1 H, (5)-H), 7.77, 7.27, (AA'BB', 4 H, Ar), 7.06 (d, J = 7.5 Hz, 1 H, NH), 4.80 (m, 1 H, CH), 4.26 (q, J = 7.3 Hz, 2 H, CO_2CH_2), 4.13 (q, J = 7.3 Hz, 2 H, CO_2CH_2), 2.73-2.82, (m, 4 H, 2° aliphatic), 2.03-2.57, (m, 6 H, 2° aliphatic), 1.62 (s, 9 H, $C(CH_3)_3$), 1.32 (t, J = 7.3 Hz, 3 H, CH_3), 1.24 (t, J = 7.3 Hz, 3 H, CH_3); HRMS m/z calcd for $C_{31}H_{40}N_5O_7$ (MH^+) 594.2927, found 594.2932.

Diethyl *N*-[4-[3-[2-(Pivaloylamino)-3,4,5,6,7,8-hexahydro-4-oxo-5-deazapteridin-6-yl]propyl]benzoyl]-L-glutamate (22b). This compound was prepared from 0.15 g of **21b** and 0.45 g (3.0 wt equivalent) of 5% palladium on carbon as described previously for the preparation of **22a**, yield 0.15 g (quantitative) of **22b** as a white microcrystalline solid: mp 196-197 °C; ^1H NMR ($CDCl_3$) δ 8.67 (b s, 1 H, (3)-H), 7.73, 7.25 (AA'BB', 4 H, Ar), 7.09 (d, J = 7.5 Hz, 1 H, NH), 4.94 (b s, 1 H, (8)-NH), 4.82 (m, 1 H, $CHCO_2Et$), 4.25 (q, J = 4.1 Hz, 2 H, CO_2CH_2), 4.12 (q, J = 7.1 Hz, 2 H, CO_2CH_2), 1.71-3.36 (m, 13 H, 2° aliphatic), 1.62 (s, 9 H, $C(CH_3)_3$), 1.32 (t, J = 7.1 Hz, 3 H, CH_3), 1.23 (t, J = 7.1 Hz, 3 H, CH_3); HRMS m/z calcd for $C_{31}H_{43}N_5O_7$ (M^+) 597.3162, found 597.2816. Anal. Calcd for $C_{31}H_{43}N_5O_7$: C, 62.29; H, 7.25; N, 11.72. Found: C, 62.07; H, 7.07; N, 11.48.

***N*-[4-[3-(2-Amino-3,4,5,6,7,8-hexahydro-4-oxo-5-deazapteridin-6-yl)propyl]benzoyl]-L-glutamic Acid (HDDATHF) (1b).** This compound was prepared from 0.16 g of **22b** and 40 mL of 1 N sodium hydroxide as described previously for the preparation of **1a** from **22a**,[9] yield 0.09 g (75%) of **1b** as a white solid: mp >250 °C; ^1H NMR (TFA-*d*, DMSO-d_6) δ 7.31, 6.93 (AA'BB', 4 H, Ar), 4.58 (m, 1 H, $CHCO_2H$), 3.19 (m, 1 H, (6)-H), 2.68 (t, J = 9.5 Hz, 2 H, benzyl), 1.47-2.48 (m, 8 H, 2° aliphatic), 1.35 (m, 2 H, 2° aliphatic), 1.04 (m, 2 H, 2° aliphatic); HRMS m/z calcd for $C_{22}H_{28}N_5O_6$ (MH^+) 458.1961, found 458.2011. Anal. Calcd for $C_{22}H_{27}N_5O_6$: C, 57.76; H, 5.95; N, 15.31. Found: C, 57.87; H, 5.94; N, 15.12.

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Registry No. **1a**, 95693-76-8; **1b**, 124018-99-1; **3**, 56-06-4; **7a**, 927-74-2; **7b**, 5390-04-5; **8**, 619-42-1; **9a**, 123910-86-1; **9b**, 123910-87-2; **10a**, 123910-88-3; **10b**, 123910-89-4; **11a**, 106200-41-3; **11b**, 123910-90-7; **12a**, 123910-83-8; **12b**, 126295-73-6; **13a**, 123910-84-9; **13b**, 123910-85-0; **14a**, 126295-74-7; **14b**, 126295-75-8; **17a**, 123910-81-6; **17b**, 123910-82-7; **18a**, 123910-91-8; **18b**, 123910-92-9; **19a**, 126295-76-9; **19b**, 126295-77-0; **20a**, 123910-93-0; **20b**, 123910-94-1; **21a**, 123910-95-2; **21b**, 123910-96-3; **22a**, 116387-28-1; **22b**, 123910-97-4; GAR TFase, 9032-02-4; $CH_2(CN)_2$, 109-77-3; $HC(OEt)_3$, 122-51-0; H-Glu(OEt)-OEt·HCl, 1118-89-4; pivalic anhydride, 1538-75-6.

