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Oxidation of Alcohols to Carbonyl Compounds with Diisopropyl Azodicarboxylate Catalyzed by Nitroxyl Radicals

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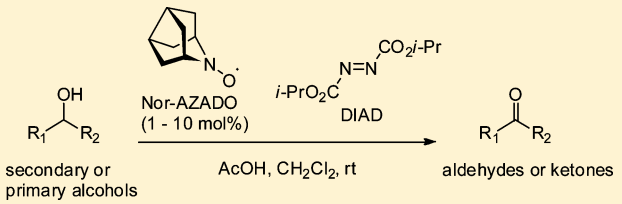
Supporting Information

ABSTRACT: A nitroxyl-radical-catalyzed oxidation of alcohols using diisopropyl azodicarboxylate (DIAD) as the terminal oxidant is reported. A variety of primary and secondary alcohols including aliphatic, benzylic, and allylic alcohols are efficiently oxidized to their corresponding aldehydes and ketones without overoxidation to carboxylic acid. 1,2-Diols are oxidized to hydroxyl ketones or diketones depending on the amount of DIAD used.



The oxidation of alcohols to their corresponding carbonyl compounds is one of the most fundamental transformations in organic synthesis, and numerous methods have been developed.[1] In recent years, a stable class of nitroxyl radicals, as exemplified by 2,2,6,6-tetramethyl piperidinyl 1-oxyl [TEMPO (**1**); Figure 1], have been extensively used as a catalyst for alcohol oxidation in a wide range of chemistry.[2,3] Typically, TEMPO-based oxidations are carried out in the presence of a catalytic amount of TEMPO and a stoichiometric amount of bulk oxidants. Positive halogen source reagents such as NaOCl[3l] are often used as bulk oxidants for TEMPO-based oxidations. Although they are useful reagents from a practical viewpoint, they often suffer from the undesirable halogenation of electron-rich moieties such as double bonds and aromatic rings. To prevent these side reactions, bis(acetoxy)iodobenzene (BAIB) is often used as a mild bulk oxidant.[3j]

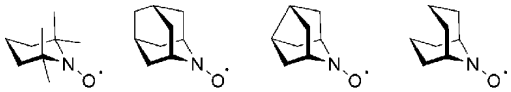


Figure 1. Structures of TEMPO and AZADOs.

We have recently disclosed that 2-azaadamantane-, 9-azanoradamantane-, and 9-azabicyclo[3.3.1]nonane-type nitroxyl radicals (AZADOs; AZADO (**2**),[4a,f] Nor-AZADO (**3**),[4c] and ABNO (**4**);[4d] Figure 1), which form a less-hindered class of nitroxyl radicals, exhibit significantly enhanced reactivity compared with TEMPO.[4] They exhibit extremely high activities toward a wide range of alcohols, including structurally hindered secondary alcohols that cannot be efficiently oxidized by TEMPO. With our continued interest in AZADOs-based oxidation, we have searched for a mild terminal oxidant that allows for a chemoselective oxidation of alcohols with electron-rich functionalities. We report herein an AZADO-catalyzed oxidation method using diisopropyl azodicarboxylate (DIAD) as the terminal oxidant.

Dialkyl azodicarboxylates, as exemplified by DIAD and diethyl azodicarboxylate (DEAD), are useful reagents in organic synthesis, especially as a Mitsunobu reagent.[5,6] They are also versatile for promoting some particular transformations including alcohol oxidation, azo-ene reaction, and hetero-Diels–Alder reaction.[7,8] Alcohol oxidation by DEAD was first reported by Yoneda et al. in 1966 with a limited number of examples.[7d] Recently, alcohol oxidation by a combination of DEAD and a Lewis acid has been reported.[8] Some primary and secondary alcohols have been oxidized to their corresponding carbonyl compounds by this method; unfortunately, the method could not be applied to allylic or propargylic alcohols because of unwanted side reactions. The oxidation of hydroxylamines to nitroso compounds by DEAD under low temperatures has also been reported.[7b] Inspired by this report, we envisioned that dialkyl azodicarboxylate is a potential oxidant for converting a nitroxyl radical into its corresponding oxoammonium ion, which is a selective and efficient oxidant for alcohols.

