Electron Impact Ionization Mass Spectra of 6-Carbamoyloxy-3-oxo-3,6-dihydro-2*H*-pyran and 5*H*-pyrano[3,2-*d*]-oxazole-2,6-dione Derivatives

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Received July 19, 1994
Revised January 3, 1995

The electron impact ionization mass spectra of 6-carbamoyloxy-3-oxo-3,6-dihydro-2*H*-pyrans show a weak molecular ion peak and a base peak of *m/z* 84 resulting from a retro Diels-Alder fragmentation. The bicyclic system 5*H*-pyrano[3,2-*d*]oxazole-2,6-dione gives a characteristic fragmentation pattern with a very stable fragment of oxazolenone.

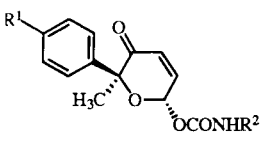
J. Heterocyclic Chem., **32**, 579 (1995).

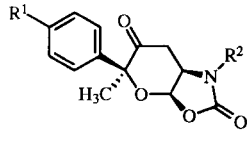
Introduction.

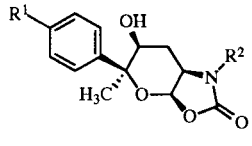
6-Hydroxy-3-oxo-3,6-dihydro-2*H*-pyrans are important intermediates for the synthesis of a variety of compounds with pharmacological interest [1-4]. In particular their allylic 6-carbamoyloxy derivatives have attracted much attention due to their potential use as anticoccidial and antimicrobial agents [5-7]. Upon treatment with sodium carbonate in acetone/water they undergo a highly stereoselective intramolecular Michael addition furnishing their corresponding 5*H*-pyrano[3,2-*d*]oxazole-2,6-diones, compounds with a novel 1,2-*cis*-fused-ring system [8], (Table 1).

Table 1

Structure of the Compounds Studied







Compound	R^1	R^2
1	Ph-S-	Me
2	Ph-S-	Et
3	Ph-S(O)-	Me
4	Ph-S(O)-	Et
5	Ph-SO_2-	Me
6	Ph-SO_2-	Et
7	Ph-S-	Me
8	Ph-S-	Et
9	Ph-S(O)-	Me
10	Ph-S(O)-	Et
11	Ph-SO_2-	Me
12	CH_3O-	Me
13	Ph-S-	Me
14	Ph-S-	Et
15	CH_3O-	Me

The fact that only limited information is available on the mass spectra of 6-substituted 3-oxo-3,6-dihydro-2*H*-pyrans [9], along with the preparation of a novel fused-ring system, has prompted us to report their synthesis and study their electron impact (EI) ionization mass spectral fragmentation.

Results and Discussion.

Chemistry.

The 6-carbamoyloxy derivatives of 3-oxo-3,6-dihydro-2*H*-pyrans **1-6** were synthesized by a base (triethylamine) catalysed reaction of the appropriate isocyanate ester with their 6-hydroxy derivatives [5,7]. Accordingly the 5*H*-pyrano[3,2-*d*]oxazole-2,6-diones **7-12** were synthesized by the base catalysed (sodium carbonate) highly stereoselective intramolecular conjugate addition on their corresponding activated allylic carbamates [8]. Reduction of **7**, **8** and **12** with lithium aluminum hydride afforded selectively and stereospecifically the thermodynamically preferred alcohols **13-15**. These compounds were characterized with the usual spectroscopic (ir and ^{1}H nmr) and analytical techniques (see Experimental).

Mass Spectroscopy.

Tables 2 and 3 list the *m/z* (relative abundance, %) values of the principal fragment ions of the studied compounds, while Figures 1, 2 and 3 illustrate, as examples, the mass spectra of **1**, **9** and **15** respectively.

Compounds **1-6**.

The mass spectra (Table 2) of compounds **1-6** show relatively small molecular ions and peaks typical of a retro-Diels-Alder type fragmentation. The main fragmentation pathways of compound **1** are summarized as a representative example in Scheme 1. The detection of both complementary fragments of the retro-Diels-Alder process (*m/z* 141 and 228 *via* pathways **A** or **B** respectively) is attributed to their comparable Ionization Potentials. However, pathway **A** is the predominant one, since fragment *m/z* 84 which arises from ion *m/z* 141, is the base peak of the spectrum. Accordingly, fragment with *m/z* 213 which is formed *via* pathway **B** by an α-cleavage of methyl radical, has relatively low abundunce.

Another possible fragmentation pathway involves the ejection of the oxo-methyl-carbonate radical forming the ion *m/z* 295 which has low relative abundunce (pathway **C**).

