The Invention of Radical Reactions. 30. Diazirines as Carbon Radical Traps. Mechanistic Aspects and Synthetic Applications of a Novel and Efficient Amination Process

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Abstract: A number of diazirines were synthesized for the purpose of exploring the addition of a carbon radical to the nitrogen–nitrogen double bond. Carbon radicals, generated from the photolysis of the *O*-acyl derivatives of *N*-hydroxy-2-thiopyridone or via radical exchange from the corresponding organotellurides, were shown to add smoothly to the diazirines leading to imines **34**. When 3-(trifluoromethyl)-3-phenyldiazirine (**13**) is used as the trap, the thus formed imines can be easily hydrolyzed to amines. A mechanism that involves dimerization of the diaziridinyl radicals **32** to produce tetraazo intermediates **33** is suggested in accord with variable temperature NMR data for the reaction. Proof for this mechanistic scheme was furthermore obtained by isolation and X-ray structure determination of **33d**. The first X-ray structure of a 3-(trifluoromethyl)-3-aryldiazirine is also reported.

Introduction and Background

The past few years have witnessed a dramatic growth in the development and use of free-radical reactions in organic synthesis.[1] This fact is mainly related to the availability of different sources of carbon radicals as well as to the selectivity and mildness of these reactions. An important group of radical reactions with widespread synthetic use is the radical-chain deoxygenation of secondary aliphatic alcohols via their xanthate derivatives using tributyltin hydride as hydrogen donor (Barton–McCombie reaction).[2] Later, this reaction was extended to primary[3] and tertiary alcohols[4] and diols.[5] With the introduction of novel reagents,[6,7] many successful applications have been reported.[8]

Another recent contribution was the use of the *O*-acyl derivatives of *N*-hydroxy-2-thiopyridone, such as **3a–e**, as convenient sources of carbon-,[9] nitrogen-,[10] and oxygen-centered[11] radicals under mild conditions by visible photolysis without

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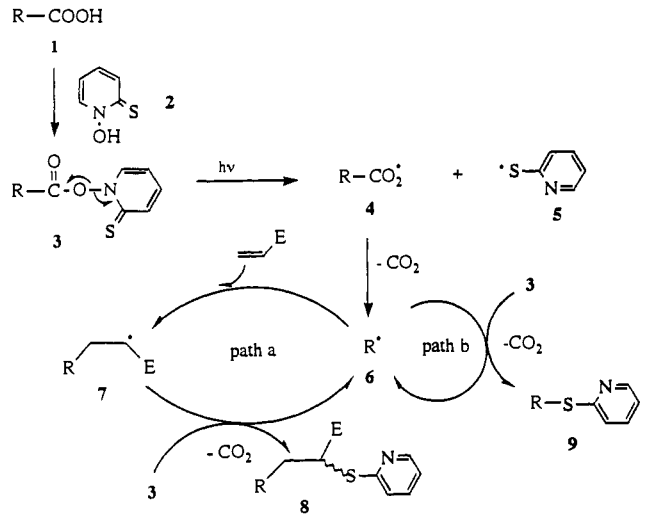
Scheme I[a]

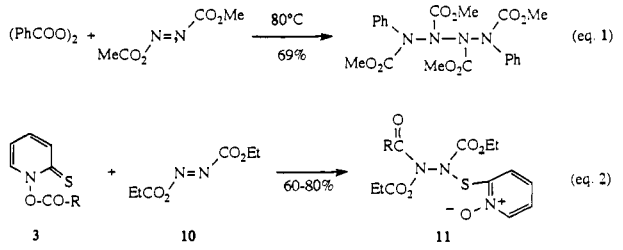


[a] For **1**, **3**, **4**, **6**, **7**, **8**, and **9**: **a**, R = $Ph(CH_2)_2$; **b**, R = C_6H_{11}; **c**, R = 1-adamantanyl; **d**, R = CH_3OCH_2; **e**, R = CH_3.

temperature restrictions. Carbon radicals[12] generated in these reactions have been used for carbon–carbon or carbon–heteroatom bond formation, thus allowing the introduction of new functional groups into organic molecules.[13]

An example of carbon–carbon bond formation via this method is depicted in Scheme I. Thus, visible-light irradiation of *O*-acyl thiohydroxamates **3** results, through homolytic cleavage of the N–O bond, in the formation of the thiyl radical **5**[14] and the acyloxy radical **4**. Acyloxy radicals decarboxylate rapidly when R is an aliphatic moiety ($k > 10^9$)[15] but are more persistent in the case of aromatic and conjugated acids ($k \approx 10^6$).[16] During the propagation step, radical **6** reacts with the olefin (path a) to produce the new carbon-centered radical **7**, which in turn attacks the thiocarbonyl of **3** to produce the addition product **8** and thus propagate the chain. Alternatively, and depending on the efficiency of a given trap toward radical **6**, this can add directly on the thiocarbonyl moiety of **3**, thus producing thioether **9** (path b).

Scheme II



As a continuation of our research, we have attempted to add a carbon-centered radical onto the nitrogen atom of a suitably substituted nitrogen-containing trap. Although the addition of a nitrogen-centered radical onto a carbon–carbon double bond is well documented,[10] there is at present little information on the amination of a carbon-centered radical.[17] In addition, it is important in the amino glycoside antibiotics to find a reagent which will replace secondary hydroxyl groups by the primary amine function using radical chemistry. There is a good precedent for the addition of phenyl radicals generated from dibenzoyl peroxide onto the nitrogen of the dialkyl azodiformates[18] (Scheme II, eq 1). We conceived that carbon radicals could easily add to the nitrogen–nitrogen double bond. However, our initial attempts with activated azo derivatives, such as **10**, were unsuccessful.[19] Due to the nucleophilicity of the thiocarbonyl group, the hydrazine derivatives **11** were formed instead, via an ionic process. We suspected that, due to ring strain, diazirines might be exceptionally reactive in radical chemistry.

In a recent communication, we reported our preliminary results for the amination of carbon radicals using 3-(trifluoromethyl)-3-phenyldiazirine.[20] We now wish to report in full our detailed study of the addition of carbon radicals on different diazirines as well as mechanistic insights for this unprecedented transformation.

Results and Discussion

Synthesis of Diazirines. Despite the relatively short history of diazirines,[21] they have become an important source for the generation of carbenes.[22] Alternatively, they are being used as

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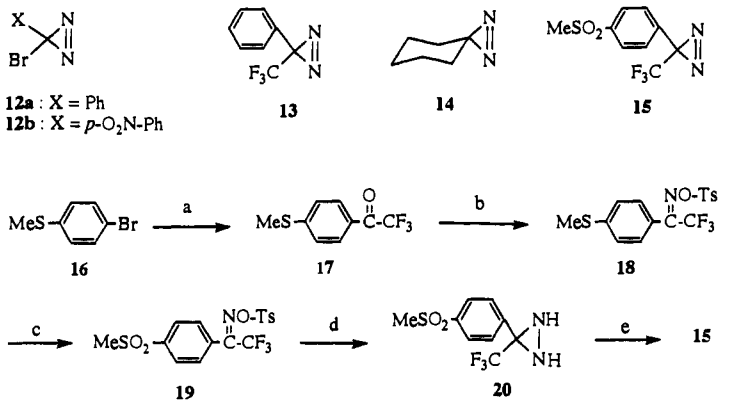
Scheme III[a]



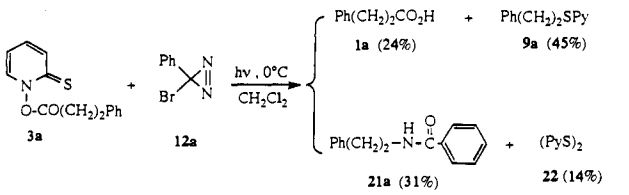
[a] Reagents and conditions: (a) Mg, THF, followed by CF_3CN, 75%; (b) NH_2OH, EtOH, pH 5, followed by TsCl, pyridine, and CH_2Cl_2, 87%; (c) *m*-CPBA, CH_2Cl_2, room temperature, 82%; (d) NH_3, Et_2O, 95%; (e) MnO_2, Et_2O, 92%.

photoaffinity reagents to label receptors.[23] 3-Bromo-3-aryldiazirines **12a**[24] and **12b**[25] were prepared from the corresponding amidine hydrochlorides according to the standard Graham oxidation.[26] 3-(Trifluoromethyl)-3-phenyldiazirine (**13**)[27] and cyclohexyldiazirine (**14**)[28] are known compounds and were synthesized from the corresponding commercially available ketones in few steps following literature procedures.

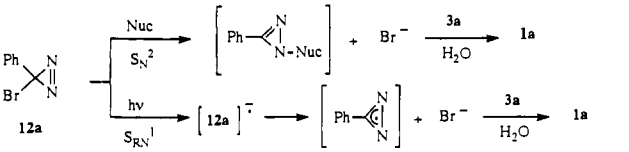
Diazirine **15** was prepared from the corresponding 4-bromothioanisole (**16**). Reaction of gaseous trifluoroacetonitrile with the Grignard salt of **16**[29] provided the desired trifluoromethyl aryl ketone **17** in 75% yield. Compound **17** was then converted to the oxime in the presence of excess hydroxylamine, generated in situ from hydroxylamine hydrochloride by continuously adjusting the pH of the solution to about 5 with 4 M aqueous NaOH. Without any purification, the oxime was O-*p*-tosylated with *p*-toluenesulfonyl chloride to give **18**, in 87% overall yield. At this point, we attempted the *m*-CPBA-mediated oxidation of the thiomethyl moiety. This afforded sulfone **19** in 82% yield as the single product. Treatment of **19** with liquid ammonia afforded diaziridine **20** in 95% yield, which was then oxidized with MnO_2 to the desired diazirine **15** in 92% yield.