We first investigated the use of dialkyl azodicarboxylate as a mild bulk oxidant for AZADO-catalyzed alcohol oxidation. The initial experiment was carried out using ABNO as the catalyst and DIAD as the bulk oxidant (Table 1).

We first treated 4-phenyl-2-butanol (**5**) with 1 mol % ABNO and 1.2 equiv of DIAD in CH_2Cl_2 at room temperature; almost no oxidation was observed even after 48 h (entry 1). We tested some additives and found that the reaction proceeds in the presence of acetic acid (entry 2).[9] The result of the control experiment carried out in the absence of ABNO indicated that ABNO mediates this oxidation (entry 3). The reaction rate and

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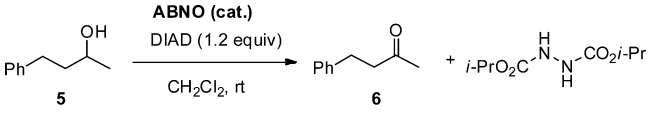
Table 1. Investigation of Reaction Conditions



5 6

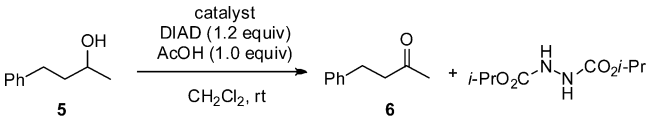
entry[a]	ABNO (mol %)	additive (equiv)	CH_2Cl_2 (M)	time (h)	yield (%)
1	1		0.5	48	trace
2	1	AcOH (1)	0.5	48	80
3		AcOH (1)	0.5	48	1
4	1	AcOH (1)	1.0	48	88
5	1	AcOH (0.1)	1.0	48	25
6	1	AcOH (2)	1.0	48	86
7	3	AcOH(1)	1.0	24	88

[a]The reactions were carried out with DIAD (1.2 equiv) at room temperature.

yield were enhanced by increasing the concentration and the catalyst loading amount (entries 4, 7).

We next compared the catalytic efficiencies of some nitroxyl radicals in this system (Table 2). Nor-AZADO and AZADO

Table 2. Comparison of Catalytic Efficiency of Nitroxyl Radicals[a]



5 6

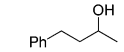
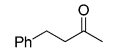
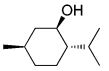
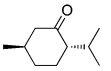
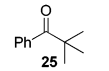
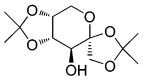
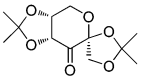
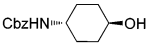
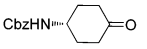
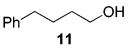
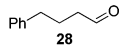
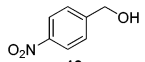
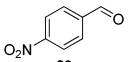
	yield (%)			
catalyst loading (mol %)	ABNO	AZADO	Nor-AZADO	TEMPO
1	88 (48 h)	81(24 h)	97 (24 h)	
3	88 (24 h)	96 (24 h)	99 (24 h)	1(24 h)

[a]The reactions were carried out with DIAD (1.2 equiv) and AcOH (1 equiv) in CH_2Cl_2 (1 M) at room temperature.

gave comparable results with a loading amount of 3 mol % and showed superior catalytic efficiency compared to ABNO. Note that TEMPO did not work as a catalyst in this system. The difference between Nor-AZADO and AZADO became apparent when the catalyst loading amount was decreased to 1 mol %; the reaction was completed within 24 h with 1 mol % Nor-AZADO to give **6** in excellent yield, whereas the oxidation using 1 mol % AZADO was not completed. We also tested azo-compounds other than DIAD, such as diphenyl azodicarboxylate (DPAD), 1,1′-(azodicarbonyl) dipiperidine (ADD), azodicalboxamide, azobenzene, and 2,2′-azopyridene, and none of them worked effectively.[10]

