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SYNTHESIS OF DIAZIRIDINES FROM OXIME ESTERS

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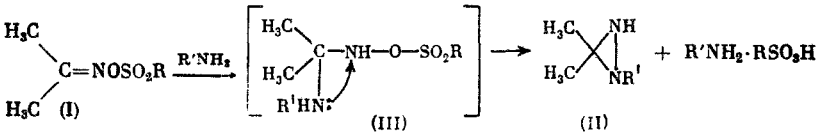
Diaziridines were first prepared from oxime esters by the reaction of cyclohexanone oxime O-sulfonic acid with NH_3 [1] (reference to unpublished work). This reaction was subsequently extended to hexafluoroacetone oxime p-toluenesulfonate [2] and dimethyl mesoxalate oxime p-toluenesulfonate [3]. Whether oxime sulfonates of carbonyl compounds with simple aliphatic groups can be used in diaziridine synthesis is doubtful because of their greater susceptibility to the Beckmann rearrangement (BR) [4]. Moreover, this reaction is known to be accelerated by the presence of strong nucleophiles. Thus, ammonia and amines form amidines [5].

Here we report a study of the synthesis of diaziridines via oxime esters with different acid components. We found that BR is the major pathway in the reaction of cyclohexanone oxime p-toluenesulfonate with primary aliphatic amines. Even at 0°C ≤ 5% of the diaziridine is formed. However, acetoxime sulfonates (I) are stable to BR and with 2 moles of the primary aliphatic amine or a large excess of NH_3 in an aprotic solvent (ether, CH_2Cl_2, THF, acetonitrile) at 20°C they form diaziridines (II) in high yield [6]; the reaction time is 2 to 8 days (Table 1).

We can rationalize the dependence of the yields of (II) on the structure of the starting amine on the basis of the conventional scheme for the diaziridine ring formation



R = n-C_4H_9 (Ia), C_6H_5 (Ib), $C_6H_4CH_3$ (Ic),

R′ = H (IIa), CH_2CH_2OH (IIb); n-C_3H_7 (IIc), i-C_3H_7 (IId), t-C_4H_9 (IIe)

Increase in the branching of the substituents in the amine inhibits the first stage of the reaction—attack by the amine on the oxime carbon.

Other things being equal, BR should require more forcing conditions, since it begins with ionization of the N—O bond, whereas the diaziridine synthesis starts with addition of the amine to the double bond, which requires less energy for cleavage of the π bond. Further, the subsequent cleavage of the N—O bond is promoted by the intramolecular nucleophilic attack of the bound amine. Consequently, under mild conditions we were able to suppress the undesirable BR, whereas at higher temperatures (60°C) as a result of the concomitant BR the yields of diaziridines were ≤ 50% even when we used amines with n-aliphatic groups.

We verified the structures of products (II) by elemental analysis, their IR and PMR spectra, and their ability to oxidize iodide ion in acidic solution. The properties of 3,3-dimethyldiaziridine [7] and 1-isopropyl-3,3-dimethyldiaziridine [8] were in agreement with literature values. Our proposed method of synthesis of (II) represents an important addition to extant methods for preparing diaziridines of this type [9].

N. D. Zelinskii Institute of Organic Chemistry, Academy of Sciences of the USSR, Moscow. Translated from Izvestiya Akademii Nauk SSSR, Seriya Khimicheskaya, No. 7, pp. 1566-1570, July, 1978. Original article submitted March 31, 1977.

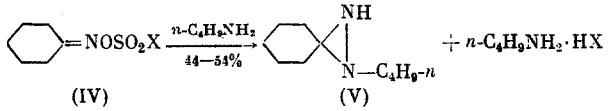
TABLE 1. Yields of Diaziridines (II) as a Function of the Structure of Acetoxime (I)

Starting (I)	Yield of (II), *%				
	(IIa)	(IIb)	(IIc)	(IId)	(IIe)
(Ia)	–	–	(92,5)	49(56)	0
(Ib)	–	–	89,5 (94,5)	36	0
(Ic)	90,5 (95)	88 (95)	(97)	26	0

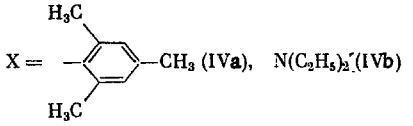
*Figures in brackets show the yields established by iodometric titration of the undistilled product.

