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Photoinduced Masked-Formylation of Vinylsulfone Derivatives with 1,3-Dioxolane. Application to the Synthesis of 3,4-Disubstituted Pyrroles

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It was found that α -cyanovinylsulfones, which were prepared by an improved Knoevenagel condensation, react readily with 1,3-dioxolane under ultraviolet irradiation in the presence of a photosensitizer. The reaction provided a new convenient method for the preparation of 3,4-disubstituted pyrroles.

We have been investigating the preparation of vinyl- and allylsulfones¹⁾ and the related new synthetic reactions.²⁾ In the course of the study, we found that vinylsulfones (<u>1</u>) react with THF (<u>2</u>) and 1,3-dioxolane (<u>3</u>) in the presence of 2,2'-azobisisobutyronitrile (AIBN) or under irradiation by ultraviolet light giving the corresponding addition products (<u>4</u>).³⁾ The addition of 1,3-dioxolane means the masked-formylation⁴⁾ on β -position of vinylsulfones.



On the other hand, we have developed the convenient methods for the preparation of substituted furans $(\underline{7})$ and pyrroles $(\underline{8})$ starting from 3-p-toluenesulfonyl-propanal ethylene acetal derivatives $(\underline{5})$ as shown in the following scheme.⁵⁾



The above masked-formylation of vinylsulfones therefore prompted us to apply it to the preparation of heterocyclic compounds such as $\underline{7}$ and $\underline{8}$. This paper describes the application of the photoinduced masked-formylation of vinylsulfones to the synthesis of 3,4-disubstituted pyrroles useful as a building block of porphynoids according to Scheme 1.

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An attempt to prepare α -cyanovinylsulfone (<u>11</u>) from aldehyde (<u>9</u>) and sulfonylacetonitrile (<u>10</u>) by general Knoevenagel condensation⁶) resulted in the formation of unseparable mixture of <u>11</u> and α -cyanoallylsulfone (<u>17</u>). The difficulty could be overcome by trapping the initially formed condensation product as a sulfide (<u>18</u>) with a thiol (especially o-toluenethiol was excellent among the examined thiols: methanethiol, t-butanethiol, benzenethiol, p-toluenethiol, otoluenethiol)⁷ followed by the oxidation⁸ with potassium peroxymonosulfate (OXONE, 2KHSO₅·KHSO₄·K₂SO₄) in two phases (CH₂Cl₂/H₂O) using a phase transfer catalyst⁹) (Scheme 2).



The masked-formylation of $\underline{11}$ was readily achieved using $\underline{3}$ as a solvent in the presence of a photosensitizer under irradiation with 300 W mercury lamp (Eiko-sha) at room temperature (Table 1).

The 3-cyano-3-sulfonylpropanal ethylene acetal derivatives $(\underline{12})$ thus obtained were next alkylated with alkyl halide and potassium carbonate in N,N-dimethylform-amide (DMF) at room temperature in good yields (Table 2).

Entry	<u>11a-e</u> , R ¹	Photosensi- tizer (1 equiv.)	Time/h ^{b)}	<u>12a-e</u> Yield/%c)	Ratio of diastereomers ^d)
1	<u>11a</u> , Ph(CH ₂) ₂	PhCOPh	2	<u>12a</u> , 79	87/13
2	<u>11b</u> , Ph	MeCOPh	2	<u>12b</u> , 89	83/17
3	<u>11с</u> , (СН ₃) ₂ СН	MeCOPh	1	<u>12c</u> , 79	51/49
4	<u>11c</u> , "	PhCOPh	0.5	<u>12c</u> , 77	51/49
5	<u>11d</u> , CH ₃ (CH ₂) ₄	MeCOPh	1	<u>12d</u> , 80	87/13
6	<u>11e</u> , CH ₃ CH ₂	PhCOPh	2	<u>12e</u> , 84	88/12

Table 1. Photoinduced Masked-Formylation of α -Cyanovinylsulfones $(<u>11</u>, R = Me)^{a}$

a) 0.1 M solution of 11 in 1,3-dioxolane was irradiated at r.t.

b) The progress of the reaction was monitored by a TLC.
c) All compounds gave the satisfactory spectral data.
d) Determined by 400 MHz H-NMR spectra.

The nitrile group of 13 was readily reduced to the amine with lithium aluminum hydride in the case of R = Me but not R = p-Tol. Therefore, the whole procedure for the preparation of 3,4-disubstituted pyrroles is herein given only for the former case. After the reduction and usual work-up, the resulting primary amines were mesylated without isolation. The crude products (14) were then cyclized to the 3,4-disubstituted N-mesylpyrroles (15) in refluxing benzene containing a catalytic amount of p-toluenesulfonic acid in good yields (Table 3).