Table 2

EI Mass Spectra (70 eV) of Allylic Carbamates **1-6**

		m/z (relative intensity, %)										
		Pathway **A**		Pathway **B**			Pathway **C**	Other Important Ions				
Compound	M^+	M– $R^1(C_6H_4)COCH_3$	*m/z* 84	$R^1(C_6H_4)COCH_3$	$[R^1(C_6H_4)CO]^+$	$[R^1(C_6H_4)COHCH_3]^+$	[M-OCONHR²]	R^1	$C_6H_5^+$	R_2NHCO^+	CH_3CO^+	Other
1	369 (7)	141 (17)	84 (100)	228 (17)	213 (23)	229 (33)	295 (5)	109 (9)	77 (6)	58 (12)	43 (26)	230 (6), 184 (11), 55 (16), 56 (13)
2	383 (5)	155 (9)	84 (100)	228 (12)	213 (19)	229 (42)	295 (7)	109 (10)	77 (7)	72 (5)	43 (35)	56 (9), 55 (9), 230 (7)
3	385 (2)	141 (7)	84 (100)	244 (33)	229 (8)	245 (57)	311 (4)	125 (17)	77 (40)	58 (23)	43 (64)	135 (36), 228 (21), 181 (25), 213 (15), 109 (42), 55 (17), 56 (12), 44 (75)
4	399 (9)	-	84 (100)	244 (55)	229 (14)	245 (66)	-	125 (16)	77 (40)	72 (17)	43 (72)	228 (53), 213 (21), 181 (27), 109 (44), 56 (46), 196 (18), 135 (56), 44 (26)
5	-	141 (9)	84 (100)	260 (4)	245 (7)	261 (21)	327 (2)	141 (9)	77 (20)	58 (8)	43 (13)	125 (11), 51 (6), 56 (9), 55 (10)
6	-	155 (4)	84 (100)	260 (2)	245 (5)	261 (19)	327 (2)	141 (5)	77 (22)	72 (4)	43 (16)	285 (3), 125 (11), 56 (10), 55 (10)

Table 3

		m/z (relative intensity, %)							
		Pathway **A**	Pathway **B**		Pathway **C**		Other Important Ions		
Compound	M^+	oxazolenone	$CH_2=C=O$	$R^1(C_6H_4)COCH_3$	$[R^1(C_6H_4)CO]^+$	$[R^1(C_6H_4COHCH_3]^+$	R^1	$C_6H_5^+$	Other
7	369 (50)	99 (24)	42 (25)	228 (90)	213 (100)	229 (15)	-	77 (13)	341 (20), 57 (25), 184 (38)
8	383 (32)	113 (23)	42 (4)	228 (100)	213 (67)	229 (27)	109 (8)	77 (9)	355 (19), 57 (8), 56 (30), 43 (23), 71 (45), 127 (13)
9	385 (35)	99 (100)	42 (70)	244 (57)	229 (14)	245 (70)	125 (8)	77 (32)	213 (24), 181 (24), 135 (55), 43 (78), 228 (50), 196 (19), 57 (47), 109 (38), 58 (34)
10	399 (14)	113 (100)	42 (20)	244 (64)	229 (43)	245 (35)	-	77 (20)	181 (15), 135 (27), 56 (41)
11	401 (1)	99 (100)	42 (11)	-	245 (4)	261 (2)	141 (2)	77 (8)	359 (3), 125 (7), 113 (10), 58 (6), 44 (12), 57 (9), 43 (10)
12	291 (8)	99 (35)	42 (42)	150 (28)	135 (100)	151 (30)	107 (5) [a]	77 (17)	248 (23), 113 (14), 88 (77) [b], 50 (94) [b], 43 (42), 91 (12), 57 (43)
13	371 (10)	99 (5)	43 (100) [c]	228 (17)	213 (20)	229 (90)	109 (26)	77 (11)	281 (20), 57 (16), 91 (30), 115 (15), 230 (14), 42 (64)
14	385 (12)	113 (33)	43 (23) [c]	228 (100)	213 (41)	229 (38)	109 (11)	77 (6)	56 (20)
15	293 (8)	99 (80)	43 (45) [c]	150 (90)	135 (100)	151 (52)	107 (4) [a]	77 (15)	58 (10), 57 (8), 42 (42)

[a] $R^1 = CH_3O\text{-}C_6H_4\text{-}$. [b] Impurities. [c] *m/z* 43: $[CH_2=C\text{-}OH]^+$.

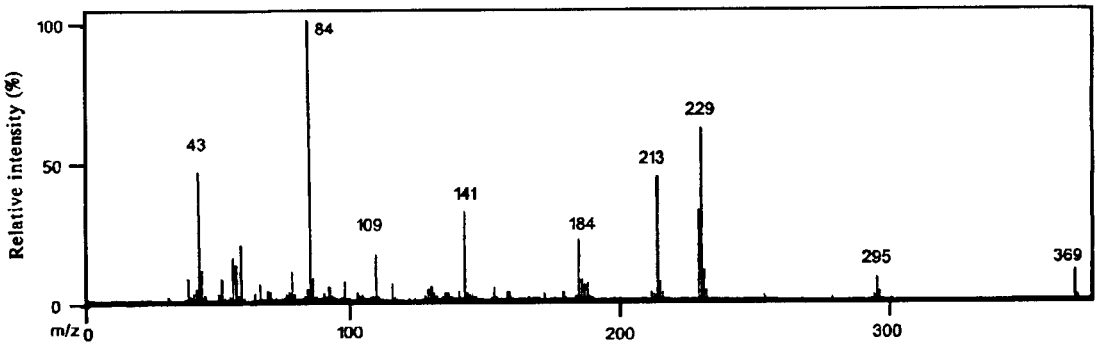


Figure 1. 70 eV mass spectrum of **1**.

