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Reaction of *Schiff* Bases of 1-Tetralone with Acid Chlorides. Stereoselective Synthesis of β-Lactams Spiroannulated with the Tetrahydronaphthalene Ring System

K. Bogdanowicz-Szwed* and **M. Krasodomska**

Department of Organic Chemistry, Jagiellonian University, PL-30060 Kraków, Poland

Summary. Arylimines of 1-tetralone (**1**) react with various substituted acetyl chlorides (**2**) in the presence of triethylamine yielding β-lactams spiroannulated with tetrahydronaphthalene (**3**). The stereochemistry of the products has been determined by NMR methods. Reactions of imines **1** with acid chlorides **2** were proved to be highly stereoselective.

Keywords. Acid chlorides; Cycloaddition; β-Lactams; Schiff bases.

Reaktion *Schiff*scher Base von 1-Tetralon mit Säurechloriden. Stereoselektive Synthese von mit dem Tetrahyronaphthalinsystem spiroannellierten β-Lactamen

Zusammenfassung. Arylimine von 1-Tetralon (**1**) reagieren in Gegenwart von Triethylamin mit substituierten Säurechloriden (**2**) zu mit Tetrahydronaphthalin spiroannellierten β-Lactamen (**3**). Die Stereochemie der Produkte wurde mittels NMR-Spektroskopie aufgeklärt. Es konnte gezeigt werden, daß die Reaktion hoch stereoselektiv verläuft.

Introduction

Preparative methods for the construction of a β-lactam ring system have been attracting much interest in connection with the development of the analogues of β-lactam antibiotics such as penicillin, cephalosporin, nocardicin and thienamycin [1]. The following general methods of synthesis of an azetidinone ring are well known: cyclization of functionalized β-amino acids [2], cycloaddition of ketenes to imines [3, 4], cyclization of ester enolates and imines [5], *Reformatsky* reaction of imines [4], and cycloaddition of active isocyanates, *e.g.* chlorosulphonylisocyanate to alkenes [6].

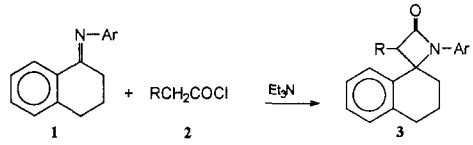
In previous communications we reported the reactions of 1-tetralone imines and enamines with arylisocyanates, arylisothiocyanates and active methylene compounds [7–9] leading to fused N and S six-membered heterocycles. In this work we report the reaction of previously described 1-tetralone imines [7] with acyl chlorides leading to β-lactams spiroannulated to the naphthalene system.

Campbell et al. [10] reported the formation of β-lactams spiroannulated with tetrahydronaphthalene by cycloaddition of 1-tetralone anil to ethoxyketene obtained by photochemical generation and rearrangement of carboethoxycarbene. Recently, *Ishibashi* [11] described the radical ring closure of the α-chloroacylated enamine of 2-tetralone leading to a β-lactam spiroannulated with a tetrahydronaphthalene moiety.

Results and Discussion

In this work we investigated the reaction of arylimines of 1-tetralone (**1**) with acid chlorides (**2**). The preparation of arylimines with electron-releasing groups was described earlier [7]. In the course of this work we have also prepared an arylimine with an electron-withdrawing NO_2 group in arylimino moiety (**1p**). Derivatives of acetic acid chloride contained various substituents such as PhO–, BzO–, Phthaloyl–N– PhS–, Cl–, *etc.* (Scheme 1).

Reactions of the appropriate imines with acid chlorides were carried out in methylene chloride in the presence of triethylamine. We noticed that the formation of β-lactams dependeds on the sequence of reagent addition. Most of the reactions were conducted by addition of the acyl chloride solution with a few drops of triethylamine to a mixture of imine and triethylamine in methylene chloride. Progress of the reaction was monitored by change of colour of the reaction mixture from yellow to brown-green. Quenching the reaction with acid, extraction, and chromatographic purification on silica gel, followed by recrystallization, afforded products **3** as colourless crystals.