Reactions of Oximes with Thianthrene Cation Radical in Nitrile Solvents. Cycloaddition To Form Oxadiazoles and Deoxygenation To Form Nitriles

Shishue Chiou, A. K. M. M. Hoque, and Henry J. Shine*

Department of Chemistry and Biochemistry, Texas Tech University, Lubbock, Texas 79409

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Reactions of eight oximes, RCH=NOH (**1a**, R = C_6H_5; **1b**, R = 4-$CH_3C_6H_4$; **1c**, R = 4-$NO_2C_6H_4$; **1d**, R = 4-$CH_3OC_6H_4$; **1e**, R = 2-$CH_3OC_6H_4$; **1f**, R = 1-naphthyl; **1g**, R = C_5H_{11}; **1h**, R = C_4H_9), with thianthrene cation radical perchlorate ($Th^{\bullet+}ClO_4^-$) in acetonitrile under argon were studied. The major product from the oxime in all cases, but of **1d**, was the nitrile, RCN. The anticipated product of oxidative cycloaddition, namely, a 3-R-5-methyl-1,2,4-oxadiazole (**2**), was obtained in substantial yield (**2d**, 66%) only in the case of **1d**. An isomeric 5-R-3-methyl-1,2,4-oxadiazole (**3**) was obtained from some reactions, that is, **3c** alone from **1c**, and a mixture of **2a** and **3a** from **1a**. Neither **2** nor **3** was obtained in measurable amounts from reactions of **1g** and **1h**. The aldehyde (RCHO) was obtained in small yields from each reaction. Thianthrene (Th) and thianthrene 5-oxide (ThO) were also major products. Studies with [^{18}O]-**1b** and [^{18}O]-**1d** showed that the oxygen atom in **2** came entirely and in ThO primarily from the oxime. Studies of workup with $H_2{}^{18}O$ showed that the workup water was the source of the oxygen atom in RCHO and to a small extent in ThO. Explanations are given for the formation of **2** by a stepwise addition of $RCH{=}NOH^{\bullet+}$ ($\mathbf{1}^{\bullet+}$) to solvent nitrile and of **3** by the reaction of solvent nitrile with an oxaziridine cation radical (**7**, obtained from $\mathbf{1}^{\bullet+}$).

Introduction

Earlier reports from this laboratory have described oxidative cycloadditions of aldehyde arylhydrazones to nitrile solvents, and oxidative intramolecular cyclizations of arylhydrazones of chalcones and benzalacetones, achieved by reaction with thianthrene cation radical ($Th^{\bullet+}$). Products of these reactions, obtained in excellent yields, were 1,2,4-triazoles (eq 1)[1-3]and pyrazoles (eq 2).[4] The cation radical was reduced to thianthrene (Th). Cyclizations of araldehyde semicarbazones into (mainly) 2-amino-1,3,4-oxadiazoles (eq 3) have been similarly achieved.[5] In each of these reactions the presence of a pyridine base, either 2,6-di-*tert*-butyl- or 2,6-di-*tert*-butyl-4-methylpyridine (DTBMP), enhanced the reaction but did not change its course. We report now the reactions of some aldoximes (**1**, RCH=NOH) in acetonitrile. Cycloaddition, with formation of oxadiazoles, is by no means the rule. The major trend is toward the formation of nitriles (RCN), a trend which is magnified by carrying out reaction in the presence of DTBMP.

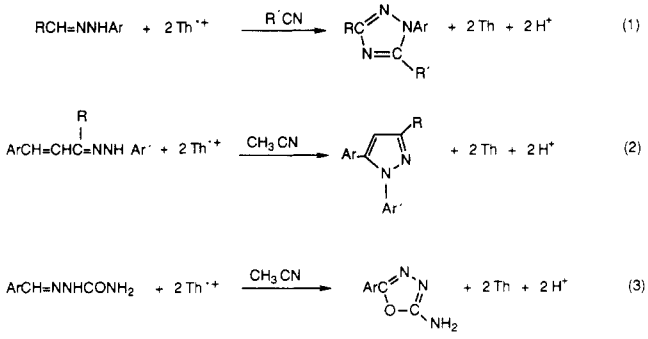

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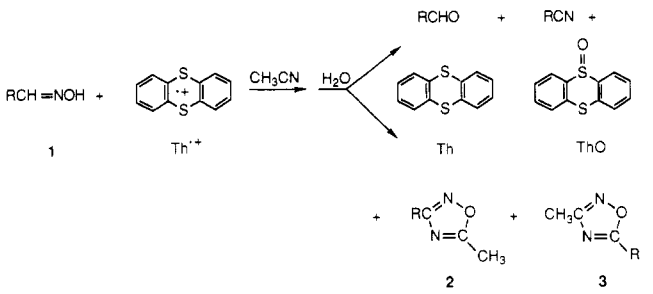
Table I. Products of Reaction of Oximes (RCH=NOH) with $Th^{\bullet+}ClO_4^-$ in Acetonitrile and Acrylonitrile[a]

		products, mmol and %[b]							acct (%) of products	
run	oxime	RCHO	RCN	recovd oxime	2	3	Th	ThO	oxime	$Th^{\bullet+}ClO_4^-$
1[c]	1a	0.069	0.327		0.024	0.068	0.592	0.397		
		13.8	65.4		4.8	13.6	59.2	39.7	97.6	98.9
2[c]	1b	0.084	0.320		0.078		0.576	0.421		
		16.8	64.0		15.6		57.6	42.1	96.4	99.7
3[d]	1b	0.040	0.168		0.037		0.284	0.215		
		16.0	67.2		14.8		56.8	43.0	98.0	99.8
4[c]	1c	0.332		0.021		0.128	0.628	0.357		
		66.4		4.2		25.6	62.8	35.7	96.2	98.5
5[e,f]	1d	0.011	0.026	0.011	0.105		0.259	0.039		
		6.9	16.3	6.9	65.6		80.9	12.2	95.7	98.7
6[a,c]	1d	0.028	0.253		0.204[g]		0.697	0.296		
		5.6	50.6		40.8		69.7	29.6	97.0	99.3
7[e,h]	1e	0.014	0.034	0.057	0.028		0.267	0.034		
		8.8	21.3	35.6	17.5		83.4	10.6	83.2	95.3
8[c,i]	1f	0.085	0.338		0.064		0.575	0.411		
		17.0	67.6		12.8		57.5	41.1	97.4	98.6
9[c]	1g	0.037	0.393	0.030	tr		0.509	0.491		
		7.4	78.6	6.0			50.9	49.1	92.0	100
10[c]	1h	0.013	0.406	0.045	tr		0.512	0.489		
		2.6	81.2	9.0			51.2	48.9	92.8	100