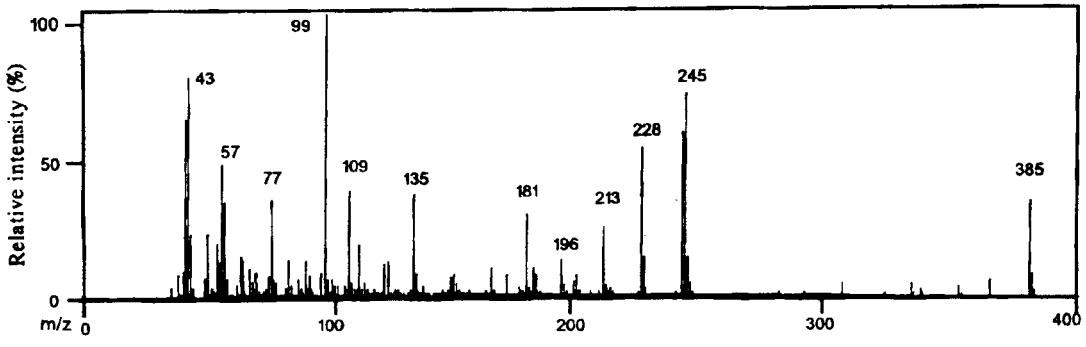


Figure 2. 70 eV mass spectrum of **9**.

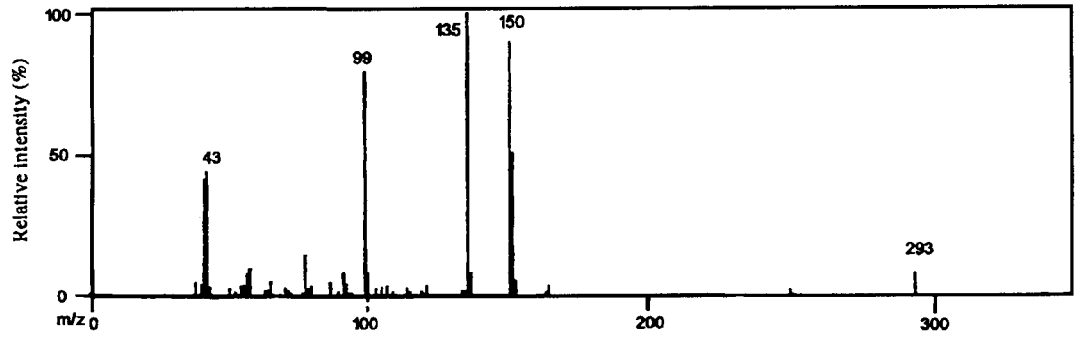


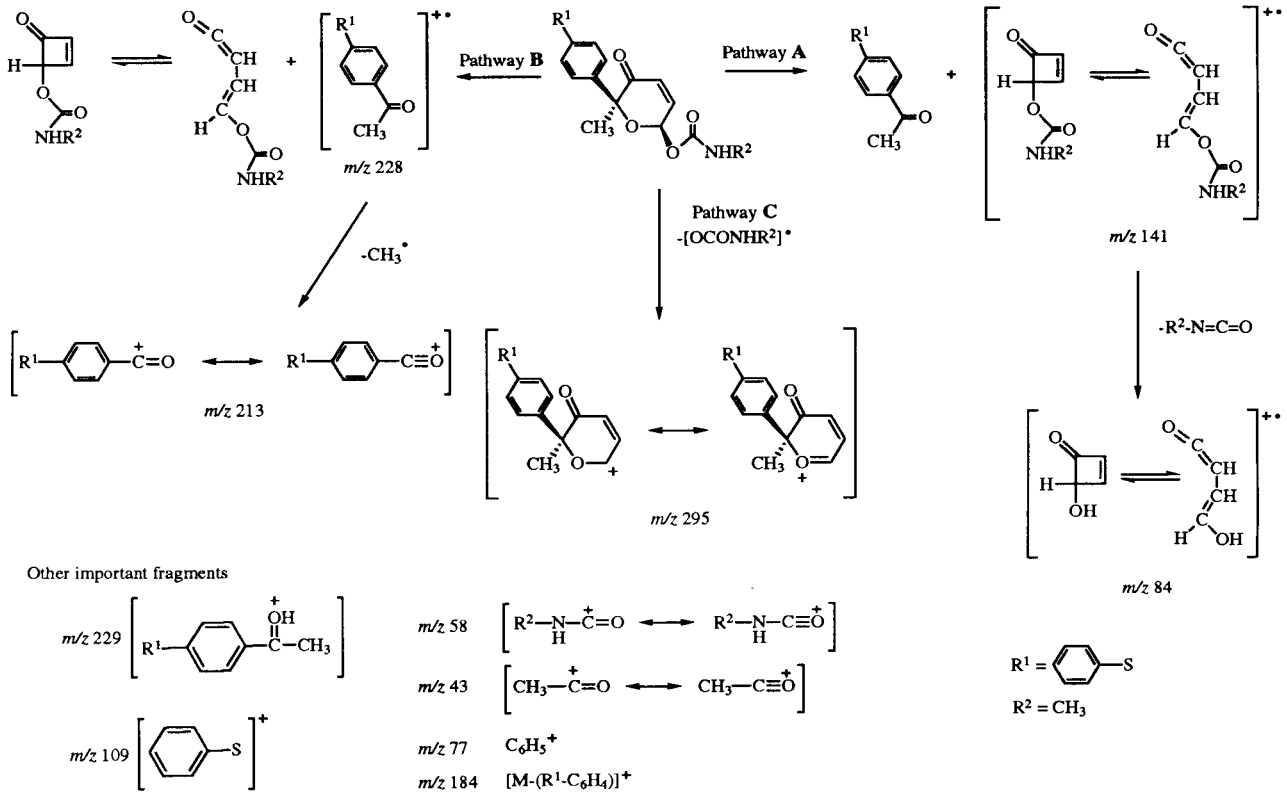
Figure 3. 70 eV mass spectrum of **15**.

