Table I. Tri- and Tetrasubstituted Olefins from α-Silyl Esters

entry (cmpd)	R^1	R^2	R^3M	R^4M	olefin	yield,[a] %
1 (11)	Me[b]	H	PhMgBr	PhMgBr	$MeCH{=}CPh_2$	85
2 (12)	Me[b]	H	n-$C_5H_{11}MgBr$	n-$C_5H_{11}MgBr$	$MeCH{=}C(n\text{-}C_5H_{11})_2$	54
3 (13)	Me	H	n-$C_6H_{13}MgBr$	n-$C_6H_{13}MgBr$	$MeCH{=}C(n\text{-}C_6H_{13})_2$	66
4 (14)	Me	H	$PhCH_2MgCl$	$PhCH_2MgCl$	$MeCH{=}C(CH_2Ph)_2$	37
5 (15)	Et	H	PhMgBr	PhLi	$EtCH{=}C(Ph)_2$	55
6 (16)	n-C_8H_{17}	H	PhMgBr	PhLi	n-$C_8H_{17}CH{=}C(Ph)_2$	20
7 (17)	n-C_8H_{17}	H	MeMgI	MeMgI	n-$C_8H_{17}CH{=}C(Me)_2$	39
8 (17)	n-C_8H_{17}	H	MeMgI	MeLi	n-$C_8H_{17}CH{=}(Me)_2$	54
9 (18)	n-C_8H_{17}	H	EtMgI	EtMgI	n-$C_8H_{17}CH{=}C(Et)_2$	9
10 (19)	n-C_8H_{17}	H	n-C_3H_7MgBr	n-C_3H_7MgBr	n-$C_8H_{17}CH{=}C(n\text{-}C_3H_7)_2$	8
11 (20)	n-C_8H_{17}	H	C_3H_5MgBr	C_3H_5MgBr	n-$C_8H_{17}CH{=}C(allyl)_2$[c]	84
12 (21)	n-C_8H_{17}	H	n-C_4H_9MgBr	n-C_4H_9Li	n-$C_8H_{17}CH{=}C(n\text{-}C_4H_9)_2$	19
13 (22)	n-C_8H_{17}	H	n-C_3H_7MgBr	MeLi	n-$C_8H_{17}CH{=}C(n\text{-}C_3H_7)Me$[d]	55
14 (23)	$CH_2{=}CH(CH_2)_7$	H	MeMgBr	MeLi	$CH_2{=}CH(CH_2)_7CH{=}C(Me)_2$	56
15 (24)	Me	Me[e]	PhMgBr	PhLi	$Me_2C{=}C(Ph)_2$	70
16 (25)	Me	Me[e]	n-C_4H_9MgBr	n-C_4H_9Li	$Me_2C{=}C(n\text{-}C_4H_9)_2$	60
17 (26)	Me	Me[e]	n-$C_6H_{13}MgBr$	n-$C_6H_{13}MgBr$	$Me_2C{=}C(n\text{-}C_6H_{13})_2$	44
18 (27)	n-C_8H_{17}	Me[f]	MeMgI	MeLi	$(n\text{-}C_8H_{17})MeC{=}CMe_2$	12

[a] Isolated yields. [b] Ethyl (trimethylsilyl)propionate prepared via methylation of ethyl (trimethylsilyl)acetate used in these reactions. [c] The allyl Grignard has been shown to add twice to other hindered esters. [d] Product is greater than 99:1 E:Z when elimination is carried out with KO-t-Bu. [e] Prepared by methylation of the lithium enolate of 4 (R = Me). [f] Prepared by methylation of 4 (R = n-C_8H_{17}).

142.5, 123.3, 32.0, 30.3, 29.6, 29.4, 29.2, 27.6, 23.2, 22.8, 14.1, 13.3, 13.0; MS, 196 (9), 55 (100). The major product was 3-dodecanone (71%).

4-Propyltridec-4-ene (19). The title compound was produced in 8% yield as above: ^{1}H NMR δ 5.2 (t, 1 H, J = 7.1 Hz), 2.1–1.9 (m, 6 H), 1.3 (bs, 12 H), 0.85 (m, 9 H); ^{13}C NMR δ 139.0, 125.3, 39.1, 32.1, 31.9, 30.2, 29.6, 29.4, 29.3, 27.7, 22.7, 21.7, 21.4, 14.2, 14.1, 14.0; MS, 224 (17), 70 (100). The major product was 4-tridecanone formed in 78% yield.

4-Allyltrideca-1,4-diene (20). The reaction of 6 mmol of allylmagnesium bromide with 2 mmol of 4 (R = n-C_8H_{17}) at reflux for 21 h gave 84% of the title compound: n_D^{20} 1.4621; IR (neat) 1635 cm^{-1}; ^{1}H NMR δ 6.15–5.51 (m, 2 H), 5.24 (t, 1 H, J = 6.1 Hz), 5.25–5.05 (m, 2 H), 5.00 (m, 2 H), 2.82–2.67 (bt, 2 H, J = 5.3 Hz), 2.20–1.80 (m, 2 H), 1.26 (bs, 12 H), 0.82 (bt, 3 H); ^{13}C NMR δ 137.1, 136.2, 135.0, 127.5, 115.7, 115.1, 41.4, 34.6, 32.0, 30.0, 29.6, 29.4, 27.9, 14.1; MS, 220 (not observed) 41 (100). Anal. Calcd for $C_{16}H_{28}$; C, 87.27; H, 12.73. Found: C, 87.09; H, 12.85.