Exploratory Photolysis of the *O*-Acyl Derivatives of Thiohydroxamates 3 with Diazirines 12a and 12b. *O*-Acyl thiohydroxamate **3a** and 3 equiv of diazirine **12a** were irradiated in dry methylene chloride solution at 0 °C using visible light (W, 300 W) (Scheme IV). After the disappearance of the starting compound **3a**, the products of the reaction were isolated, identified by GC–MS, IR, and NMR spectra, and compared to authentic samples. Formation of thioether **9a** (45%) can easily be explained according to Scheme I. Of greater interest was the isolation of benzamide **21a** (31%), in which formation of a new carbon–nitrogen bond had occurred via radical addition of the carbon radical **6a** onto one of the nitrogens of diazirine **12a**.

Scheme IV



Scheme V



Carboxylic acid **1a**, isolated from this reaction, results from hydrolysis of the starting thiohydroxamate **3a**. Two different mechanisms may account for its formation. S_N2' addition of the electron-rich thiocarbonyl group on the nitrogen of the diazirine can result in the formation of Br^- during the photolysis, which, in turn, can attack the activated carbonyl moiety of **3a** to produce the corresponding acid bromide. The latter, after hydrolysis, could provide **1a**. Alternatively, a visible-light-induced $S_{RN}1$ chain-type process can generate the Br^- (Scheme V). In order to distinguish between these two possible mechanisms, we briefly investigated the reaction of **3a** and **12a** under the same conditions in the absence of light. After 12 h in the dark, we could not detect any formation of **1a**. This result is accounted for by the $S_{RN}1$ mechanism, in accord with the literature.[25]

In order to trap any HBr formed during this reaction, we repeated the reaction in the presence of 3 equiv of different bases, such as pyridine, triethylamine, and sodium bicarbonate. However, in all these cases, the amount of carboxylic acid **1a** obtained was increased to 70–100% yield. Addition of weak acids, such as acetic and malonic acids, or of camphorsulfonic acid into the reaction mixture had no effect on the formation and distribution of final products.

We then investigated the photolysis of thiohydroxamates **3a–c** at low temperature in an attempt to decrease the rate of the

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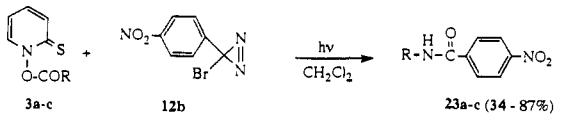
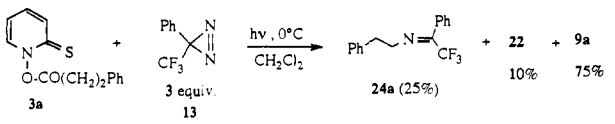
Table I. Photolysis of Thiohydroxamates **3** in the Presence of **12a**

			products formed (% from ^{1}H NMR)			
			R–NHCOPh	R–CO_2H	R–SPy	$(SPy)_2$
T (°C)	**3**	**12a** (equiv)	**21**	**1**	**9**	**22**
0	**a**, R = $Ph(CH_2)_2$	1	27	17	56	14
		3	31	24	45	14
		5	33	26	41	15
	b, R = C_6H_{11}	1	50	5	45	22
		3	54	7	39	25
		5	55	8	36	25
	c, R = 1-adamantamyl	1	51	5	45	25
		3	57	5	39	27
		5	59	8	36	31
−60	**a**, R = $Ph(CH_2)_2$	1	60	8	5	35
		3	68	21		31
		5	71	23		37
	b, R = C_6H_{11}	1	70	8	5	45
		3	82	8		45
		5	82	10		45
	c, R = 1-adamantamyl	1	61	5	8	44
		3	74	9	5	45
		5	74	14		40

Scheme VI



Scheme VII



hydrolysis and the formation of sulfides **9a–c**. Indeed, photolysis of **3a–c** at −60 °C resulted in the formation of amides **21a–c** in yields of up to 82% (Table I). Similar results were obtained when thiohydroxamates **3a–c** were photolyzed in the presence of diazirine **12b** (Scheme VI). Once more, *p*-nitrobenzamides **23a–c** were produced in moderate to good yields, together with **1a–c**, **9a–c**, and **22**.

Exploratory Photolysis of 3 with 3,3-Dialkyldiazirines 13, 14, and 15. Following the interesting results previously obtained, we were encouraged to attempt the photolysis of **3a** in the presence of diazirine **13**. Irradiation (W, 300 W) of **3a** with 3 equiv of **13** in dry methylene chloride solution at 0 °C afforded thioether **9a** (75%), trifluoroacetophenone imine **24a** (25%), and disulfide **22** (10%) (Scheme VII).

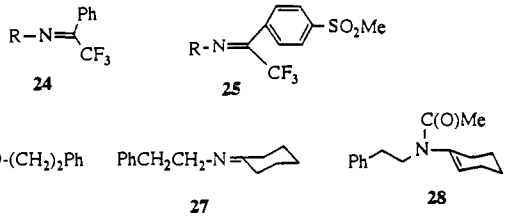
Formation of compound **24a** during the photolysis results from the addition of **6a** onto the nitrogen of **13**, since no reaction occurred in the dark even after 24 h.

In an attempt to increase the formation of the trifluoroacetophenone imine, we studied the reaction of **6a** with diazirine **15** under the same conditions as previously used. However, despite the electron-withdrawing effect of the methanesulfonyl group grafted in the *para* position of the aromatic ring, there was no increase in the yield of **25a** (Table II).

We further conducted the photolysis of **3a** in the presence of an equal amount of diazirines **13** and **15**. In this case, we were able to detect the formation of imines **24a** and **25a** in equal yield (15%). Therefore, given the additional steps required for the preparation of compound **15**, we focused our attention on the easily prepared diazirine **13**.

We also investigated the reaction of thiohydroxamate **3a** in the presence of 5 equiv of diazirine **14** under standard irradiation conditions. Along with disulfide **22** and thioether **9a**, we also isolated amide **26** in 23% yield (Chart I). We conceived that **26** was obtained by reaction of the imine intermediate **27** with

Chart I[a]



[a] For **24** and **25**: **a**, R = $PhCH_2CH_2$; **b**, R = C_6H_{11}; **c**, R = 1-adamantanyl.

Table II. Comparison of Diazirines **13** and **15**

		imines obtained (%)	
3 (equiv)	**13** or **15** (equiv)	**24a**	**25a**
1	1.5	20	18
1	3	25	23
1	5	32	29

unreacted **3a**. In order to confirm this hypothesis, we conducted the same reaction in the presence of 5 equiv of acetic anhydride and we were able to isolate enamide **28** in 38% yield. Indeed, formation of the intermediate *N*-cyclohexylimine **27**[30] accounts for the formation of compounds **26** and **28**, as we proved by independently preparing and reacting **27** with **3a** and acetic anhydride, respectively.

The effect of temperature during the irradiation of thiohydroxamate **3a** in the presence of **13** was also studied. The results are shown in Table III.

Mechanistic Studies of the Reaction between Thiohydroxamates 3 and the Diazirines. Intrigued by the formation of compounds **21**, **23–26**, and **28**, where a carbon–nitrogen bond was created under radical conditions, we decided to investigate further the mechanism of these unprecedented reactions. The carbon radical **6** formed during the irradiation of **3** may add to the nitrogen–nitrogen double bond of the diazirines to form the new nitrogen-centered diaziridinyl radical **32**. Existence of these moieties is well documented in the literature,[31] and they are considered to be π-radicals with the unpaired electron located in a predominantly 2p orbital of the nitrogen. More recently, the generation, EPR identification, and decay kinetics of the diazirinyl radicals, such as **29**, have been reported in the pioneering work of Ingold and

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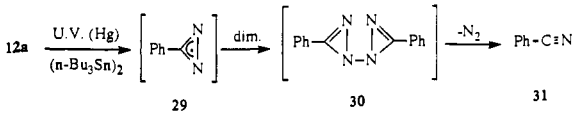
Table III. Reaction of **3** with **13** under **Different** Conditions

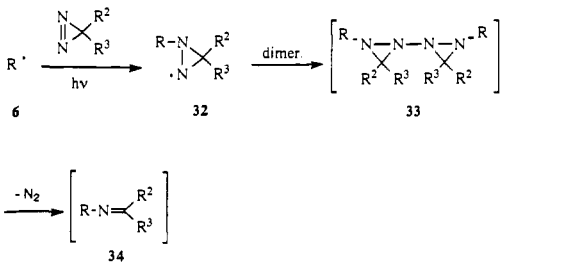
entry	3 (1 equiv)	13 (equiv)	T (°C)	products formed[a] (%) sulfide **9**	imine **24**
1	**3a**	1	0	80	20
2		3	0	75	25
3		5	0	68	32
4		20	0	29[b]	71[b]
5		5	−60	55	45
6		20	−60	19[b]	79[b]
7	**3b**	1	0	68	32
8		3	0	59	41
9		5	0	52	48
10		20	0	11[b]	89[b]
11	**3c**	1	0	70	30
12		3	0	65	31
13		5	0	61	39
14		20	0	20[b]	80[b]
15	**3d**	1	0	68	32
16		3	0	51	49
17		5	0	39	61
18		20	0	6[b]	94[b]

[a] Yields are based on ^{1}H NMR measurements using CH_2Cl_2 as internal standard and are normalized to 100% for 9 + 24. [b] Yields are based on ^{1}H NMR measurements of the crude mixture after removal of excess **13** under vacuum.

