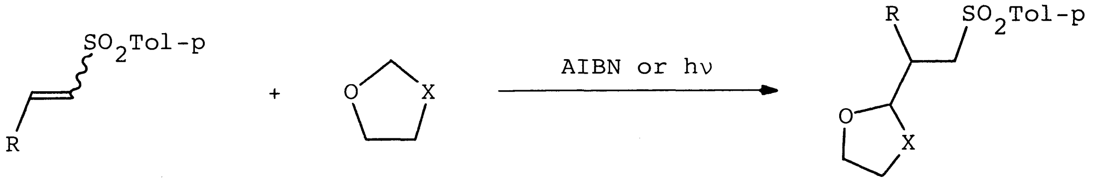
CHEMISTRY LETTERS, pp. 813-816, 1988.

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

Katsuhiko INOMATA,* Hiroshi SUHARA, Hideki KINOSHITA,
and Hiroshi KOTAKE
Department of Chemistry, Faculty of Science, Kanazawa University, Kanazawa 920

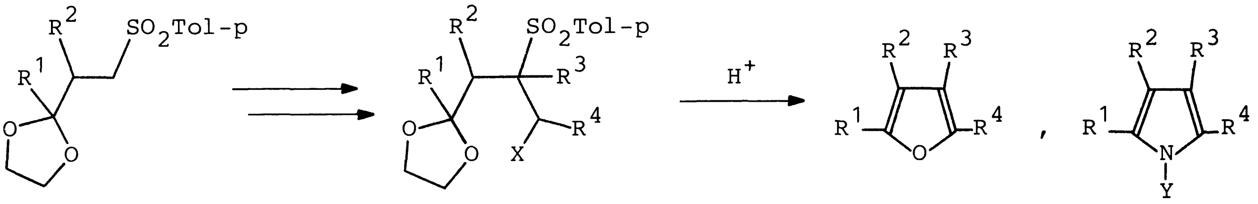
It was found that α-cyanovinylsulfones, which were prepared by an improved Knoevenagel condensation, react readily with 1,3-dioxolane under ultraviolet irradiation in the presence of a photosensitizer. The reaction provided a new convenient method for the preparation of 3,4-disubstituted pyrroles.

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 (1) react with THF (2) and 1,3-dioxolane (3) in the presence of 2,2'-azobisisobutyronitrile (AIBN) or under irradiation by ultraviolet light giving the corresponding addition products (4).3) The addition of 1,3-dioxolane means the masked-formylation4) on β-position of vinylsulfones.



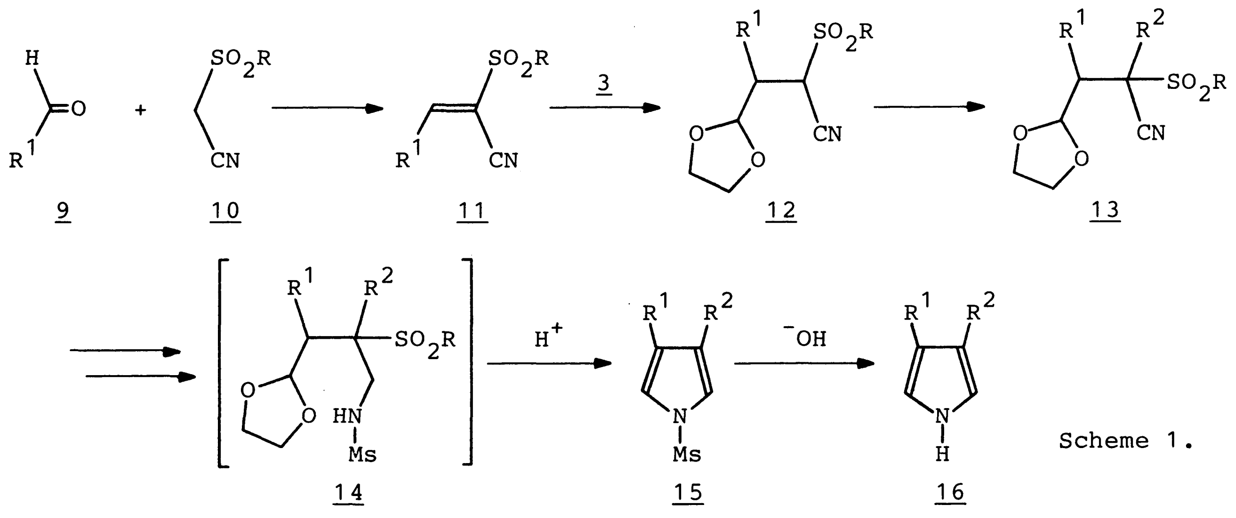
1 2 (X = CH_2) 3 (X = O) 4 (X = CH_2 or O)