[a] Only run 6 was carried out in CH_2=CHCN. [b] % data are given in the second entry of each run. [c] $Th^{\bullet+}ClO_4^-$ (1.0 mmol), oxime (0.50 mmol). [d] $Th^{\bullet+}ClO_4^-$ (0.50 mmol), oxime (0.25 mmol); ^{18}O-labeled oxime was used. [e] $Th^{\bullet+}ClO_4^-$ (0.32 mmol), oxime (0.16 mmol). [f] ThO_2 (tr) was also obtained. [g] 2i. [h] ThO_2 (0.002 mmol, 1.3%) was also obtained. [i] An earlier result with 1f gave 2f and a small amount of 3f.[13] We were unable to reproduce this result.

Scheme I



Results

The oximes used had R = C_6H_5 (**1a**), 4-$CH_3C_6H_4$ (**1b**), 4-$NO_2C_6H_4$ (**1c**), 4-$CH_3OC_6H_4$ (**1d**), 2-$CH_3OC_6H_4$ (**1e**), 1-naphthyl (**1f**), C_5H_{11} (**1g**), and C_4H_9 (**1h**). Reactions were carried out either by adding CH_3CN by syringe to a septum-capped flask containing the solids $Th^{\bullet+}ClO^{4-}$, 1, and (where necessary) DTBMP under argon, or by mixing solutions of $Th^{\bullet+}ClO^{4-}$ and 1 that had been separately degassed in the arms of a Y-tube. In the latter case argon was introduced prior to mixing. Reactions in the absence of added DTBMP were slow, as judged by the disappearance of the color of $Th^{\bullet+}$, and were continued for periods of 2–3 days. Reactions in the presence of DTBMP were complete within 5–10 min. After treatment with aqueous $NaHCO_3$ (to neutralize $HClO_4$ that had been formed) and workup, the mixture of products was analyzed quantitatively by capillary gas chromatography (GC) and the use of authentic compounds.

Products obtained from reaction of $Th^{\bullet+}$ and 1 are shown in Scheme I. The scheme shows the aldehyde and nitrile (RCHO and RCN) corresponding with 1 (RCH=NOH), two oxadiazoles (**2** and **3**), thianthrene (Th), and its 5-oxide (ThO). RCHO and RCN were formed in all reactions. On the other hand, whether **2** and/or **3** was formed depended on the nature of R. These variations are to be seen in the tables. Table I lists products of reactions in the absence of DTBMP. For the most part a good accounting of the reactants was achieved. That is, the quantitative GC assays accounted for 92–98% of the oxime (except in the case of **1e**) and 95–100% of the $Th^{\bullet+}$. Oxadiazole formation was substantial (65.6%) only in the case of **1d** (R = 4-$CH_3OC_6H_4$). Here too, a small amount of **1d** (0.011 mmol, 6.9%) remained unused, so that the conversion into **2d** was, in fact, nearly 71%. Even in the case of **1e** (R = 2-$CH_3OC_6H_4$) oxadiazole formation was small, amounting to a conversion of only 27%, after allowing for incomplete reaction. Small amounts of **2b** were obtained from **1b** (R = 4-$CH_3C_6H_4$) and of **2f** from **1f** (R = 1-naphthyl), while only traces (observed by GC) of **2** were obtained from the alkyl oximes **1g** (R = C_5H_{11}) and **1h** (R = C_4H_9). A mixture of oxadiazoles (**2a** and **3a**) was obtained from **1a** (R = C_6H_5), while in the case of **1c** (R = 4-$NO_2C_6H_4$) only **3c** was obtained. In all reactions except that of **1d** the nitrile (RCN) was the dominant product. The aldehyde (RCHO) was also formed in significant amounts. It was not possible to separate *p*-nitrobenzaldehyde and *p*-nitrobenzonitrile on the SE-30 column, and therefore their mixture is expressed quantitatively as if only the nitrile were present (run 4). GC–MS showed, in fact, that the nitrile was the major component of the mixture. Thianthrene 5-oxide (ThO) is often obtained as a side product in reactions of $Th^{\bullet+}$, arising from hydrolysis of $Th^{\bullet+}$ by water[6] either present adventitiously or added during workup. In the present reactions, however, the ThO was a primary rather than a side product of all reactions, and, as will be brought out later, its amount in each case is related to those of the aldehyde and nitrile.

In Table II are listed the products of reactions in the presence of DTBMP. Again, accounting for reactants is quite good. The effect of the base was to prevent oxadiazole formation in all cases but that of **1d**, and to enhance formation of the nitrile, even in that case, too. The presence of the base diminished to some extent in some cases, but did not suppress in any case, the formation of aldehyde. The effect of added base on the relative yields of aldehyde and nitrile can be seen in the reactions of **1a**. In the absence of base (Table I) these yields were approximately 14 and 65%. In the presence of base the yields were 7 and 83% (Table II, run 11), while the trend in yields