Having identified the optimum reaction conditions, we explored the substrate applicability to the oxidation system using Nor-AZADO as the catalyst (Table 3). A variety of alcohols were efficiently oxidized to their corresponding carbonyl compounds with 1−10 mol % catalyst. Aliphatic and benzylic secondary alcohols, including a sugar derivative (**9**), an *N*-protected amine (**10**), a nucleoside derivative (**18**), and a pyridine derivative (**20**), were effectively oxidized (entries 1−7, 19, 22, 23). Relatively acid-labile isopropylidene and TBS-protecting group remained after the reaction (entries 6, 19). Primary alcohols were also oxidized to their corresponding aldehydes in high yield without overoxidation to carboxylic acids (entries 8−17, 24, 25). Note that 4-thiomethylbenzyl

Table 3. Scope of the Nor-AZADO/DIAD/AcOH System

entry[a]	substrate	Nor-AZADO (mol%)	time (h)	temp	product	yield (%)
1		1	24	rt		97
2	5	1	8	reflux	6	99
3		3	48	rt		95
4	7	3	8	reflux	24	90
5		1	24	reflux		87
	8				25	
6		1	10	reflux		91
	9				26	
7[b]		3	11	reflux		90
	10				27	
8		3	5	rt		86
	11				28	
9		3	5	rt		95
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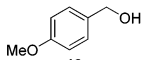
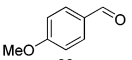
11		3	2.5	rt		98
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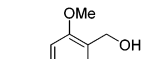
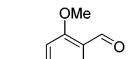
13		3	3	rt		95
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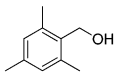
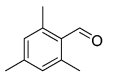
15		1	5.5	reflux		96
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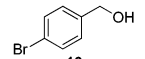
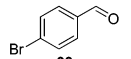
16		1	2	reflux		93
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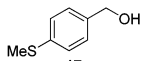
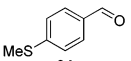
17		1	1.5	reflux		93
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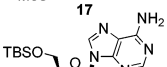
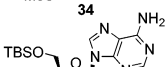
18[d]		3	24	rt		19
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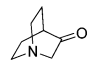
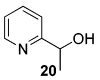
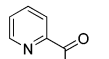
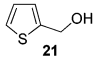
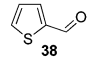
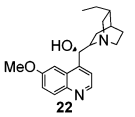
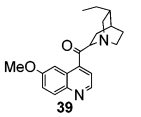
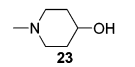
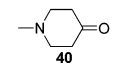
20[c,d]		3	34	rt		24
21[c,d]	19	10	8	rt	36	87
22		3	8	rt		87
23	20	1	5	reflux	37	78
24		3	5	rt		90
25	21	1	2	reflux	38	89
26[c,d]		10	24	rt		0
	22				39	
27[c,d]		10	24	rt		0
	23				40	

[a]The reactions were carried out with DIAD (1 equiv) and AcOH (1 equiv) in CH_2Cl_2 (1 M) unless otherwise noted. [b]1.1 equiv of DIAD was used. [c]2 equiv of DIAD was used. [d]2 equiv of AcOH was used.

alcohol (**17**) having a sulfide group was oxidized chemoselectively to its corresponding aldehyde (**34**) (entry 17).