The treatment of 15 with 2 M-KOH in methanol under refluxing afforded the demesylated 3,4-disubstituted pyrroles (16)^{5d)} in quantitative yields except 15f which was surprisingly not affected at all under the conditions.

As described above, the present photoinduced masked-formylation of α -cyano-

Entry	<u>12a-e</u> , R ¹	R ² X (equiv.)	Reaction time at r.t. ^{b)}	Yield of <u>13a-i</u> /% ^{C)}
1	<u>12a</u> , Ph(CH ₂) ₂	CH ₃ CH ₂ I (1.5)	1.5 d	<u>13a</u> , 74
2	<u>12a</u> , "	CH ₃ (CH ₂) ₂ I (1.5)	1.5 d	<u>13b</u> , 76
3	<u>12b</u> , Ph	CH ₃ (CH ₂) ₂ I (1.2)	4.5 h	<u>13c</u> , 78
4	<u>12b</u> , "	CH ₃ (CH ₂) ₅ I (1.5)	3.5 h	<u>13d</u> , 82
5	<u>12b</u> , "	$H_2C=CHCH_2Br$ (1.2)	1 h	<u>13e</u> , 78
6	<u>12с</u> , (СН ₃) ₂ СН	CH ₃ (CH ₂) ₅ I (1.2)	5 d	<u>13f</u> , 90
7	<u>12d</u> , CH ₃ (CH ₂) ₄	CH ₃ CH ₂ I (1.5)	2.5 d	<u>13</u> g, 90
8	<u>12d</u> , "	CH ₃ (CH ₂) ₂ I (1.5)	2.5 d	<u>13h</u> , 75
9	<u>12е</u> , СН ₃ СН ₂	PhCH ₂ Br (1.5)	9.5 h	<u>13i</u> , 94

Table 2.	Alkylation of 3-Cyano-3-mesylpropanal	Ethylene	Acetal
	Derivatives $(12, R = Me)^{a}$		

a) 1.5 equiv. of K_2CO_3 was used as a base in DMF. b) The progress of²the reaction was monitored by a TLC.

c) Obtained as a mixture of diastereomers. The spectral data for

new compounds were in accordance with the structures assigned.

Entry	<u>13a-i</u>		Reduction	Yield of	Refluxing	Yield of
	R ¹	R ²	time/h	<u>15a-i</u> /% ^{b)}	hydrolysis ^C	<u>16a-i</u> /% ^{b)}
1	Ph(CH ₂) ₂	CH ₃ CH ₂	1	<u>15a</u> , 84	2 h	<u>16a</u> , quant
2	"	CH ₃ (CH ₂) ₂	1.5	<u>15b</u> , 73	1.5 h	<u>16b</u> , quant
3	Ph	CH ₃ (CH ₂) ₂	1.5	<u>15c</u> , 68	10 min	<u>16c</u> , quant
4		CH ₃ (CH ₂) ₅	. 3	<u>15d</u> , 74	10 min	<u>16d</u> , quant
5		H ₂ C=CHCH ₂	2.5	<u>15e</u> , 55	10 min	<u>16e</u> , quant
6	(CH ₃) ₂ CH	CH ₃ (CH ₂) ₅	1	<u>15f</u> , 57	2 h	d)
7	CH ₃ (CH ₂) ₄	CH ₃ CH ₂	1.5	<u>15</u> g, 82	4 h	<u>16g</u> , quant
8	"	CH ₃ (CH ₂) ₂	1.5	<u>15h</u> , 90	4.5 h	<u>16h</u> , quant
9	сн ₃ сн ₂	PhCH ₂	2	<u>15i</u> , 61	1 h	<u>16i</u> , quant

Table 3. Formation of 3,4-Disubstituted N-Mesyl- and N-Demesylpyrroles $(15 \text{ and } 16) \text{ from } 13 (R = Me)^{a}$

a) (1) LiAlH₄ (4 equiv.) in Et_2O at r.t. (2) CH_3SO_2Cl (2 equiv.)/ Et_3N (2.2 equiv.) in CH₂Cl₂ at r.t. for 10 min. (3) p-TolSO₃H (catalytic amount) in benzene/refluxed for 15 min.

b) All compounds gave the satisfactory spectral data.

c) Refluxed in 2 M-KOH in methanol.

d) 15f was recovered quantitatively.

vinylsulfone derivatives with 1,3-dioxolane provided a new convenient method for the preparation of 3,4-disubstituted pyrroles. Further work is in progress in our labolatory.

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