General Procedure for Reaction with a Grignard Reagent Followed by an Organolithium Reagent. The α-silyl ester was reacted with 2 equiv of Grignard reagent in THF at reflux, the reaction was cooled to 0 °C, and 3 equiv of lithium reagent in ether were added followed by a 24-h reflux period. The reaction was cooled to room temperature and 9 equiv of KO-t-Bu was added, and the reaction was refluxed for 1 h. Workup as before gave the olefins.

5-Butyltetradec-5-ene (21). Title compound produced in 19% yield: n_D^{20} 1.4495; ^{1}H NMR δ 5.17 (t, 1 H, J = 7.0 Hz), 2.21–1.70 (m, 6 H), 1.26 (bs, 20 H), 1.05–0.73 (m, 9 H); ^{13}C NMR δ 139.5, 124.8, 36.8, 32.0, 30.9, 30.6, 30.3, 29.8, 29.6, 29.4, 27.8, 23.0, 22.8, 22.6, 14.1; MS, 252 (25), 55 (100). 5-Tetradecanone was produced in 78% yield.

(*E*)-4-Methyltridec-4-ene (22). Treatment of 4 (R = n-C_8H_{17}) with n-propylmagnesium bromide followed by methyllithium as above gave 55% yield of the title compound: n_D^{20} 1.4420; ^{1}H NMR δ 5.14 (tq, 1 H, J = 7.0 Hz, 1.22 Hz), 1.97 (t, 4 H), 1.60 (s, 3 H), 1.36 (bs, 14 H), 0.90 (bt, 3 H); ^{13}C NMR δ 134.8, 124.8, 41.9, 31.9, 30.0, 29.6, 29.4, 27.9, 22.7, 21.0, 15.8, 14.1, 13.7; MS, 196 (24), 55 (100). Anal. Calcd for $C_{14}H_{28}$: C, 85.71: H, 14.29. Found, C, 85.63: H, 14.35. GC–MS analysis with a capillary columnm (15 m SE-30) showed the sample to have an E:Z ratio of greater than 99:1. This same column separated a 70:30 E:Z mixture formed by boron fluoride etherate elimination (see text).

11-Methyldodeca-1,10-diene (23). The title compound was formed in 56% yield: n_D^{20} 1.4479; ^{1}H NMR δ 6.02–5.59 (m, 1 H), 5.21–4.86 (m, 3 H), 2.30–1.75 (m, 4 H), 1.68 (bs, 3 H), 1.59 (bs, 3 H) 1.30 (bs, 10 H); ^{13}C NMR δ 139.2, 131.0, 125.0, 114.2, 33.9, 30.0, 29.5, 29.4, 29.3, 29.0, 28.1, 25.7, 17.7; MS, 180 (7), 69 (100).

1,1-Diphenyl-2-methylpropene (24). The title compound was formed in 70% yield: n_D^{16} 1.5950; ^{1}H NMR δ 7.22 (s, 10 H), 1.78 (s, 6 H); ^{13}C NMR δ 143.3, 137.2, 135.3, 130.9, 129.8, 128.7, 127.8, 127.1, 126.0, 22.4, MS, 208 (80), 115(100).

2-Methyl-3-butylhept-2-ene (25). The title compound was formed in 60% yield: n_D^{20} 1.4415; ^{1}H NMR δ 2.20–1.89 (m, 4 H), 1.64 (s, 6 H), 1.48–1.07 (m, 8 H), 0.88 (bt, 6 H); ^{13}C NMR δ 133.2, 123.9, 32.3, 31.2, 23.0, 20.2, 14.1; MS, 168 (17), 83 (100). Anal. Calcd for $C_{12}H_{24}$: C, 85.71: H, 14.29. Found: C, 85.61: H, 14.36.

2-Methyl-3-*n*-hexylnon-2-ene (26). The title compound was formed in 44% yield, purified by preparative GLC (3% SE-30); n_D^{20} 1.4540; ^{1}H NMR δ 2.20–1.7 (m, 4 H), 1.64 (s, 6 H), 1.28 (bs, 16 H), 1.05–0.70 (bt, 6 H); ^{13}C NMR δ 133.2, 123.9, 32.6, 31.9, 29.7, 28.9, 22.7, 20.2, 14.1; MS, 224 (41), 8 (100). Anal. Calcd for $C_{16}H_{32}$: C, 85.71: H, 14.29. Found: C, 85.54; H, 14.32.

2,3-Dimethyl-2-undecene (27). This compound was formed in 12% yield and identified by GC–MS only.