We also tested some substrates containing amine functionalities. In the case of 3-quinuclidinol (**19**), its corresponding ketone was obtained in high yield, although 10 mol % catalyst was needed

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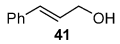
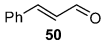
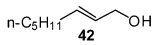
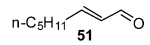
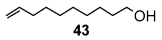
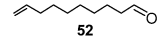
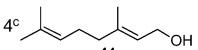
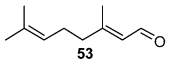
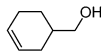
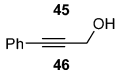
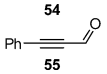
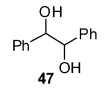
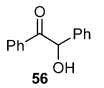
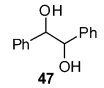
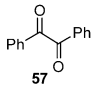
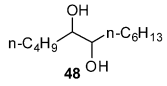
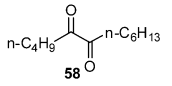
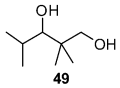
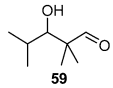
(entry 21). However, the reaction failed to proceed in the cases of other aminoalcohols such as **22** and **23** (entries 26, 27).

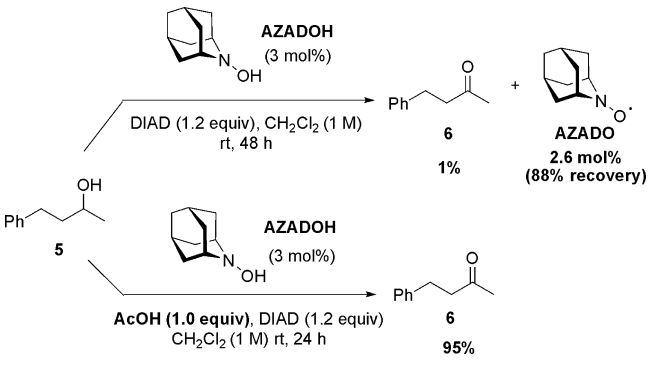
We then tested double- and triple-bond-containing substrates and diols (Table 4). A variety of double-and triple-bond-containing alcohols were oxidized in high yield at room temperature (entries 1–6). Note that 1,2-diol was oxidized to a hydroxyl ketone or a diketone depending on the amount of DIAD used (entries 7–9).[11] Primary alcohol was oxidized selectively over secondary alcohol in the case of the diol **49**, which has both primary and secondary alcohols (entry 10).

Table 4. Scope of the Nor-AZADO/DIAD/AcOH System

entry[a]	substrate	Nor-AZADO (mol%)	time (h)	temp	product	yield (%)
1[b]	 **41**	1	10	rt	 **50**	97
2	 **42**	3	8	rt	 **51**	87
3	 **43**	3	5	rt	 **52**	85
4[c]	 **44**	3	3	rt	 **53**	87
5	 **45**	3	8	rt	 **54**	81
6	 **46**	3	4	rt	 **55**	90
7	 **47**	3	6	rt	 **56**	89
8[d]	 **47**	3	6	reflux	 **57**	92
9[d]	 **48**	3	24	rt	 **58**	81
10	 **49**	3	5.5	rt	 **59**	83

[a]The reactions were carried out with DIAD (1 equiv) and AcOH (1 equiv) in CH_2Cl_2 (1 M) unless otherwise noted. [b]1.2 equiv of DIAD was used. [c]1.1 equiv of DIAD was used. [d]2 equiv of DIAD was used.

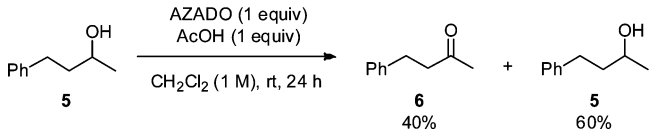
Scheme 1. Oxidation with Hydroxyl Amine



AZADOH and DIAD in the absence of acetic acid; almost no alcohol oxidation was observed after 48 h, but AZADOH was oxidized to a nitroxyl radical, AZADO. In contrast, alcohol oxidation proceeded smoothly in the presence of acetic acid with AZADOH to give **6** in high yield. These results indicate that AZADO is not oxidized into an oxoammonium ion, which is an active oxidant of typical nitroxyl-radical-catalyzed alcohol oxidation, by DIAD in the absence of acetic acid. Thus, the oxoammonium salt was thought to be generated by an acid-catalyzed disproportionation of the nitroxyl radical.[2f,12,13]

We conducted the oxidation of **5** with stoichiometric amount of AZADO and acetic acid in the absence of DIAD, wherein **6** was obtained in 40% yield, indicating that about half the amount of the active oxoammonium salt was generated from AZADO by acid disproportionation (Scheme 2).