Finally, partial fragmentation of the molecule containing the R^1 (phenylthio, phenylsulfinyl, phenylsulfonyl or methoxyphenyl) or R^2 (methyl or ethyl) groups give rise to several other fragments (*m/z* 109, 141, 77 *etc*, from fragments containing the R^1 moiety and *m/z* 58, 72 *etc* from fragments containing the R^2 moiety) which are depicted in Scheme 1 and listed in Table 2.

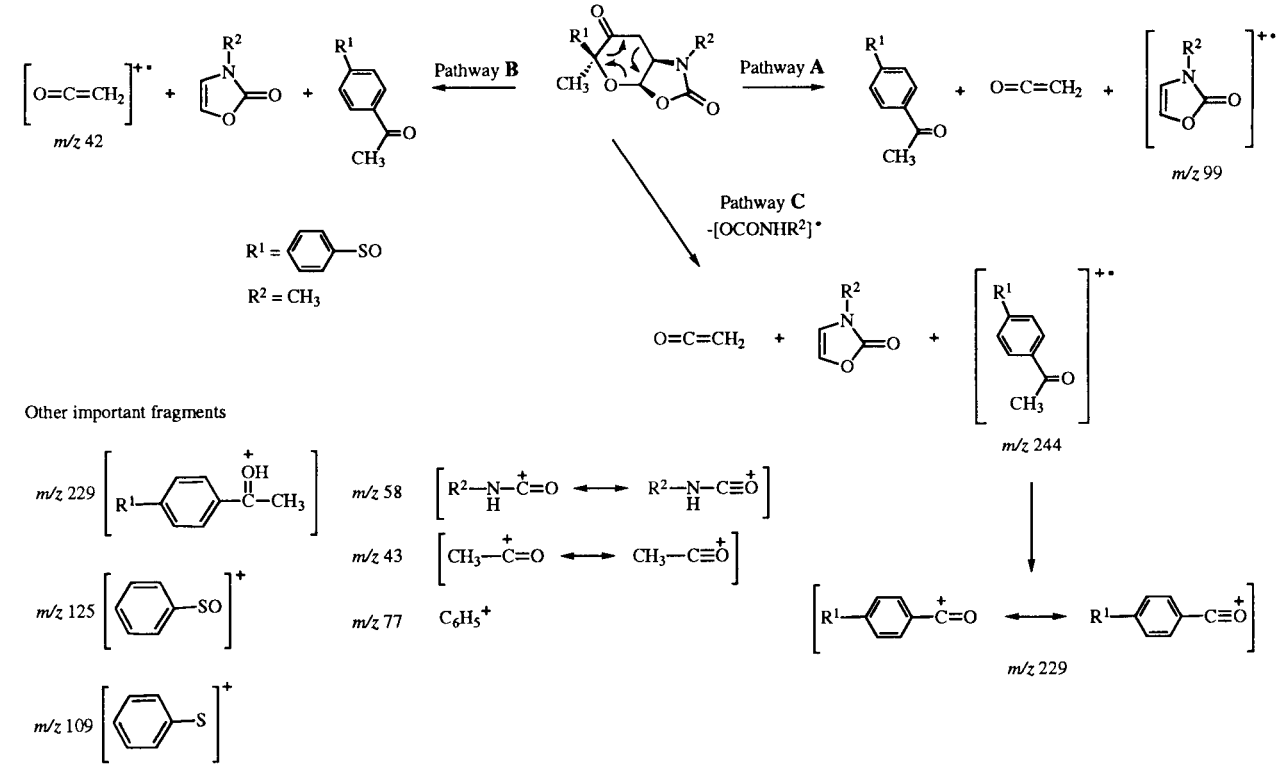
Compounds **7-12**.