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Registry No. 4 (R = Me), 77772-22-6; 4 (R = Et), 89638-15-3; 4 (R = n-C_8H_{17}), 89638-16-4; 4 (R = $CH_2{=}CH(CH_2)_7$), 89968-59-2; 6 (R^1 = R^2 = Me), 91413-17-1; 6 (R^1 = n-C_8H_{17}, R^2 = Me), 91586-15-1; 11, 778-66-5; 12, 91586-16-2; 13, 91586-17-3; 14, 40558-71-2; 15, 1726-14-3; 16, 1530-27-4; 17, 56888-88-1; 18, 68066-08-0; 19, 91586-18-4; 20, 91586-19-5; 21, 91586-20-8; (*E*)-22, 91586-21-9; (*Z*)-22, 91586-22-0; 23, 18625-77-9; 24, 781-33-9; 25, 91586-23-1; 26, 91586-24-2; 27, 91586-25-3; PhBr, 108-86-1; n-$C_5H_{11}Br$, 110-53-2; n-$C_6H_{13}Br$, 111-25-1; $PhCH_2Cl$, 100-44-7; MeI, 74-88-4; EtI, 75-03-6; n-C_3H_7Br, 106-94-5; C_3H_5Br, 106-95-6; n-C_4H_9Br, 109-65-9; PhLi, 591-51-5; MeLi, 917-54-4; n-C_4H_9Li, 109-72-8; ethyl 2-(trimethylsilyl)propionate, 13950-55-5.

Oxidation of 4-Aryl-Substituted Isoxazolin-5-ones. A New Synthesis of 2,5-Diaryl-1,3-oxazin-6-ones

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The oxidation of a large number of 3,4-disubstituted isoxazolin-5-ones has been achieved with active manganese dioxide as well as with peroxyformic acid. In the first case

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Table I. Characterization of New Compounds[a]