The susceptibility to BR is known to diminish with reduction in the strength of the acid incorporated in the oxime ester [10]. By utilizing this distinctive property, we were able to synthesize diaziridine (V) in moderate yield from cyclohexanone oxime sulfonates (IV) incorporating weaker acids than p-toluenesulfonic acid [11].

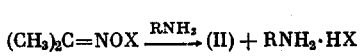
We prepared esters (IV) in high yield from cyclohexanone oxime and sulfonyl chlorides and used them without preliminary purification



(IV) (V)



We also examined the possibility of using oxime phosphates, sulfinates, and oxime carboxylates in diaziridine synthesis. We found that only phosphates form diaziridines fairly readily [Table 2, compounds (VIa), (VIb))]. The not very high yields are apparently due to side reactions of alkylation or phosphorylation, to which alkyl and aryl phosphates are susceptible [16]. The BR of (VIa) and (VIb) is scarcely possible under the conditions of the diaziridine synthesis (20°C), since these compounds can be distilled at fairly high temperatures



(VI)

Oxime esters have at least two centers that are susceptible to nucleophilic attack – the central atom of the acid component and the oxime carbon. Attack on the central atom is sterically hindered in sulfonates. Moreover, since the five-coordinate state is not characteristic for sulfur, change in the bond angles in the approach to the transition state is energetically unfavorable [17].

In oxime carboxylates the carbonyl carbon is sterically accessible and the most electrophilic. This is evidently why the reaction of hexafluoroacetone oxime benzoate with NH_3 gives benzamide [2] and why we were unable to prepare diaziridines by reaction of primary amines with some very different oxime carboxylates [Table 2, (VIc)].

We chose mesitoate to block attack at the carbonyl group. In this case the amine does attack the oxime carbon, giving diaziridines in good yield [Table 2, (VId)].

Acetoxime sulfinates are not converted to diaziridines by amines [compound (VIe)] again apparently as a result of the steric accessibility of the central atom of the acid component, where the attack is again directed. Sulfinate sulfur is more accessible than sulfonate sulfur. For example, in the solvolysis of ethyl p-toluenesulfinate, n-butyl alcohol attacks the sulfur atom to form a four-coordinate transition state [18].

Thus, in the reaction of oxime esters with primary amines important factors in directing the reaction toward diaziridine formation are the stability of the esters toward BR and the steric inaccessibility of the central atom of the acid component.

TABLE 2. Yields of Diaziridines (II) as a Function of the Structure of Oximes (VI) (R = n-C_3H_7)

(VI)	X	Reaction conditions (in ether)	Yield of (II), %
(VIa)	(O)P(OC$_6$H$_5$)$_2$	10 days 20°	52
(VIb)	(O)P(OC$_3$H$_7$-*i*)$_2$	5 days 20°	67
(VIc)	$COCH_3$ [12]	10 days 20°	0
	COC_6H_5 [13]	The same	0
	$COCH_2Cl$, $-COCHCl_2$	" "	0
	$COCCl_3$ [14]	" "	0
(VId)	CO-2,4,6-(CH$_3$)$_3$C$_6$H$_2$	50 h 40°	82
(VId)*	The same	100 h 40°, 10 atm	50
(VIe)	(O)$SOCH_3$ [15]	76 h 20°	0
	(O)SOC$_3$H$_7$-*i* (VIe-1)	The same	0
	(O)SC$_6$H$_4$CH$_3$ (VIe-2)	" "	0

*R = H.

EXPERIMENTAL

The PMR spectra were recorded on a Perkin–Elmer R-12 (60 MHz) (chemical shifts are quoted on the δ scale, ppm); the IR spectra, on a UR-10 (cm^{-1}) instrument.