Scheme VIII[a]



Suggested reaction pathway:



[a] For **32**, **33**, and **34**: R^2 = Ph, R^3 = Br, **34** leads to **21a–c**; R^2 = *p*-O_2N-Ph, R^3 = Br, **34** leads to **23a–c**; R^2 = Ph, R^3 = CF_3, **34** isolated as **24a–c**; R^2 = *p*-Ms-Ph, R^3 = CF_3, **34** isolated as **25a–c**; R^2, R^3 = C_6H_{10} **34** leads to **26** or **28**.

Maeda.[32] These authors have generated the diazirinyl radical **29** by UV photolysis of diazirine **12a** in the presence of hexa-*n*-butylditin. They concluded from decay kinetic data that a bimolecular self-reaction of these radicals takes place, leading to the formation of benzonitrile **31** (Scheme VIII).

In accordance with these results and the fact that nitrogen-centered radicals do not add on the thiocarbonyl moiety,[10] we propose a dimerization of radical **32** leading to the corresponding tetraazo **33**. Smooth elimination of one molecule of N_2 could then yield imine **34**. When diazirines **12a** or **12b** were used as traps, further hydrolysis of the α-bromophenylimines thus formed, could lead to the benzamides **21a–c** and **23a–c**. When diazirines **13** or **15** were used as traps, the resulting imines **24** and **25** were stable and isolable. Finally, when cyclohexyldiazirine (**14**) was used as a trap, an anionic reaction of **34** with unreacted **3a** occured, leading to amide **26** (Scheme VIII).

Tetraazo compounds of the type **33** are known to be stable when electron-withdrawing substituents are attached on the nitrogens.[18] With this in mind, we decided to study the addition of a carbon radical onto diazirine **13**. We followed the progress of the reaction with low-temperature ^{13}C NMR. We chose to analyze the addition of the more nucleophilic radical **6d** since better yields of imine **24d** have been observed in this case.[33] The irradiation was conducted in an NMR tube in the presence of 5 equiv of **13** at −60 °C, using deuteriochloroform as solvent. After the end of the reaction, the ^{13}C NMR spectrum of the crude mixture taken at −60 °C showed the complete disappearance of starting **3d** and the absence of imine **24d**. Besides the signals at 56.3 and 73.3 ppm due to the expected sulfide **9d**, we were able to detect four new signals at 57.3, 57.5, 85.2, and 86.5 ppm. By gradually raising the temperature (10 °C/h), we could observe the smooth disappearance of these signals and the appearance of two new peaks at 55.9 and 84.1 ppm that corresponded to the final imine **24d** (Figure 1). We have found that **24d** is formed above −10 °C. At this temperature, the set of peaks at 57.5 and 86.5 ppm had completely disappeared. The other set of peaks at 57.3 and 85.2 ppm disappears above 40 °C, leading again to imine **24d**.

We suspected that these sets of peaks corresponded to two diastereomeric forms of tetraazo **33d**. As one of its forms seemed to be stable at room temperature, we therefore decided to isolate it. Indeed, by carefully controlling the temperature of the reaction, not to exceed 25 °C, we were able to isolate and completely characterize **33d**. Its good crystalline form also allowed us to collect X-ray data, thus proving its structure (Figure 2). The structure of **33d** is completely symmetrical, and this explains why only two peaks corresponding to the CH_3OCH_2 moiety are observed in the ^{13}C NMR.

It is worth mentioning that this is the first X-ray structure for this class of tetraazo derivatives.

Amination of a Carbon Radical via Its Thiohydroxamate and/or Its Organotelluride Derivatives. Our preliminary studies indicated that 3-(trifluoromethyl)-3-phenyldiazirine (**13**) is the most convenient trap for the addition of carbon radicals **6** onto nitrogen. We investigated the reactivity of diazirine **13** in the presence of different thiohydroxamates **3a–d** (Table III). Photolysis of 1 equiv of **3a–d** in the presence of varying amounts of **13** at 0 °C in methylene chloride (0.2 M initial concentration of **3**) furnished the corresponding imines **24a–d** in yields of up to 89%. As expected, nucleophilic carbon radicals added more efficiently to the diazirines, presumably due to the closer interaction of the SUMO orbital of the carbon radical **6** with the LUMO orbital of the nitrogen–nitrogen double bond. It is important to mention that diazirines as a class are unusually volatile so that the excess of **13** used during this transformation can easily be recovered by simple Kugelrohr distillation of the crude mixture (53–55 °C at 30 mmHg). Hydrolysis of **13a–c** to the desired amines **35a–c** can easily be accomplished under very mild conditions in a refluxing mixture of ethanol/water using $B(OH)_3$ as catalyst[34] (Scheme IX). It is worth mentioning that during the hydrolysis, the trifluoroacetophenone, which constitutes the starting material for the preparation of **13**, can be generated and recycled, giving an additional advantage to the whole amination process.

(32) Maeda, Y.; Ingold, K. U. *J. Am. Chem. Soc.* **1979**, *101*, 837–840.

(33) For a discussion of the reactivity of alkoxymethyl radicals, see: Rawal, V. H.; Singh, S. P.; Dufour, C.; Michoud, C. *J. Org. Chem.* **1991**, *56*, 5245–5247 and references cited there.

(34) Barton, D. H. R.; Motherwell, W. B.; Wozniak, J.; Zard, S. Z. *J. Chem. Soc., Perkin Trans. I* **1985**, 1865–1869.

(35) Barton, D. H. R.; Ozbalik, N.; Sarma, J. C.; *Tetrahedron Lett.* **1988**, *29*, 6581–6584. Barton, D. H. R.; Ramesh, M. *J. Am. Chem. Soc.* **1990**, *112*, 891–892. Barton, D. H. R.; Dalko, P. I.; Géro, S. D. *Tetrahedron Lett.* **1991**, *32*, 4713–4716. Barton, D. H. R.; Géro, S. D.; Quiclet-Sire, B.; Samadi, M.; Vincent, C. *Tetrahedron* **1991**, *47*, 9383–9392. Barton, D. H. R.; Camara, J.; Cheng, X.; Géro, S. D.; Jaszberenyi, J. Cs.; Quiclet-Sire, B. *Tetrahedron* **1992**, *48*, 9261–9276. Han, L. B.; Ishihara, K.-I.; Kambe, N.; Ogawa, A.; Ryu, I.; Sonoda, N. *J. Am. Chem. Soc.* **1992**, *114*, 7591–7592. Chen, C.; Crich, D.; Papadatos, A. *J. Am. Chem. Soc.* **1992**, *114*, 8313–8314. For related work with iodides, see: Curran, D. P.; Chang, C.-T. *J. Org. Chem.* **1989**, *54*, 3140–3157. Snieckus, V.; Cuevas, J.-C.; Sloan, C. P.; Liu, H.; Curran, D. P. *J. Am. Chem. Soc.* **1990**, *112*, 896–898.

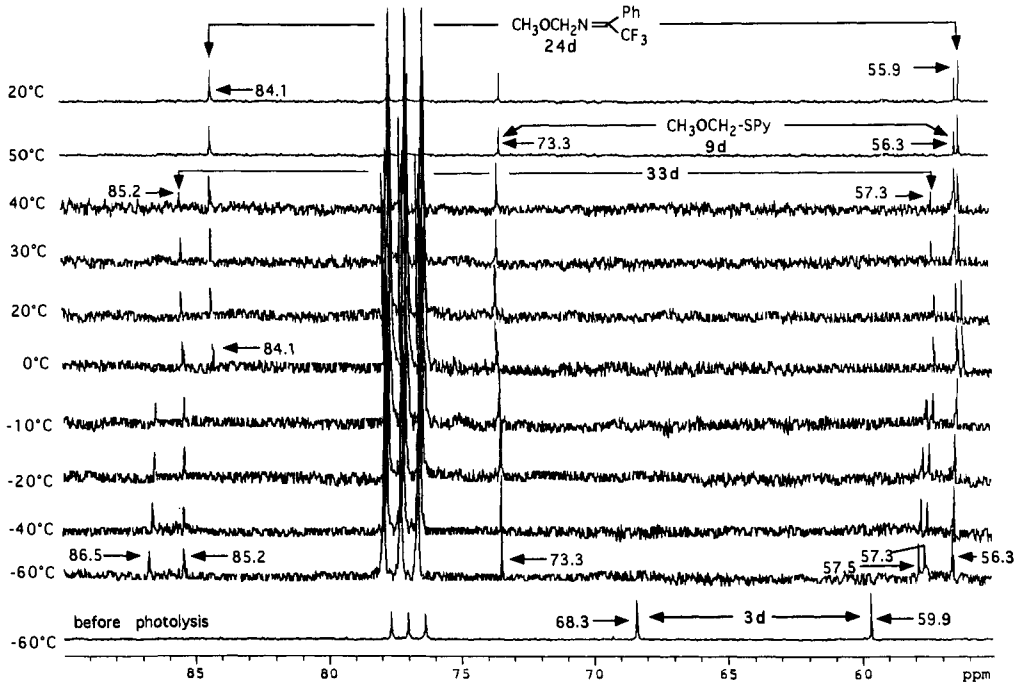


Figure 1. Variable temperature ^{13}C NMR of the reaction between **3d** and diazirine **13**.

