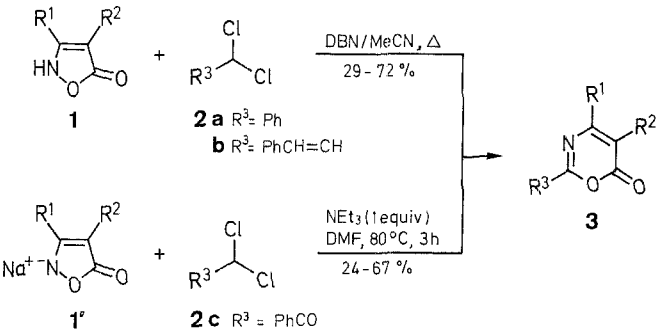


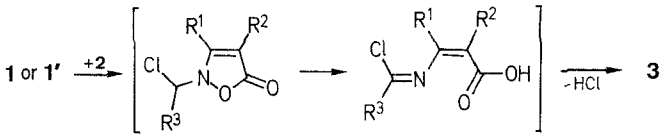
1 2a R³ = Ph; b R³ = PhCH=CH

1′ 2c R³ = PhCO

3

1, 1′	R¹	R²	1, 1′	R¹	R²
a	Me	CH_2Ph	e	Ph	CH_2Ph
b	Me	n-$C_{16}H_{33}$	f	Me	$CH_2CH_2CO_2Et$
c	Me	CH_2CO_2Me	g	Me	Ph
d	Ph	Me			

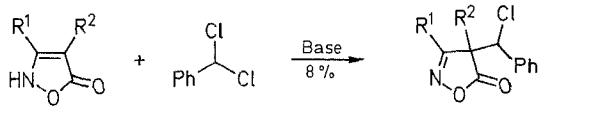
We suggest that the oxazinones **3** are formed by the initial attack of the dihalo compound **2** at position 2 of the isoxazolyl anion, followed by ring opening and cyclization with hydrogen chloride elimination, in analogy with previously reported reaction paths.[2,3]



The results are reported in Table 1. The structure of new compounds follows from analytical and spectroscopic data (Table 2); moreover, compound **3da** has been previously reported.[4]

By-products are always present, but they are formed in appreciable amount only when R^1 is a bulky group which hinders the reaction at position 2 of the isoxazolone nucleus. Indeed, from the reaction between isoxazolones **1d,e** and (dichloromethyl) benzene **(2a)**, compounds **4** and **5** were isolated as a diastereoisomeric mixture besides the expected oxazinones.

The 3,4,4-trisubstituted isoxazolin-5-one structure was assigned to compounds **4** and **5** on the basis of analytical and spectroscopic data (Tables 1 and 2). The carbonyl absorption band in the infrared spectra was present in the range of 1775–1780 cm^{-1}, in good agreement with the reported data for 3,4,4-trisubstituted isoxazolin-5-ones.[5] These derivatives arise from the attack of the dihalo compound at position 4 of the isoxazolyl anion.



1d,e 2a

4 R^1 = Ph, R^2 = CH_3

5 R^1 = Ph, R^2 = $PhCH_2$

Melting points are uncorrected. Reagent quality solvents were used without further purification. IR spectra were determined with a Perkin-Elmer 298 instrument, in Nujol mull for solids and liquid film for oils. ^{1}H-NMR spectra were recorded on a Varian Em-390. Column chromatography was performed on Merck Kieselgel 60, 0.063–0.2 mm. The starting materials were prepared according to literature procedures: **1a**;[6] **1b, c, f**;[2] **1d**;[7] **1e**;[8] **1g**.[9]

1,3-Oxazin-6-ones from 5(2*H*)-Isoxazolones

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The reaction of 5(2*H*)-isoxazolones **1** with 1,1-dihalocompounds, in the presence of a base, affords 1,3-oxazin-6-ones **3**.

1,3-Oxazin-6-ones have been proved to be versatile intermediates in heterocyclic synthesis.[1] 5(2*H*)-Isoxazolones have been found to be a very good starting material for simple and high yield-synthesis of 1,3-Oxazin-6-ones, e.g. 2-dialkylamino-1,3-oxazin-6-ones and 2,3-dihydro-1,3-oxazin-6-ones.[2,3] We now wish to report that 1,3-oxazin-6-ones **3** can be obtained from 3,4-disubstituted isoxazolin-5-ones **1**, by reaction with 1,1-dihalo compounds **2** in the presence of a base. As 1,1-dihalocompounds, we used (dichloromethyl)benzene **(2a)**, 3,3-dichloro-1-phenyl-1-propene **(2b)**, and 2,2-dichloroacetophenone **(2c)**.