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



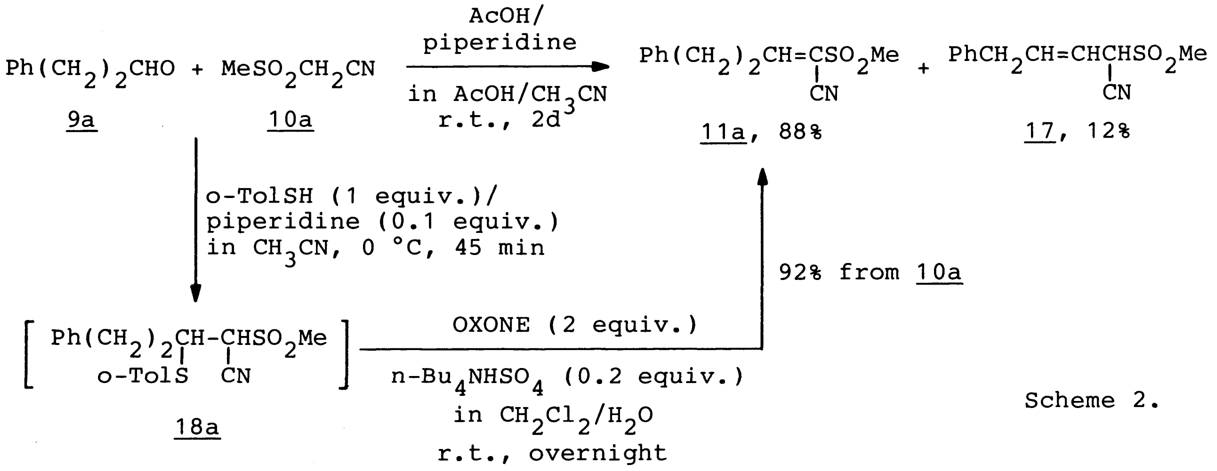
5 6 7 (X = OH) 8 (X = NHY)

The above masked-formylation of vinylsulfones therefore prompted us to apply it to the preparation of heterocyclic compounds such as 7 and 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.



Scheme 1.

An attempt to prepare α-cyanovinylsulfone (11) from aldehyde (9) and sulfonylacetonitrile (10) by general Knoevenagel condensation[6)] resulted in the formation of unseparable mixture of 11 and α-cyanoallylsulfone (17). The difficulty could be overcome by trapping the initially formed condensation product as a sulfide (18) with a thiol (especially o-toluenethiol was excellent among the examined thiols: methanethiol, t-butanethiol, benzenethiol, p-toluenethiol, o-toluenethiol)[7)] followed by the oxidation[8)] with potassium peroxymonosulfate (OXONE, $2KHSO_5 \cdot KHSO_4 \cdot K_2SO_4$) in two phases ($CH_2Cl_2/H_2O$) using a phase transfer catalyst[9)] (Scheme 2).



Scheme 2.

The masked-formylation of 11 was readily achieved using 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 (12) thus obtained were next alkylated with alkyl halide and potassium carbonate in N,N-dimethylformamide (DMF) at room temperature in good yields (Table 2).

Table 1. Photoinduced Masked-Formylation of α-Cyanovinylsulfones (11, R = Me)[a)]

Entry	11a-e, R^1	Photosensitizer (1 equiv.)	Time/h[b)]	12a-e Yield/%[c)]	Ratio of diastereomers[d)]
1	11a, $Ph(CH_2)_2$	PhCOPh	2	12a, 79	87/13
2	11b, Ph	MeCOPh	2	12b, 89	83/17
3	11c, $(CH_3)_2CH$	MeCOPh	1	12c, 79	51/49
4	11c, "	PhCOPh	0.5	12c, 77	51/49
5	11d, $CH_3(CH_2)_4$	MeCOPh	1	12d, 80	87/13
6	11e, CH_3CH_2	PhCOPh	2	12e, 84	88/12

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 ^{1}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-

Table 2. Alkylation of 3-Cyano-3-mesylpropanal Ethylene Acetal Derivatives (12, R = Me)[a)]