compd	yield, %	mp/bp (mmHg), °C	IR,[b] cm^{-1}	^1H NMR[c] ($CDCl_3$)
1b	90	49–51[d]	3200, 1730, 1665	12.25 (d, 1, 13),[e] 7.25 (m, 5)
1c	92	44–47[d]	3150, 1650, 1585	12.18 (d, 1, 13),[e] 7.46 (d, 2, 9), 7.25 (d, 1, 13),[f] 7.18 (d, 2, 9)
1d	94	105–110 (0.4)	1725, 1660, 1610	12.08 (d, 1, 13),[e] 7.27 (d, 1, 13),[f] 7.18 (d, 2, 9), 6.9 (d, 2, 9), 3.82 (s, 3)
1e	87	undistilled	1730, 1655, 1610	12.2 (d, 1, 13),[e] 7.3 (m, 5), 2.4 (s, 3)
1f	83	98–101[d]	3140, 1665, 1635	7.8 (d, 1, 12),[f] 7.3 (m, 4), 5.7 (d, 1, 12)[e]
1g	92	71–73[d]	3160, 1650, 1635	7.73 (d, 1, 14),[f] 7.2 (m, 4), 6 (d, 1, 14),[e] 2.22 (s, 3)
1h	88	108–111 (0.3)	1700, 1630	8.65 (m, 1), 7.75 (m, 2), 7.2 (m, 2), 4.2 (m, 4), 1.3 (m, 6)
2b	77	134–135[d]	3060, 1720, 1700	10 (bs, 1),[e] 9.17 (s, 1), 7.8 (d, 2, 9), 7.45 (d, 2, 9)
2c	80	120–121[g]	3000 b, 1748, 1705	10.8 (bs, 1)[e] 9.18 (s, 1), 7.76 (d, 2, 9), 7.58 (d, 2, 9)
2d	85	112–114[h]	3200 b, 1740, 1700	9 (s, 1), 7.2 (bs, 1),[e] 7.7 (d, 2, 9), 6.98 (d, 2, 9), 3.8 (s, 3)
2e	70	124–126[h]	3000 b, 1735, 1685	10 (bs, 1),[e] 9.07 (s, 1), 7.68 (d, 2, 9), 7.23 (d, 2, 9), 2.34 (s, 3)
2f	78	101–104[h]	3000 b, 1670, 1605	11.4 (bs, 1),[e] 8.28 (s, 1), 7.4–7 (m, 4), 2.38 (s, 3)
2g	80	104–106[d]	3000 b, 1740, 1700	11.1 (s, 1),[e] 8 (s, 1), 7.25 (m, 4), 2.38 (s, 3)
2h	20	203–204[i]	3250, 1670, 1645	8.75 (s, 1), 8.25 (s, 1), 7.9 (m, 2), 7.1 (m, 1)[l]
3a	57	113	1800, 1778	8.6 (s, 1), 8 (s, 1), 7.4 (m, 10)[m]
3b	91	119	1790, 1778, 1740	insoluble
3c	66	125	1800, 1777	insoluble
3d	72	111–112	1795, 1775, 1730	8.6 (s, 1), 8 (s, 1), 7.6 (m, 4), 7.2 (m, 4), 4 (s, 6)[m]
3e	90	114	1780, 1745	8.58 (s, 1), 8 (s, 1), 7.3 (m, 8), 2.5 (s, 3), 2.36 (s, 3)[m]
3f	59	109–111	1780, 1745, 1700	8.57 (s, 1), 8.02 (s, 1), 7.35 (m, 8), 2.5 (s, 3), 2.32 (s, 3)[m]
4a	80	130–133[h]	3400 b, 2205, 1710	9.4 (bs, 1),[e] 8.1 (m, 2), 7.9 (s, 1), 7.6 (m, 8)
4b	79	158–159[h]	3300 b, 2210, 1705	8 (m, 3), 7.48 (m, 6)
4c	75	178–182[h]	2700 b, 2220, 1775	8.08 (s, 1), 7.9 (d, 2, 9), 7.75 (d, 2, 9), 7.6 (d, 2, 9), 7.48 (d, 2, 9)
4d	72	151–153[h]	3000 b, 2220, 1725	8.07 (s, 1), 7.98 (d, 2, 9), 7.6 (d, 2, 9), 7 (m, 4), 3.95 (s, 3), 3.87 (s, 3)
4e	89	136–138[n]	3000 b, 2210, 1783	12.1 (bs, 1)[e] 8 (s, 1), 7.9 (d, 2, 9), 7.35 (m, 6), 2.45 (s, 3), 2.4 (s, 3)
4f	70	121–122[d]	3000 b, 2210, 1700	8.15 (s, 1), 7.9 (m, 2), 7.45 (m, 6), 2.5 (s, 3), 2.43 (s, 3)
5a	96	132–135[d]	2210, 1730, 1600	8.05 (m, 3), 7.58 (m, 8), 4.04 (s, 3)
5b	95	164–166[h]	2210, 1710, 1600	7.9 (m, 3), 7.45 (m, 6), 4 (s, 3)
5c	96	179–180[h]	2205, 1708, 1597	7.87 (m, 3), 7.5 (m, 6), 4 (s, 3)
5d	97	157–159[h]	2210, 1740, 1600	8 (d, 2, 9), 7.85 (s, 1), 7.53 (d, 2, 9), 7 (d, 2, 9), 6.95 (d, 2, 9), 4.03 (s, 3), 3.94 (s, 3), 3.9 (s, 3)
5e	94	137–139[h]	2200, 1733, 1593	7.9 (s, 1), 7.9 (d, 2, 9), 7.43 (d, 2, 9), 7.24 (d, 2, 9), 7.2 (d, 2, 9), 4 (s, 3), 2.41 (s, 3), 2.38 (s, 3)
5f	97	113–114[d]	2205, 1728, 1600	7.93 (s, 1), 7.88 (m, 2), 7.38 (m, 6), 4 (s, 3), 2.417 (s, 3), 2.412 (s, 3)
6b	85	155–156[h]	1730, 1600	8.3 (s, 1), 8.15 (d, 2, 9), 7.8 (d, 2, 9), 7.71 (d, 2, 9), 7.58 (d, 2, 9)[l]
6c	81	183–184[d]	1750, 1610, 1590	8.15 (d, 2, 9), 8 (s, 1), 7.63 (m, 6)
6d	82	164–165[h]	1750, 1610	8.18 (s, 1), 8.12 (d, 2, 9), 7.7 (d, 2, 9), 7.15 (d, 2, 9), 7.02 (d, 2, 9) 3.9 (s, 3), 3.85 (s, 3)[l]
6e	86	162–163[d]	1727, 1600	8.18 (d, 2, 9), 8 (s, 1), 7.62 (d, 2, 9), 7.32 (d, 2, 9), 7.28 (d, 2, 9) 2.5 (s, 3), 2.45 (s, 3)
6f	66	89–90[d]	1740, 1600, 1575	8.1 (m, 2), 8 (s, 1), 7.4 (m, 6), 2.49 (s, 3), 2.46 (s, 3)
6g	86	97–98[d]	1737, 1607	8.18 (dd, 1, 7, 2), 7.8 (s, 1), 7.3 (m, 7), 2.8 (s, 3), 2.38 (s, 3)
7a	98	203–204	3140, 1680, 1655	13.5 (bs, 1),[e] 12 (d, 1, 10),[e] 7.9 (m, 3), 7.4 (m, 8)
7b	96	233–234	3340, 1692, 1658	13.2 (bs, 1),[e] 11.8 (d, 1, 10),[e] 7.93 (d, 2, 9), 7.72 (d, 1, 10),[f] 7.70 (d, 2, 9), 7.44 (s, 4)[l]
7c	95	208–209	3340, 1690, 1655	13.3 (bs, 1),[e] 11.76 (d, 1, 11),[e] 7.84 (s, 4), 7.7 (d, 1, 11),[f] 7.6 (d, 2, 9) 7.37 (d, 2, 9)
7d	94	210–211	3330, 1680, 1663	13.2 (bs, 1),[e] 11.73 (d, 1, 10),[e] 7.88 (d, 2, 9), 7.63 (d, 1, 10),[f] 7.33 (d, 2, 9), 7.15 (d, 2, 9), 6.93 (d, 2, 9), 3.9 (s, 3), 3.8 (s, 3)
7e	96	213–214	3330, 1685, 1660	12 (bs, 1),[e] 10.75 (d, 1, 11),[e] 7.8 (d, 2, 9), 7.67 (d, 1, 11),[f] 7.52 (d, 2, 9) 7.25 (m, 4), 2.43 (s, 3), 2.34 (s, 3)[l]
7f	97	186–187	3140, 1680, 1655	13.1 (bs, 1),[e] 11.8 (d, 1, 11),[e] 7.65 (m, 5), 7.2 (m, 4), 2.45 (s, 3), 2.35 (s, 3)[l]
7g	95	237–238	3310, 1690, 1660	13 (bs, 1),[e] 11.2 (d, 1, 11),[e] 7.5 (m, 5), 7.23 (m, 4), 2.53 (s, 3), 2.27 (s, 3)[l]