Cyclohexanone Oxime Mesitylenesulfonate (IVa). To a solution of cyclohexanone oxime (5.65 g, 0.05 mole) and triethylamine (5.05 g, 0.05 mole) in ether (50 ml) at 0°C was added portionwise mesitylenesulfonyl chloride (10.9 g, 0.05 mole). The reaction mixture was stirred at 0-5°C for 10 h. The resulting precipitate was filtered off and washed with ether. The solvent was stripped to give (IVa) (11.4 g, 77.5%), mp 74°C. PMR spectrum (CCl_4): 1.82 s (6H, 3,4,5-H_2), 2.37 diffuse s (4H, 2,6-H_2), 2.66 s (3H, p-CH_3Ph), 2.86 s [6H, 2,6-(CH$_3$)$_2$Ph], 7.70 s (2H, 3,5-H).

Cyclohexanone Oxime N,N-Diethylaminosulfonate (IVb). To a suspension of $NaNH_2$ (1 g, 0.025 mole) in benzene (100 ml) at −10°C was added portionwise cyclohexanone oxime (2.83 g, 0.025 mole). The reaction mixture was stirred at −10 to 0°C for 1 h, whereupon $ClSO_2N(C_2H_5)_2$ (4.28 g, 0.025 mole) in ether (5 ml) was added dropwise. The resulting salt was filtered off and benzene and ether were evaporated under vacuum to give (IVb) (5.2 g, 84%). PMR spectrum (CCl_4): 1.08 t (6H, CH_3), 1.67 s (6H, 3,4,5-H_2), 2.22 diffuse s (4H, 2,6-H_2), 3.35 q (4H, CH_2).

Acetoxime Mesitoate (VId). To a mixture of acetoxime (10.95 g, 0.15 mole) and triethylamine (15.15 g, 0.15 mole) in ether (150 ml) at 0°C was added dropwise mesitoyl chloride (25.6 g, 0.15 mole). The reaction mixture was refluxed with stirring for 15 h. The resulting precipitate was filtered off and extracted with ether. The ethereal extract was washed with water and dried over $MgSO_4$. Ether was stripped. The residue was distilled under vacuum to give (VId) (25.4 g, 91%), bp 122°C (1 mm); n_D^{20} 1.5262. PMR spectrum (CCl_4): 1.9 d (6H, $=C(CH_3)_2$), 2.18 s, (3H, p-CH_3Ph), 2.22 s [6H, 2,6-(CH$_3$)$_2$Ph]; 6.79 s (2H, 3,5-H). Found: C 71.34; H 7.91; N 6.15%. $C_{13}H_{17}NO_2$. Calculated: C 71.20; H 7.82; N 6.38%.

3,3-Dimethylaziridine (IIa). A cooled autoclave was charged with acetoxime p-toluenesulfonate (Ic) (22.7 g, 0.1 mole) [19] in CH_2Cl_2 (35 ml) and liquid NH_3 (30 g, 1.765 mole). The reaction mixture was left at 20°C for 8 days. After removal of the precipitate the yield of (IIa) was 95% (iodometric). The solvent was stripped on a column. The residue was distilled from KOH to give (IIa) (6.51 g, 90.5%), bp 103-106°C, mp 39-40°C (from pentane) [7].

Similarly acetoxime mesitoate (VId) (5.4 g, 0.0264 mole) in ether (25 ml) and liquid NH_3 (100 ml) at 40°C gave (IIa) (0.95 g, 50%).

1-n-Propyl-3,3-dimethyldiaziridine (IIc). To acetoxime benzenesulfonate (Ib) (8 g, 0.0376 mole) [5] in CH_2Cl_2 (15 ml) was added n-propylamine (4.5 g, 0.0763 mole). The reaction mixture was stirred at 20°C for 7 days. The precipitated salt was filtered off and the solvent was stripped. The yield of the crude product was 94.5% (iodometric). Distillation gave (IIc) (3.84 g, 89.5%) with bp 67-68.5°C (76 mm); n_D^{20} 1.4236. PMR spectrum ($CHCl_3$): 0.30 t (3H, C–C–CH_3), 1.29 s [6H, C(CH$_3$)$_2$], 1.64 m (2H, CCH_2C), 2.19 s (1H, NH), 2.40 m (2H, NCH_2). Found: C 63.12; H 12.33; N 24.75%. $C_6H_{14}N_2$. Calculated: C 63.11; H 12.35; N 24.53%.