Scheme 2. Oxidation with Nitroxyl Radical and Acetic Acid



On the basis of the above observations, we propose a possible reaction pathway (Figure 2). Two molecules of AZADO were disproportionated to give AZADOH and an oxoammonium salt with the aid of acetic acid. The oxoammonium salt thus generated oxidizes an alcohol to give its corresponding carbonyl compound and AZADOH. AZADOH is then converted to AZADO by DIAD to establish the catalytic cycle.

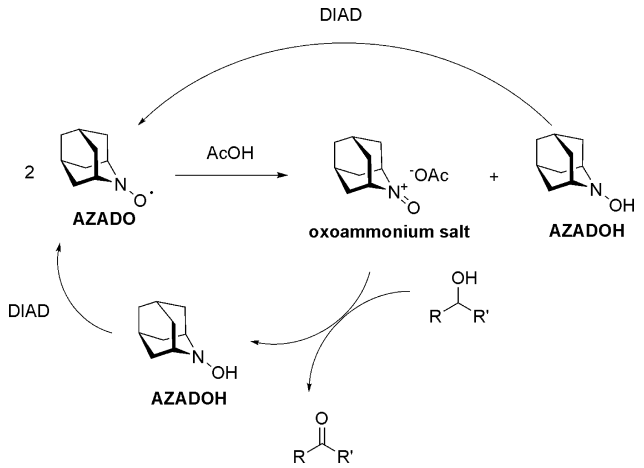


Figure 2. Proposed reaction pathway for alcohol oxidation with DIAD/AcOH/AZADOs.

In conclusion, we have demonstrated that a combination of AZADOs, DIAD, and acetic acid is an efficient system for alcohol oxidation. The described procedure is simple, mild, and applicable to a variety of alcohols including 1,2-diol. This mild system would find good use in the alcohol oxidation of a variety of substrates that cannot tolerate strong oxidants.

EXPERIMENTAL SECTION

General Experimental Procedures. The reagents were purchased from commercial sources and used without further purification, unless otherwise stated. Reactions were monitored by thin-layer chromatography (TLC) carried out on 0.25 mm Merck silica gel plates (60F-254). Column chromatograpy was performed using silica gel 60 (particle size, 0.063–0.210 mm). The eluents employed are reported as volume:volume percentages.

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Chemical shift (δ) is reported in parts per million (ppm) downfield relative to tetramethylsilane (TMS) or $CDCl_3$ (77.10 ppm). Coupling constants (J) are reported in Hz. Multiplicities are reported using the following abbreviations: s, singlet; d. doublet; t, triplet; q, quartet; m, multiplet; br, broad.

Representative Procedure for Oxidation of Alcohols. A solution of 4-phenyl-2-butanol (**5**) (97.7 mg, 0.651 mmol), Nor-AZADO (90.0 μg, 0.00651 mmol), acetic acid (37.0 μL, 0.651 mmol), and DIAD (0.128 mL, 0.651 mmol) in CH_2Cl_2 (0.65 mL) was refluxed with stirring for 8 h. Saturated $NaHCO_3$ (2 mL) was added and extracted with CH_2Cl_2. The organic layer was dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by silica gel column chromatography [hexane/Et_2O (4:1 v/v)] to afford 2-phenyl-butan-2-one (**6**) (95.1 mg, 0.642 mmol, 99%) as a colorless oil.