[a] Satisfactory combustion analytical data (±0.3%) for C, H, and N were obtained. [b] Nujol mull for solids and liquid film for oils. [c] Multiplicity, signal intensity (H), and coupling constant (hertz) indicated by values in parentheses. Chemical shifts of COOR groups are not reported. [d] From CH_2Cl_2–hexane. [e] Exchange with D_2O. [f] Singlet after D_2O. [g] Washed with Et_2O. [h] From CH_2Cl_2–Et_2O. [i] From CH_2Cl_2–MeOH. [l] Me_2SO. [m] CF_3COOD. [n] From THF–Et_2O.

oxidative coupling products were obtained,[1] while in the second case 3,4,4-trisubstituted 4-hydroxy-2-isoxazolin-5-ones were formed.[2]

We report here that the title compounds can be oxidized, by manganese dioxide or by peroxyformic acid, giving, in both cases, oxidative coupling derivatives of the C–N type, from which 1,3-oxazin-6-ones can be easily obtained in quantitative yields.

The 4-arylisoxazolin-5-ones **2** were prepared by reaction between the corresponding 2-aryl-2-formyl acetates **1** and hydroxylamine hydrochloride in methanol–water solution (Scheme I). The isoxazolin-5-one **2h** was obtained in a similar way from ethyl 3-ethoxy-2-(2-pyridyl)acrylate (**1h**).

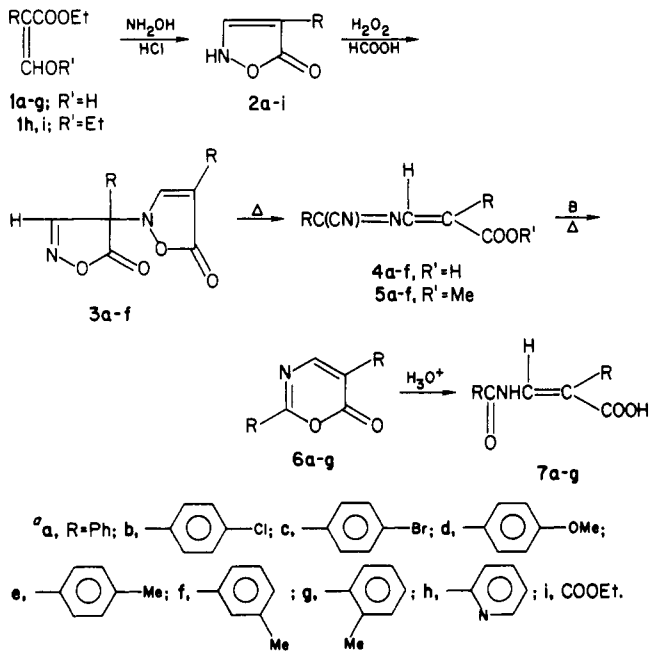
While the corresponding alkyl derivatives are unstable,[3] the 4-arylisoxazolones **2** are stable compounds which are synthesized in high yields. From ^1H NMR data, all these compounds exist mainly in the NH tautomeric form in chloroform solution. Compounds **2a**[3] and **2i**[4] have been previously reported.

When a formic acid solution of the isoxazolones **2** is treated with 30% hydrogen peroxide, an exothermic reaction takes place and the oxidation product **3** crystallize out from the reaction mixture with good yields and in a pure state. However, we were unable to isolate pure **3g**.

The structures **3** follow from analytical and spectroscopic data as well as from the chemical behavior. The compounds **3** are crystalline solids which decompose explosively on heating above the melting point. With organic

(1) Beccalli, E. M.; Marchesini, A.; Gioia, B. *J. Heterocycl. Chem.* **1980**, *17*, 763.
(2) Baldoli, C.; Beccalli, E. M.; Licandro, E.; Marchesini, A. *Gazz. Chim. Ital.* **1981**, *111*, 347.
(3) De Sarlo, F.; Dini, G. *J. Heterocycl. Chem.* **1967**, *4*, 533.
(4) Claisen, L. *Leibigs Ann. Chem.* **1897**, *297*, 75.

Scheme I[a]



solvents they lose carbon dioxide, often in an high exothermic reaction, as in Me_2SO with formation of deep yellow to red solutions. By refluxing **3** in THF solution, the 2-aza-1-cyano-1,3-diene-4-carboxylic acids **4** were obtained in 70–87% yields. The corresponding methyl esters **5** were obtained by reaction of **4** with an ethereal solution of diazomethane. The stereochemistry of the C–C double bond follows from the structure of the cyclic precursor **3**. Although the stereochemistry of the C–N double bond is unknown, the ^1H NMR spectra of compounds **4** and **5** suggest they are pure stereoisomers.

In the presence of a base, the acids **4** gave, in 66–86% yields, the corresponding 1,3-oxazin-6-ones **6** with cyanide elimination. The 1,3-oxazin-6-one **6a** has been previously reported.[5] Analytical and spectroscopic data agree with the reported structures **6**. On acidic hydrolysis the oxazinones **6** gave the corresponding enamido acids **7**. The oxazinones **6** may be obtained directly, in 82–86% yields, by heating a THF slurry of compounds **3** in the presence of triethylamine.