1 2 3

3	Ar	R
a	C_6H_5-	C_6H_5O-
b	C_6H_5-	$C_6H_5CH_2O$-
c	C_6H_5-	CH_3O-
d	C_6H_5-	CH_3CH_2O-
e	C_6H_5-	Cl-
f	C_6H_5-	Pht-
g	*p*-CH_3O-C_6H_4-	C_6H_5O-
h	*p*-CH_3O-C_6H_4-	$C_6H_5CH_2O$-
i	*p*-CH_3O-C_6H_4-	CH_3O-
j	*p*-CH_3O-C_6H_4-	CH_3CH_2O-
k	*p*-CH_3O-C_6H_4-	Cl-
l	*p*-CH_3O-C_6H_4-	Pht-
m	*p*-Br-C_6H_4-	C_6H_5O-
n	*p*-Cl-C_6H_4-	C_6H_5O-
o	*p*-CH_3-C_6H_4-	C_6H_5O-
p	*p*-$NO_2C_6H_4$-	C_6H_5O-
q	*p*-CHO-C_6H_4-	PhS-

Scheme 1

Reaction of imine **1a** with phenoxyacetic chloride (**2a**) leading to **3a** was chosen as representative for establishing the structures of all products and for comparison of the reactivities of other 1-tetralone imines with various acyl chlorides.

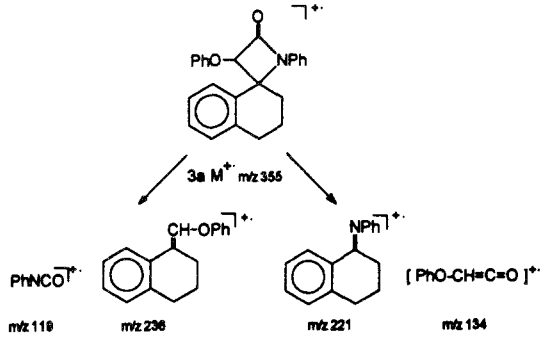
Analytical and MS spectral data for **3a** were in agreement with the expected β-lactame structure.

The IR spectrum revealed an intensive band at 1735 cm^{-1} characteristic for the carbonyl stretch of the azetidinone ring. The ^1H NMR spectrum displayed the multiplets of 14 aromatic protons. The six aliphatic protons of the three methylene groups of the tetraline skeleton appeared as four multiplets

with intensity 1 ($\delta = 1.69$, 2.59, 2.74, 2.90 ppm) and one multiplet with intensity 2 ($\delta = 2.00$ ppm). The singlet at $\delta = 5.13$ ppm was assigned to the hydrogen attached to C–3′ of the azetidinone ring.

The analysis of the DEPT ^{13}C NMR spectrum of **3a** allowed us to assign the signals for all carbon atoms. The characteristic carbon atoms of the azetidinone ring resonate at $\delta = 163.21$ ppm (CO), $\delta = 90.21$ ppm (C–3′), and at $\delta = 68.08$ ppm (C–4′ spiro atom; see Experimental).

The MS spectrum of **3a** revealed the molecular ion at $m/z = 355$. In general, two distinct modes of fragmentation were found, and may be considered as the reverse [2 + 2] cycloaddition (Scheme 2). The first pathway involves the formation of intensive ions at $m/z = 119$ and $m/z = 236$ which correspond to phenylisocyanate and phenoxymethylene-1-tetraline, respectively. The presence of an intense ion at $m/z = 221$ due to 1-tetralone anil suggested the second pathway of fragmentation, although the ion at $m/z = 134$, corresponding to phenoxyketene, was not observed, presumably because of its further decomposition. This type of fragmentation was also observed for other β-lactams synthesized in this work and is in agreement with literature reports [12].



Scheme 2

All synthesized β-lactams contain two chiral centres at C–3′ and at the spiro atom C4′. ^1H NMR spectra of all compounds **3** revealed one methine signal which occurred in the range of 4.44–5.15 ppm, depending on the substituent attached to C–3′. The presence of only one signal indicates that the reactions of **1** with **2** give one diastereoisomer exclusively. Since *Campbell et al.* [10] reported the formation of two diastereoisomeric β-lactams by reaction of carboethoxycarbene with 1-tetralone anil (**1**), we tried to find out whether formation of diastereoisomeric compounds depends on the type of substituent or on the method of construction of azetidinone ring.

Reaction of **1** with ethoxyacetic chloride **2** in the presence of triethylamine yielded **3d** as the sole product. Its structure was confirmed by TLC and ^1H NMR and IR spectra of the crude reaction mixture and the pure sample of **3d**. The IR spectrum revealed one intensive band at 1745 cm^{-1}; the ^1H NMR spectrum gave only one signal for the H–C3′ proton. Analytical and spectral data of **3d** were in agreement with the expected azetidinone structure, but in some extent different from those reported by *Campell et al.* [10a]. Taking into account these data we assume that the diastereoselectivity in the formation of these β-lactams depends on the method of synthesis.