4-Phenylbutan-2-one (6). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.28 (m, 2H), 7.22−7.16 (m, 3H), 2.89 (t, J = 7.5 Hz, 2H), 2.75 (m, 2H), (t, J = 7.5 Hz, 2H), 2.14 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 207.8, 140.9, 128.4, 128.2, 126.0, 45.1, 30.0, 29.6. IR (neat, cm^{-1}): 1717. MS m/z: 148 (M^+), 148 (100%). HRMS (EI) calcd for $C_{10}H_{12}O$: 148.0888, found 148.0873.

Menthone (24). ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.35 (ddd, J = 12.8, 3.7, 2.3 Hz, 1H), 2.18−1.81 (m, 6H), 1.43−1.29 (m, 2H), 1.01 (d, J = 6.3 Hz, 3H), 0.91 (d, J = 6.8 Hz, 3H), 0.85 (d, J = 6.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 212.3, 55.8, 50.8, 35.4, 33.9, 27.8, 25.8, 22.2, 21.2, 18.6. IR (neat, cm^{-1}): 1711. MS m/z: 154 (M^+), 112 (100%). HRMS (EI) calcd for $C_{10}H_{18}O$: 154.1358, found 154.1343.

2,2-Dimethyl-1-phenylpropan-1-one (25). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.68 (d, J = 7.3 Hz, 2H), 7.48−7.38 (m, 3H), 1.35 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 209.2, 138.6, 130.7, 128.0, 127.8, 44.1, 28.0. IR (neat, cm^{-1}): 1676. MS m/z: 162 (M^+), 105 (100%). HRMS (EI) calcd for $C_{11}H_{14}O$: 162.1045, found 162.1050.

1,2:4,5-Di-*O*-isopropylidene-*β*-D-*erythro*-2,3-hexadiulo-2,6-pyranose (26). ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.73 (d, J = 5.6 Hz, 1H), 4.61 (d, J = 9.4 Hz, 1H), 4.53(m, 1H), 4.39 (dd, J = 13.5, 2.2 Hz, 1H), 4.12 (d, J = 13.5 Hz, 1H), 4.00 (d, J = 9.4 Hz, 1H), 1.55 (s, 3H), 1.47 (s, 3H), 1.40 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 196.9, 113.8, 110.6, 104.1, 77.9, 75.9, 70.0, 60.1, 27.1, 26.5, 26.0, 26.0. IR (neat, cm^{-1}): 1749. MS m/z: 259 (M^+ + H), 114 (100%). HRMS (EI) calcd for $C_{12}H_{19}O_6$: 259.1182 (M^+ + H), found 259.1164.

***trans*-4-Carbobenzyloxiaminocyclohexanone (27).** ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.37−7.31 (m, 5H), 5.12 (s, 2H), 4.75 (br s, 1H), 3.99 (br s, 1H), 2.45−2.40 (m, 4H), 2.28−2.24 (m, 2H), 1.75−1.59 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 209.5, 155.6, 136.3, 128.5, 128.2, 128.1, 66.8, 47.9, 38.8, 32.1. IR (neat, cm^{-1}): 1704, 1530. MS m/z: 247 (M^+), 91 (100%). HRMS (EI) calcd for $C_{14}H_{17}NO_3$: 247.1208, found 247.1206.

4-Phenylbutanal (28). ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.74 (d, J = 1.5 Hz, 1H), 7.30−7.15 (m, 5H), 2.65 (t, J = 7.7 Hz, 2H), 2.43 (dt, J = 7.2, 1.5 Hz, 2H), 1.95 (tt, J = 7.7, 7.2 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 202.2, 141.2, 128.4, 128.3, 126.0, 43.1, 34.9, 23.6. IR (neat, cm^{-1}): 1724. MS m/z: 148 (M^+), 104 (100%). HRMS (EI) calcd for $C_{10}H_{12}O$: 148.0888, found 148.0873.