The intensity of the molecular ion peaks of these compounds which contain the novel structural framework of 2*H*-pyrano[3,2-*d*]oxazole-2,6-dione (Table 3) demonstrates their stability as compared to the allylic carbamate precursors, while Scheme 2 exemplifies the main fragmentation pathways of compound **9**. The existence of a base peak corresponding to the oxazolenone fragment (*m/z* 99 or 113 for methyl or ethyl derivatives respectively) suggests that the predominant fragmentation pathway involves the formation of this ion *via* simultaneous elimination of ketene and the corresponding aromatic ketone R^1COCH_3 (Pathway **A**). The observed charge retention on the latter fragments with the formation of the ions *m/z* 42 and 244 (Pathways **B** and **C** respectively) indicates that all these ions have comparable Ionization Potentials. However, in the case of compounds **7**, **8** and **12** Pathway **C** is the predominant, since the fragment corresponding to the aromatic ketone is the base peak of the spectrum (Table 3).

Scheme 1: Main Fragmentation Pathways of Compound **1**, as a Representative Example for Carbamoyloxypyrans **1-6**



Scheme 2: Main Fragmentation Pathways of Compound **9**, as a Representative Example for Oxazolendiones **7-12**



It is also noticeable that further decomposition of these ions occurs *via* the same fragmentation processes which was observed for compounds **1-6**.

Compounds **13-15**.

The fragmentation pattern of these compounds resembles those of **7-12** with the exception that [CH_2=C-OH] with *m/z* 43 was detected as the main decomposition fragment of the pyran ring along with a weaker peak which corresponds to ketene (*m/z* 42). Their main fragmentation pathway however is **C** with the exception of compound **13** wich decomposes mainly *via* pathway **B**.

EXPERIMENTAL

General Procedures.

All melting points are in degrees Centigrade and were determined in open capillary tubes with a Büchi melting point apparatus and are uncorrected. Analytical thin layer chromatography (tlc) was performed with 0.2 mm silica gel coated plastic sheets with fluorescent indicator UV_{254} (Merck) and a mixture of 2:2:1:1 benzene/tetrahydrofuran/diethyl ether/hexane as elusion solvent. All column chromatography was done by the flash chromatography technique and the column packing was Merck 32-63 μm. The nmr spectra were recorded on General Electric QE-300 (300 MHz) in the indicated solvents. Chemical shifts are reported in part per million from tetramethylsilane as internal standard (δ scale); multiplicities indicated s (singlet), d (doublet), t (triplet), q (quadruplet), m (multiplet) or br (broadened). Infrared (ir) spectra were obtained on a Perkin Elmer Model 283 B (4,000-200 cm^{-1}) spectrophotometer, from samples prepared in accordance with the potassium bromide disk technique. Peaks are reported in cm^{-1} with the following relative intensities: s (strong, 67-100%), m (medium, 34-66%) and w (weak, 0-33%). Microanalytical data were provided by the Microanalytical Service Laboratory of NRC "Democritos", Athens, Greece.

The mass spectra were recorded on a Varian MAT CH-5 mass spectrometer using the direct sample insertion system with the lowest feasible temperature (130-180°) and ionization by electron impact at 70 eV. The accelerating voltage was 6 kV, the temperature of the ion source was ~200° and the emission current ~100 mA.

2-[*p*-(Phenylthio)phenyl]-2-methyl-6-[[(ethylamino)carbonyl]-oxy]-3-oxo-3,6-dihydro-2*H*-pyran **2**.

To a stirred solution of 6-hydroxy-2-[*p*-(phenylthio)phenyl]-2-methyl-3-oxo-3,6-dihydro-2*H*-pyran (10 g, 0.032 mole) and ethyl isocyanate (9 ml, 0.13 mole) in dry ether (150 ml), triethylamine (12 ml, 1.2 moles) was added portionwise. When the end of the reaction was confirmed by tlc (Rf 0.35), the mixture was washed with water to neutrality and dried over magnesium sulfate. The solvent was evaporated under reduced pressure and the remaining residue was chromatographed (1:1 diethyl ether/hexane as eluant) yielding 9.5 g (yield 77%) of **2** (white crystals from ether, mp 122-123°); ir: ν max (cm^{-1}) 1685 s [conjugated C=O], 1725 s [O-C=O], 3380 m [N-H], 1250 s, 1010 s [C-O], 1215 m [C-N], 3060 w, 1590 m, 1510 s, 820 m [aromatic]; ^{1}H nmr (deuteriochloroform): δ 7.41-7.25 [m, 9H, aromatic], 6.73 [dd, J = 10.3, 1.7, 1H, H-C(5)], 6.39 [dd, J = 1.7, 1.3, 1H, H-C(6)], 6.22 [dd, J = 10.3, 1.3, 1H, H-C(4)], 4.98 [br, 1H, NH], 3.29 [dq, J = 7.2, 4.7, 2H, N-$CH_2$$CH_3$], 1.65 [s, 3H, CH_3], 1.18 [t, J = 7.2, 3H, N-$CH_2$$CH_3$].