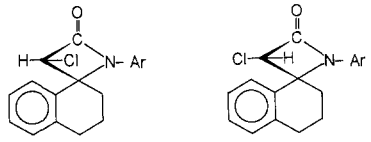
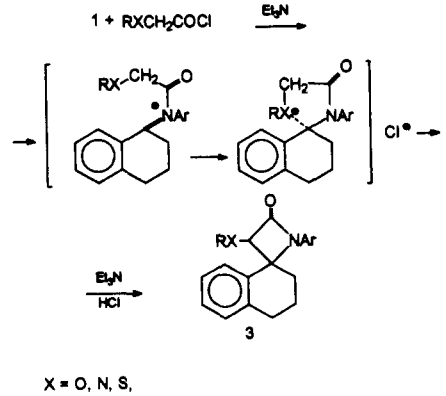


Fig. 1

To assign the relative configuration at carbons C–3′ and C–4, a ^{1}H NOE difference experiment was performed. Compound **3e** was chosen as the model compound. In the difference spectrum was observed on irradiating H–C3′ enhancement (6.4%) of the aromatic proton (7.31 ppm). This signal is a doublet with a coupling constant of 8 Hz indicating the presence of one *ortho* neighbour. The chemical shift of this signal allowed us to assign it to H–C8. Therefore, the homonuclear NOE difference experiment proves the structure to correspond to diastereoisomer A, (Fig. 1) *i.e.* the proton attached to carbon C–3′ is directed towards the aromatic moiety of the tetrahydronaphthalene skeleton. Inspection of *Dreiding* models of **3** confirm that structure A since it is less sterically hindered than B.

We found considerable influence of the type of substituents in arylimines **1** and in acyl chlorides **2** on the yields of the products **3**. In the case of imines we noticed an increase of yield when electron-releasing substituents were present in the arylimine moiety. Particularly good results were obtained in the case of *p*-methoxyanil substituted 1-tetraloneimine. Since the reaction with phenacyl chloride failed, we used derivatives of acetyl chlorides which contained phenoxy, methoxy, phthalimide and chloro substituents. Examination of the results shows that only acid chlorides containing atoms with a lone electron pair in the α position react with imines to yield β-lactams. The results can be best explained by assuming that these atoms play an important role in a transition state involved in β-lactam formation. Our results are in agreement with observations suggesting that atoms of this type can form a five-membered transition state (Scheme 3) [13, 14].



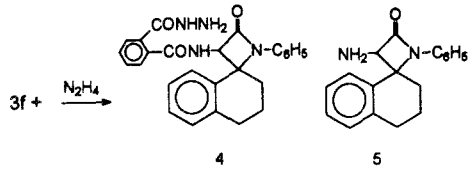
Scheme 3

Recently, convenient procedure for the synthesis of β-lactams was reported [15, 16]. It involves the reaction of imines with acids in presence of chlorosulphinyl-

methylene-N, N-dimethylammonium chloride, formed by the reaction of thionyl chloride with *DMF*. Taking advantage of the above procedure, we applied it to the preparation of some β-lactams to compare selectivity and yields of both pathways. The reaction of imine **1** (Ar = C_6H_5, $CH_3OC_6H_4$) with phenoxyacetic acid and phthaloylglycine in presence of this reagent gave compounds **3a**, **g** and **3f**, **l**, respectively. The obtained products were found to be identical in all respects with those synthesised in the reaction of imines with acid chlorides, but yields were lower. Using this procedure, we also obtained small amounts of β-lactam **3q** which could not be obtained using phenylthioacetic acid chloride and imine **1**.

Subsequently we have examined the rearrangements of some β-lactams **3**. Rearrangement involves cleavage of amide N–C2 or N–C4 bonds [12], yielding acyclic or enlarged cyclic compounds. These reactions are usually promoted by electrophilic or nucleophilic agents.

