Ring Opening Reactions of Indeno[1,2-*c*]isoxazolones [1]

Thomas L. Lemke* and Kailash N. Sawhney

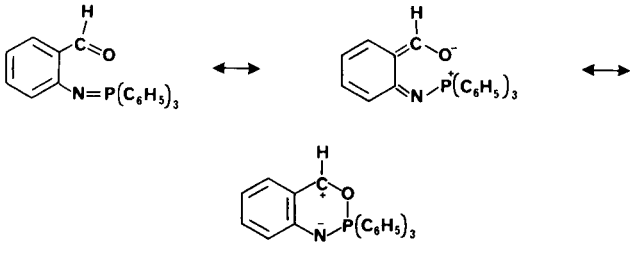
Department of Medicinal Chemistry and Pharmacognosy, College of Pharmacy, University of Houston, Houston, Texas 77004

Received February 1, 1983

Nucleophilic attack of 8-substituted indeno[1,2-*c*]isoxazol-7-ones (**1**) and 3-phenylindeno[1,2-*c*]isoxazol-4-one (**4**) by dimethylsulfoxide or triphenylphosphine results in cleavage of the nitrogen-oxygen bond of the isoxazole ring leading to the formation of sulfoximides (**2** and **5**) and phosphazenes (**3** and **8**).

J. Heterocyclic Chem., **20**, 899 (1983).

The cleavage of the N-O bond of the isoxazole ring with various reagents is a well-known reaction [2]. A nucleophilic reagent which has not been extensively explored for such reactions is triphenylphosphine. Nomura and coworkers [3] first reported the addition of triphenylphosphine to benzisoxazole to give (2-acylphenyl)iminotriphenylphosphoranes, the stability of which was explained by postulating the formation of a resonance stabilized chelate as shown below.



Recently, Sutter and Weis [4] have reported a related ring cleavage of 6*H*-anthra[1,9-*cd*]isoxazol-6-ones and of anthra[1,9-*cd*:5,10-*c'*,*d'*]isoxazole by this and other reagents such as sulfoxides and alkyl or arylphosphites. By this method these workers were able to prepare a variety of substituted anthraquinones having triphenylphosphazeno-, sulfoximido- and dialkyl or diarylphosphoramidic groups attached to 1- and the 1,5-positions of the anthraquinone systems. These reactions proceed readily and in good yields. The ring cleavage reaction with dimethylsulfoxide is considered to proceed *via* a four-membered cyclic intermediate which is similar to that accepted for the Wittig reaction.

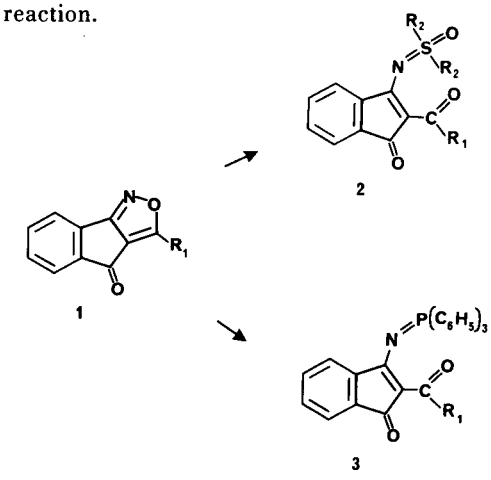
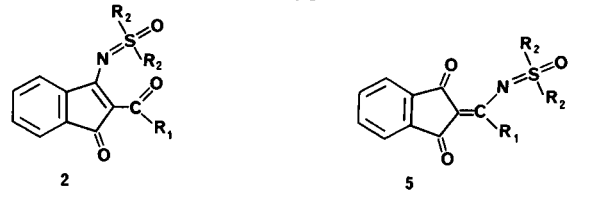