Anal. Calcd. for $C_{21}H_{21}NO_4S$ (383.45): C, 65.78; H, 5.52; N, 3.66. Found: C, 65.49; H, 5.27; N, 3.42.

2-[*p*-(Benzenesulfinyl)phenyl]-2-methyl-6-[[(methylamino)carbonyl]oxy]-3-oxo-3,6-dihydro-2*H*-pyran **3**.

2-[*p*-(Benzenesulfonyloxy)phenyl]-6-hydroxy-2-methyl-3-oxo-3,6-dihydro-2*H*-pyran (15 g, 0.046 mole) and methyl isocyanate (8 ml, 0.14 mole) in dry methylene chloride (200 ml) was treated with triethylamine (12 ml, 1.2 mole) as before, affording after chromatographic purification (7:3 diethyl ether/ethyl acetate) 10.6 g (yield 58%) of **3** (white crystals from ether, mp 124-125°; Rf 0.15); ir: ν max (cm^{-1}) 1690 s [conjugated C=O], 1735 s [O-C=O], 3295 w [N-H], 1220 m [C-N], 1255 s, 1015 m [C-O], 1040 m [S-O], 3070 w, 1595 m, 1490 s, 820 s [aromatic]; ^{1}H nmr (deuteriochloroform): δ 7.67-7.29 [m, 9H, aromatic], 6.72 [dd, J = 10.3, 1.8, 1H, H-C(5)], 6.37 [dd, J = 1.8, 1.2, 1H, H-C(6)], 6.18 [dd, J = 10.3, 1.2, 1H, H-C(4)], 5.22 [m, 1H, NH], 2.85 [d, J = 4.6, 3H, N-CH_3], 1.64 [s, 3H, CH_3].

Anal. Calcd. for $C_{20}H_{19}NO_5S$ (385.42): C, 62.32; H, 4.97; N, 3.64. Found: C, 62.62; H, 4.91; N, 3.37.

2-[*p*-(Benzenesulfinyl)phenyl]-2-methyl-6-[[(ethylamino)carbonyl]oxy]-3-oxo-3,6-dihydro-2*H*-pyran **4**.

2-[*p*-(Benzenesulfonyloxy)phenyl]-6-hydroxy-2-methyl-3-oxo-3,6-dihydro-2*H*-pyran (10 g, 0.03 mole) and ethyl isocyanate (9 ml, 0.13 mole) in dry methylene chloride (200 ml) was treated with triethylamine (12 ml, 1.2 moles) as described for compound **2**, affording after evaporation of the solvents 11 g (yield 90%) of **4** as an amorphus solid (one spot by tlc) which gave satisfactory mass spectrum and was used for the next step without further purification.

2-[*p*-(Benzenesulfonyl)phenyl]-2-methyl-6-[[(ethylamino)carbonyl]oxy]-3-oxo-3,6-dihydro-2*H*-pyran **6**.

2-[*p*-(Benzenesulfonyl)phenyl]-6-hydroxy-2-methyl-3-oxo-3,6-dihydro-2*H*-pyran (6.9 g, 0.02 mole) and ethyl isocyanate (7 ml, 0.1 mole) in dry ether (300 ml) was treated with triethylamine (12 ml, 1.2 moles) as before affording after chromatographic purification (9:1 diethyl ether/ethyl acetate) 7.5 g (yield 90%) of **6** (white crystals from ethyl acetate/hexane, mp 154-155°; Rf 0.17); ir: ν max (cm^{-1}) 1690 s [conjugated C=O], 1765 s [O-C=O], 3440 m [N-H], 1230 s, 1010 s [C-O], 1300 m, 1160 m [SO_2], 3060 w, 1600 s, 1505 s, 820 s [aromatic], ^{1}H nmr (deuteriochloroform): δ 7.94 [m, 4H, aromatic], 7.67 [dd, J = 8.5, 1.5, 2H, aromatic], 7.55 [m, 1H, aromatic], 7.51 [dd, J = 8.5, 1.5, 2H, aromatic], 6.76 [dd, J = 10.3, 1.8, 1H, H-C(5)], 6.39 [dd, J = 1.8, 1.4, 1H, H-C(6)], 6.20 [dd, J = 10.3, 1.4, 1H, H-C(4)], 5.18 [t, J = 5.6 1H, NH], 3.28 [dq, J = 7.2, 5.6, 2H, N-$CH_2$$CH_3$], 1.65 [s, 3H, CH_3], 1.17 [t, J = 7.2, 3H, N-$CH_2$$CH_3$].