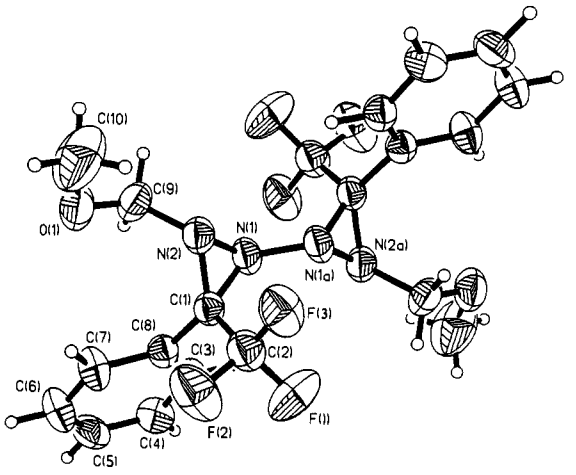
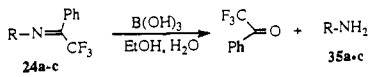


Figure 2. Thermal ellipsoid plot (50% probability) of **33d**. Hydrogen atoms have been drawn as spheres with arbitrary radii. Selected bond lengths and angles are as follows: N(1)–C(1), 1.464(5) Å; N(2)–C(1), 1.442(6) Å; N(1)–N(2), 1.473(5) Å; N(1)–N(1A), 1.473(7) Å; N(2)–C(9), 1.469(7) Å; C(1)–N(1)–N(1A), 111.9(4)°; N(1)–C(1)–N(2), 60.9-(3)°; N(1)–N(2)–C(9), 110.9(3)°; N(2)–N(1)–N(1A), 106.7(4)°; N(1)–N(2)–C(1), 60.3(3)°; C(1)–N(2)–C(9), 117.6(4); N(2)–N(1)–C(1), 58.8(3)°.

Scheme IX[a]

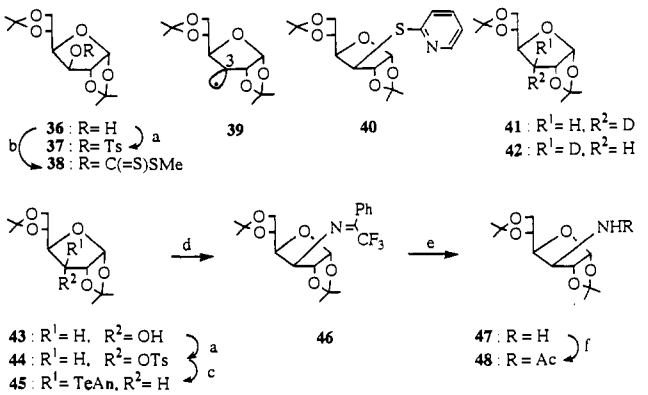


[a] **35a**, R = $Ph(CH_2)_2$, 91%; **35b**, R = C_6H_{11}, 87%; **35c**, R = 1-adamantanyl, 96%.

It has recently been shown that organotellurium derivatives[35] can be effective precursors of carbon radicals. Such organotellurium species can be simply prepared from the corresponding *O*-tosylates or halides by S_N2 displacement of the leaving group with the sodium salt of the telluride. The latter is formed in situ by $NaBH_4$ reduction of the corresponding dianisyl ditelluride in alcoholic media.

All our attempts to prepare the corresponding telluride from tosylate **37** of diacetone glucose (**36**) failed, presumably due to the steric hindrance at the *endo* face toward an S_N2 displacement.

Scheme X[a]



[a] Reagents and conditions: (a) TsCl, pyridine, CH_2Cl_2, room temperature; (b) ref 2; (c) $(AnTe)_2$, $NaBH_4$, *t*-BuOH, 72%; (d) **13** (×20), **3e** (×2), *hν* CH_2Cl_2, 0 °C, 95%; (e) $B(OH)_3$, $EtOH/H_2O$, reflux 87%; (f) Ac_2O, pyridine, CH_2Cl_2, 90%.

We were, however, able to prepare the telluro carbohydrate **45** from the corresponding allose derivative **44** in refluxing *tert*-butyl alcohol (72%). The radical exchange reaction of **45** to **46** was "triggered" by the *O*-acyl derivative of *N*-hydroxy-2-thiopyridone **3e**. Thus, visible-light irradiation of **3e** produced methyl radicals **6e**, which reacted smoothly with telluride **45** to generate the carbohydrate radical **39**. In the presence of excess diazirine **13**, radical **39** furnished imine **46** (95%). Hydrolysis of **46** in a refluxing solution of ethanol/water, using $B(OH)_3$ as catalyst, yielded the amino sugar **47** (87%) which was further converted to the known acetamide **48**,[36] mp 94–96 °C ($CHCl_3$/hexanes), $[\alpha]^{25}_D$ = –44.1° (*c* 1.2, $CHCl_3$).

Of particular interest was the stereochemistry of the imino carbohydrate **46**, since the 3β-isomer was formed exclusively. To further confirm these results, we irradiated[37] the known xanthate **38** with thiohydroxamate **3e** in refluxing methylene chloride and we isolated thioether **40** (exclusively 3β) in 77% yield. Alter-

(36) (a) Williams, D. T.; Jones, J. K. N. *Can. J. Chem.* **1967**, *45*, 7–9. (b) Brimacombe, J. S.; Bryan, J. G. H.; Husain, A.; Stacey, M.; Tolley, M. S. *Carbohydr. Res.* **1967**, *3*, 318–324.

(37) Barton, D. H. R.; Tachdjian, C. *Tetrahedron* **1992**, *48*, 7109–7120.

natively, reaction of **38** with diazirine **13**, initiated by thiohydroxamate **3e**, resulted in the formation of **46** in moderate yield (60%).

There is good precedent for the high level of the stereoselectivity obtained with radical **39** formed in the 3-position of the glucofuranosyl ring. Stick *et al.*[38] have earlier demonstrated that the reduction of xanthate **38** in the presence of the tri-*n*-butyltin deuteride in refluxing toluene proceeded with good diastereoselectivity (**41**/**42**: 85/15) for the addition of the deuterium from the β-face. The reason for this high selectivity results from the 1,2-acetonide group induced steric hindrance at the *endo* α-face of the five-membered ring. The addition therefore proceeds preferentially from the *exo* face. This principle was used successfully in the synthesis of several natural compounds.[39,40] Recently, very remarkable progress in acyclic stereochemical control in free-radical reactions has been achieved using chiral auxiliaries.[41]

Crystal Structure of Diazirine 15

The surprisingly good crystalline form of diazirine **15** allowed us to collect low-temperature X-ray data for this compound (Figure 3). At present, to the best of our knowledge, there is no X-ray structure reported in the literature of a 3-(trifluoromethyl)-3-aryldiazirine ring; the only crystal structure information concerning the diazirine ring was recently provided by two different α-chloro diazirines.[42] Therefore, these data can provide valuable information concerning the structure–reactivity relationship in this exciting class of molecules. We intend to use these data, together with those available from the literature, for theoretical calculations on the radicophilicity of diazirines, like **15**, in comparison with the lack of reactivity found in many N=N structures.

Despite the electron-withdrawing effect of the methanesulfonyl moiety grafted onto the *para* position of the phenyl ring, there is little or no difference between the bond distances and angles of the free diazirine ring compared with its analogues (Table IV). This result explains the similar affinity of carbon radicals toward the diazirines studied in this work and furthermore indicates the limitation of this new reaction. It is also of interest to point out the equal bond distance and electronic density (within experimental error) of the two carbon–nitrogen bonds of the ring in all the diazirines examined.[44]

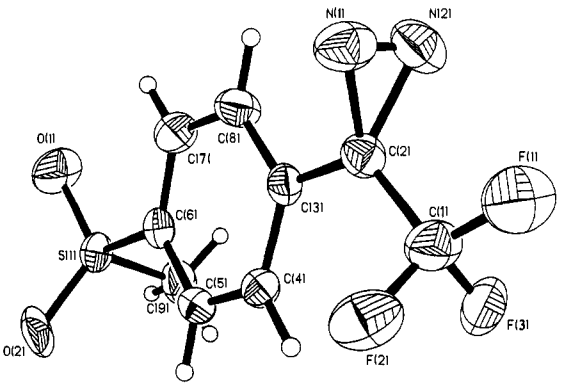


Figure 3. Thermal ellipsoid plot (50% probability) of **15**. Hydrogen atoms have been drawn as spheres with arbitrary radii. Selected bond lengths and angles are as follows: N(1)–N(2), 1.228(9) Å; N(1)–C(2), 1.496(7) Å; N(2)–C(2), 1.490(7) Å; C(1)–C(2), 1.493(9) Å; C(2)–C(3), 1.479(9) Å; N(2)–N(1)–C(2), 65.5(4)°; N(1)–N(2)–C(2), 66.0(4)°; N(1)–C(2)–N(2), 48.6(4)°; N(1)–C(2)–C(1), 15.5(6)°; N(2)–C(2)–C(1), 114.5(5)°; N(1)–C(2)–C(3), 118.2(5)°; N(2)–C(2)–C(3), 118.3-(5)°.