Under equivalent conditions acetoxime butanesulfonate (Ia) and p-toluenesulfonate (Ic) gave (IIc) in > 90% yield. The reaction was carried out in CH_2Cl_2, ether, THF, and acetonitrile. The yield of (IIc) from acetoxime diphenyl phosphate (VIa) (13.6 g, 0.045 mole) [20] and n-propylamine (5.3 g, 0.09 mole) in ether (30 ml) (20°C, 240 h) was 52%; from acetoxime diisopropyl phosphate (VIb) (11.8 g, 0.05 mole) and n-propylamine (5.9 g, 0.1 mole) in ether (35 ml) (20°C, 5 days) it was 67%. Compound (IIc) was also prepared from (VId) and n-propylamine in ether (40°C, 50 h) in 82% yield.

1-Isopropyl-3,3-dimethyldiaziridine (IId). Acetoxime butanesulfonate (Ia) (5.7 g, 0.0296 mole) (prepared as an undistillable oil after [19]) and isopropylamine (3.49 g, 0.0592 mole) were mixed in ether (10 ml), and left at 20°C for 8 days. The yield of (IId) was 56% (iodometric); distillation gave 1.65 g (49%), bp 53-55°C (60 mm); n_D^{20} 1.4268, cp [8]. The yields of (IId) from acetoxime benzenesulfonate and p-toluenesulfonate were, respectively, 36 and 26%.

1-(β-Hydroxyethyl)-3,3-dimethyldiaziridine (IIb). This was prepared by the procedure of the preceding synthesis from acetoxime p-toluenesulfonate (Ic) and ethanolamine in CH_2Cl_2, yield 88%, bp 58-59°C (1 mm); n_D^{20} 1.4690. PMR spectrum (CCl_4): 1.23 s, 1.28 s, [6H, $C(CH_3)_2$], 2.48 m (3H, NCH_2 and NH), 3.55 t (2H, CCH_2O), 4.05 s (1H, OH). IR spectrum: 3200 (ν NH), 3300 (ν OH). Found: C 51.42; H 10.45; N 24.54%. $C_5H_{12}N_2O$. Calculated: C 51.69; H 10.41; N 24.12%.

1-n-Butyl-3,3-pentamethylenediaziridine (V). A mixture of (IVb) (4.96 g, 0.02 mole) and n-butylamine (4.38 g, 0.06 mole) in ether (10 ml) was left at 20°C for 8 days. Water (10 ml) was added, the organic layer was removed, and the aqueous layer was extracted with CH_2Cl_2 until it no longer gave a positive reaction with acid KI solution. The organic extracts were combined and dried over $MgSO_4$. The solvent was stripped. The residue was distilled under vacuum to give (V) (1.8 g, 54%), bp 80°C (3 mm); 110°C (12 mm); n_D^{20} 1.4730. PMR spectrum:(CH_2Cl_2): 0.90 t (3H, $CCCCH_3$), 1.48 m (4H, CCH_2CH_2C), 1.57 br s (10H, ring CH_2), 2.26 m (3H, NCH_2 and NH). IR spectrum: 3220 (νNH). Found: C 71.14; H 11.75; N 16.70%. $C_{10}H_{20}N_2$. Calculated: C 71.45; H 11.90; N 16.65%.

Similarly, (IVa) (7.4 g, 0.025 mole) and n-butylamine (4.2 g, 0.058 mole) in CH_2Cl_2 (7 ml) gave (V) (1.85 g, 44%) (iodometric).

Acetoxime Diisopropyl Phosphate (VIb). To a mixture of acetoxime (8.32 g, 0.114 mole) and pyridine (9 g, 0.114 mole) in benzene (70 ml) at 5°C was added diisopropyl phosphorochloridate (22.9 g, 0.114 mole). The reaction mixture was stirred at 20°C for 2 days. Water (30 ml) was added. The organic layer was removed and dried over $MgSO_4$. After evaporation of benzene the residue was distilled to give (VIb) (22.95 g, 85%), bp 107°C (2 mm); n_D^{20} 1.4320. PMR spectrum ($CHCl_3$): 1.3 d [12H, $(CH_3)_2C$], 1.95 s [6H, $(CH_3)_2C=$], 4.63 m (2H, CH). IR spectrum: 1670 (ν C=N). Found: C 45.32; H 8.51; N 6.00; P 12.92%. $C_9H_{20}NPO_4$. Calculated: C 45.56; H 8.49; N 5.90; P 13.05%.