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Table II. Products of Reaction of Oximes (RCH=NOH) with $Th^{\bullet+}ClO_4^-$ in the Presence of Base (2,6-Di-*tert*-butyl-4-methylpyridine) in Acetonitrile[a]

		products, mmol and %[b]						acct (%) of products	
run[c]	oxime	RCHO	RCN	Th	ThO	base[d]	2	oxime	$Th^{\bullet+}ClO_4^-$
11	**1a**	0.036	0.413	0.531	0.443	1.37			
		7.2	82.6	53.1	44.3	91.3		89.8	97.4
12	**1a**	0.055	0.396	0.528	0.436	1.40[e]			
		11.0	79.2	52.8	43.6	93.3		90.2	96.4
13	**1a**	0.074	0.368	0.552	0.399	1.42[f]			
		14.8	73.6	55.2	39.9	94.7		88.4	95.1
14	**1b**	0.037	0.423	0.520	0.463	1.38			
		7.4	84.6	52.0	46.3	92.0		90.0	98.3
15	**1b**[g]	0.042	0.413	0.526	0.456	1.40	tr		
		8.4	82.6	52.6	45.6	93.3		91.0	98.2
16[h]	**1b**	0.037	0.419	0.507	0.454	1.38	tr		
		7.4	83.8	50.7	45.4	92.0		91.2	96.1
17	**1c**	0.454		0.536	0.454	1.43	tr		
		90.8		53.6	45.4	95.3		90.8	99.0
18	**1d**	0.036	0.327	0.568	0.399	1.39	0.087[i]		
		7.2	65.4	56.8	39.9	92.7	17.4	90.0	96.7
19	**1d**[g]	0.028	0.331	0.593	0.382	1.41	0.098[i]		
		5.6	66.2	59.3	38.2	94.0	19.6	91.4	97.5
20[h]	**1d**	0.031	0.340	0.581	0.388	1.36	0.096[i]		
		6.2	68.0	58.1	38.8	90.7	19.2	93.4	96.9
21	**1d**	0.034	0.350	0.553	0.403	2.80[j]	0.073[i]		
		6.8	70.0	55.3	40.3	93.3	14.6	91.4	95.6
22	**1f**	0.033	0.442	0.528	0.473	1.47			
		6.6	88.4	52.8	47.3	97.9		95.0	100
23	**1g**	0.023	0.451	0.511	0.474	1.45	tr		
		4.6	90.2	51.1	47.4	97.0		94.8	98.5
24	**1h**	0.020	0.455	0.505	0.475	1.44			
		4.0	91.0	50.5	47.5	96.0		95.0	98.0

[a] $Th^{\bullet+}ClO_4^-$ (1.0 mmol), RCH=NOH (0.50 mmol), and base (1.50 mmol) were used in each run, unless otherwise stated. [b] % data are given in the second entry of each run. [c] Runs are numbered successively from Table I. [d] Recovered. [e] Base was added 1 h after reaction began. [f] Base was added 12 h after reaction began. [g] ^{18}O-Labeled oxime. [h] Workup with $H_2{}^{18}O$. [i] **2d**. [j] 3.0 mmol of base was used.

Table III. Comparison of Summary Yields[a] of Aldehyde (RCHO) and Nitrile (RCN) vs Thianthrene 5-Oxide (ThO) from Reactions of Oximes (RCH=NOH) with $Th^{\bullet+}ClO_4^-$

		yield, mmol				yield, mmol	
run[b]	oxime	RCHO + RCN	ThO	run[b]	oxime	RCHO + RCN	ThO
1	**1a**	0.396	0.397	13[e]	**1a**	0.442	0.399
2	**1b**	0.404	0.421	14	**1b**	0.460	0.463
3	**1b**	0.208	0.215	15[f]	**1b**	0.455	0.456
4	**1c**	0.332	0.357	16[g]	**1b**	0.456	0.454
5	**1d**	0.037	0.039	17	**1c**	0.454	0.454
6[c]	**1d**	0.281	0.296	18	**1d**	0.363	0.399
7	**1e**	0.048	0.034	19[f]	**1d**	0.359	0.382
8	**1f**	0.423	0.421	20[g]	**1d**	0.371	0.388
9	**1g**	0.430	0.491	21[h]	**1d**	0.384	0.403
10	**1h**	0.419	0.489	22	**1f**	0.475	0.473
11	**1a**	0.449	0.443	23	**1g**	0.474	0.474
12[d]	**1a**	0.451	0.436	24	**1h**	0.475	0.475

[a] Data from Table I and II. [b] Runs 1–10 without, runs 11–24 with added base. [c] In $CH_2{=}CHCN$. [d] Base added 1 h after reaction began. [e] Base added 12 h after reaction began. [f] ^{18}O-Oxime was used. [g] Workup with $H_2{}^{18}O$. [h] 3.0 mmol instead of 1.5 mmol of base was used.

was toward more aldehyde and less nitrile by delaying the addition of base to the reaction mixture (Table II, runs 12 and 13). On the other hand, doubling the amount of base did not much affect the relative yields of aldehyde and nitrile in reactions of **1d** (Table II, runs 18 and 21).

In Table III a comparison is made of the yield of ThO with the sum of the yields of aldehyde and nitrile. It is apparent that these yields are equated. In some cases the sum of yields is exactly that of ThO; in others the yields are quite close, and in the remainder the differences may be attributed to experimental errors. The data indicate that ThO is formed whenever aldehyde and nitrile are formed.

The fate of the oxygen atom in an oxime and the source of the oxygen atom in the aldehyde, **2**, and ThO were traced with the use of ^{18}O-labeling. Data are given in Table IV. ^{18}O-Enrichment in a product was measured as the (M + 2)/M ratio by GC–MS. The measurements are not as precise as obtainable by selected ion monitoring but are satisfactory for our purpose. Comparison of runs 2 and 3, 14 and 15, and 18 and 19 shows that the oxygen atom in **2** and ThO comes from the oxime. That is, the labeling in **2b**, as shown by run 3 without added base, and run 15 with added base, and the labeling in **2d** (run 19) arises from addition of the oxime to solvent nitrile. Runs 15 and 19 show that the origin of the oxygen atom in the ThO is also the oxime. The result (46.7%) from run 3 appears to be questionable, but in that run some of the ThO may have been formed by workup hydrolysis of unused $Th^{\bullet+}$, and would thus be $Th^{16}O$. It seems clear that the oxygen atom in the aldehyde is supplied not by the oxime but by workup water (runs 16 and 16a). Measurements were made on *p*-tolualdehyde (from **1b**) only. We found it difficult to quantify the ^{18}O content in the aldehyde, as shown by the duplicate experiments. When $H_2{}^{18}O$ was used in the workup, ^{18}O did not appear in **2b**, and did not,

