A Convenient and Regioselective Synthesis of 4,6-Diaryl-2,3,4,7-tetrahydrooxepin-2-ones[1] and 1,4-Diphenyl-2,3,4,7-tetrahydro-1*H*-azepin-2-one

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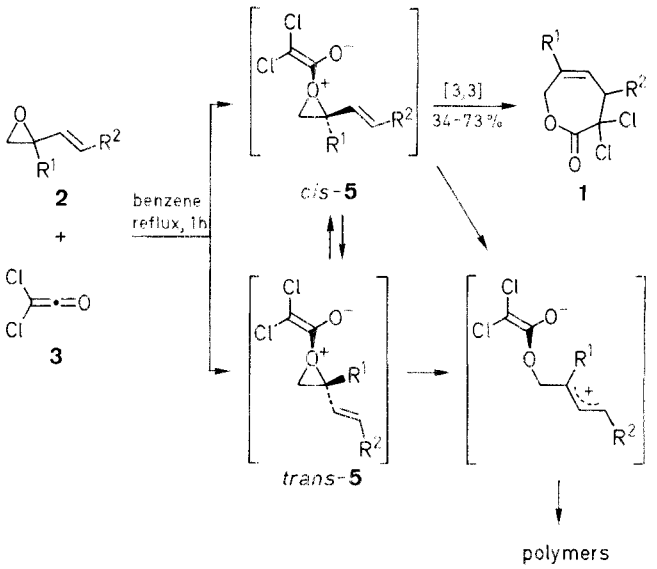
Reactions of 2-vinyloxiranes and 2-vinylaziridine with dichloroketene gave the corresponding 2,3,4,7-tetrahydrooxepin-2-ones and 2,3,4,7-tetrahydroazepin-2-one derivatives, respectively.

Synthesis of lactone derivatives is one of the intensive subjects of organic chemistry, because of their occurrence in natural products and synthetic utilities as acylating reagents.[2] For the synthesis of ε-lactones, the most widely used method is a Baeyer Villiger oxidation of the appropriately substituted cyclohexanones.[3-5]

In this paper, we wish to report a convenient and regioselective synthesis of 4,6-diaryl-2,3,4,7-tetrahydrooxepin-2-ones **1** from cycloaddition reaction between easily available 2-vinyloxiranes **2**[6,7] and dichloroketene (**3**)[8-12] and further application for the synthesis of 2,3,4,7-tetrahydro-1*H*-azepin-2-one **4**.

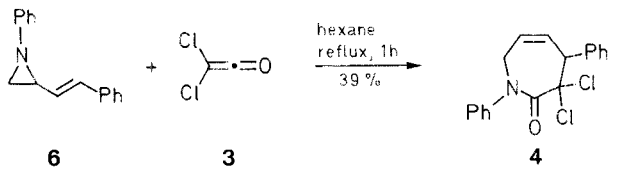
The ketene **3**, *in situ* generated by dehydrochlorination of dichloroacetyl chloride, reacted with 2-vinyloxiranes **2** in refluxing benzene to give 3,3-dichloro-2,3,4,7-tetrahydrooxepin-2-ones **1** without formation of 2-yliden-1,3-dioxolanes or γ-lactones.[13-15]



1, 2	R^1	R^2	1, 2	R^1	R^2
a	H	Ph	**d**	Ph	4-$MeOC_6H_4$
b	Ph	Ph	**e**	Ph	4-ClC_6H_4
c	Ph	4-$CH_3C_6H_4$	**f**	4-$MeOC_6H_4$	Ph

Use of the ketene **3** generated from trichloroacetyl chloride and zinc[16] gave poor results, probably due to ring opening or polymerization of the oxirane **2a**. Use of ether, tetrahydrofuran, or hexane as a solvent also gave poor results. The reaction of **2f** with **3** at 20 °C gave higher yield of **1f** than that at 80 °C. The reaction may proceed via nucleophilic addition of oxygen atom of **2** to the carbonyl carbon of the ketene **3** to form the oxonium salt **5**. [3,3]-Sigmatropic rearrangement of the intermediate *cis*-**5** could give the ε-lactones **1**.[17,18]

Instead of the oxiranes **2**, use of *N*-phenyl-2-(2-phenylvinyl)-aziridine **6**[19] led to the formation of 3,3-dichloro-1,4-diphenyl-2,3,4,7-tetrahydro-1*H*-azepin-2-one **(4)** in 39% yield. Similar ring expansions of vinylaziridines were reported.[17,18]



6 **3** **4**

Further studies on the reactions of the ketene **3** with 2-vinyloxiranes **1** and 2-vinylaziridines **6** having other substituents such as aliphatic groups are now in progress.

