, 4H, $C\underline{H}_2CH_3$, $J = 7.2$ Hz), 7.82 (m, 1H, Is), 7.94 (d, 1H, Is, $J = 6.8$ Hz), 7.99 (d, 2H, Is, $J = 4.0$ Hz), 8.12 (d, 1H, Is, $J = 8.0$ Hz), 8.30 (t, 1H, Is, $J = 7.2$ Hz), 9.27 (s, 1H, H_1 (Is))	1658	–	–
14a	1.13 (t, 3H, $CH_2C\underline{H}_3$, $J = 7.2$ Hz), 1.35 (t, 3H, $CH_2C\underline{H}_3$, $J = 7.2$ Hz), 4.08 (q, 2H, $C\underline{H}_2CH_3$, $J = 7.2$ Hz), 4.32 (q, 2H, $CH_2C\underline{H}_3$, $J = 7.2$ Hz), 7.76 (d, 2H, Ar, $J = 9.2$ Hz), 7.90 (m, 1H, Is), 8.08 (m, 3H, Is), 8.18 (d, 2H, Ar, $J = 9.2$ Hz), 8.16–8.23 (m, 1H, Is), 8.33 (d, 1H, Is), $J = 6.8$ Hz), 9.34 (s, 1H, H_1 (Is))	1591	1591	1714
15a	1.21 (t, 3H, $CH_2C\underline{H}_3$, $J = 7.2$ Hz), 1.32 (t, 3H, $CH_2C\underline{H}_3$, $J = 7.2$ Hz), 2.95 (s, 6H, CH_3S), 4.23–4.48 (m, 4H, $C\underline{H}_2CH_3$), 7.61 (d, 2H, Ar, $J = 8.8$ Hz), 7.87 (s, 1H, CH), 7.95 (t, 1H, Is, $J = 7.2$ Hz), 8.07–8.17 (m, 2H, Is), 8.24 (d, 1H, Is, $J = 6.4$ Hz), 8.25 (d, 2H, Ar, $J = 8.8$ Hz), 8.41 (d, 1H, Is, $J = 6.8$ Hz), 8.60 (d, 1H, Is, $J = 8.4$ Hz), 10.29 (s, 1H, H_1 (Is)), 10.77 (bs, 1H, H^+)	1751	1715	1751
14b	(^{1}H NMR at +20°C) 1.20 (t, 3H, $CH_2C\underline{H}_3$, $J = 7.2$ Hz), 1.33 (t, 3H, $CH_2C\underline{H}_3$, $J = 7.2$ Hz), 4.15–4.24 (m, 2H, $C\underline{H}_2CH_3$), 4.25–4.34 (m, 2H, $C\underline{H}_2CH_3$), 7.37–8.39 (m, 13H, H_{arom}), 9.36 (s, 1H, H_1 (Is)) (^{1}H NMR at +55°C) 1.30 (t, 3H, $CH_2C\underline{H}_3$, $J = 7.2$ Hz), 1.33 (t, 3H, $CH_2C\underline{H}_3$, $J = 7.2$ Hz), 4.21 (q, 2H, $C\underline{H}_2CH_3$, $J = 7.2$ Hz), 4.31 (q, 2H, $C\underline{H}_2CH_3$, $J = 7.2$ Hz), 7.37–8.39 (m, 13H, H_{arom}), 9.37 (s, 1H, H_1 (Is))	1583	1583	1712

Is = isoquinoline.

*N-[(N-Ethoxycarbonyl-N-3,4-dichlorophenylcarbamoyl)ethoxycarbonylmethyl]pyridinium Methosulfate (***10d***)*

$MeSO_2OH$ (0.83 g, 8.68 mmol) was added dropwise to a stirred yellow solution of **9d** (3.69 g, 8.68 mmol) in CH_2Cl_2 (20 ml). The colorless solution that formed was evaporated to dryness under reduced pressure. The residue was washed by ethyl ether and recrystallized from acetone to obtain white crystals. ^{13}C NMR δ: 13.63 ($OCH_2\underline{C}H_3$), 39.31 (CH_3S), 64.10 ($O\underline{C}H_2CH_3$), 64.50 ($O\underline{C}H_2CH_3$), 75.79 (CH), 127.82–127.04 ($C_{2,6}$ (Ar)), 130.25 (C_5 (Ar)), 130.65 (C_β (Py)), 132.53 (C—Cl), 132.91 (C—Cl), 135.75 (N—C (Ar)), 146.16 (C_γ (Py)), 147.59 (C_α (Py)), 152.98 (C(O)N), 162.84 (N$\underline{C}$OOEt) 164.64 ($\underline{C}$OOEt).