Table IV. ^{18}O Content of Products of Reaction of 1b and 1d with $Th^{\bullet+}ClO_4^-$

run[b]	oxime	^{18}O-labeled compd	product and % (M + 2)[a] ArCHO[c]	2[c]	ThO[c]
2	1b	none	0[d]	0[d]	9.0
3[e]	1b	1b[f]	0.74	71.2	46.7
14	1b	none	0[d]	0[d]	9.0
15	1b	1b[f]	0[d]	72.4	71.1
16	1b	H_2O[g]	13.2	0[d]	10.3
16a[h]	1b	H_2O[g]	24.6	0[d]	11.7
18	1d	none	i	0.94	10.1
19	1d	1d[j]	i	66.6	70.5
20	1d	H_2O[g]	i	1.1	9.8

[a] Determined from GC–MS measurements. [b] Runs 2 and 3 in absence, all other runs in presence of DTBMP. [c] % (M + 2) in each unenriched compd was calculated to be: $CH_3C_6H_4CHO$ (0.54), **2b** (0.83), $CH_3OC_6H_4CHO$ (0.79), **2d** (1.04), ThO (9.87). [d] Too small to be seen in the GC–MS spectrum. [e] Reaction was worked up after 48 h, and some $Th^{\bullet+}ClO_4^-$ is believed to have been unreacted. [f] % (M + 2) in labeled **1b** was 64.8. [g] ^{18}O content 50%; 0.50 mL of $H_2{}^{18}O$ was used, followed 30 min later by a small amount of unenriched solid $NaHCO_3$. [h] Duplicate experiment. [i] Not measured. [j] % (M + 2) in labeled **1d** was 66.6.

Table V. Effect of O_2 on the Products of Reaction of $Th^{\bullet+}ClO_4^-$ with *p*-Anisaldoxime (1d)

products, mmol	run[a] 5[b]	25[c]
ArCHO	0.011	0.006
ArCN	0.026	0.018
2d	0.105	0.111
Th	0.259	0.010
ThO	0.039	0.288
ThO_2	tr	0.009

[a] $Th^{\bullet+}ClO_4^-$ (0.32 mmol), **1d** (0.16 mmol). [b] Under argon; 0.011 mmol of **1d** was recovered. [c] Under O_2.

it seems, appear in the ThO either. The latter point is discussed later.

All of the reactions reported in Tables I and II took place in an argon atmosphere. When air or oxygen was present the reactions took a slightly different course. The aldehyde, nitrile, and oxadiazole were formed, but almost of all the Th was converted into ThO. This is shown with **1d** in Table V. That is, the amount of Th obtained from reaction of **1d** was reduced from 0.259 mmol (81% of the $Th^{\bullet+}$) for reaction under argon to 0.01 mmol (3.1% of the $Th^{\bullet+}$) for reaction under oxygen, with a corresponding increase in the amount of ThO.

In some of the reactions that were carried out under argon (Table I, runs 5 and 7) thianthrene *cis*-5,10-dioxide (ThO_2) was obtained, in either traces or small amounts. ThO_2 became a more evident product in reactions carried out under oxygen, as is shown in Table V. The significance of this finding and of the effect of oxygen on the reactions will be reported in detail in a separate communication.

Experimental Section

The preparation of $Th^{\bullet+}ClO_4^-$ and the details of other routine experimental procedures have been given earlier.[3] Oximes were prepared by standard procedures and had satisfactory melting points. The preparation of authentic 3,5-disubstituted 1,2,4-oxadiazoles has been described earlier.[7] Quantitative gas chromatographic (GC) analyses were carried out with a 25-m, 0.25-mm diameter SE-30 capillary column and the use of naphthalene as an internal standard. ^{18}O-Labeled *p*-tolualdoxime (**1b**) and *p*-anisaldoxime (**1d**) were prepared as described for acetoxime.[8] The M/(M + 2) ratios obtained by GC–MS were 100:64.8 for [^{18}O]-**1b** and 100:66.6 for [^{18}O]-**1d**, as compared to 100:0.58 and 100:0.61, respectively, for unenriched oximes. Reactions of oximes with $Th^{\bullet+}ClO_4^-$ were carried out in general ways and are described with the following examples.

Reaction of $Th^{\bullet+}ClO_4^-$ with Benzaldoxime (1a) in Acetonitrile. (A) In the Absence of DTBMP. Run 1. The oxime (60.5 mg, 0.50 mmol) and $Th^{\bullet+}ClO_4^-$ (315 mg, 1.0 mmol) were placed in a septum-capped, argon-filled flask containing a magnetic stirrer. CH_3CN (20 mL) was added by syringe and the mixture was stirred for 48 h, after which time the solution still had the color of $Th^{\bullet+}$. Dilute $NaHCO_3$ solution (10 mL) was added and the mixture was extracted with 4 × 10 mL of CH_2Cl_2. The dried ($MgSO_4$) CH_2Cl_2 solution was evaporated to give 282 mg of residue. The residue was dissolved in 10 mL of CH_2Cl_2 for assay by GC. Results are given in Table I.