In a simpler way, they may be obtained by active manganese dioxide oxidation of the isoxazolones **2** in dichloromethane solution, followed by treatment with triethylamine. In this case the dimeric intermediates **3** cannot be isolated: in the presence of the MnO_2 excess they decompose giving the acids **4**. Pure **3** behave in the same way in similar conditions as well as in the presence of silica gel.

The isoxazolones **2h** and **2i** failed to give any oxidation product: this would be ascribed to the presence of an electron-withdrawing group.

Our work provides an easy entry to new 1,3-oxazin-6-ones, and to 2-azabutadienes bearing electron-withdrawing groups. The synthetic potential of such a class of compounds is well documented.[6]

Experimental Section

All melting and boiling points are uncorrected. IR spectra were determined with a Perkin-Elmer 377 instrument. ^1H NMR spectra were recorded on a Varian EM-390 or on a Bruker WP80SY spectrometer with tetramethylsilane as an internal standard. Column chromatography was performed on Merck Kieselgel 60, 0.063–0.200 mm. Magnesium sulfate was used as drying agent. Evaporation was carried out in vacuo (rotary evaporation).

Preparation of Ethyl 2-Aryl-2-formylacetates 1a–g. General Procedure. A NaH 80% suspension (0.2 mol) was added, over a period of 30 min at room temperature with stirring and under a dry nitrogen stream, to a solution of the ethyl arylacetate (0.05 mol, commercial source) in ethyl formate (80 mL). During the addition the temperature in some case rises 35–40 °C. The reaction mixture was stirred at room temperature (compounds **1a–d**, **1h**, **1e,f** 2.5 h; **1g**, 6 h) and then added to dilute HCl (4.5%, 230 mL). Extraction with Et_2O (2 × 150 mL), drying, and evaporation of solvents afforded the crude products, purified by distillation or crystallization. Compound **1a** has been previously reported.[7]

Preparation of Ethyl 3-Ethoxy-2-(2-pyridyl)acrylate (1h). A mixture of ethyl (2-pyridyl)acetate (6.8 g, commercial source), $ZnCl_2$ (200 mg), acetic anhydride (40 mL), and ethyl orthoformate (40 mL) was heated under reflux for 8 h. After evaporation to dryness, Et_2O (150 mL) was added, and the organic solution was washed with aqueous $NaHCO_3$ and H_2O and then dried. Removal of the solvent followed by distillation of the residue gave pure **1h**.

Preparation of 4-Arylisoxazolin-5-ones 2a–h. General Procedure. A solution of NH_2OH·HCl (0.15 mol) in water (15 mL) was added to a solution of the ester **1** (0.1 mol) in MeOH (100 mL), and the mixture was heated to reflux for 1 h. The residue from the solvent evaporation was taken up in water (80 mL), and, after cooling in ice, the isoxazolone **2** was filtered off and recrystallized or washed with the reported solvent. In the case of the ester **1h**, pyridine (0.2 mol) was added to the reaction mixture.

Preparation of 4-Aryl-4-[1-(4-aryl-5-oxo-2-isoxazolinyl)]-2-isoxazolin-5-ones 3a–f. General Procedure. The isoxazolone **2** (2 g) was dissolved in HCOOH (20 mL) at 40 °C, and then 30% H_2O_2 (4 mL) was added with stirring. The temperature was maintained at 35–40 °C with external cooling and then allowed to raise to ambient temperature. A solid separated from the reaction mixture and, after cooling at 0 °C for 30 min, this was suction filtered, washed with HCOOH (5 mL) and a 3:1 mixture of hexane–Et_2O (80 mL), and air-dried to yield the dimeric derivative **3**. No TLC analysis was possible: on silica gel, decomposition to compounds **4** was immediate.

Preparation of 1,4-Diaryl-1-cyano-2-azabuta-1,3-diene-4-carboxylic Acids 4a–f and of Corresponding Methyl Esters 5a–f. General Procedure. The dimeric derivative **3** (1 g) was dissolved in THF (50 mL) and the mixture slowly heated to reflux. Evolution of CO_2 was observed and the color changed to deep yellow or red. After 30 min, solvent evaporation gave pure **4** which was crystallized from reported solvent. A sample of acid **4** was dissolved in THF and then treated with an ethereal solution of diazomethane. Usual workup gave pure methyl ester **5**. These compounds melt with decomposition, affording the corresponding oxazinones **6**.

Preparation of 2,5-Diaryl-1,3-oxazin-6-ones 6a–f from the Dimers 3. General Procedure. The dimeric compound **3** (1 g) was dissolved in THF (50 mL) and the mixture was slowly heated to reflux. After 15 min, triethylamine (3 mL) was added and the solution heated to reflux for 15 min. The color changed from deep yellow or red to pale yellow. Solvent evaporation and silica gel chromatography of the residue (eluant CH_2Cl_2–hexane, 1:1, v/v) gave pure oxazinones **6**.