***p*-Nirobenzaldehyde (29).** ^{1}H NMR (400 MHz, $CDCl_3$): δ 10.16 (s, 1H), 8.40 (dd, J = 8.8, 1.8 Hz, 2H), 8.08 (dd, J = 8.8, 1.8 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 192.3, 150.6, 140.1, 130.6, 124.2. IR (neat, cm^{-1}): 1709, 1537. MS m/z: 131 (M^+), 151 (100%). HRMS (EI) calcd for $C_7H_5NO_3$: 151.0269, found 151.0253.

***p*-Methoxybenzaldehyde (30).** ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.89 (s, 1H), 7.84 (d, J = 8.7 Hz, 2H), 7.01 (d, J = 8.4 Hz, 2H), 3.89 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 190.7, 164.6, 131.9, 129.9, 114.3, 55.5. IR (neat, cm^{-1}): 1684. MS m/z: 136 (M^+), 135 (100%). HRMS (EI) calcd for $C_8H_8O_2$: 136.0524, found 136.0526.

2,4-Dimethoxybenzaldehyde (31). ^{1}H NMR (400 MHz, $CDCl_3$): δ 10.30 (s, 1H), 7.82 (d, J = 8.7 Hz, 1H), 6.55 (dd, J = 8.4, 2.9 Hz, 1H), 6.45 (d, J = 2.9 Hz, 1H), 3.91 (s, 3H), 3.88 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 188.3, 166.2, 163.6, 130.7, 119.1, 105.7, 97.9, 55.6, 55.6. IR (neat, cm^{-1}): 1670, 1266. MS m/z: 166 (M^+), 166 (100%). HRMS (EI) calcd for $C_9H_{10}O_3$: 166.0630, found 166.0625.

2,4,5-Trimethylbenzaldehyde (32). ^{1}H NMR (400 MHz, $CDCl_3$): δ 10.57 (s, 1H), 6.90 (s, 2H), 2.60 (s, 6H), 2.32 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 192.9, 143.8, 141.4, 130.5, 130.0, 21.4, 20.5. IR (neat, cm^{-1}): 1686. MS m/z: 148 (M^+), 148 (100%). HRMS (EI) calcd for $C_{10}H_{12}O$: 148.0888, found 148.0878.

***p*-Bromobenzaldehyde (33).** ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.98 (s, 1H), 7.75 (d, J = 8.7 Hz, 1H), 7.69 (d, J = 8.2 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 191.0, 135.1, 132.4, 130.9, 129.8. IR (neat, cm^{-1}): 1688, 1066. MS m/z: 184 (M^+), 185 (100%). HRMS (EI) calcd for C_7H_5BrO: 183.9524, found 183.9523.

***p*-(Methylthio)benzaldehyde (34).** ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.92 (s, 1H), 7.77 (d, J = 8.7 Hz, 2H), 7.33 (d, J = 8.2 Hz, 2H), 2.54 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 191.2, 147.9, 133.0, 130.0, 125.2, 14.7. IR (neat, cm^{-1}): 1695. MS m/z: 152 (M^+), 152 (100%). HRMS (EI) calcd for C_8H_8OS: 152.0296, found 152.0290.

9-(2′,5′-Bis-*O*-(*tert*-butyldimethylsilyl)-*β*-D-*erythro*-pentofuran-3-ulosyl)-9*H*-adenine (35). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.36 (s, 1H), 8.14 (s, 1H), 6.13 (d, J = 8.2 Hz, 1H), 5.85 (br s, 2H), 4.94 (d, J = 8.2 Hz, 1H), 4.29 (br s, 1H), 3.97 (m, 2H), 0.92 (s, 9H), 0.72 (s, 9H), 0.10 (s, 3H), 0.07 (s, 3H), −0.02 (s, 3H), −0.20 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 208.6, 155.5, 153.4, 150.4, 138.5, 119.8, 85.0, 82.4, 77.8, 62.4, 25.8, 25.3, 18.2, 18.0, −4.8, −5.5, −5.6, −5.7. IR (neat, cm^{-1}): 1788, 1647, 1595, 1577. MS m/z: 436 (M^+ − tBu), 301 (100%). HRMS (EI) calcd for $C_{22}H_{39}N_5O_4Si_2$: 493.2541, found 493.2511.