(B) In the Presence of DTBMP. Run 11. The procedure described above was repeated, with the difference that 308 mg (1.5 mmol) of DTBMP was added to the flask before injection of CH_3CN. The color of $Th^{\bullet+}$ disappeared within 5 min, leaving a light yellow solution which was stirred overnight. Workup gave 585 mg of light yellow solid whose components were assayed by GC. Results are given in Table II.

(C) With Delayed Addition of DTBMP. Runs 12 and 13. The procedure of run 1 was repeated with the difference that a solution of 308 mg (1.5 mmol) of DTBMP in 10 mL of CH_3CN was added to the reaction solution 1 h (run 12) and 12 h (run 13) after reaction had been started. In each case the persisting color of $Th^{\bullet+}$ was dispelled immediately on addition of the DTBMP, leaving a light brown solution. Workup was then continued in the usual way (Table II).

Reaction of $Th^{\bullet+}ClO_4^-$ with 1d in the Absence of DTBMP. (A) In the Absence of O_2. Run 5. $Th^{\bullet+}ClO_4^-$ (100 mg, 0.32 mmol) was placed in one arm, and **1d** (24 mg, 0.16 mmol) in the other arm of a septum-capped Y-tube. The tube was evacuated at 0.5 Torr and filled with argon. Into each arm was injected 10 mL of CH_3CN after which the tube was degassed by the freeze–thaw method three times. The two solutions were mixed at room temperature and kept under vacuum for 3 days. Workup followed in the usual way (Tables I and V).

(B) Under O_2. Run 25. The procedure of run 5 was repeated with the difference that the dry Y-tube was filled with O_2 instead of argon. The tube was then connected to a balloon of O_2, CH_3CN was injected into each arm, and the two solutions were mixed. Within 20 min the color of $Th^{\bullet+}$ faded to light pink, but after overnight stirring the solution had become dark red. Workup followed in the usual way (Table V).

Reaction of $Th^{\bullet+}ClO_4^-$ with ^{18}O-Labeled *p*-Anisaldoxime (1d) in the Presence of DTBMP. Run 19. The reactants were 315 mg (1.0 mmol) of $Th^{\bullet+}ClO_4^-$, 76.5 mg (0.50 mmol) of [^{18}O]-**1d**, and 308 mg (1.5 mmol) of DTBMP. Reaction was complete within 5 min of stirring. The mixture of products was assayed in the usual way (Table II); appropriate components were also assayed for ^{18}O content by capillary GC–MS (Table IV).

Reaction of $Th^{\bullet+}ClO_4^-$ with 1d. Workup with $H_2{}^{18}O$. Run 20. The usual procedure was employed. After overnight stirring of the mixture, 0.5 mL of 50% $H_2{}^{18}O$ was injected, and this was followed by addition of solid $NaHCO_3$. The residue (574 mg) after workup was assayed by GC (Table II) and GC–MS (Table IV).

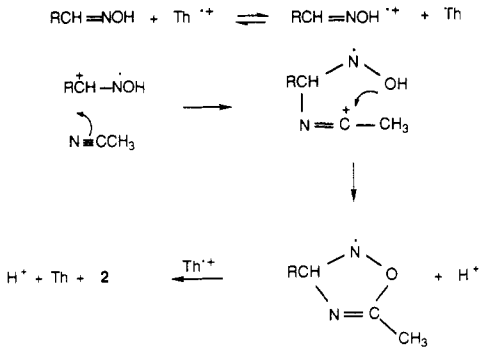
Reaction of $Th^{\bullet+}ClO_4^-$ with 1d in Acrylonitrile. Formation of 3-*p*-Anisyl-5-vinyl-1,2,4-oxadiazole (2i). Run 6. In the usual way, 20 mL of acrylonitrile was added to a mixture of 315 mg (1.0 mmol) of $Th^{\bullet+}ClO_4^-$ and 75.5 mg (0.50 mmol) of **1d**. The mixture was stirred overnight, after which 10 mL of dilute $NaHCO_3$ was added to the pink solution. Workup gave 308 mg of residue. Assay by GC gave 41% of **2i**[7] along with the other anticipated products (Table I). Neither the isomeric oxidiazole (**3i**) nor the isomeric 3-*p*-anisyl-5-cyano-2-oxazoline was detected by GC and GC-MS.

Control Reaction of $Th^{\bullet+}ClO_4^-$ with DTBMP. To a septum-capped flask containing 315 mg (1.0 mmol) of $Th^{\bullet+}ClO_4^-$ and 308 mg (1.5 mmol) of DTBMP under argon was added 20 mL of CH_3CN. The intense color of $Th^{\bullet+}$ persisted during 24 h of stirring. Workup in the usual way gave 529 mg of residue. GC

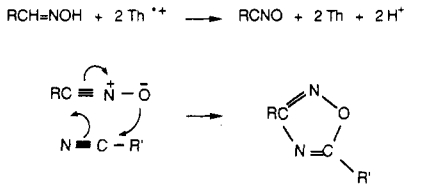
(7) Chiou, S.; Shine, H. J. *J. Heterocycl. Chem.* **1989**, *26*, 125.

(8) Rajendran, G.; Van Etten, R. L. *Inorg. Chem.* **1986**, *25*, 876.

Scheme II



Scheme III



analysis gave 0.569 mmol (57%) of Th, 0.423 mmol (42%) of ThO, and 1.42 mmol (95%) of DTBMP.

Oxidation Potentials. Cyclic voltammograms of the oximes were completely irreversible, even up to a scan rate of 500 mV/s. They were run in CH_3CN with 0.1 M $Bu_4N^+BF_4^-$ ($TBABF_4$) as supporting electrolyte, a platinum disk working electrode and a reference cell of Ag/0.01 M $AgNO_3$/0.1 M $TBABF_4$ in dry CH_3CN. Each of the oximes **1a–f** gave two well-defined anodic peaks, the first of each of which is listed in Table VI. The anodic waves of **1g** and **1h** were ill-defined, each having a shallow broad peak in the region of 1.3 V.