3,3-Dichloro-4-phenyl-2,3,4,7-tetrahydrooxepin-2-one (1a):
To a solution of 2-(2-phenylvinyl)oxirane[6] (**2a**, 0.292 g, 2.0 mmol) and NEt_3 (1.01 g, 10 mmol) in anhydrous benzene (30 mL), a solution of dichloroacetyl chloride (1.47 g, 10 mmol) in anhydrous benzene (20 mL) is added dropwise within 30 min with refluxing. After refluxing for additional 60 min, the mixture is diluted with benzene (50 mL), washed with H_2O (3 × 100 mL), and dried over anhydrous Na_2SO_4. After removal of the solvent, the residue is chromatographed on silica gel column (eluent: hexane/CH_2Cl_2, 2:1), to give 0.376 g (73%) of **1a** as white plates; mp 111–114°C (Et_2O/hexane).

3,3-Dichloro-1,4-diphenyl-2,3,4,7-tetrahydro-1*H*-azepin-2-one (4):
To a solution of *N*-phenyl-2-(2-phenylvinyl)aziridine[19] (**6**, 0.221 g, 1.0 mmol) and NEt_3 (0.202 g, 2.0 mmol) in anhydrous hexane (15 mL), a solution of dichloroacetyl chloride (0.295 g, 2.0 mmol) in anhydrous hexane (10 mL) is added dropwise within 30 min with refluxing. After refluxing for additional 60 min, the solvent is removed, and the residue is dissolved in CH_2Cl_2 (100 mL). The solution is washed with H_2O