Table IV. Comparison[42] of Bond Lengths and Angles in Diazirines[a]

	bond lengths (Å)		bond angles (degrees)	
compound	N=N	C=N	M—C—N	ef
15[b]	1.228(9)	1.490(7)	48.5(4)	this work
H_2CN_2	1.228(3)	1.482(3)	48.9	43a
p-O_2N-PhOCH_2-C(Cl)N_2[b]	1.229(3)	1.460(1)	49.8(1)	42b
$(Me)_2CN_2$	1.235(5)	1.490(10)	48.9	43c
$MeHCN_2$	1.235(5)	1.481(10)	49.3(3)	43e
$MeClCN_2$	1.241(5)	1.462	50.2(5)	43d
$(C_{10}H_7CH_2)ClCN_2$[b]	1.244(10)	1.465(10)	50.3(5)	42a
F_2CN_2	1.293(9)	1.426(4)	53.9(4)	43b

[a] Unless otherwise specified, dimensions were derived from rotational spectra. [b] Data were derived from single-crystal X-ray diffraction.

Conclusions

Carbon radicals generated from the corresponding thiohydroxamates via visible-light irradiation and from the corresponding organotellurides via radical exchange add readily to the nitrogen–nitrogen double bond of diazirines to produce diaziridinyl radicals. These later furnish, after dimerization and subsequent extrusion of N_2, imines **34**, which, in the case of 3-(trifluoromethyl)-3-phenyldiazirine (**13**), can be easily hydrolyzed to the desired amines **35**. The reaction sequence was easily applied to the synthesis of protected kanosamine **48**, with high diastereoselectivity in the carbon–nitrogen bond formation. The whole sequence proved to be very mild and efficient and provides an alternative procedure for the conversion of a carboxylic acid or an alcohol to the corresponding nor-amine through radical processes.

Experimental Section

General Methods. NMR spectra were determined for solutions in deuteriochloroform on a Varian Gemini 200 or a Varian XL 200E spectrometer, operated at 200 MHz for ^1H NMR and 50 MHz for ^{13}C

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NMR. Chemical shifts are reported (δ) relative to TMS. Melting points were determined with a Kofler hot-stage apparatus and are uncorrected. IR spectra were recorded on a Perkin-Elmer 881 spectrophotometer in chloroform solutions. GC–MS data were obtained on a Hewlett-Packard 5890 GC–MS system with a 5971 mass selective detector. Mass spectra were obtained on a VG Analytical 70S high-resolution, double-focusing magnetic sector mass spectrometer with an attached VG 11/250J data system in the EI mode. Microanalyses were performed by Atlantic Microlab Inc., Norcross, GA. Solvents and reagents were purified according to standard laboratory techniques. *N*-Hydroxy-2-thiopyridone was isolated from its sodium salt (Omadine). A 40% solution of the sodium salt of *N*-hydroxy-2-thiopyridone was a kind gift of the Olin Corp., Cheshire, CT. Other reference compounds and starting materials were purchased from Aldrich Chemical Co., Inc., Milwaukee, WI.

Synthesis and Characterization of Starting Materials and Products. Compounds 3a–e. *N*-Hydroxy-2-thiopyridone (**2**) was reacted with the corresponding carboxylic acids **1a–d** in the presence of *N,N'*-dicyclohexylcarbodiimide (DCC), following literature methods,[19] to afford the *O*-acyl derivatives **3a–d**. Compound **3e** was prepared from the corresponding acetyl chloride as previously described.[37]

***N*-((Methoxyacetyl)oxy)-2-thiopyridone (3d).** DCC (10.3 g, 50 mmol) was added portionwise to a solution of *N*-hydroxy-2-thiopyridone (**2**) (6.4 g, 50 mmol) and methoxyacetic acid (**1d**) (4.5 g, 50 mmol) in dry methylene chloride (100 mL) in the dark at 0 °C. The reaction mixture was stirred for 24 h at room temperature, and then the 1,3-dicyclohexylurea, which was formed during the reaction, was removed by gravity filtration. The yellow solution was then washed twice with a cold saturated aqueous solution of $NaHCO_3$ and extracted with methylene chloride. The organic layer was dried over magnesium sulfate and concentrated under vacuum at room temperature in the dark. Chromatography on silica gel using AcOEt as solvent afforded, then, compound **3d** as a yellow liquid (7.1 g, 72%) that slowly solidified when kept at −20 °C: mp 28–29 °C; IR ($CHCl_3$, cm^{-1}) 1808, 1610; ^1H NMR δ 3.58 (s, 3H), 4.49 (s, 2H), 6.75 (m, 1H), 7.25 (m, 1H), 7.7 (m, 2H); ^{13}C NMR δ 59.9, 68.3, 113.1, 133.5, 136.9, 137.5, 166.9, 174.6; MS (EI, *m/z*) 155 (12), 140 (89), 125 (32), 112 (100), 78 (61). Anal. Calcd for $C_8H_9NO_3S$: C, 48.22; H, 4.55. Found: C, 48.48; H, 4.74.

Thioether 9d. A solution of thiohydroxamate **3d** (1 g, 5 mmol) in dry methylene chloride (10 mL) was irradiated under argon at 0 °C with two tungsten lamps (GE, 150 W) from a distance of about 20 cm. The consumption of **3d** was followed by TLC and completed after 30 min. The solvent was then removed under reduced pressure, and the crude residue was chromatographed on silica gel. Thioether **9d** was eluted with hexanes/ether, 9:1, as a colorless liquid (472 mg, 61%): IR ($CHCl_3$, cm^{-1}) 3064, 2988, 1539, 1445, 1080; ^1H NMR δ 3.39 (s, 3H), 5.32 (s, 2H), 6.95 (m, 1H), 7.24 (m, 1H), 7.5 (m, 1H), 8.45 (m, 1H); ^{13}C NMR δ 56.3, 73.3, 119.9, 122.5, 136.1, 149.2, 157.5; MS (EI, *m/z*) 155 (12), 140 (81), 125 (31), 112 (100). Anal. Calcd for C_7H_9NOS: C, 54.16; H, 5.84; N, 9.02. Found: C, 54.02; H, 5.89; N, 8.96.

α-Bromo Diazirines. Compounds **12a**[24] and **12b**[25] were prepared by the Graham[26] oxidation of the appropriate amidinium salts using freshly prepared NaOBr solution. Their spectroscopic and physical data were identical to those reported in the literature.

3,3-Dialkyldiazirines. Known procedures were used to prepare the corresponding diaziridines of **13**[27] and **14**.[28] The reported method for the oxidation of the diaziridines to diazirines was modified in order to avoid the use of silver salts. Instead, MnO_2 was used as oxidant.[45] A general procedure is as follows. A solution of the diaziridine (1 mmol) in 10 mL of ether was added slowly at 0 °C to a stirred suspension of MnO_2 (3 mmol) in 20 mL of ether. The mixture was stirred for an additional hour and then filtered through Celite, and the filtrate was concentrated in a vacuum (40 mmHg) at 10 °C. The residues were distilled, 40–60 °C/20 mmHg, with a Kugelrohr apparatus to afford the diazirines as colorless liquids.

4-(Methylthio)trifluoroacetophenone *O*-(*p*-Tolylsulfonyl)oxime (18). The Grignard reagent of **16** was prepared by reaction of 4-bromothioanisole (20.3 g, 100 mmol) with magnesium turnings (2.7 g, 110 mmol) in dry THF (150 mL) under argon. Gaseous trifluoroacetonitrile was then slowly introduced into the flask below the surface of the cloudy solution over a period of 1 h at 0 °C.[29] After being stirred for an additional hour, the mixture was slowly poured into 200 mL of cold 6 N aqueous HCl and extracted with ether (300 mL). The ether layer was dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was then filtered through a short pad of silica gel. The crude 4-(methylthio)-trifluoroacetophenone (17.6 g, 75%) was converted to the corresponding oxime following the literature procedure.[27] 4-(Methylthio)trifluoroacetophenone oxime (10.2 g, 43.4 mmol) and *p*-toluenesulfonyl chloride (9 g, 47.4 mmol) were then dissolved in dry methylene chloride (50 mL) and treated at 0 °C with freshly distilled dry pyridine (3.8 g, 47.4 mmol). The mixture was stirred for 12 h at room temperature and then washed with water, 0.1 M aqueous HCl, and saturated aqueous $NaHCO_3$. The organic layer was extracted with methylene chloride, dried over magnesium sulfate, and concentrated at reduced pressure. Tosylate **18** was obtained pure following recrystallization from methylene chloride/ethyl alcohol as a white solid (14.6 g, 87%): mp 113–114 °C (CH_2Cl_2/EtOH); IR ($CHCl_3$, cm^{-1}) 1593, 1384, 1193, 1147; ^1H NMR δ 2.46 (s, 3H), 2.49 (s, 3H), 7.22–7.4 (m, 6H), 7.9 (d, 2H, J = 8 Hz); ^{13}C NMR δ 14.5, 21.5, 120.3, 125.5, 129.0, 129.3, 130.0, 131.3, 144.7, 146.3; MS (EI, *m/z*) 389 (35), 155 (100), 91 (81). Anal. Calcd for $C_{16}H_{14}F_3NO_3S_2$: C, 49.35; H, 3.62; N, 3.60. Found: C, 49.24; H, 3.63; N, 3.58.

