

NITROOLEFINS. I. A NEW AND CONVENIENT ACCESS TO INDOLIZINES AND
PYRAZOLO[1,5-a]PYRIDINES USING 1-NITRO-2-(PHENYLTHIO)ETHYLENE

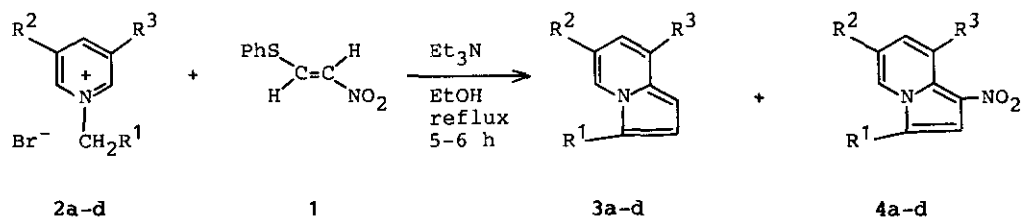
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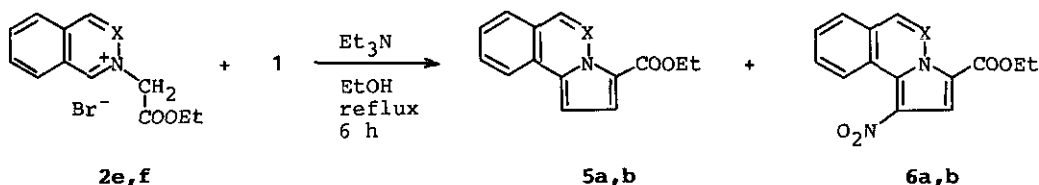
Abstract——1-Nitro-2-(phenylthio)ethylene (**1**) reacts with a variety of N-ylides and N-imines (pyridinium, isoquinolinium, quinolinium, phthalazinium N-ylides and N-imines) in the presence of triethylamine to give the corresponding fused pyrrole and pyrazole derivatives (indolizines, pyrrolo[2,1-a]isoquinoline, pyrrolo[2,1-a]phthalazine, pyrazolo[1,5-a]pyridine, pyrazolo[5,1-a]quinoline, and pyrazolo[5,1-a]isoquinoline) along with the corresponding 1-nitropyrrolopyridines and 1-nitropyrazolopyridines, respectively, in moderate yields.

Nitroolefins are useful reagents not only for the synthesis of heterocycles but also for various synthetic transformations.¹⁻⁴ The presence of electron-donating groups on the vicinal olefinic carbon atom has made this nitroolefin moiety especially reactive and attractive for the synthesis of a wide variety of nitrogen- and sulfur-containing heterocyclic compounds. Among these polarized nitroolefins, ketene dithioacetals,⁵ ethoxymethylene compounds,^{6,7} and aminomethylene compounds^{8,9} are widely used. Recently, 1-nitro-2-(phenylthio)ethylene (**1**)³ was prepared conveniently by the reaction of acetoxynitroethane with thiophenol followed by treatment with sulfur chloride and triethylamine. To our knowledge, **1**, known as a precursor to sulfinyl or sulfonynitroethylenes, has been allowed to react only with pyrrole to give 1-nitro-2-pyrrolylethylene,³ although the electrophilic reagent **1** may be a potential building block for the synthesis of heterocyclic compounds. Indeed we report herein that **1** is an efficient and unprecedented reagent for the synthesis of indolizine and pyrazolopyridine derivatives.

The reaction of 1-ethoxycarbonylmethylpyridinium bromide (2a) with 1 in the presence of triethylamine in ethanol gave the desired ethyl indolizine-3-carboxylate (3a) in 56.5% yield, along with ethyl 1-nitroindolizine-3-carboxylate (4a) in 38.8% yield. Similarly 1-ethoxycarbonylmethyl-3,5-dimethylpyridinium bromide (2b) reacted with 1 to give ethyl 6,8-dimethylindolizine-3-carboxylate (3b) in 55.8% yield. 3-Cyanoindolizine derivatives (3c, d)¹⁰ were also obtained from the corresponding 1-cyanomethylpyridinium bromides (2c, d). 1-Nitro-6,8-dimethylindolizines (4b, d) could not be almost detected in the reaction mixture in the cases of 2b and 2d, although similar results were found in the reaction of 3,5-dimethylpyridinium N-ylides with nitroketene dithioacetal.¹¹ Furthermore reactions of 1 with 2e and 2f under the similar conditions of the synthesis of indolizines gave the corresponding cyclized products, ethyl pyrrolo[2,1-a]isoquinoline-3-carboxylate (5a), ethyl pyrrolo[2,1-a]phthalazine-3-carboxylate (5b), together with ethyl 1-nitro-substituted derivatives, 6a and 6b, respectively, in yields as indicated in Scheme 1.