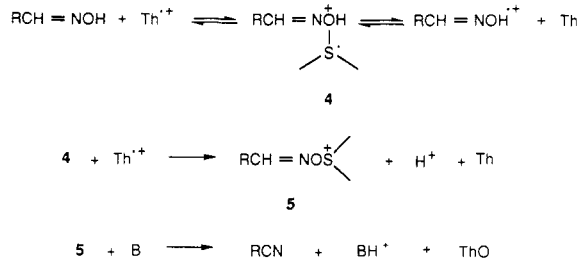
Discussion

It is necessary to account for the formation of two oxadiazoles (**2** and **3**), the nitrile and aldehyde, and the effect of base on promoting nitrile formation. Furthermore, it is necessary to accomodate the ^{18}O data.

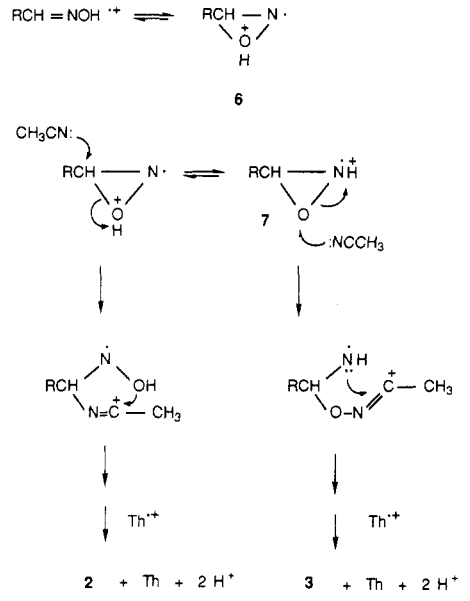
The simplest interpretation of the formation of **2** is the analogue of our finding in the reactions of hydrazones[1-3] and is shown in Scheme II. There, the oxime cation radical undergoes stepwise addition to acetonitrile. ^{18}O-Labeled oxime thus becomes ^{18}O-labeled **2**. The possibility that complete oxidation of an oxime could first provide a nitrile oxide for cycloaddition to solvent nitrile (Scheme III) is ruled out by our result with reaction of **1d** in acrylonitrile (run 6, Table I). 3-(4-Methoxyphenyl)-5-vinyl-1,2,4-oxadiazole (**2i**) was formed, in almost 41% yield. Nitrile oxides undergo pericyclic addition to the vinyl group of acrylonitrile,[9] because that group has higher dienophilic reactivity than the nitrile function.[10] Had the nitrile oxide been formed from **1d** in run 6, cycloaddition should have given 3-(4-methoxyphenyl)-5-cyano-2-oxazoline rather than **2i**. Stepwise addition (Scheme II) is proposed therefore, beginning with a Ritter-like reaction of solvent nitrile with the oxime cation radical. If this is the route to **2**, it must be a parallel one to other routes to the other products.

An explanation of the formation of ThO is shown in Scheme IV. We propose that $Th^{\bullet+}$ bonds at the oxygen

Scheme IV



Scheme V



atom of the oxime and that the intermediate (**4**) thus formed is oxidized by a second molecule of $Th^{\bullet+}$, giving intermediate **5**. ThO is then eliminated from **5** by a deprotonation which leads also to RCN. The function of added DTBMP is to promote the elimination reaction, which, in the absence of DTBMP, must be initiated by solvent. Scheme IV explains the ^{18}O-labeling of ThO when [^{18}O]-**1** is used. But, if Scheme IV were the sole source of ThO, we should find equal yields of ThO and RCN, yet our data (Tables I and II) do not support such a finding. Instead, the yield of ThO is equatable to the sum of the yields of nitrile and aldehyde (Table III). This point is discussed further, later. Scheme IV allows also for the formation of the oxime cation radical. That is, the oxime cation radical needed for cycloaddition may not necessarily be formed directly by one-electron transfer (Scheme II). In this sense, Scheme IV is analogous to the complexation mechanism that has been popularized for cation radical–nucleophile reactions by Parker,[11] in which **4** would then be a complex, rather than a covalently bound pair. It may well be that this is, in fact, the route to **5**. In any case, the scheme would provide the oxime cation radical needed for cycloaddition in Scheme II.

An oxime cation radical in the open chain form shown in Schemes II and IV cannot lead to an isomeric oxadiazole (**3**). We propose, therefore, that an oxaziridine cation radical (**7**, Scheme V) is formed and serves as the source formation of **3**. The scheme shows the opening of the N–O bond, required for the formation of **3**, that is brought about by attack of solvent nitrile on **7**. Scheme V shows also how

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(10) Huisgen, R.; Grashey, R.; Seidel, M.; Wallbillich, G.; Knupfer, H.; Schmidt, R. *Justus Liebigs Ann. Chem.* **1962**, *653*, 105.

(11) Hammerich, O.; Parker, V. D. *Adv. Phys. Org. Chem.* **1984**, *20*, 55–189.