*N-[(N-Ethoxycarbonyl-N-4-nitrophenylcarbamoyl)ethoxycarbonylmethyl]pyridinium Methosulfate (***10f***)*

$MeSO_2OH$ (0.024 g, 0.25 mmol) was added dropwise to stirred yellow solution of **9f** (0.10 g, 0.25 mmol) in CH_2Cl_2 (2 ml). A colorless solution that resulted was evaporated to dryness under reduced pressure. The residue was washed by ethyl ether and recrystallized (ether/THF) to obtain white crystals.

*N-[(N-Ethoxycarbonyl-N-4-nitrophenylcarbamoyl)ethoxycarbonylmethyl]pyridinium bis-methosulfate (***11f***)*

$MeSO_2OH$ (0.05 g, 0.50 mmol) was added dropwise to a stirred yellow solution of **9f** (0.10 g, 0.25 mmol) in CH_2Cl_2 (2 ml). A colorless solution that resulted was evaporated to dryness under reduced pressure. The residue was washed by ethyl ether and recrystallized from THF to obtain white crystals. ^{13}C NMR δ: 9.87 ($OCH_2\underline{C}H_3$), 35.11 (CH_3S), 60.86 ($O\underline{C}H_2CH_3$), 60.90 ($O\underline{C}H_2CH_3$), 71.93 (CH), 120.07–124.06 (Ar), 125.83 (C_β (Py)), 137.75 (N—C (Ar)), 141.95 (C_γ (Py)), 143.79 (C_α-(Py)), 148.68 (C(O)N), 158.62 (N$\underline{C}$OOEt) 160.36 ($\underline{C}$OOEt).

*Thermolysis of (***9b***)*

Ylide **9b** (1 g, 0.28 mmol) was heated (130°C) under N_2 for 1 h. The resulting mixture was cooled to room temperature and extracted with boiling acetone. Evaporation of the solvent gave a powder, which was recrystallized from acetone. Yield 60%, mp 174°C. The ^{1}H NMR spectrum gave the signals of the starting ylide **7**.

Isoquinolinium ylide (**12**) was obtained by the literature method [5].

*Isoquinolinium (N-Ethoxycarbonyl-N-4-nitrophenylcarbamoyl)ethoxycarbonylmethylide (***14a***)*

A mixture of ylide **12** (2 g, 6.96 mmol) and 4-nitrophenyl isocyanate (2.3 g, 14.02 mmol) in $CHCl_3$ (25 ml) was left for 24 h at room temperature. The reaction mixture was filtered, and petroleum ether was added dropwise to the filtrate. The precipitate that formed was filtered off and dried under reduced pressure without heating to obtain orange powder.

*Isoquinolinium (N-Ethoxycarbonyl-N-1-naphthylcarbamoyl)ethoxycarbonylmethylide (***14b***)*

A mixture of ylide **12** (2 g, 6.96 mmol) and 1-naphthyl isocyanate (2.4 g, 14.20 mmol) in CH_2Cl_2 (25 ml) was left for 8 days at room temperature. Completion of the reaction was monitored by ^{1}H NMR spectroscopy. The reaction mixture was filtered, and petroleum ether was added dropwise to the filtrate. An oil that formed was stirred in the mixture of ethyl ether and petroleum ether. An orange powder **14b** that formed was filtered off and dried under reduced pressure without heating.

*N-[(N-Ethoxycarbonyl-N-4-nitrophenylcarbamoyl)ethoxycarbonylmethyl]isoquinolinium bis-methosulfate (***15a***)*

$MeSO_2OH$ (0.42 g, 4.43 mmol) was added dropwise to a stirred yellow solution of **14b** (1 g, 2.21 mmol) in CH_2Cl_2 (10 ml). A colorless solution that resulted was evaporated to dryness under reduced pressure. The residue was washed by ethyl ether and recrystallized from acetone to obtain white crystals. ^{13}C NMR δ: 9.93 ($OCH_2\underline{C}H_3$), 35.44 (CH_3S), 60.52 ($O\underline{C}H_2CH_3$), 61.07 ($O\underline{C}H_2CH_3$), 71.74 (CH), 120.59–148.74 (C_{arom}), 148.94 (C(O)N), 159.19 ($N\underline{C}OOEt$) 161.06 ($\underline{C}OOEt$).

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