Entry	12a-e, R^1	R^2X (equiv.)	Reaction time at r.t.[b)]	Yield of 13a-i/%[c)]
1	12a, $Ph(CH_2)_2$	CH_3CH_2I (1.5)	1.5 d	13a, 74
2	12a, "	$CH_3(CH_2)_2I$ (1.5)	1.5 d	13b, 76
3	12b, Ph	$CH_3(CH_2)_2I$ (1.2)	4.5 h	13c, 78
4	12b, "	$CH_3(CH_2)_5I$ (1.5)	3.5 h	13d, 82
5	12b, "	$H_2C{=}CHCH_2Br$ (1.2)	1 h	13e, 78
6	12c, $(CH_3)_2CH$	$CH_3(CH_2)_5I$ (1.2)	5 d	13f, 90
7	12d, $CH_3(CH_2)_4$	CH_3CH_2I (1.5)	2.5 d	13g, 90
8	12d, "	$CH_3(CH_2)_2I$ (1.5)	2.5 d	13h, 75
9	12e, CH_3CH_2	$PhCH_2Br$ (1.5)	9.5 h	13i, 94

a) 1.5 equiv. of K_2CO_3 was used as a base in DMF.
b) The progress of the 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.

Table 3. Formation of 3,4-Disubstituted N-Mesyl- and N-Demesylpyrroles (15 and 16) from 13 (R = Me)[a)]

Entry	13a-i		Reduction	Yield of	Refluxing time for hydrolysis[c)]	Yield of
	R^1	R^2	time/h	15a-i/%[b)]		16a-i/%[b)]
1	$Ph(CH_2)_2$	CH_3CH_2	1	15a, 84	2 h	16a, quant
2	"	$CH_3(CH_2)_2$	1.5	15b, 73	1.5 h	16b, quant
3	Ph	$CH_3(CH_2)_2$	1.5	15c, 68	10 min	16c, quant
4	"	$CH_3(CH_2)_5$	3	15d, 74	10 min	16d, quant
5	"	$H_2C{=}CHCH_2$	2.5	15e, 55	10 min	16e, quant
6	$(CH_3)_2CH$	$CH_3(CH_2)_5$	1	15f, 57	2 h	d)
7	$CH_3(CH_2)_4$	CH_3CH_2	1.5	15g, 82	4 h	16g, quant
8	"	$CH_3(CH_2)_2$	1.5	15h, 90	4.5 h	16h, quant
9	CH_3CH_2	$PhCH_2$	2	15i, 61	1 h	16i, quant

a) (1) $LiAlH_4$ (4 equiv.) in Et_2O at r.t. (2) CH_3SO_2Cl (2 equiv.)/Et_3N (2.2 equiv.) in CH_2Cl_2 at r.t. for 10 min. (3) p-$TolSO_3H$ (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.

This work is partly supported by the Research Grant-in-Aid from The Ministry of Education, Science and Culture (No. 62540376).

References

1) K. Inomata, S. Sasaoka, T. Kobayashi, Y. Tanaka, S. Igarashi, T. Ohtani, H. Kinoshita, and H. Kotake, Bull. Chem. Soc. Jpn., 60, 1767 (1987) and references cited therein; T. Kobayashi, Y. Tanaka, T. Ohtani, H. Kinoshita, K. Inomata, and H. Kotake, Chem. Lett., 1987, 1209.
2) K. Inomata, S. Igarashi, M. Mohri, T. Yamamoto, H. Kinoshita, and H. Kotake, Chem. Lett., 1987, 707 and references cited therein.
3) Presented at the 54th National Meeting of the Chemical Society of Japan, Tokyo, April 1987.
4) C. Giordano, F. Minisci, E. Vismara, and S. Levi, J. Org. Chem., 51, 536 (1986); M. Matsukawa, J. Inanaga, and M. Yamaguchi, Tetrahedron Lett., 28, 5877 (1987).
5) a) K. Inomata, S. Aoyama, and H. Kotake, Bull. Chem. Soc. Jpn., 51, 930 (1978); b) H. Kotake, K. Inomata, H. Kinoshita, S. Aoyama, and Y. Sakamoto, Heterocycles, 10, 105 (1978); c) K. Inomata, Y. Nakayama, M. Tsutsumi, and H. Kotake, ibid., 12, 1467 (1979); d) H. Kinoshita, K. Inomata, M. Hayashi, T. Kondoh, and H. Kotake, Chem. Lett., 1986, 1033.
6) G. Jones, Org. React., 15, 204 - 599 (1967); F. D. Popp and A. Catala, J. Org. Chem., 26, 2738 (1961).
7) W. E. Parham and F. L. Ramp, J. Am. Chem. Soc., 73, 1293 (1951).
8) S. Ranganathan, D. Ranganathan, and S. K. Singh, Tetrahedron Lett., 28, 2893 (1987).
9) R. Curci, M. Fiorentino, L. Troisi, J. O. Edwards, and R. H. Pater, J. Org. Chem., 45, 4758 (1980).

(Received February 16, 1988)