Table VI. Peak Oxidation Potentials of Oximes

oxime	E_p, V[a]	oxime	E_p, V[a]	oxime	E_p, V[a]
1a	1.74	**1d**	1.22	**1g**	*b*
1b	1.49	**1e**	1.34	**1h**	*b*
1c	2.06	**1f**	1.31		

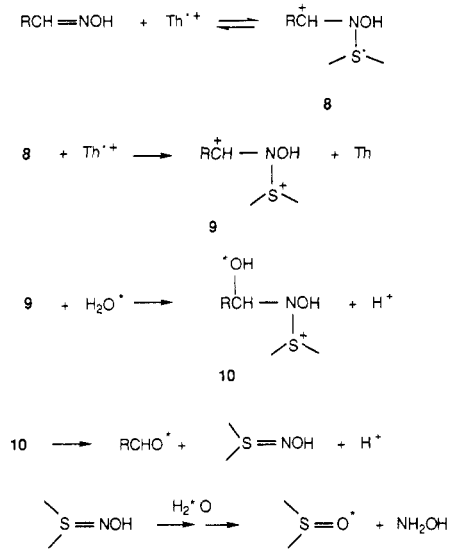
[a] In CH_3CN, vs Ag/0.01 M $AgNO_3$. [b] Broad inflection in the anodic wave.

intermediate **6**, the precursor of **7**, could serve for the formation of **2**, but we do not favor that route to **2**. The reason is that in that case understanding the effect of the structure of R on oxadiazole formation would be difficult. Formation of **2** is favored by oximes RCH=NOH in whose cation radicals delocalization of positive charge is more likely to be accommodated by R, for example, **1d**$^{\bullet+}$. In contrast, oxaziridine cation radical formation (**6**) is favored by localization of charge in the azomethine linkage, for example, with **1c**$^{\bullet+}$. Conversion of **6** into **7** would be facilitated by the $HClO_4$ that is generated in the formation of oxadiazoles, and would be inhibited accordingly by the presence of DTBMP. We would expect that delocalization of positive charge in RCH=NOH$^{\bullet+}$ should be reflected in relative oxidation potentials of oximes in our series **1a-h** and, hence, in the formation of **2** and/or **3**. Anodic peak potentials (E_p) from the irreversible cyclic voltammograms of **1a-f** are given in Table VI and, qualitatively, are in line with expectation. That is, **1d** (E_p = 1.22 V) leads only to **2d**, while **1c** (E_p = 2.06 V) leads only to **3c**. Between these extremes are **1b** (E_p = 1.49 V), **1e** (E_p = 1.34 V), and **1f** (E_p = 1.31 V) which gave only **2b**, **2e**, and **2f**, respectively, and **1a** (E_p = 1.74 V) which gave a mixture of **2a** and **3a**. It is not clear to us why **1g** and **1h**, with ill-defined peaks near 1.3 V, gave neither **2** nor **3**, but only large amounts of the corresponding nitriles.

The overall view of the behavior of oximes in reaction with Th$^{\bullet+}$, then, is that intermediates **4** and **5** (Scheme IV) are readily formed and, in the presence of DTBMP particularly, are conveyed onward to nitrile. Where an oxime cation radical is stabilized by charge delocalization, e.g., as in **1d**$^{\bullet+}$, it can undergo cycloaddition for formation of **2**, whereas charge localization promotes the formation of **3**.

Schemes II, IV, and V accomodate formation of all products and ^{18}O data except the aldehyde. This product seems to be formed at the workup stage when water is added. Its formation also appears to be linked to that of ThO, yet the ^{18}O label that appears in the aldehyde when $H_2{}^{18}O$ is used in workup does not seem to appear in the ThO. We suggest that aldehyde formation may originate from yet another intermediate (**9**) resulting from attack of Th$^{\bullet+}$ on the oxime's nitrogen atom (Scheme VI). Reactions of ammonia, and primary and secondary alkylamines, at the sulfur atom of Th$^{\bullet+}$ and analogous cation radicals have been reported and may serve as precedents for this suggestion.[6,12] Intermediate **9** would have to be durable for later reaction with added water and become labeled aldehyde when the water was labeled. The hydroxysulfilimine that is formed along with RCHO would

Scheme VI



also have to undergo hydrolysis, and in that case lead to Th^{18}O. The data in Table IV (runs 16, 16a, and 20) show, in fact, very small increases in the % (M + 2) as compared with the average of measured values for unenriched ThO (9.4, runs 2, 14, and 18). The ThO results obtained from using $H_2{}^{18}O$ are thought to reflect the insensitivity of our GC–MS measurements to detecting small amounts of Th^{18}O in a mixture with Th^{16}O. That is, although Th^{18}O should be formed along with RCH^{18}O (Scheme VI), by far the major part of thianthrene 5-oxide formed in these reactions is Th^{16}O and comes from nitrile formation (Scheme IV). The amount of Th^{16}O formed in that way overshadows in GC–MS measurement of the (M + 2)/M ratio the amount of Th^{18}O arising from hydrolyses by $H_2{}^{18}O$. It is possible to derive the approximate ratio of Th^{16}O/Th^{18}O from the data in Table II, run 16, in which quenching with 50% $H_2{}^{18}O$ was used. The amount of RCH^{18}O (and the equivalent amount of Th^{18}O) formed is (0.037)/2 mmol, whereas the amount of Th^{16}O is 0.454 - (0.037)/2 mmol, a ratio of Th^{16}O/Th^{18}O of 23.5:1. GC–MS measurements of the *m/e* ratio 234/232 for an authentic, control mixture of this kind gave the % (M + 2) as 10.6.

The stoichiometry of each of the reactions we have described calls for two units of Th$^{\bullet+}$ for each unit of oxime. Our balance of products is in accord with this requirement. For example, the ratio of the summation of products (in mmol) derived from Th$^{\bullet+}$ and **1** in runs 1–4 ranges from 2.02 to 2.07. The ratio in runs 10–23 ranges from 2.07 to 2.18, the larger values resulting from somewhat lower (~ 90%) recoveries of oxime products.

We turn last and briefly to the effect of oxygen on the reaction. Reactions carried out under oxygen led to the conversion of Th into ThO (Table V). We shall report later the catalytic oxygenation of many-fold amounts of added Th and of other sulfides.

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