4-(Methylsulfonyl)trifluoroacetophenone *O*-(*p*-Tolylsulfonyl)oxime (19). 3-Chloroperoxybenzoic acid (*m*-CPBA, 4.3 g, 25 mmol) was added portionwise to a solution of tosylate **18** (3.89 g, 10 mmol) in dry methylene chloride (50 mL) at 0 °C. The solution was allowed to warm to room temperature and stirred overnight. The mixture was then washed with saturated aqueous $NaHCO_3$ and extracted with methylene chloride. The organic layer was dried over magnesium sulfate and concentrated under vacuum. Tosylate **19** was obtained pure after recrystallization from methylene chloride/ethyl alcohol as a white solid (3.45 g, 82%): mp 169–170 °C (CH_2Cl_2/EtOH); IR ($CHCl_3$, cm^{-1}) 1595, 1390, 1320, 1177, 1152; ^1H NMR δ 2.50 (s, 3H), 3.12 (s, 3H), 7.4 (d, 2H, J = 8 Hz), 7.6 (d, 2H, J = 8 Hz), 7.9 (d, 2 H, J = 8 Hz), 8.1 (d, 2H, J = 8 Hz); ^{13}C NMR δ 21.6, 44.1, 128.1, 129.4, 129.6, 129.9, 130.2, 130.8, 143.6, 146.8; MS (EI, *m/z*) 421 (0.7), 281 (22), 182 (35), 155 (100), 91 (96). Anal. Calcd for $C_{16}H_{14}F_3NO_5S_2$: C, 45.60; H, 3.35; N, 3.32. Found: C, 45.49; H, 3.38; N, 3.27.

3-(Trifluoromethyl)-3-(4-(methylsulfonyl)phenyl)diaziridine (20). A suspension of tosylate **19** (2.0 g, 4.75 mmol) in dry ether (50 mL) was cooled to −78 °C. Liquid ammonia (10 mL) was then added, and the mixture was stirred in a sealed flask at room temperature for 12 h. The excess ammonia was then evaporated at room temperature and the mixture washed with water. The organic layer was extracted twice with methylene chloride, dried over magnesium sulfate, and concentrated under vacuum. The resulting solid was then crystallized from methylene chloride/hexanes to afford diaziridine **20** (1.2 g, 95%): mp 125–126 °C (CH_2Cl_2/hexanes); IR ($CHCl_3$, cm^{-1}) 3288, 3054, 1315, 1144; ^1H NMR δ 2.46 (d, 1H, J = 8 Hz), 2.98 (d, 1H, J = 8 Hz), 3.06 (s, 3H), 7.83 (d, 2H, J = 8 Hz), 7.97 (d, 2H, J = 8 Hz); ^{13}C NMR δ 44.2, 57.1, 57.8, 120.3, 125.8, 127.7, 129.3, 137.2, 142.0; MS (EI, *m/z*) 266 (2.2), 265 (51), 245 (33), 186 (100). Anal. Calcd for $C_9H_9F_3N_2O_2S$: C, 40.60; H, 3.41; N, 10.52. Found: C, 40.96; H, 3.51; N, 10.60.

3-(Trifluoromethyl)-3-((4-methylsulfonyl)phenyl]diazirine (15). A solution of diaziridine **20** (0.27 g, 1 mmol) in 10 mL of ether was added slowly at 0 °C to a stirred suspension of MnO_2 (0.26 g, 3 mmol) in 20 mL of ether. The mixture was stirred for an additional hour and then filtered through Celite, and the filtrate was concentrated under vacuum (40 mmHg) at 10 °C. The resulting solid was crystallized from ether/hexanes to afford compound **15** (0.24 g, 92%): mp 83–84 °C (ether/hexanes); IR ($CHCl_3$, cm^{-1}) 1571, 1317, 1187, 1151; ^1H NMR δ 3.08 (s, 3H), 7.4 (d, 2H, J = 8 Hz), 8.0 (d, 2H, J = 8 Hz); ^{13}C NMR δ 44.0, 118.9, 124.4, 127.4, 128.0, 134.9, 141.8; MS (EI, *m/z*) 264 (0.5), 238 (21), 223 (30), 103 (100). Anal. Calcd for $C_9H_7F_3N_2O_2S$: C, 40.91; H, 2.67; N, 10.60. Found: C, 40.97; H, 2.70; N, 10.55.

General Procedure for the Radical Addition of the Acyl Derivatives 3a–c to Diazirines 12a,b. All operations were performed under argon using degassed, dry dichloromethane as solvent. A solution of diazirine **12a** (0.59 g, 3 mmol) and the *O*-acyl derivative **3a** (0.26 g, 1 mmol) in 15 mL of dry methylene chloride under argon at 0 °C was irradiated with two tungsten lamps (GE, 150 W) in a Pyrex flask from a distance of about 20 cm. The consumption of **3a** was followed by TLC and completed after 2 h. The solvent was removed under reduced pressure at room temperature, and the crude residue was chromatographed on silica gel. Most of the excess **12a** was eluted with hexanes in the first fraction. Benzamide **21a** (70 mg, 31%) was eluted with hexanes/ether, 3:7: mp 114 °C (CH_2Cl_2/hexanes); IR ($CHCl_3$, cm^{-1}) 3450, 1655, 1514; ^1H NMR δ 2.95 (t, 2H, J = 7 Hz), 3.7–3.8 (q, 2H, J = 7 Hz), 6.4 (b s, 1H), 7.2–7.45 (m, 8H), 7.7 (m, 2H); ^{13}C NMR δ 35.6, 41.1, 126.4, 126.7, 128.4, 128.6, 128.7, 131.3, 134.5, 138.8, 167.4; MS (EI, *m/z*) 225 (19),

(44) As additional proof, the *ab initio* calculations on **15** also indicate that the carbon–nitrogen bond lengths are equivalent (J. H. Riebenspies, unpublished results).

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134 (15), 105 (100). Anal. Calcd for $C_{15}H_{15}NO$: C, 79.97; H, 6.71; N, 6.21. Found: C, 79.72; H, 6.68; N, 6.12. *N*-(2-Phenylethyl)-4-nitrobenzamide (**23a**): mp 149–151 °C (CH_2Cl_2/hexanes) (lit.[46] mp 151 °C). *N*-Cyclohexylbenzamide (**21b**): mp 146–147 °C (CH_2Cl_2/EtOH) (lit.[47] mp 146 °C). *N*-Cyclohexyl-4-nitrobenzamide (**23b**): mp 201–202 °C (CH_2Cl_2/EtOH) (lit.[47] mp 200–202 °C). *N*-(1-Adamantanyl)benzamide (**21c**): mp 151–152 °C (CH_2Cl_2/hexanes) (lit.[48] mp 152–153 °C). *N*-(1-Adamantanyl)-4-nitrobenzamide (**23c**): mp 180–182 °C (CH_2Cl_2/hexanes) (lit.[48] mp 182–183 °C). Compounds **21a–c** and **23a–c** were compared with authentic samples prepared from the corresponding amine with the appropriate benzoyl chloride according to the literature method.[49]

Compound 26. To a solution of thiohydroxamate **3a** (0.26 g, 1 mmol) in dry methylene chloride (5 mL) was added diazirine **14** (0.55 g, 5 mmol) under argon, and the mixture was photolyzed at 0 °C until decoloration. Then, the reaction mixture was concentrated under vacuum and the crude residue chromatographed on silica gel. Amide **26** (58 mg, 23%) was eluted with hexanes/ether, 5:5: mp 95–96 °C (benzene/hexanes); IR ($CHCl_3$, cm^{-1}) 3443, 1660, 1510; ^1H NMR δ 2.4 (t, 2H, J = 7 Hz), 2.73 (t, 2H, J = 7 Hz), 2.95 (t, 2H, J = 7 Hz), 3.45 (m, 2H), 5.6 (s, 1H), 7.05–7.3 (m, 10H); ^{13}C NMR δ 31.7, 35.6, 38.4, 40.6, 126.2, 126.4, 128.3, 128.5, 128.6, 128.7, 138.9, 140.9, 172.1; MS (EI, m/z) 253 (53), 133 (55), 104 (100); HRMS calcd for $C_{17}H_{19}NO$ 253.1466, found 253.1454.

Enamide 28. To a solution of thiohydroxamate **3a** (0.26 g, 1 mmol) in dry methylene chloride (5 mL) containing acetic anhydride (0.51 g, 5 mmol) was added diazirine **14** (0.55 g, 5 mmol) under argon, and the mixture was photolyzed at 0 °C until decoloration. Then, the reaction mixture was concentrated under vacuum and the crude residue chromatographed on silica gel. Enamide **28** (92 mg, 38%) was eluted with hexanes/ether, 5:5, as a colorless liquid: IR ($CHCl_3$, cm^{-1}) 1715, 1634, 1397, 1362; ^1H NMR δ 1.5–1.8 (m, 4H), 2.02 (s, 3H), 2.0–2.2 (m, 4H), 2.8–2.9 (t, 2H, J = 7 Hz), 3.6–3.7 (m, 2H), 5.65 (m, 1H), 7.2–7.4 (m, 5H); ^{13}C NMR δ 21.3, 21.5, 22.6, 24.5, 27.6, 34.1, 47.1, 126.2, 127.5, 128.4, 128.9, 139.3, 139.4, 170.3; MS (EI, m/z) 243 (21), 152 (30), 139 (32), 110 (100). Anal. Calcd for $C_{16}H_{21}NO$: C, 78.97; H, 8.70. Found: C, 78.77; H, 8.74.