Table I



Compound No.	R_1	R_2	Reaction Time	Mp °C	Yield %	Molecular Formula	Analysis % Calcd./Found			
2a	C_6H_5	CD_3	10 days	185-186 (a)	92	$C_{18}H_9D_6NO_3S$	C, 65.22;	H + D, 6.40;	N, 4.23;	S, 9.68
							C, 65.14;	H + D, 6.43;	N, 4.22;	S, 9.63
2b	C_6H_5	CH_3	13 days	184-186 (a)	92	$C_{18}H_{15}NO_3S$	C, 66.44;	H, 4.65;	N, 4.31	
							C, 66.36;	H, 4.66;	N, 4.28	
2c	$C(CH_3)_3$	CH_3	11 days	84-86 (b)	75	$C_{16}H_{19}NO_3S$	C, 62.92;	H, 6.27;	N, 4.59;	S, 10.50
							C, 62.85;	H, 6.31;	N, 4.55;	S, 10.45
5a	C_6H_5	CD_3	18 hours	199-201 (c)	83	$C_{18}H_{19}D_6NO_3S$	C, 65.22;	H, 4.56;	N, 4.23;	S, 9.68
							C, 65.04;	H, 4.62; (d)	N, 4.17;	S, 9.61
5d	C_6H_5	CH_3	18 hours	202-204 (a)	59	$C_{18}H_{15}NO_3S$	C, 66.44;	H, 4.65;	N, 4.31;	S, 9.86
							C, 66.29;	H, 4.67;	N, 4.29;	S, 9.89

(a) From ethyl acetate-petroleum ether (35-60°). (b) From cyclohexane-petroleum ether (35-60°). (c) From toluene. (d) Deuterium analyzed as hydrogen.

In this communication, we wish to report an extension of this finding to the indeno[1,2-*c*]isoxazole system. Thus, 8-phenylindeno[1,2-*c*]isoxazol-7-one (**1a**, $R_1 = C_6H_5$) [5], 8-*t*-butylindeno[1,2-*c*]isoxazol-7-one (**1b**, $R_1 = C(CH_3)_3$) [6] and 3-phenylindeno[1,2-*c*]isoxazol-4-one (**4a**, $R_1 = C_6H_5$) [5] react with hexadeuteriodimethylsulfoxide, dimethylsulfoxide and triphenylphosphine to give sulfoximides (**2a-c** and **5a,b**) and triphenylphosphazenes (**3a,b** and **8a**). Contrary to the finding of Sutter and Weis [4], the indenoisoxazolones react slowly with dimethylsulfoxide. The reaction with triphenylphosphine, however, is relatively fast. In the reaction of 3-phenylindeno[1,2-*c*]isoxazol-4-one (**4a**), trace amounts of spiroazirine **6** [7] and 2-benzoyl-3-amino-2-inden-1-one (**7**)[8] are also obtained besides the sulfoximide **5a**. Reaction of 3-*t*-butylindeno[1,2-*c*]isoxazol-4-one (**4b**, $R_1 = C(CH_3)_3$) with these reagents was unsuccessful, which may be attributed to the steric crowding at the nitrogen of the isoxazole ring due to the bulky *t*-butyl group. This steric hindrance prevents the attack of the reagent on the nitrogen of the isoxazole, a finding which has also been observed by Sutter and Weis [4].

The structures of all the new compounds were confirmed on the basis of the elemental analysis, nmr, ir and mass spectral data. The results have been summarized in Tables I-II.

EXPERIMENTAL

Melting points were determined on Thomas-Hoover unimelt apparatus and are uncorrected. Infrared spectra were recorded on a Perkin-Elmer 283 as potassium bromide pellets. All ^{1}H-nmr spectra were recorded on a Varian EM 360 spectrometer in deuteriochloroform using tetramethylsilane as an internal reference. Chemical shifts are quoted in parts per million (s = singlet, m = multiplet). All ^{13}C experiments were performed in deuteriochloroform on an FT-80 A nmr spectrometer system operating in the Fourier transform mode at 20 MHz. Chemical shifts are quoted in parts per million downfield from tetramethylsilane. Low resolution mass spectra were recorded on a Finnigan 6000 equipped with a model 6115 data system. Microanalyses were performed by Atlantic Microlabs, Atlanta, Georgia.