Optimum results were obtained when the reaction of **2a** and **2b** with the 5(2*H*)-isoxazolones **1** was carried out in acetonitrile and in the presence of two equivalents of 1,5-diazabicyclo[4.3.0] non-5-ene (DBN). In the case of **2c** the use of the sodium salt **1′** in dimethylformamide in the presence of equimolecular amount of triethylamine is preferred. Although in somes cases the yields are moderate (Table 1), the corresponding oxazinones can in all cases easily be obtained in a pure state by column chromatography on silica gel.

Table 1. Compounds **3aa–3gc** Prepared

Product[a]	R^3	Ratio of Eluent[b]	Yield (%)	mp (°C) (solvent)[c]	Molecular Formula[d] or Lit. mp (°C)
3aa	Ph	2:1	72	99–101 (CH_2Cl_2/Hx)	$C_{18}H_{15}NO_2$ (277.3)
3ab	PhCH=CH	3:1	51	107–108 (ether/Hx)	$C_{20}H_{17}NO_2$ (303.3)
3ba	Ph	2:1	50	54–56 (ether/Hx)	$C_{27}H_{41}NO_2$ (411.6)
3bb	PhCH=CH	3:1	38	53–54 (Hx)	$C_{29}H_{43}NO_2$ (437.6)
3bc	PhCO	1:1	67	59–61 (Hx)	$C_{28}H_{41}NO_3$ (439.6)
3ca	Ph	1:1	29	91 (ether/Hx)	$C_{14}H_{13}NO_4$ (259.2)
3cc	PhCO	–[e]	24	56 (ether/Hx)	$C_{15}H_{13}NO_5$ (287.3)
3da	Ph	2:1	40[f]	118 (ether/Hx)	119–120[4]
3db	PhCH=CH	3:1	40	124–126 (ether/Hx)	$C_{19}H_{15}NO_2$ (289.3)
3dc	PhCO	–[e]	61	132–134 (ether)	$C_{18}H_{13}NO_3$ (291.3)
3ea	Ph	3:1	29[g]	148–150 (ether/Hx)	$C_{23}H_{17}NO_2$ (339.4)
3ec	PhCO	1:1	64	138 (ether)	$C_{24}H_{17}NO_3$ (367.4)
3fa	Ph	1:1	48	58–59 (Hx)	$C_{16}H_{17}NO_4$ (287.3)
3fc	PhCO	–[e]	35	97 (ether/Hx)	$C_{17}H_{17}NO_5$ (315.3)
3gb	PhCH=CH	2:1	68	117–118 (ether/Hx)	$C_{19}H_{15}NO_2$ (289.3)
3gc	PhCO	–[e]	39	122 (ether/Hx)	$C_{18}H_{13}NO_3$ (291.3)

[a] For R^1 and R^2 see reaction scheme.
[b] Eluent: petroleum ether/CH_2Cl_2.
[c] Hx = *n*-hexane.
[d] Satisfactory elemental analyses obtained: C, H, N ±0.2.
[e] Eluent: CH_2Cl_2.
[f] Besides **3da**, 8% of compound **4** was also isolated. **4**: mp 89°C from ether/Hx; $C_{17}H_{14}ClNO_2$ (299.7).
[g] Compound **5** was isolated as a by-product in 8% yield. **5**: oil, $C_{23}H_{18}ClNO_2$ (375.8).