General Procedure for the Addition of 3a–d to Diazirines 13 and 15. To a solution of the *O*-acyl derivative **3a** (0.56 g, 1 mmol) in dry methylene chloride (5 mL) was added diazirine **13** (3.72 g, 20 mmol) under argon, and the solution was irradiated with two tungsten lamps (GE, 150 W) in a Pyrex flask from a distance of about 20 cm, until the disappearance of **3a**. The methylene chloride was then removed under vacuum at room temperature and the residue subjected to Kugelrohr distillation to recover most of the excess **13**. Imine **24a** (0.19 g, 70%) was isolated by column chromatography on silica gel, eluting with hexanes: bp 122 °C (1 mmHg); IR ($CHCl_3$, cm^{-1}) 1725, 1670, 1351, 970; ^1H NMR δ 2.95 (t, 2H, J = 7 Hz), 3.61 (qt, 2H, J_1 = 7 Hz, J_2 = 1 Hz), 6.8–6.9 (m, 2H), 7.0–7.1 (m, 2H), 7.2–7.4 (m, 6H); ^{13}C NMR δ 36.4, 54.7, 126.3, 127.4, 128.3, 128.5, 129.0, 129.8, 130.1, 139.0; MS (EI, m/z) 277 (10), 208 (26), 186 (100), 91 (85). Anal. Calcd for $C_{16}H_{14}F_3N$: C, 69.30; H, 5.09; N, 5.05. Found: C, 69.33; H, 5.01; N, 5.11.

Imine 24b: 86%; bp 76–78 °C (0.3 mmHg); IR ($CHCl_3$, cm^{-1}) 1719, 1663, 1326, 970; ^1H NMR δ 1.1–1.3 (m, 3H), 1.5–1.8 (m, 7H), 3.22 (m, 1H), 7.15–7.25 (m, 2H), 7.35–7.5 (m, 3H); ^{13}C NMR δ 23.9, 25.2, 33.0, 61.2, 127.5, 128.7, 129.7, 135.5; MS (EI, m/z) 255 (10), 166 (71), 104 (100). Anal. Calcd for $C_{14}H_{16}F_3N$: C, 65.86; H, 6.32; N, 5.48. Found: C, 65.99; H, 6.33; N, 5.50.

Imine 24d: 93%; IR ($CHCl_3$, cm^{-1}) 1721, 1668, 1351, 970; ^1H NMR δ 3.46 (s, 3H), 4.74 (q, 2H, J_1 = 2 Hz), 7.2–7.3 (m, 2H), 7.4–7.5 (m, 3H); ^{13}C NMR δ 56.4, 84.4, 126.9, 129.0, 130.1, 135.9; MS (EI, m/z) 217 (35), 186 (42), 148 (41), 117 (46), 91 (100), 77 (91). Anal. Calcd for $C_{10}H_{10}F_3NO$: C, 55.30; H, 4.64. Found: C, 55.09; H, 4.69.

Tetraazo 33d. To a solution of the *O*-acyl derivative **3d** (0.5 g, 2.5 mmol) in dry methylene chloride (20 mL) was added diazirine **13** (3.72 g, 20 mmol) under argon, and the solution was irradiated at –60 °C with two tungsten lamps (GE, 150 W) in a Pyrex flask from a distance of about 20 cm, until the disappearance of **3d**. The methylene chloride and the excess **13** were then removed under vacuum (0.3 mmHg) at 0 °C and the residue was subjected to silica gel chromatography. Compound **33d** was eluted with hexanes in the first fraction (120 mg, 21%) and crystallized with ether/hexanes at –20 °C: mp 117–118 °C (ether/hexanes); IR ($CHCl_3$, cm^{-1}) 2998, 2957, 1318, 1196, 1170, 1141; ^1H NMR δ 3.6 (s, 3H), 3.7 (d, 1H, J = 8 Hz), 3.8 (d, 1H, J = 8 Hz), 7.4–7.5 (m, 3H), 7.6–7.7 (m, 2H); ^{13}C NMR δ 57.5, 85.4, 127.4, 128.3, 130.1, 130.6; MS (EI, m/z) 217 (35), 186 (42), 148 (41), 117 (46), 91 (100), 77 (91). Anal. Calcd for $C_{20}H_{20}F_6N_4O_2$: C, 51.95; H, 4.36; N, 12.12. Found: C, 52.02; H, 4.32; N, 12.12.

Detection of the Intermediate Tetraazo 33. Thiohydroxamate **3d** (70 mg, 0.27 mmol) was dissolved in deuteriochloroform (0.6 mL) and poured into an NMR tube. To this solution was added diazirine **13** (0.25 g, 1.3 mmol), and the mixture was irradiated with two tungsten lamps (GE, 150 W) at –60 °C. The progress of the reaction was followed by TLC. After the consumption of **3d**, the ^{13}C NMR spectra of the solution were recorded at a range of temperatures from –60 to 50 °C.

General Procedure for the Hydrolysis of Imines 24 to Amines 36. To a solution of imine **24a** (0.19 g, 0.68 mmol) in ethanol (5 mL) was added $B(OH)_3$ (0.085 g, 1.4 mmol) followed by H_2O (1 mL), and the mixture was heated at 80 °C for 8 h. The solvents were then removed under reduced pressure, and the residue was poured into water (15 mL), acidified to pH 1 with the addition of 5 mL HCl (6 N), and washed with ether. The aqueous layer was then basified with K_2CO_3 at pH 12 and extracted twice with ether. The organic layer was dried over magnesium sulfate, filtered, and concentrated under vacuum to afford 2-phenylethylamine **36a** (0.075 g, 91%).

3-((4-Methoxyphenyl)telluro)-3-deoxy-1,2:5,6-di-*O*-isopropylidene-D-glucofuranose (45). The dianisyl ditelluride[50] (1.4 g, 3 mmol) was dissolved in 40 mL of *tert*-butyl alcohol and introdued into a dry, three-neck, round-bottom flask equipped with a reflux condenser and a gas exit. To this brown-red mixture was added portionwise $NaBH_4$ (0.3 g, 8 mmol) over a period of 30 min. The addition was accompanied by formation of hydrogen gas and the decoloration of the reaction mixture that indicated complete conversion of the ditelluride to its sodium salt. A solution of tosylate **44** (2.48 g, 6 mmol) in dry THF (30 mL) was then transferred into the flask under argon, and the resulting mixture was heated for 12 h at 80 °C. The solvents were then removed under reduced pressure, and the residue was washed with water and extracted with CH_2Cl_2. The organic layer was dried over magnesium sulfate, filtered, and concentrated. Column chromatography of the residual liquid afforded telluride **45** (2.06 g, 72%) as a yellow liquid: $[\alpha]^{25}_D$ = –76.71° (*c* 0.92, $CHCl_3$); IR ($CHCl_3$, cm^{-1}) 2991, 1707, 1584, 1484, 1456, 1371, 1239, 1040; ^1H NMR δ 1.22, 1.37, 1.44, 1.47 (4 s, 12H), 3.81 (s, 3H), 3.85–4.25 (m, 5H), 4.84 (d, 1H, J = 3.4 Hz), 5.55 (d, 1H, J = 3.4 Hz), 6.8 (d, 2H, J = 8.8 Hz), 7.8 (d, 2H, J = 8.8 Hz); ^{13}C NMR δ 25.0, 26.1, 26.4, 26.7, 33.6, 55.0, 67.7, 78.3, 80.4, 87.8, 99.0, 104.6, 109.4, 111.3, 115.1, 142.2, 160.1; MS (EI, m/z) 477 (0.1), 462 (0.2), 325 (21), 281 (28), 229 (100). Anal. Calcd for $C_{19}H_{26}O_6Te$: C, 47.74; H, 5.48. Found: C, 47.66; H, 5.45.

3β-[((Trifluoromethyl)phenylmethyl)imino]-3-deoxy-1,2:5,6-di-*O*-isopropylidene-D-glucofuranose (46). Telluride **45** (150 mg, 0.31 mmol) and diazirine **13** (1.15 g, 6.2 mmol) were dissolved in dry dichloromethane (5 mL) at 0–5 °C under argon. To this mixture was added **3e** (10 mg, 0.06 mmol) at 20-min intervals (180 mg total weight of **3e**) while the solution was photolyzed with two tungsten lamps (GE, 150 W). The progress of the reaction was monitored by TLC. When all the telluro carbohydrate had reacted, the solvent was removed in vacuum followed by Kugelrohr distillation to recover most of the excess **13**. Imine **46** (122 mg, 95%) was isolated as a clear liquid from the residue by column chromatography on silica gel (hexanes/ether, 8:2): $[\alpha]^{25}_D$ = –2.41° (*c* 2.88, $CHCl_3$); IR ($CHCl_3$, cm^{-1}) 2890, 1706, 1678, 1372, 1198, 1142, 1076, 971, 770; ^1H NMR δ 1.30, 1.32, 1.34, 1.47 (4 s, 12H), 3.90–4.20 (m, 5H), 4.36 (d, 1H, J = 3.6 Hz), 6.1 (d, 1H, J = 3.6 Hz), 7.35–7.52 (m, 5H); ^{13}C NMR δ 25.3, 26.3, 26.7, 26.8, 67.8, 68.0, 72.7, 82.1, 85.3, 105.9, 109.0, 112.0, 127.9, 128.7, 129.7, 130.2; MS (EI, m/z) 415 (0.1), 400 (38), 342 (61), 286 (65), 227 (71), 198 (80), 158 (51), 101 (100). Anal. Calcd for $C_{20}H_{24}F_3NO_5$: C, 57.83; H, 5.82. Found: C, 58.21; H, 6.18.