Anal. Calcd. for $C_{21}H_{21}NO_6S$ (415.45): C, 60.71; H, 5.09; N, 3.37. Found: C, 60.88; H, 5.19; N, 3.41.

2-[*p*-(Phenylthio)phenyl]-2-methyl-6-[[(methylamino)carbonyl]oxy]-3-oxo-3,6-dihydro-2*H*-pyran **1**, see ref [8].

2-[*p*-(Benzylsulfonyl)phenyl]-2-methyl-6-[[(methylamino)carbonyl]oxy]-3-oxo-3,6-dihydro-2*H*-pyran **5**, see ref [8].

5-[4-(Benzenesulfinyl)phenyl]-1,5-dimethyldihydro-[1*H*,7*H*]-5*H*-pyrano[3,2-*d*]oxazole-2,6-dione **9**.

To a solution of **3** (5 g, 13 mmoles) in acetone (100 ml), a saturated solution of sodium carbonate (40 ml) was added in one pot under stirring. After 30 minutes of vigorous stirring tlc (Rf 0.05) showed that the reaction was completed. The reaction mixture was diluted with methylene chloride and washed successively with water and a saturated solution of ammonium chloride. The organic layer was separated, dried over magnesium sulfate and evaporated to dryness under reduced pressure affording an amorphous pale yellow solid. Crystallization from ethyl acetate furnished **9** as analytically pure white crystals (4.5 g, yield 90%); mp 185-187°; ir: ν max (cm^{-1}) 1710 s [C=O], 1735 s [O-C=O], 1270 s, 1080 m, 1010 m [C-O], 1045 m [S-O], 3060 w, 1490 m, 685 m [aromatic]; ^1H nmr (deuteriochloroform): δ 7.71-7.44 [m, 9H, aromatic], 6.21 [d, J = 7.5, 1H, H-C(3α)], 4.40 [dt, J = 7.5, 3.1, 1H, H-C(7α)], 2.88 [dd, J = 14.2, 3.9, 1H, H-C(7)], 2.86 [s, 3H, N-CH_3], 2.64 [dd, J = 14.2, 2.7, 1H, H-C(7)], 1.72 [s, 3H, CH_3].

Anal. Calcd. for $C_{20}H_{19}NO_5S$ (385.42): C, 62.32; H, 4.97; N, 3.64. Found: C, 62.40; H, 4.91; N, 3.54.

5-[4-(Benzenesulfinyl)phenyl]-1-ethyl-5-methyldihydro-[1*H*,7*H*]-5*H*-pyrano[3,2-*d*]oxazole-2,6-dione **10**.

A solution of **4** (11 g, 27 mmoles) in acetone (100 ml), was treated with a saturated solution of sodium carbonate (40 ml) as before. Crystallization from acetone/hexane gave analytically pure **10** as white crystals (9 g, yield 82%); mp 156-157°; Rf 0.07; ir: ν max (cm^{-1}) 1710 s [C=O], 1740 s [O-C=O], 1260 s, 1180 m, 1010 s [C-O], 1045 m [S-O], 3060 w, 1590 s, 1515 m, 760 s [aromatic]; ^1H nmr (deuterioacetone): δ 7.66-7.39 [m, 9H, aromatic], 6.12 [d, J = 7.4, 1H, H-C(3α)], 4.44 [dt, J = 7.4, 3.5, 1H, H-C(7α)], 3.46 [dq, J = 7.2, 14.4, 1H, N-CH_2CH$_3$], 3.02 [dq, J = 7.2, 14.4, 1H, N-CH_2CH$_3$], 2.78 [dd, J = 14.2, 3.9, 1H, H-C(7)], 2.53 [dd, J = 14.2, 2.6, 1H, H-C(7)], 1.64 [s, 3H, CH_3], 1.08 [t, J = 7.2, 3H, N-CH_2CH_3].

Anal. Calcd. for $C_{21}H_{21}NO_5S$ (399.45): C, 63.14; H, 5.30; N, 3.51. Found: C, 62.95; H, 5.21; N, 3.34.

1,5-Dimethyl-5-[4-(methoxy)phenyl]dihydro-[1*H*,7*H*]-5*H*-pyrano[3,2-*d*]oxazole-2,6-dione **12**.