Table. 2,3,4,7-Tetrahydrooxepin-2-ones **1** and -1*H*-azepin-2-one **4**

Product	Yield[a] (%)	mp (°C)	Molecular Formula[b]	IR (KBr)[c] ν(cm^{-1})	^{1}H-NMR ($CDCl_3$)[d] δ, J(Hz)	^{13}C-NMR ($CDCl_3$)[d] δ	MS (20 eV)[e] m/z (M^+)
1a	73 0[f] 0[g] trace[h] 0[i] 41[j]	111–114 (Et_2O/hexane)	$C_{12}H_{10}Cl_2O_2$ (257.1)	1725 (C=O)	4.37 (m, 1H, CH); 5.03 (ddd, 1H, J = 1.8, 5.0, 16.8, CHH); 5.41 (qd, 1H, J = 2.4, 16.8, CHH); 5.87 (ddd, 1H, J = 2.4, 5.4, 12.4, CH=CH); 5.95 (ddd, 1H, J = 2.4, 5.0, 12.4, CH=CH); 7.34 (s, 5H, H_{arom})	58.8, 69.2, 86.7, 124.0, 128.5, 128.8, 129.6, 130.3, 135.0, 162.3 (C=O)	256
1b	71	118–120 (Et_2O/hexane)	$C_{18}H_{14}Cl_2O_2$ (333.2)	1760 (C=O)	4.56 (ddd, 1H, J = 1.5, 2.4, 5.8, CH); 5.38 (m, 1H, CHH); 5.74 (td, 1H, J = 2.4, 16.3, CHH); 6.02 (dd, 1H, J = 2.4, 5.8, CH=C); 7.3–7.4 (m, 10H, H_{arom})	58.9, 72.0, 86.4, 126.5, 127.6, 128.5, 128.6, 128.80, 128.83, 130.4, 135.2, 136.5, 139.1, 162.4 (C=O)	332
1c	70	116–121 (Et_2O/hexane)	$C_{19}H_{16}Cl_2O_2$ (347.2)	1740 (C=O)	2.34 (s, 3H, CH_3); 4.51 (m, 1H, CH); 5.36 (m, 1H, CHH); 5.75 (ddd, 1H, J = 2.2, 2.4, 16.5, CHH); 6.01 (dd, 1H, J = 2.2, 6.2, CH=C); 7.1–7.4 (m, 9H, H_{arom})	21.1, 58.5, 71.9, 86.5, 126.4, 127.8, 128.4, 128.8, 129.4, 130.2, 132.1, 136.1, 138.8, 139.1, 162.4 (C=O)	346
1d	54	112–113 (Et_2O)	$C_{19}H_{16}Cl_2O_3$ (363.2)	1745 (C=O)	3.79 (s, 3H, CH_3); 4.50 (ddd, 1H, J = 1.1, 2.2, 6.2, CH); 5.35 (dd, 1H, J = 1.1, 16.5, CHH); 5.75 (td, 1H, J = 2.2, 16.5, CHH); 6.01 (dd, 1H, J = 2.2, 6.2, CH=C); 6.8–7.4 (m, 9H, H_{arom})	55.3, 58.2, 72.0, 86.6, 114.0, 126.5, 126.9, 127.8, 128.4, 128.8, 131.6, 136.0, 139.2, 160.0, 162.5 (C=O)	362
1e	58	115–119 (Et_2O/hexane)	$C_{18}H_{13}Cl_3O_2$ (367.7)	1740 (C=O)	4.54 (ddd, 1H, J = 1.5, 2.4, 6.0, CH); 5.38 (ddd, 1H, J = 0.6, 1.5, 16.5, CHH); 5.73 (td, 1H, J = 2.4, 16.5, CHH); 5.98 (m, 1H, CH=C); 7.3–7.4 (m, 9H, H_{arom})	58.1, 72.0, 86.1, 126.5, 127.0, 128.6, 128.9, 131.7, 133.7, 134.9, 137.0, 138.8, 162.2 (C=O)	366
1f	34 67[k]	143–145 (EtOH/EtOAc)	$C_{19}H_{16}Cl_2O_3$ (363.2)	1750 (C=O)	3.81 (s, 3H, CH_3); 4.54 (ddd, 1H, J = 1.5, 2.2, 6.2, CH); 5.36 (m, 1H, CHH); 5.69 (td, 1H, J = 2.2, 16.4, CHH); 5.95 (dd, 1H, J = 2.2, 6.2, CH=C); 6.9–7.4 (m, 9H, H_{arom})	55.3, 58.8, 72.0, 86.5, 114.2, 126.4, 127.7, 128.6, 128.8, 130.4, 131.3, 135.4, 136.0, 159.8, 162.5 (C=O)	362
4	39[l] 31[m]	173–177 (EtOH)	$C_{18}H_{15}NOCl_2$ (332.2)	1660 (C=O)	4.4–4.5 (m, 2H, CHH and CH); 4.92 (m, 1H, CHH); 5.88 (dddd, 1H, J = 0.8, 2.0, 4.8, 12.0, CH=CH); 5.95 (dddd, 1H, J = 0.8, 2.4, 5.6, 12.0, CH=CH); 7.2–7.5 (m, 10H, H_{arom})	52.5, 58.9, 90.4, 124.1, 126.0, 127.4, 128.3, 128.5, 129.4, 129.8, 130.5, 136.0, 145.7, 153.4 (C=O)	331

[a] Isolated yields.
[b] Satisfactory microanalyses obtained: C ± 0.17, H ± 0.19.
[c] Recorded by Jasco IR-G.
[d] Recorded by Jeol JNM GX-270.
[e] Recorded by Hitachi RMU-6M (Cl = ^{35}Cl).
[f] The ketene **3** was generated from trichloroacetyl chloride and zinc in the presence of $P(O)Cl_3$ for 4 h in Et_2O at 35°C[16]; mole ratio **2**/**3** = 1:1.1.
[g] The oxirane **2a** was recovered; solvent: Et_2O (35°C); mole ratio **2**/**3** = 1:1.1.
[h] Solvent: THF (66°C); mole ratio: **2**/**3** = 1:1.1.
[i] Solvent: hexane (68°C); mole ratio: **2**/**3** = 1:1.1.
[j] Mole ratio: **2**/**3** = 1:1.1.
[k] Reaction was carried out at 20°C.
[l] Solvent: hexane (68°C); mole ratio: **6**/**3** = 1:2.
[m] Solvent: benzene (80°C); mole ratio: **6**/**3** = 1:5.

(3 × 100 mL), then dried over anhydrous Na_2SO_4. After removal of the solvent, the residue is triturated with Et_2O (0.5 mL) to give 0.129 g (39%) of **4** as white powder; mp 173–177°C (EtOH).

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