3-Acetamido-3-deoxy-1,2:5,6-di-*O*-isopropylidene-D-glucofuranose (48). To a solution of imine **46** (100 mg, 0.24 mmol) in ethanol (6 mL) and water (1 mL) was added $B(OH)_3$ (30 mg, 0.5 mmol), and the resulting mixture was heated at 80 °C for 8 h. The solvents were then removed under reduced pressure, and the residue was poured into water (15 mL) and extracted twice with CH_2Cl_2. The organic layer was dried over magnesium sulfate, filtered, and concentrated to 5 mL. To this solution

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was added dry pyridine (5 mL) followed by the addition of acetic anhydride (50 mg, 0.5 mmol). The reaction mixture was then stirred at room temperature overnight. The solvents were then removed under vacuum, and the residue was washed with water and extracted with CH_2Cl_2. The organic layer was dried and concentrated. Acetamide **48**[51] was obtained after recrystallization from $CHCl_3$/hexanes (56 mg, 78%): mp 94–96 °C ($CHCl_3$/hexanes), $[\alpha]^{25}_D = -44.1°$ (*c* 1.2, $CHCl_3$); IR ($CHCl_3$, cm^{-1}) 3621, 3018, 2400, 1672, 1508, 1421, 1374, 1213, 1017; ^1H NMR δ 1.23, 1.29, 1.37, 1.44 (4 s, 12H), 1.94 (s, 3H), 3.8 (dd, 1H, J_1 = 6.4 Hz, J_2 = 6 Hz), 4.0–4.15 (m, 2H), 4.25–4.4 (m, 2H), 4.52 (d, 1H, J = 4 Hz), 5.8 (m, 1H, J = 4 Hz), 6.65 (b d, 1H, J = 6.8 Hz); ^{13}C NMR δ 23.1, 24.9, 25.9, 26.4, 26.5, 55.9, 66.7, 73.0, 77.3, 84.1, 104.1, 109.6, 111.8, 149.5, 170.0; MS (EI, *m/z*) 301 (0.2), 286 (100), 228 (61), 207 (63), 168 (61), 142 (91), 101 (80), 85 (77).

3β-(2-Pyridylthio)-3-deoxy-1,2:5,6-di-*O*-isopropylidene-D-glucofuranose (40). To a refluxing solution of xanthate **38** (0.7 g, 2 mmol) in dry methylene chloride (10 mL) was added portionwise (10 times over a period of 2 h) thiohydroxamate **3e** (1 g, 6 mmol) while the mixture was continuously irradiated with two tungsten lamps (GE, 150 W). The consumption of the starting material was followed by TLC. After evaporation of the solvent, the residue was chromatographed on silica gel and gave **40** as a white solid (0.54 g, 77%): mp 138–139 °C (CH_2Cl_2/hexanes), $[\alpha]^{25}_D = -56.7°$ (*c* 3.6, $CHCl_3$); IR ($CHCl_3$, cm^{-1}) 2990, 1577, 1450, 1373, 1063; ^1H NMR δ 1.31, 1.32, 1.42, 1.57 (4 s, 12H), 4.1 (m, 2H), 4.3 (m, 1H), 4.42 (dd, 1H, J_1 = 3.9 Hz, J_2 = 4 Hz), 4.6 (d, 1H, J = 4 Hz), 4.7 (d, 1H, J = 3.6 Hz), 5.9 (d, 1H, J = 3.6 Hz), 6.99 (m, 1H), 7.20 (m, 1H), 7.5 (m, 1H), 8.5 (m, 1H); ^{13}C NMR δ 25.1, 26.3, 26.6, 26.8, 50.1, 67.5, 74.1, 79.2, 86.3, 104.8, 109.4, 112.0, 119.8, 122.8, 135.9, 149.7, 156.6; MS (EI, *m/z*) 353 (4), 338 (60), 252 (21), 194 (100). Anal. Calcd for $C_{17}H_{23}NO_5S$: C, 57.77; H, 6.56; N, 3.96. Found: C, 57.72; H, 6.59; N, 3.95.

X-ray Crystallographic Analysis for Compounds 15 and 33d. Colorless plates [0.1 × 0.38 × 0.41 mm] of **15** and [0.01 × 0.15 × 0.22 mm] of **33d** were mounted on glass fibers with epoxy cement at room temperature. The crystal of **15** was cooled to 165 K in a N_2 cold stream (Siemens LT-2) while the crystal of **33d** was kept at room temperature. Preliminary examination and data collection were performed on a Siemens R3m/V X-ray diffractometer (oriented graphite monochromator; Mo Kα λ = 0.71073-Å radiation) for **15** and on a Rigaku AFC5R X-ray diffractometer (oriented graphite monochromator; Cu Kα λ = 1.54178-Å radiation) for **33d**. Cell parameters for **15** (monoclinic, $P2_1/c$ (No. 14) α = 14.858(4) Å, b = 5.190(2) Å, c = 15.394(4) Å, β = 113.79(2)°, V = 1086.2(6) Å^3, D_x = 1.616 g cm^{-3}, μ = 0.317 mm^{-1}, Z = 4, F(000) = 536 e$^-$) and **33d** (monoclinic, $C2/c$ (No. 15) a = 22.633(4) Å, b = 13.422(2) Å, c = 7.497(1) Å, β = 103.69(1)°, V = 2212(1) Å^3, D_x = 1.388 g cm^{-3}, μ = 1.078 mm^{-1}, Z = 4, F(000) = 952 e$^-$) were calculated from the least-squares fitting of the setting angles for 25 and 50 carefully selected reflections for **15** and **33d**, respectively. Omega scans for several intense reflections indicated good crystal quality for both crystals.

Data were collected for $4.0° \le 2\theta \le 50.0°$ [θ–2θ scans, $-17 \le h \le 16$, $-6 \le k \le 0$, $0 \le l \le 18$] at 165 K for **15** and for $5.0° \le 2\theta \le 120.0°$ [θ–2θ scans, $0 \le h \le 25$, $0 \le k \le 15$, $-8 \le l \le 8$] at 296 K for **33d**. Scan range, on ω, for the data collection was 2.00° plus Kα separation for **15** and $0.945 + 0.30 \tan(\theta)°$ for **33d**. Both data sets were collected with variable scan rates (for **15**, 2.0–14.7° min^{-1} and for **33d**, 4.0–16° min^{-1}). For **33d**, weak reflections were rescanned for added precision. Three control reflections, collected every 97 reflections for **15** and **33d**, showed no significant trends. Background measurements for **15** and **33d** were by the stationary-crystal and stationary-counter technique at the beginning and end of each scan for 0.50 min of the total scan time.

Lorentz and polarization corrections were applied to 2212 reflections for **15** and 1785 reflections for **33d**. A semiempirical absorption correction was applied to both data sets (for **15**, T_{max} = 0.9760, T_{min} = 0.8257 and for **33d**, T_{max} = 0.9990, T_{min} = 0.9080). A total of 1364 unique reflections (R_{int} = 0.05),[52] with $|I| \ge 2.0\sigma I$ for **15**, and a total of 894 unique reflections (R_{int} = 0.03),[52] with $|I| \ge 2.0\sigma I$ for **33d**, were used in further calculations. The structures of **15** and **33d** were solved by direct methods [SHELXLS, SHELXTL-PLUS program package, Sheldrick (1990)].[53] Full-matrix least-squares anisotropic refinement for all non-hydrogen atoms [SHELXLS, SHELXTL-PLUS program package, Sheldrick (1990); number of least-squares parameters = 155 for **15** and 146 for **33d**; quantity minimized $\sum w(F_o - F_c)^2$; $w^{-1} = \sigma^2 F + gF^2$, g = 0.00010 for **15** and g = 0.000001 for **33d**][53] yielded R = 0.054, R_w = 0.074, and S = 2.96 for **15** and R = 0.051, R_w = 0.051, and S = 1.34 for **33d** at convergence[52] [largest Δ/σ = 0.0016 for **15** and 0.0006 for **33d**; mean Δ/σ = 0.0002 for **15** and 0.0002 for **33d**; largest positive peak in the final Fourier difference map = 0.54 e$^-$ Å^3 for **15** and 0.18 e$^-$ Å^3 for **33d**; largest negative peak in the final Fourier difference map = –0.42 e$^-$ Å^3 for **15** and –0.20 e$^-$ Å^3 for **33d**]. The extinction coefficient χ {where $F^* = F_c/[1 + 0.002\chi F_c^2/\sin(2\theta)]^{0.25}$} was refined to 0.0003(3) for **15** and 0.0008(2) for **33d**.[54] For **15** and **33d**, the hydrogen atoms were placed in idealized positions with isotropic thermal parameters fixed at 0.08 Å^2. Neutral-atom scattering factors and anomalous scattering correction terms were taken from *International Tables for X-ray Crystallography*.[55,56]

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Supplementary Material Available: Tables of atomic coordinates, bond lengths, and bond angles for compounds **15** and **33d** (10 pages); tables of observed and calculated structure factors (13 pages). Ordering information is given on any current masthead page.

(51) The different data previously reported for compound **48** prompted us to prepare this compound by the literature method (ref 36). The compound thus prepared was recrystallized from $CHCl_3$/hexanes and had mp = 95–96 °C, $[\alpha]^{25}_D$ –43.4° (*c* 0.75, $CHCl_3$), in accordance with the data reported in ref 36b. The lower values for the melting point and optical rotation reported in ref 36a are presumably due to the different recrystallization solvent system (H_2O, MeOH) used in this work.

(52) Residuals: $R_{int} = [\sum F^2 - (F_{mean})^2]/[\sum F^2]$; $R = \sum|F_o - F_c|/\sum F_o$; $R_w = \{[\sum w(F_o - F_c)^2]/[\sum w(F_o)^2]\}^{1/2}$; $S = \{[\sum w(F_o - F_c)^2]/[N_{data} - N_{parameters}]\}^{1/2}$.

(53) All crystallographic calculations were performed with SHELXTL-PLUS (4.11) (Sheldrick, G. M. Institut für Anorganische Chemie der Universität, Tammannstrasse 4, D-3400, Göttingen, Germany).

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