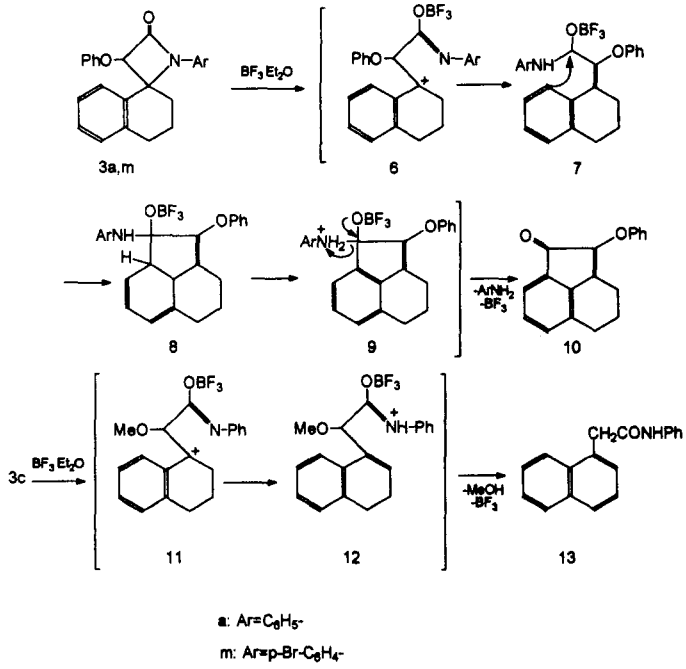
At first we were interested in removing the phthaloyl protecting group of **3f** by heating it with hydrazine hydrate in ethanolic solution. Work up of the reaction mixture afforded two products: hydrazide **4** and 3-amino azetidinone **5** (Scheme 4).



Scheme 4

The β-lactams **3** turned out to be stable in conc. sulphuric acid and in ethanolic sodium ethoxide solution; however, they underwent rearrangement under the influence of boron trifluoride etherate. Depending upon the substituents present in the azetidinone ring at C–3′ these reactions may proceed by pathways giving different type of products. When **3a**,**m** were heated in toluene in the presence of boron trifluoride etherate, compound **10** was isolated in 41% and 33% yields, respectively. Analytical and spectral data of **10** combined with molecular mass determination ($m/z = 262$) indicate that both reactions occurred with splitting off arylamine moieties. On the basis of these data, an acenaphthenone structure was assigned to **10** (Scheme 5). The ^{1}H NMR spectrum of **10** revealed a broad multiplet of six aliphatic protons at 2.25–3.75 ppm and a multiplet of eight aromatic protons at 7.00–7.60 ppm. The IR spectrum of **10** exhibited a CO-band at 1750 cm^{-1}. Reaction of **3c** performed under the same conditions, yielded 1-naphthylacetanilide **13**, identical with that described in Ref. [17].

To explain these reactions, we propose the following mechanism: the boron trifluoride catalyzed reaction of β-lactams **3a**,**m** and **3c** proceeds *via* cleavage of the N–C4′ bond yielding carbonium ions **6** or **11**. The proton shift of H–C(3′) in carbonium ion **6** involves an amide intermediate **7**. In the next step, a boron trifluoride catalyzed intramolecular electrophilic substitution of **7** yields **10**. In the case of carbonium ion **11**, derived from **3c**, the proton shift from H–C(2) of the hydronaphthalene moiety yields the intermediate **12**, which subsequently undergoes dehydrogenation and simultaneous removal of the methoxy group giving 1-naphthyl acetanilide **13**.



Scheme 5

Experimental

Melting points were measured on a Boetius apparatus and are corrected. IR spectra were recorded on a Bruker IFS spectrometer in nujol hexachlorobutadiene mulls. ^1H NMR spectra were obtained on Tesla BS 567 A (100 MHz) and Bruker AM 400 (400 MHz) NMR spectrometers in $CDCl_3$ or *DMSO* using *TMS* as an internal standard. ^{13}C NMR spectra were recorded in $CDCl_3$ at 100 MHz on a Bruker AM 400 spectrometer. Mass spectra were measured on a LKB 9000S (70 eV) spectrometer and elemental analyses were carried out on a Perkin Elmer Analyser 240 in the Regional Laboratory of Physico-Chemical Analyses and Structural Studies in Kraków.

1-Tetralone arylimines **1** were obtained according to the procedure described in Ref. [7]. Imines with *p*-tolyl and *p*-nitrophenyl groups were not described; they were synthesized in the similar manner.

p-Tolylimine of 1-tetralone

Yellow prisms from ligroin, m.p. 64–66°C; yield: 77%; IR: 1625 cm^{-1} (C=N); ^1H NMR ($CDCl_3$ ppm): 1.95 (q, 2H, CH_2), 2.34 (s, 3H, CH_3), 2.49 (t, 2H, CH_2), 2.92 (t, 2H, CH_2), 6.82–8.26 (m, 8H, arom.).

p-Nitrophenylimine of 1-tetralone

Pale yellow prisms from ethanol, m.p. 150–152°C; yield: 45%; IR: 1625 cm^{-1} (C=N); ^1H NMR ($CDCl_3$ ppm): 1.92 (q, 2H, CH_2), 2.59 (t, 2H, CH_2), 2.95 (t, 2H, CH_2), 6.65–8.29 (m, 8H, arom).