A solution of 2-[*p*-(methoxyphenyl)]-2-methyl-6-[[(methylamino)carbonyl]oxy]-3-oxo-3,6-dihydro-2*H*-pyran (15 g, 50 mmoles) in acetone (250 ml) was treated with a saturated solution of sodium carbonate (80 ml) as described for compound **10**. Crystallization from ethyl acetate/hexane gave analytically pure **12** as white crystals (14.2 g, yield 95%); mp 141-142°; Rf 0.1; ir: ν max (cm^{-1}) 1730 s [C=O], 1765 s [O-C=O], 1255 s, 1180 m, 995 s [C-O], 3080 w, 1590 s, 1510 m, 755 s [aromatic]; ^1H nmr (deuteriochloroform): δ 7.45 [dd, J = 8.9, 1.9, 2*H*, aromatic], 6.88 [dd, J = 8.9, 1.9, 2*H*, aromatic], 6.19 [d, J = 7.4, 1H, H-C(3α)], 4.38 [dt, J = 7.4, 3.4, 1H, H-C(7α)], 3.79 [s, 3H, O-CH_3], 2.96 [dd, J = 14.2, 4.1, 1H, H-C(7)], 2.86 [s, 3H, N-CH_3], 2.63 [dd, J = 14.2, 3.1, 1H, H-C(7)], 1.72 [s, 3H, CH_3].

Anal. Calcd. for $C_{15}H_{17}NO_5$ (291.30): C, 61.83; H, 5.89; N, 4.81. Found: C, 61.75; H, 6.03; N, 4.75.

5-[4-(Phenylthio)phenyl]-1,5-dimethyldihydro-[1*H*,7*H*]-5*H*-pyrano[3,2-*d*]oxazole-2,6-dione **7**, see ref [7].

5-[4-(Phenylthio)phenyl]-1-ethyl-5-methyldihydro-[1*H*,7*H*]-5*H*-pyrano[3,2-*d*]oxazole-2,6-dione **8**, see ref [7].

5-[4-(Benzenesulfonyl)phenyl]-1,5-dimethyldihydro-[1*H*,7*H*]-5*H*-pyrano[3,2-*d*]oxazole-2,6-dione **11**, see ref [7].

1,5-Dimethyl-5-[4-(phenylthio)phenyl]-6-hydroxyperhydropyrano[3,2-*d*]oxazole-2-one **13**.

To a solution of **7** (0.2 g, 0.5 mmole) in anhydrous tetrahydrofuran (25 ml) cooled to 0°, lithium aluminum hydride (10 mg, 0.25 mmole) was added portionwise with stirring. The cooling bath was removed and after 1 hour of stirring, tlc (Rf 0.02) showed that the reaction was completed. A calculated amount of saturated solution of ammonium chloride was added dropwise and the mixture was filtered on Celite. The filtrate was evaporated under reduced pressure to afford after crystallization from acetone/hexane white crystals of **13** (0.16 g, yield 82%); mp 205-207°; ir: ν max (cm^{-1}) 3490 m [O-H], 1755 s [O-C=O], 1100 m, 1005 s [C-O], 3080 w, 1590 s, 1510 m [aromatic]; ^1H nmr (deuterioacetone): δ 7.69-7.29 [m, 9H, aromatic], 5.63 [d, J = 5.3, 1H, H-C(3α)], 4.11 [m, 1H, H-C(6)], 3.69 [m, 1H, H-C(7α)], 2.93 [d, disappeared on addition of deuterium oxide, J = 7.6, 1H, OH], 2.91 [s, 3H, N-CH_3], 2.04 [m, 2H, H-C(7)], 1.54 [s, 3H, CH_3].

Anal. Calcd. for $C_{20}H_{21}NO_4S$ (371.45): C, 64.67; H, 5.70; N, 3.77. Found: C, 64.52; H, 5.77; N, 3.69.

1,5-Dimethyl-5-[4-(methoxy)phenyl]-6-hydroxyperhydropyrano[3,2-*d*]oxazole-2-one **15**.

A solution of **12** (5 g, 17 mmoles) in anhydrous tetrahydrofuran (25 ml) cooled to 0° was treated with lithium aluminum hydride (300 mg, 30 mmoles) as described for compound **13** yielding 4.2 g (84%) of the title compound **15** as white crystals, mp 145-146°; Rf 0.11; ir: ν max (cm^{-1}) 3490 m [O-H], 1760 s [O-C=O], 1180 m, 1030 s [C-0], 3060 w, 1590 m, 1510 m [aromatic]; ^1H nmr (deuterioacetone): δ 7.45 [d, J = 8.5, 2H, aromatic], 6.91 [d, J = 8.5, 2H, aromatic], 5.57 [d, J = 5.6, 1H, H-C(3α)], 4.33 [m, 1H, H-C(6)], 4.17 [m, 1H, H-C(7α)], 3.79 [s, 3H, O-CH_3], 3.83 [d, disappeared on addition of deuterium oxide, J = 6.8, 1H, OH], 2.82 [s, 3H, N-CH_3], 2.02 [m, 2H, H-C(7)], 1.48 [s, 3H, CH_3].

Anal. Calcd. for $C_{15}H_{19}NO_5$ (293.31): C, 61.41; H, 6.53; N, 4.78. Found: C, 61.37; H, 6.65; N, 4.72.

5-Ethyl-1-methyl-5-[4-(phenylthio)phenyl]-6-hydroxyperhydropyrano[3,2-*d*]oxazole-2-one **14**, see ref [7].

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