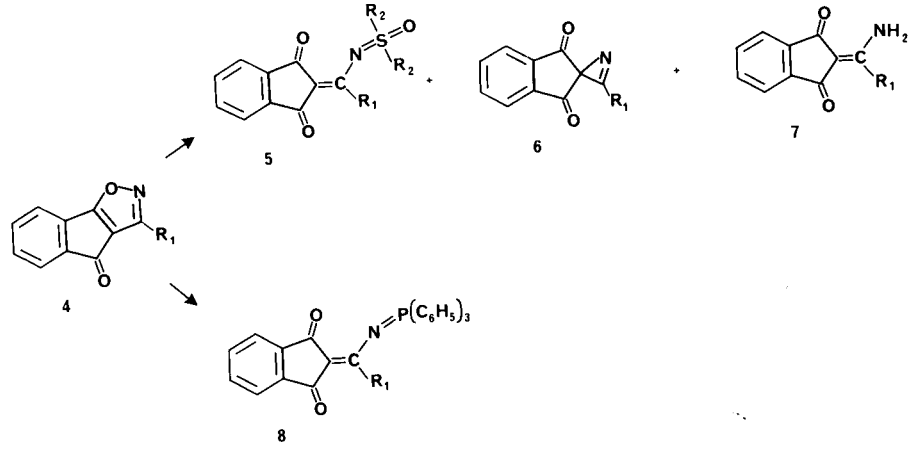
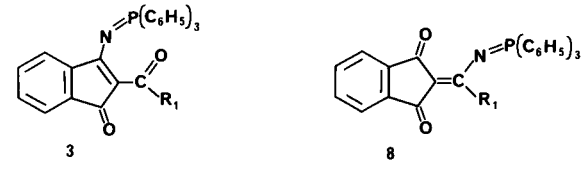


Table II



Compound No.	R_1	Reaction Solvent	Reaction Time	Mp °C	Yield %	Molecular Formula	Analysis % Calcd./Found		
3a	C_6H_5	Toluene	45 minutes	228-230 dec (a)	97	$C_{34}H_{24}NO_2P$	C, 80.14;	H, 4.75;	N, 2.75
							C, 80.01;	H, 4.80;	N, 2.72
3b	$C(CH_3)_3$	Toluene	22 hours	204-206 dec (b)	54	$C_{32}H_{28}NO_2P$	C, 78.51;	H, 5.76;	N, 2.82
							C, 78.58;	H, 5.82;	N, 2.77
8a	C_6H_5	Toluene	5 hours	241-243 dec (c)	89	$C_{34}H_{24}NO_2P$	C, 80.14;	H, 4.75;	N, 2.75
							C, 79.88;	H, 4.82;	N, 2.70

(a) From ethyl acetate. (b) From toluene-petroleum ether (35-60°). (c) From chloroform-cyclohexane.

Sulfoximide (**2b**).

A solution of **1a** (0.4 g, 1.6 mmoles) was prepared in 15 ml of dimethylsulfoxide with heat. Nitrogen gas was bubbled through the solution for 5 minutes and the flask was sealed. The mixture was stirred in an oil bath at 85-90° for 13 days. Dimethylsulfoxide was removed under vacuum distillation and the residue treated with 5 ml of water. The aqueous mixture was extracted with chloroform (50 ml) and the chloroform extract dried over anhydrous magnesium sulfate. Removal of the solvent gave 0.5 g of residue which was chromatographed on florisil (40 g) using ethyl acetate/toluene (35:65) as the eluting solvent. Early fractions gave 0.05 g of the starting isoxazole. Further elution gave 0.425 g of sulfoximide **2b** which was recrystallized from ethyl acetate/petroleum ether (35-60°) as yellow crystals, mp 184-186°; ^{1}H-nmr: δ 3.48 (s, 6), 7.32-7.59 (m, 7), 7.64-7.97 (m, 2); ^{13}C-nmr: δ 193.73 (C=O), 192.44 (C=O), 167.76 (>=C<^{N}), 113.84 (>=C<^{N}), 44.45 (S-CH_3); ir: 1670, 1630 cm^{-1}; ms: m/z 325 (M^+, 12%), 310 (M^+—15, 8%), 248 (M^+-77, 16%), 77 (C_6H_5, 100%).

Using this procedure the following additional compounds were made.

Sulfoximide **2a**.

This compound had ir: 2260, 2140, 1675, 1630 cm^{-1}; ms: m/z 331 (M^+, 69%), 313 (M^+-18, 12.1%), 254 (M^+-77, 100%), 247 (M^+-84, 44.6%).

Sulfoximide **2c**.