General Procedures for the Synthesis of β-Lactams

Method a: To a stirred and cooled (0–5°C) solution of imine **1** (0.01 mol) and triethylamine (0.03 mol) in dry methylene chloride, a solution of the acid chloride **2** (0.01 mol) in dry methylene chloride with

triethylamine (0.005 mol) was added dropwise. The reaction mixture was allowed to come to room temperature. The progress of the reaction was monitored by TLC. In some cases the reaction mixture had to be refluxed for 2 hours. After washing with water and 1 *N* HCl the organic layer was dried ($MgSO_4$). Evaporation of the solvent gave an oily product which was treated with methanol and further purified by column chromatography on silica gel using chloroform as eluent. Recrystallization from methanol furnished the pure product as colourless prisms.

Method b: A mixture of benzene (5 ml), *DMF* (1 ml, 0.012 mol), and thionyl chloride (0.8 ml, 0.011 mol) was placed in a dropping funnel. After 5 min. two phases appeared and the lower layer was separated as chlorosulphinylmethylene N,N-dimethylmmonium chloride. This reagent (0.01 mol) was added to a cooled and stirred solution or suspension of carboxylic acid (0.01 mol) in methylene chloride. After 10 min., imine **1** (0.01 mol) and subsequently triethylamine (0.03 mol) in methylene chloride was added. The reaction mixture was stirred overnight at room temperature. After washing with water and drying ($MgSO_4$), the crude product was purified in the similar way as described in *Method a.*

^{13}C NMR spectral data of compounds **3a** and **3e** ($CDCl_3$, ppm):
3a: 163.23 (C–2'), 157.22, 138.27, 135.89, 131.31, 129.17, 128.96, 128.29, 128.12, 125.71, 124.24, 122.62, 118.55, 117.39 (aromatic C), 90.21 (C–3'), 68.08 (C–4'), 31.10, 28.87, 20.57 (aliphatic C); **3e**: 161.38 (C–2'), 138.12, 135.71, 134.40, 129.71, 128.96, 128.57, 127.24, 125.13, 124.41, 118.06 (aromatic C), 68.92 (C–3'), 65.01 (C–4'), 28.96, 27.49, 20.52 (aliphatic C).

Synthesis of compounds **4** *and* **5**

Compound **3f** (1.5 g, 0.0036 mol) was pulverized and suspended in 70 ml of ethanol and 3.6 ml of a 1 *M* solution of hydrazine hydrate (0.0036 mol) in 5 ml of ethanol were added. After refluxing for 2 h, the mixture was stored overnight. The crude precipitate of **4** was separated and recrystallized from ethanol. Colourless prisms, m.p. 200–203°C; yield: 65%; IR: 1759, 1643, 1629 cm^{-1} (CO), 3326, 3242 cm^{-1} (NH).

To separate **5**, the ethanolic solution of **4** was evaporated and the residue was treated with 25 ml of hydrochloric acid (1:1) and refluxed fro 2 h. The solid was separated and treated with hot water. The aqueous and acid extracts were combined and acidified additionally with 3 ml of HCl conc. After standing overnight, the precipitated amine hydrochloride was filtered off and crystallized from ethanol. Colourless prisms, m.p. 203–205°C; yield: 61%; IR: 1760 cm^{-1} (CO); 3400, 2600–2900 cm^{-1} (NH·HCl).

11-Phenoxy-1,2,3,4-tetrahydro-acenaphthylen-10-one (**10**)

A mixture of 1.0 g of the respective β-lactam (3 mmol of **3a**, 2.3 mmol of **3m**), 1.0 ml of boron trifluoride etherate and 100 ml toluene were refluxed for 60 h. The solution was cooled and washed with water (100 ml). The organic layer was dried ($MgSO_4$). Evaporation of the solvent gave a brown oil. Trituration with methanol yielded the solid product. Purification by column chromatography on silica gel using chloroform as eluent and further crystallization from ethanol or methanol yielded the analytically pure product. Colourless needless, m.p. 152–154°C; yield: 41% from **3a**, 33% from **3m**; IR: 1660 cm^{-1} (CO); ^1H NMR ($CDCl_3$, ppm): 2.25–3.75 (m, 6H, CH_2), 7.00–7.60 (m, 8H, arom.); MS: $m/z = 262$ (100%).