Acetoxime Isopropoxysulfinate (VIe-1). To a mixture of acetoxime (7.3 g, 0.1 mole) and triethylamine (10.1 g, 0.1 mole) in ether (100 ml) at a temperature between −5 and 0°C was added dropwise isopropoxysulfinyl chloride (14.25 g, 0.1 mole). The reaction mixture was stirred at 20°C for 3 h, whereupon the precipitated salt was filttred off. The solvent was stripped and the residue was distilled to give (VIe-1) (12.3 g, 66.6%), bp 66°C (2 mm); n_D^{20} 1.4445. PMR spectrum (neat): 1.22 d [6H, $(CH_3)_2C$], 1.91 s [6H, $(CH_3)_2C=$], 5.01 m (1H, CH). IR spectrum: 1660 (ν C=N). Found: C 40.35; H 7.25; N 7.62; S 18.03%. $C_6H_{13}NO_3S$. Calculated: C 40.20; H 7.31; N 7.81; S 17.89%.

Acetoxime p-Toluenesulfinate (VIe-2). To a suspension of $NaNH_2$ (2.24 g, 0.055 mole) in absolute benzene (25 ml) at 15°C was added acetoxime (3.65 g, 0.05 mole). The reaction mixture was stirred at 15-20°C for 16 h. Then p-toluenesulfinyl chloride (8.725 g, 0.05 mole) was added at 10°C. The mixture was stirred at 15-20°C for 8 h and left overnight. Then NaCl was filtered off and the solvent was stripped to give (VIe-2) (10.02 g, 95%) (undistillable oil); n_D^{20} 1.5432. PMR spectrum (CCl_4): 1.76 d [6H, $C(CH_3)_2$], 2.34 s (3H, p-CH_3Ph), 7.3 m (4H, C_6H_4). IR spectrum: 1610 (ν C=N).

CONCLUSIONS

1. We have examined the formation of diaziridines from oximeesters and primary aliphatic amines and ammonia.

2. We suggest a new method for the synthesis of 3,3-dialkyl- and 1,3,3,-trialkyldiaziridines.

3. We include an analysis of the structural factors, whereby we were able to use oxime carboxylates in diaziridine synthesis for the first time.

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REACTIONS OF PERFLUOROOXAALKYL KETONES WITH NUCLEOPHILES

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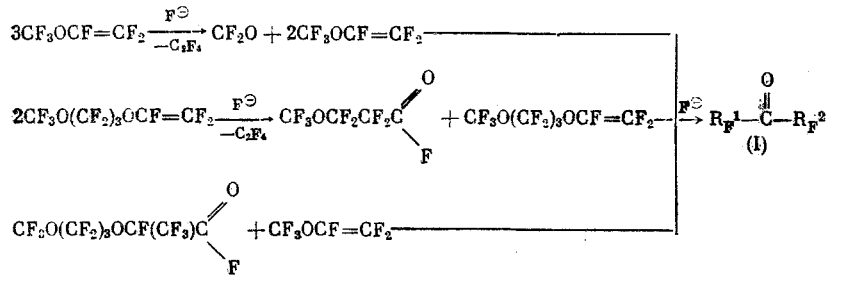
UDC 542.91:547.446

The structure of the groupings attached to the keto group markedly affects the chemical properties of fluorine-containing ketones. For example, sterically hindered ketones, notably bis(perfluoroisopropyl) ketone [1], do not participate in many reactions characteristic of hexafluoroacetone [2].

We decided to look at the influence of branched perfluorooxaalkyl groups on the chemistry of perfluorooxaalkyl ketones [3, 4], which we synthesized by the scheme



$R_F^1 = R_F^2 = CF(CF_3)OCF_3$ (Ia), $R_F^1 = CF_2CF_2OCF_3$, $R_F^1 = CF(CF_3)OCF_3$, $R_F^2 = CF(CF_3)O(CF_2)_3OCF_3$ (Ic)

$R_F^2 = CF(CF_3)O(CF_2)_3OCF_3$ (Ib),

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