This compound had ^{1}H-nmr: δ 1.29 (s, 9), 3.43 (s, 6), 7.27-7.45 (m, 4); ^{13}C-nmr: δ 210.52 (C=O), 192.31 (C=O), 164.94 (>=C<^{N}), 117.85 (>=C<^{N}), 44.32 (S-CH_3); ir: 1680, 1640 cm^{-1}; ms: m/z 305 (M^+, 10.7%), 248 (M^+-57, 53.4%).

Sulfoximide **5a**.

This compound had ir: 2280, 2260, 2140, 1650 cm^{-1}; ms: m/z 331 (M^+, 29.4%), 247 (M^+-84, 68%), 190 (M^+-141, 46.7%), 66 (CD_3SO, 100%).

Sulfoximide **5b**.

This compound had ^{1}H-nmr: δ 3.22 (s, 6), 7.41 (s, 5), 7.47-7.87 (m, 4); ^{13}C-nmr: δ 190.4 (C=O), 166.37 (>=C<^{N}), 115 (>=C<^{N}), 44.96 (S-CH_3); ir: 1650 cm^{-1}; ms: m/z 325 (M^+, 13.4%), 247 (M^+-78, 54.7%), 190 (M^+-135, 44%), 63 (CH_3SO, 100%).

Phosphazene **3a**.

A suspension of **1a** (0.3 g, 1.2 mmoles) and triphenylphosphine (0.6 g, 2.3 mmoles) in 5 ml of toluene was heated under reflux in an oil bath for 45 minutes. The solvent was removed by distillation and the residue treated with 20 ml of ethyl ether. The yellow crystalline material that remained undissolved in ether was filtered. This material (0.6 g) was recrystallized from ethyl acetate as yellow crystals, mp 228-230°; ir: 1680, 1620 cm^{-1}; ms: m/z 509 (M^+, 54.7%), 432 (M^+-77, 44%), 404 (M^+-105, 44.7%), 201 (M^+-308, 60%), 183 (M^+-326, 93.3%), 108 (P-C_6H_5, 84%).

Using this procedure the following compounds were prepared.

Phosphazene **3b**.

The reaction was carried out as above and the solvent removed. The residue was treated with a minimum amount of ethyl ether to dissolve the material. Petroleum ether (35-60°) was added until the solution had attained a permanent turbidity. The mixture, on standing overnight at room temperature, gave a yellow crystalline compound which was filtered and recrystallized from toluene/petroleum ether (35-60°) mp 204-206°; ^{1}H-nmr: δ 0.9 (s, 9), 7.2-8.12 (m, 19); ir: 1680, 1630 cm^{-1}; ms: m/z 489 (M^+, 4%), 432 (M^+-57, 38%), 201 (M^+-288, 89.3%), 183 (M^+-306, 100%), 108 (P-C_6H_5, 92%).

Phosphazene **8a**.

This compound had ir: 1665 cm^{-1}; ms: m/z 509 (M^+, 10%), 183 (M^+-326, 100%), 108 (P-C_6H_5, 62.7%).

Acknowledgement.

Support of this research by the Robert A. Welch Foundation (Grant E-791) is gratefully acknowledged.

REFERENCES AND NOTES

[1] Presented in part at the 184th ACS National Meeting, Kansas City, Missouri, Organic Section, Abstract 113, September 12-17, 1982.

[2] K. H. Wunsch and A. J. Boulton in "Indoxazenes and Anthranils", in "Advances in Heterocyclic Chemistry", Vol 18, A. R. Katritzky and A. J. Boulton, eds, Academic Press, New York, New York, 1967, p 303.

[3] Y. Nomura, Y. Kikuchi and Y. Takeuchi, *Chem. Letters*, 575 (1974).

[4] P. Sutter and C. D. Weis, *J. Heterocyclic Chem.*, **19**, 997 (1982).

[5] T. L. Lemke and K. N. Sawhney, to be published.

[6] T. L. Lemke, K. N. Sawhney and B. K. Lemke, *J. Heterocyclic Chem.*, **19**, 363 (1982).

[7] L. Geita, I. Dalberga, A. Grinvalde and I. Jankovska, *Khim. Geterotsikl. Soedin*, 65 (1976); *Chem. Abstr.*, **85**, 20963z (1976).

[8] T. L. Lemke and K. N. Sawhney, *J. Heterocyclic Chem.*, **19**, 1335 (1982).