1-Naphthylacetanilide **13**

4.0 g (14 mmol) β-lactam **3c**, 4.0 ml boron trifluoride etherate and 400 ml toluene were heated under reflux for 60 h. The solution was cooled and washed with water (200 ml). The organic layer was dried ($MgSO_4$); evaporation of solvent gave a brown oil. Trituration with methanol and crystallization from ethanol yielded 1-naphthylacetanilide. Colourless needless, m.p. 162–164°C, (Ref. [17]: 157–158°C); yield: 19%; IR: 1660 cm^{-1} (CO), 3310 cm^{-1} (NH); ^1H NMR ($CDCl_3$, ppm): 4.17 (s, 2H, CH_2); 7.03–7.98

Table 1. Yields, physical properties, and spectroscopic data of compounds **3a–3q**

	Yield (%)	M.p. (°C)	Formula, mol. mass	IR (cm^{-1})	^1H NMR δ (ppm)	MS (*m/z*)
3a	51[a] 28[b]	145–147	$C_{24}H_{21}NO_2$ 355.44	1735 (CO)	1.69 (m, 1H) 2.00 (m, 2H) 2.59 (m, 1H) 2.74 (m, 1H) 2.90 (m, 1H) 5.13 (s, 1H, CH) 6.73–7.50 (m, 14H, arom.)	355 $M^{+\cdot}$ 236 $[C_{17}H_{16}O]^{+\cdot}$ 221 $[C_{16}H_{15}N]^{\cdot}$ 119 $[C_6H_5NCO]^{+\cdot}$ 91 $[C_6H_5N]^{+\cdot}$ 77 $[C_6H_5]^{+\cdot}$
3b	25[a]	177–179	$C_{25}H_{23}NO_2$ 369.46	1751 (CO)	1.70–3.05 (m, 6H, CH_2) 4.45 (s, 1H, CH) 4.30 (dd, $J = 11.5$, Hz, 2H, CH_2) 6.96–7.50 (m, 14H, arom.)	369 $M^{+\cdot}$ 250 $[C_{18}H_{18}O]^{+\cdot}$ 221 $[C_{16}H_{15}N]^{\cdot}$ 119 $[C_6H_5NCO]^{+\cdot}$ 91 $[C_6H_5N]^{+\cdot}$ 77 $[C_6H_5]^{+\cdot}$
3c	38[a]	103–105	$C_{19}H_{19}NO_2$ 293.36	1737 (CO)	1.66–3.06 (m, 6H, CH_2) 3.11 (s, 3H, OCH_3) 4.26 (s, 1H, CH) 7.00–7.41 (m, 9H, arom.)	293 $N^{\cdot}$ 221 $[C_{16}H_{15}N]^{\cdot}$ 174 $[C_{12}H_{14}O]^{+\cdot}$ 119 $[C_6H_5NCO]^{+\cdot}$ 91 $[C_6H_5N]^{+\cdot}$ 77 $[C_6H_5]^{+\cdot}$
3d	34[a]	120–121	$C_{20}H_{21}NO_2$ 307.39	1743 (CO)	0.87 (t, 3H, CH_3) 1.86–3.00 (m, 6H, CH_2) 3.00–3.50 (dq, 2H, CH_2) 4.35 (s, 1H, CH) 7.00–7.52 (m, 9H, arom.)	307 $M^{\cdot}$ 221 $[C_{16}H_{15}N]^{\cdot}$ 188 $[C_{13}H_{16}O]^{+\cdot}$ 119 $[C_6H_5NCO]^{\cdot}$ 91 $[C_6H_5N]^{+\cdot}$ 77 $[C_6H_5]^{+\cdot}$
3e	7[a]	125–128	$C_{18}H_{16}ClNO$ 297.78	1755 (CO)	2.11 (m, 2H, CH_2) 2.43 (m, 2H, CH_2)	297 $M^{+\cdot}$ 221 $[C_{16}H_{15}N]^{+\cdot}$

Table 1. (continued)