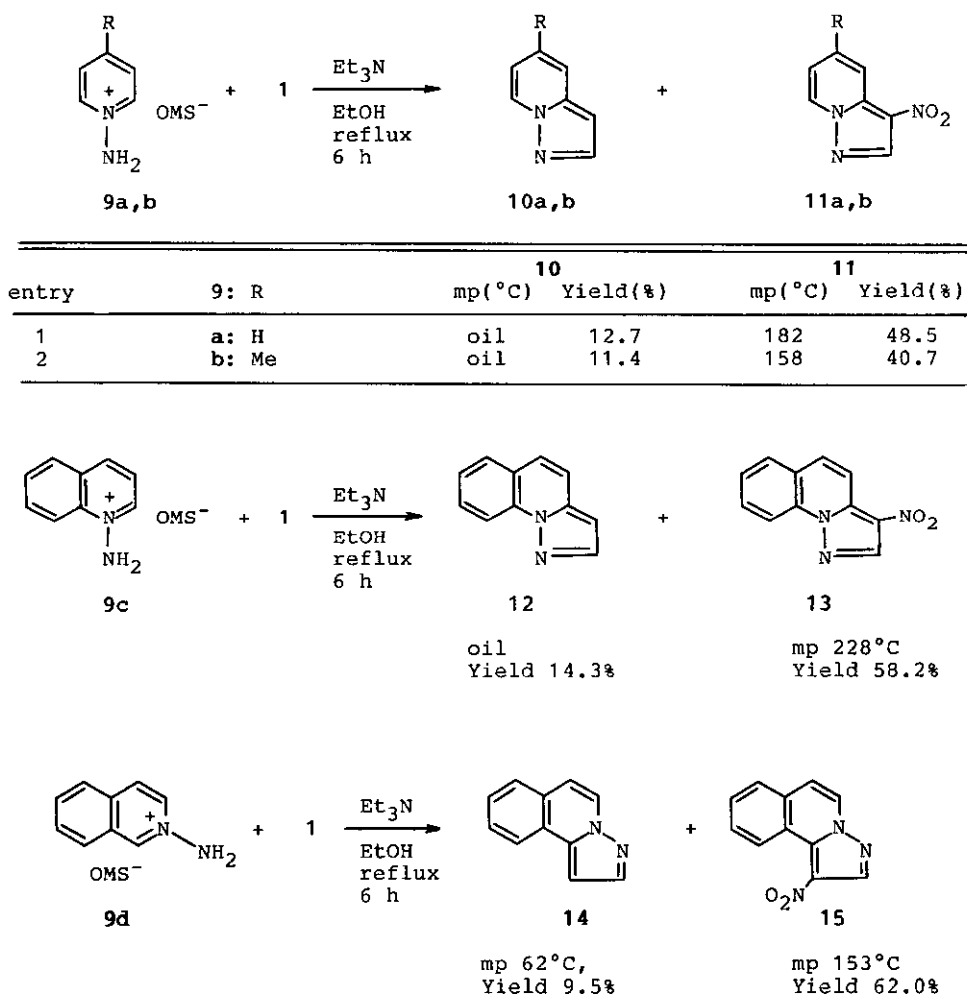
entry	2: R ¹	R ²	R ³	mp(°C)	3 Yield(%)	mp(°C)	4 Yield(%)
1	a: COOEt	H	H	oil	56.5	139	38.8
2	b: COOEt	Me	Me	48	55.8	---	trace
3	c: CN	H	H	48	73.3	231	17.6
4	d: CN	Me	Me	108	54.7	---	----



entry	2: X	mp(°C)	5 Yield(%)	mp(°C)	6 Yield(%)
1	e: CH	94	51.0	167	34.9
2	f: N	115	35.0	212	7.0

Scheme 1

This method using **1** can be readily applied to the synthesis of pyrazolo[5,1-*a*]pyridines. Thus we attempted to synthesize pyrazolopyridine derivatives which were known as very important and interesting intermediates for the synthesis of pharmacologically active compounds and dyes.¹² The reaction of 1-aminopyridinium mesitylenesulfonates (**9a, b**) with **1** in the presence of triethylamine gave the desired pyrazolo[5,1-*a*]pyridines (**10a, b**) and 1-nitropyrazolo[5,1-*a*]pyridine derivatives (**11a, b**) in yields as shown in Scheme 2. Pyrazolo[5,1-*a*]quinolines (**12, 13**) and pyrazolo[5,1-*a*]isoquinolines (**14, 15**) were also prepared from **9c** and **9d** in a manner similar to that described for the synthesis of pyrazolo[5,1-*a*]pyridines (**10, 11**).



Scheme 2

In conclusion, it has been proved that 2-nitro-1-(phenylthio)ethylene (1) is a very useful electrophilic reagent for the synthesis of indolizine and pyrazolo-pyridine derivatives. Related works are now under active progress.

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16. Satisfactory elemental analysis and spectral data were obtained for all new compounds.
17. Similar reaction mechanism for the formation of indolizines and 1-nitro-indolizines is shown in Refer. 3, 5, and 11 and the following paper: Y. Tominaga, et. al., Yakugaku Zasshi, 1984, 104, 440.