Preparation of 2,5-Diaryl-1,3-oxazin-6-ones 6a–g from Isoxazolin-5-ones 2. General Procedure. The isoxazolin-5-one **2** (1 g) was dissolved in CH_2Cl_2 (80 mL) and then active MnO_2 (4 g) was added. After being stirred at room temperature for 15 min, the mixture was filtered on Celite 535. Triethylamine was added to the filtrate and the solution heated to reflux for 15 min. Workup as previously described afforded the oxazinones **6a–g**. The oxazinones **6a–f** were obtained in 80–85% yields. The oxazinone **6g** was obtained only by this method.

Ring Opening of Oxazinones 6. Preparation of 2-Aryl-3-aminoprop-2-enoic Acids 7a–g. The 1,3-oxazin-6-one **6** (0.5

(5) Eiden, F.; Nagar, B. S. *Naturwissenschaften* **1963**, *50*, 403.
(6) Boger, D. L. *Tetrahedron* **1983**, *39*, 2869.
(7) Marx, J. N.; Argyle, J. C.; Norman, L. R. *J. Am. Chem. Soc.* **1974**, *96*, 2121.

g) was dissolved in dioxane (15 mL) and then diluted HCl (4.5%, 5 mL) was added. The solution was heated to reflux for 5 min. The solvent was evaporated and water added (25 mL). Filtration, after cooling in ice for 10 min, gave pure acid **7** with quantitative yields.

Registry No. **1a**, 17838-69-6; **1b**, 33691-09-7; **1c**, 91632-23-4; **1d**, 29969-62-8; **1e**, 62833-11-8; **1f**, 91632-24-5; **1g**, 91632-25-6; **1h**, 91632-26-7; **2a**, 17147-69-2; **2b**, 91632-27-8; **2c**, 91670-46-1; **2d**, 91632-28-9; **2e**, 91632-29-0; **2f**, 91632-30-3; **2g**, 91632-31-4; **2h**, 91632-32-5; **3a**, 91632-33-6; **3b**, 91632-34-7; **3c**, 91632-35-8; **3d**, 91632-36-9; **3e**, 91632-37-0; **3f**, 91632-38-1; **4a**, 91632-52-9; **4b**, 91632-53-0; **4c**, 91632-54-1; **4d**, 91669-97-5; **4e**, 91632-55-2; **4f**, 91632-56-3; **5a**, 91632-57-4; **5b**, 91632-58-5; **5c**, 91632-59-6; **5d**, 91632-60-9; **5e**, 91632-61-0; **5f**, 91632-62-1; **6a**, 91632-39-2; **6b**, 91632-40-5; **6c**, 91632-41-6; **6d**, 91632-42-7; **6e**, 91632-43-8; **6f**, 91632-44-9; **6g**, 91632-45-0; **7a**, 91632-46-1; **7b**, 91632-47-2; **7c**, 91632-48-3; **7d**, 91632-49-4; **7e**, 91632-50-7; **7f**, 91632-51-8; **7g**, 91670-47-2; $PhCH_2COOEt$, 101-97-3; ClC_6H_4-4-CH_2COOEt, 14062-24-9; BrC_6H_4-4-CH_2COOEt, 14062-25-0; $MeOC_6H_4$-4-CH_2COOEt, 14062-18-1; MeC_6H_4-4-CH_2COOEt, 14062-19-2; MeC_6H_4-3-CH_2COOEt, 40061-55-0; MeC_6H_4-2-CH_2COOEt, 40291-39-2; HCOOEt, 109-94-4; $HC(OEt)_3$, 122-51-0; NH_2OH, 7803-49-8; H_2O_2, 7722-84-1; MnO_2, 1313-13-9; ethyl 2-pyridylacetate, 2739-98-2.

Optically Active Nitrogen Ligands. 1. Synthesis of Two Optically Active Monoalkyl-Substituted 2-(2′-Pyridyl)pyridines

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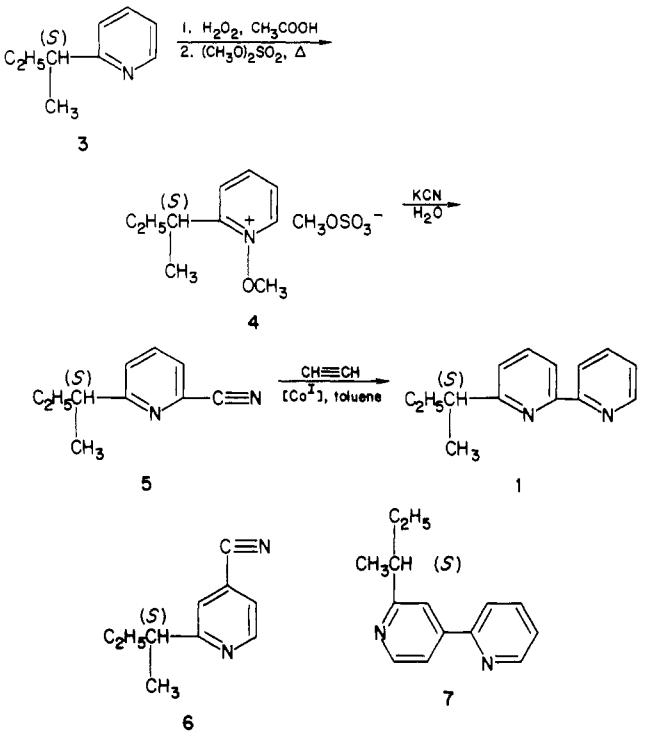
Rhodium(I) and iridium(I) complexes with 2,2′-bipyridines are reported to display a remarkable catalytic activity toward the reduction of olefins and ketones both by molecular hydrogen and by H-transfer at room temperature and atmospheric pressure.[1-3]