	Yield (%)	M.p. (°C)	Formula, mol. mass	IR (cm^{-1})	^1H NMR δ (ppm)	MS (*m/z*)
					2.93 (m, 2H, CH_2)	178 $[C_{11}H_{11}Cl]^{+\cdot}$
					4.79 (s, 1H, CH)	91 $[C_6H_5N]^{+\cdot}$
					7.00–7.35 (m, 9H, arom.)	77 $[C_6H_5]^{+\cdot}$
3f	42[a]	235–238	$C_{26}H_{20}N_2O_3$	1784 (CO)	1.25–3.00 (m, 6H, CH_2)	408 $M^{+\cdot}$
	13[b]		408.46	1759 (CO)	5.22 (s, 1H, CH)	289 $[C_{19}H_{15}NO_2]^{+\cdot}$
				1727 (CO)	7.00–7.95 (m, 13H, arom.)	221 $[C_{16}H_{15}N]^{+\cdot}$
						119 $[C_6H_5NCO]^{+\cdot}$
						91 $[C_6H_5N]^{\cdot}$
						77 $[C_6H_5]^{+\cdot}$
3g	59[a]	108–110	$C_{25}H_{23}NO_3$	1749 (CO)	1.67–2.91 (m, 6H, CH_2)	386 $M^{+\cdot}$
	44[b]		385.46		3.72 (s, 3H, OCH_3)	251 $[C_{17}H_{17}NO]^{+\cdot}$
					5.08 (s, 1H, CH)	236 $[C_{17}H_{16}O]^{+\cdot}$
					6.67–7.53 (m, 13H, arom.)	149 $[CH_3OC_6H_4NCO]^{+\cdot}$
						121 $[CH_3OC_6H_4N]^{+\cdot}$
						91 $[C_6H_5N]^{+\cdot}$
						77 $[C_6H_5]^{+\cdot}$
3h	78[a]	165–167	$C_{26}H_{25}NO_3$	1749 (CO)	1.60–3.03 (m, 6H, CH_2)	399 $M^{+\cdot}$
			399.49		3.72 (s, 3H, OCH_3)	251 $[C_{17}H_{17}NO]^{+\cdot}$
					4.44 (s, 1H, CH)	250 $[C_{18}H_{18}O]^{+\cdot}$
					4.23 (dd, $J = 11.0$ Hz, 2H, CH)	149 $[CH_3OC_6H_4NCO]^{+\cdot}$
					6.50–7.50 (m, 13H, arom.)	121 $[CH_3OC_6H_4N]^{+\cdot}$
						91 $[C_6H_5N]^{+\cdot}$
						77 $[C_6H_5]^{+\cdot}$
3i	58[a]	145–147	$C_{20}H_{21}NO_3$	1747 (CO)	1.86–3.00 (m, 6H, CH_2)	323 $M^{+\cdot}$
			323.39		3.10 (s, 3H, OCH_3)	251 $[C_{17}H_{17}NO]^{+\cdot}$
					3.72 (s, 3H, OCH_3)	174 $[C_{12}H_{14}O]^{+\cdot}$
					4.25 (s, 1H, CH)	149 $[CH_3OC_6H_4NCO]^{+\cdot}$

(Continued)

Table 1. (Continued)

	Yield (%)	M.p. (°C)	Formula, mol. mass	IR (cm^{-1})	^1H NMR δ (ppm)	MS (*m/z*)
					6.50–7.43 (m, 8H, arom.)	91 $[C_6H_5N]^{+\cdot}$ 77 $[C_6H_5]^{+\cdot}$
3j	24[a]	104–105	$C_{21}H_{23}NO_3$ 337.42	1743 (CO)	0.87 (t, 3H, CH_3) 1.84–3.00 (6H, CH_2) 3.30 (dq, 2H, CH_2) 3,71 (s, 3H, OCH_3) 4.34 (s, 1H, CH) 6.70–7.47 (m, 8H, arom.)	337 $M^{+\cdot}$ 251 $[C_{17}H_{17}NO]^{+\cdot}$ 188 $[C_{13}H_{16}O]^{+\cdot}$ 149 $[CH_3OC_6H_4NCO]^{+\cdot}$ 91 $[C_6H_5N]^{+\cdot}$ 77 $[C_6H_5]^{+\cdot}$
3k	19[a]	133–135	$C_{19}H_{18}ClNO_2$ 327.81	1749 (CO)	1.75–3.00 (m, 6H, CH_2) 3.73 (s, 3H, OCH_3) 4.79 (s, 1H, CH) 6.70–7.51 (m, 8H, arom.)	327 $M^{+\cdot}$ 251 $[C_{17}H_{17}NO]^{+\cdot}$ 178 $[C_{11}H_{11}Cl]^{+\cdot}$ 149 $[CH_3OC_6H_4NCO]^{+\cdot}$ 121 $[CH_3OC_6H_4N]^{+\cdot}$ 91 $[C_6H_5N]^{+\cdot}$ 77 $[C_6H_5]^{+\cdot}$
3l	49[a] 27[b]	250–252	$C_{27}H_{22}N_2O_4$ 438.48	1785 (CO) 1755 (CO) 1714 (CO)	1.25–3.00 (m, 6H, CH_2) 3.75 (s, 3H, OCH_3) 5.22 (s, 1H, CH) 7.00–7.95 (m, 12H, arom.)	438 $M^{+\cdot}$ 289 $[C_{19}H_{15}NO_2]^{+\cdot}$ 251 $[C_{17}H_{17}NO]^{+\cdot}$ 149 $[CH_3OC_6H_4NCO]^{+\cdot}$ 121 $[CH_3OC_6H_4N]^{+\cdot}$ 91 $[C_6H_5]^{+\cdot}$ 77 $[C_6H_5]^{+\cdot}$
3m	69[a]	144–146	$C_{24}H_{20}BrNO_2$ 434.33	1743 (CO)	1.58–2.81 (m, 6H, CH_2) 5.09 (s, 1H, CH) 6.65–7.45 (m, 13H, arom.)	434; 436 $M^{+\cdot}$ 300; 302 $[C_{16}H_{14}BrN]^{+\cdot}$ 236 $[C_{17}H_{16}O]^{+\cdot}$ 198; 200 $[BrC_6H_4NCO]^{+\cdot}$ 169; 171 $[BrC_6H_4N]^{+\cdot}$ 91 $[C_6H_5N]^{+\cdot}$ 77 $[C_6H_5]^{+\cdot}$