Table 2. Spectral Data of New Products **3–5** Prepared

Product	IR (KBr/film) ν(cm^{-1})	^{1}H-NMR ($CDCl_3$/TMS) δ, J(Hz)
3aa	1720	2.4 (s, 3H); 3.9 (s, 2H); 7.29 (s, 5H); 7.43 (m, 3H); 8.2 (m, 2H)
3ba	1730, 1600	0.9 (m, 3H); 1.3 (m, 28H); 2.37 (s, 3H); 2.53 (t, 2H, J = 7); 7.43 (m, 3H); 8.2 (m, 2H)
3ca	1750, 1725, 1617	2.38 (s, 3H); 3.63 (s, 2H); 3.78 (s, 3H); 7.48 (m, 3H); 8.2 (m, 2H)
3ea	1722, 1598	4.03 (s, 2H); 7.2 (m, 5H); 7.5 (m, 8H); 8.28 (m, 2H)
3fa	1730, 1605	1.28 (t, 3H, J = 7.5); 2.43 (s, 3H); 2.76 (m, 2H); 2.83 (m, 2H); 4.16 (q, 2H, J = 7.5); 7.45 (m, 3H); 8.2 (m, 2H)
3ab	1705, 1625	2.33 (s, 3H); 3.9 (s, 2H); 6.65 (d, 1H, J = 16.5); 7.4 (m, 10H); 7.8 (d, 1H, J = 16.5)
3bb	1730, 1632	0.9 (m, 3H); 1.3 (m, 28H); 2.3 (s, 3H); 2.5 (m, 2H); 6.63 (d, 1H, J = 16.5); 7.4 (m, 5H); 7.8 (d, 1H, J = 16.5)
3db	1720, 1625	2.23 (s, 3H); 6.75 (d, 1H, J = 16.5); 7.5 (m, 10H); 7.85 (d, 1H, J = 16.5)
3gb	1736, 1632	2.29 (s, 3H); 6.73 (d, 1H, J = 16.5); 7.4 (m, 10H); 7.9 (d, 1H, J = 16.5)
3bc	1736, 1662, 1618	0.86 (m, 3H); 1.3 (m, 28H); 2.49 (s, 3H); 2.53 (t, 2H, J = 7); 7.56 (m, 3H); 8.16 (m, 2H)
3cc	1730, 1670, 1630	2.4 (s, 3H); 3.65 (s, 2H); 3.78 (s, 3H); 7.53 (m, 3H); 8.16 (m, 2H)
3dc	1736, 1669, 1620	2.33 (s, 3H); 7.5 (m, 8H); 8.2 (m, 2H)
3ec	1728, 1652, 1612	4.06 (s, 2H); 7.2 (m, 5H); 7.5 (m, 8H); 8.2 (m, 2H)
3fc	1730, 1679, 1632	1.3 (t, 3H, J = 7.5); 2.47 (s, 3H); 2.73 (m, 2H); 2.86 (m, 2H); 4.16 (q, 2H, J = 7.5); 7.56 (m, 3H); 8.16 (m, 2H)
3gc	1729, 1651, 1605	2.35 (s, 3H); 7.5 (m, 8H); 8.2 (m, 2H)
4	1775	1.73 (s, 1.5H); 1.9 (s, 1.5H); 5.05 (s, 0.5H); 5.2 (s, 0.5H); 7.0–7.8 (m, 10H)
5	1780	3.1–4.0 (m, 2H); 5.4 (s, 0.5H); 5.5 (s, 0.5H); 7.0–8.0 (m, 15H)

Reaction of 3,4-Disubstituted 5(2*H*)-Isoxazolones 1 with (Dichloromethyl)benzene (2a) or 3,3-Dichloro-1-phenyl-1-propene (2b); General Procedure:

DBN (1.2 mL, 10 mmol) and the appropriate 1,1-dihalo compound **2a** or **2b** (7.5 mmol) are added to a solution of the 5(2*H*)-isoxazolone **1** (5 mmol) in acetonitrile (30 mL). The mixture is heated under reflux (5 h for **2a** and 2.5 h for **2b**).[10] After evaporation of the solvent, water (50 mL) is added and the mixture extracted with CH_2Cl_2 (2 × 40 mL). The organic layer is dried ($MgSO_4$), filtered and evaporated. The residue is purified by column chromatography on silica gel to give pure oxazinones **3aa–gb** (Tables 1 and 2).

Chromatography of the reaction mixture from **1d** and **2a** gives **4** in 8% yield as first eluted with petroleum ether/CH_2Cl_2, 2:1 (Table 1).

Chromatography of the reaction mixture from **1e** and **2a** gives **5** in 8% yield as first eluted with petroleum ether/CH_2Cl_2, 3:1 (Table 1).

Sodium Salts 1′ of 5(2*H*)-Isoxazolones 1; General Procedure:

A methanolic solution of NaOMe, prepared from MeOH (10 mL) and Na (230 mg, 10 mmol) is added to a solution of the isoxazolin-5-one **1b–g** (10 mmol) in MeOH (30 mL). After evaporation of the solvent, the residue is dried for 30 min at 60°C/5 mbar.

Reaction of 3,4-Disubstituted 5(2*H*)-Isoxazolones 1 with 2,2-Dichloroacetophenone (2c); General Procedure:

The sodium salt of the appropriate isoxazolin-5-one (**1′b–g**, 5 mmol) is dissolved in DMF (30 mL) and then Et_3N (0.7 mL, 5 mmol) and α,α-dichloroacetophenone (**2c**, 1.3 mL, 10 mmol) are added. The mixture is heated at 80°C for 3 h. After evaporation of the solvent, water (50 mL) is added and the mixture extracted with CH_2Cl_2 (2 × 40 mL). The organic layer is dried ($MgSO_4$), filtered and evaporated. The residue is purified by column chromatography on silica gel to give pure oxazinones **3bc–gc** (see Tables 1 and 2).

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