With the aim of making a new class of chiral complexes available and of investigating their effectiveness in asymmetric homogeneous catalysis, we undertook a study on a generalizable procedure to obtain optically active 2-(2′-pyridyl)pyridines (2,2′-bipyridines) with high optical purity. To our knowledge, no optically active title compounds have been reported in the literature so far; even monoalkyl-substituted 2,2′-bipyridines are very seldom described.[4-6]

In this paper the results obtained in the synthesis of (+)-(*S*)-2-(2′-pyridyl)-6- (**1**) and (+)-(*S*)-2-(2′-pyridyl)-4-*sec*-butylpyridine (**2**) are presented.

The reaction sequence leading to **1** is shown in Scheme I. Starting with the readily accessible (+)-(*S*)-2-*sec*-butylpyridine[7] (**3**) we obtained the key intermediate nitrile **5** by treatment of the *N*-oxide with dimethyl sulfate followed by reaction of the pyridinium compound **4** with potassium cyanide[8] (Scheme I). The overall yield was 60%; as expected,[8] the isomeric 2-*sec*-butyl-4-cyanopyridine (**6**) (Scheme I) was formed too: the ratio of the two isomers **5** and **6** was 70/30 (determined by GLC). Isomerically pure **5** was easily obtained by column chromatography on silica gel using benzene as the eluant.[9] The yield of pure **5** was about 30% based on starting **3** (Scheme I).

Scheme I[a]



[a] [Co^I] = (π-Cyclopentadienyl)cobalt 1,5-cyclooctadiene.

The cyclization reaction with acetylene was carried out by using (π-cyclopentadienyl)cobalt 1,5-cyclooctadiene as the catalytic precursor and toluene as the solvent following the procedure described by Bönneman and Brinkmann[10] and produced the expected bipyridine **1** in about 80% yield free from other heterocyclic byproducts.

(+)-(*S*)-2-(2′-Pyridyl)-6-*sec*-butylpyridine (**1**) was isolated in about 25% overall yield based on starting **3** as a 99% pure oil, and its identity was confirmed by NMR and MS analysis (see Experimental Section).

For the preparation of the 2,2′-bipyridine **2**, the crucial intermediate 1,5-dialdehyde (**9**) was easily provided by rhodium-catalyzed hydroformylation of (+)-(*S*)-1,1-diethoxy-3-*sec*-butyl-3-butene (**8**), prepared in turn with about 95% optical purity from (+)-(*S*)-*sec*-butylallylmagnesium chloride.[11] Compound **9** was converted into compound **10** by reaction with 2-lithiopyridine at −70 °C,[12,13] followed by oxidation of the resulting pyridinecarbinol with activated MnO_2 at room temperature[14] (Scheme II).

(1) Zassinovich, G.; Camus, A.; Mestroni, G. *Inorg. Nucl. Chem. Lett.* **1976**, *12*, 865.
(2) Mestroni, G.; Zassinovich, G.; Camus, A. *J. Organomet. Chem.* **1977**, *140*, 63.
(3) Zassinovich, G.; Mestroni, G.; Camus, A. *J. Organomet. Chem.* **1979**, *168*, 137.
(4) Micetich, R. G. Abramovich, R. A. "Pyridine and its Derivatives"; Interscience: New York, 1974; Suppl. Part 2, p 373.
(5) Schmalzl, K. J.; Summers, L. A. *Austr. J. Chem.* **1977**, *30*, 657.
(6) Newkome, G. R.; Puckett, W. E.; Kiefer, G. E.; Gupta, V. K.; Xia, Y.; Coreil, M.; Hackney, M. A. *J. Org. Chem.* **1982**, *47*, 4116.
(7) Tatone, D.; Cong Dich, T.; Nacco, R.; Botteghi, C. *J. Org. Chem.* **1975**, *40*, 2987.
(8) Feely, W. E.; Beavers, E. M. *J. Am. Chem. Soc.* **1959**, *81*, 4004.
(9) An alternative experimental procedure can be followed for getting isomerically pure **1**. Cyclization of the 70/30 mixture of cyanopyridines **5** and **6** under the usual conditions gives a mixture of bipyridines **1** and **7** (Scheme I) in 82% yield with practically identical composition. Column chromatography under the same conditions on the bipyridine mixture affords quite pure **1** in 22% yield based on starting **3**.
(10) Bönneman, H.; Brinkmann, R. *Synthesis* **1975**, 600.
(11) Caccia, G.; Chelucci, G.; Botteghi, C. *Synth. Commun.* **1981**, *11*, 71.
(12) Wibaut, J. P.; Jonge, A. P.; van der Voort, H. C. P.; Otto, P. P. H. L. *Recl. Trav. Chim. Pays-Bas* **1951**, *70*, 1054.
(13) Sperber, N.; Papa, D.; Schwenk, E.; Sherlock, N. *J. Am. Chem. Soc.* **1951**, *73*, 3856.

0022-3263/84/1949-4290$01.50/0