Table 1. (continued)

	Yield (%)	M.p. (°C)	Formula, mol. mass	IR (cm^{-1})	^1H NMR δ (ppm)	MS (*m/z*)
3n	42[a]	131–133	$C_{24}H_{20}ClNO_2$ 389.88	1743 (CO)	1.67–2.88 (m, 6H, CH_2) 5.14 (s, 1H, CH) 6.70–7.50 (m, 13H, arom.)	389 $M^{+\cdot}$ 255 $[C_{16}H_{14}ClN]^{+\cdot}$ 236 $[C_{17}H_{16}O]^{\cdot}$ 153 $[ClC_6H_4NCO]^{+\cdot}$ 126 $[ClC_6H_4N]^{+\cdot}$ 91 $[C_6H_5N]^{+\cdot}$ 77 $[C_6H_5]^{+\cdot}$
3o	35[a]	125–127	$C_{25}H_{23}NO_2$ 369.46	1743 (CO)	1.61–2.93 (m, 6H, CH_2) 2.27 (s, 3H, CH_3) 5.09 (s, 1H, CH) 6.67–7.51 (m, 13H, arom.)	369 $M^{+\cdot}$ 236 $[C_{17}H_{16}O]^{+\cdot}$ 235 $[C_{17}H_{17}N]^{+\cdot}$ 133 $[CH_3C_6H_4NCO]^{+\cdot}$ 91 $[C_6H_5N]^{+\cdot}$ 77 $[C_6H_5]^{+\cdot}$
3p	25[a]	153–155	$C_{24}H_{20}N_2O_4$ 400.43	1755 (CO)	1.55–2.91 (m, 6H, CH_2) 5.16 (s, 1H, CH) 6.67–8.18 (m, 13H, arom.)	400 $M^{+\cdot}$ 266 $[C_{16}H_{14}N_2O_2]^{\cdot}$ 236 $[C_{17}H_{16}O]^{\cdot}$ 164 $[NO_2C_6H_4NCO]^{+\cdot}$ 136 $[NO_2C_6H_4N]^{\cdot}$ 91 $[C_6H_5N]^{+\cdot}$ 77 $[C_6H_5]^{+\cdot}$
3q	5[b]	173–175	$C_{25}H_{23}NO_2S$ 401.52	1746 (CO)	1.96–2.80 (m, 6H, CH_2) 3.33 (s, 3H, OCH_3) 4.44 (s, 1H, CH) 6.63–7.39 (m, 13H, arom.)	401 $M^{+\cdot}$ 252 $[C_{17}H_{16}S]^{+\cdot}$ 251 $[C_{17}H_{17}NO]^{+\cdot}$ 149 $[CH_3OC_6H_4NCO]^{+\cdot}$ 121 $[CH_3OC_6H_4N]^{+\cdot}$ 91 $[C_6H_5N]^{+\cdot}$ 77 $[C_6H_5]^{+\cdot}$

All elemental analyses (C, H, N) are in agreement with the calculated values; superscripts a, and b, refer to the method of synthesis (cf. Experimental).

(m, 12H, arom.); MS (*m/z*): 261 (M^+), 168 ($M-C_6H_5NH_2^+$), 142 ($M-C_6H_5NHCO^+$), 128 ($C_{10}H_8^+$), 92 ($C_6H_5NH^+$), 77 ($C_6H_5^+$).

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