3-Quinoclidinone (36). ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.30 (s, 2H), 3.07−2.89 (m, 4H), 2.46 (quin, J = 3.0 Hz, 1H), 2.03−1.98 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 219.6, 62.8, 46.9, 39.6, 25.6. IR (neat, cm^{-1}): 1725. MS m/z 125 (M^+), 97 (100%). HRMS (EI) calcd for $C_7H_{11}NO$: 125.0841, found 125.0834.

2-Acetylpyridine (37). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.69 (br d, J = 4.1 Hz, 1H), 8.05 (d, J = 8.0 Hz, 1H), 7.84 (td, J = 7.7, 1.7 Hz, 1H), 7.49−7.30 (m, 1H), 2.73 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 200.0, 153.6, 148.9, 136.8, 127.0, 121.6, 25.7. IR (neat, cm^{-1}): 1700; EI-MS m/z: 121 (M^+), 79 (100%). HRMS (EI) calcd for C_7H_7NO: 121.0528, found 121.0529.

2-Thiophencarboxyaldehyde (38). ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.96 (d, J = 1.0 Hz, 1H), 7.80−7.77 (m, 2H), 7.22 (dd, J = 4.8, 3.9 Hz, 1H), 2.54 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 182.9, 144.1, 136.2, 135.1, 128.3. IR (neat, cm^{-1}): 1672, 1419, 729. MS m/z: 112 (M^+), 112 (100%). HRMS (CI) calcd for C_5H_5OS: 113.0061 (M^+ + H), found 113.0066.

Cinnamylaldehyde (50). ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.72 (d, J = 7.8 Hz, 1H), 7.59−7.56 (m, 2H), 7.49−7.42 (m, 4H), 6.74 (dd, J = 15.9, 7.7 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 193.7, 152.7, 134.0, 131.2, 129.1, 128.6, 128.5. IR ($CHCl_3$, cm^{-1}): 1681. MS m/z: 132 (M^+), 131 (100%). HRMS (EI) calcd for C_9H_8O: 132.0575, found 132.0558.

2-Octenal (51). ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.51 (d, J = 7.7 Hz, 1H), 6.85 (dt, J = 15.5, 6.8 Hz, 1H), 6.12 (ddt, J = 15.5, 7.7, 1.4 Hz, 1H), 2.36−2.31 (m, 2H), 1.55−1.28 (m, 2H), 1.37−1.30 (m, 4H), 0.92−0.89 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 194.1, 158.9, 133.0, 32.7, 31.3, 27.5, 22.4, 13.9. IR (neat, cm^{-1}): 1693, 1637. MS m/z: 116 (M^+), 70 (100%). HRMS (EI) calcd for $C_8H_{14}O$: 126.1045, found 126.1050.

9-Decenal (52). ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.77 (d, J = 1.9 Hz, 1H), 5.86−5.75 (m, 1H), 5.02−4.92 (m, 2H), 2.42 (dt, J = 7.2, 1.9 Hz, 2H), 2.04 (tt, J = 7.7, 7.2 Hz, 2H), 1.65−1.61 (m, 2H), 1.40−1.32 (m, 8H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 202.8, 139.0, 114.2, 43.9, 33.7, 29.2, 29.1, 28.8, 28.8, 22.0. IR (neat, cm^{-1}): 1727, 1640. MS m/z: 154 (M^+), 68 (100%). HRMS (EI) calcd for $C_{10}H_{18}O$: 154.1358, found 154.1369.

***trans*-3,7-Dimethyl-2,6-octadienal (53).** ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.99 (d, J = 7.7 Hz, 1H), 5.88 (d, J = 8.2 Hz, 1H), 5.07 (m, 1H), 2.25−2.19 (m, 4H), 2.17 (s, 3H), 1.69 (s, 3H), 1.61 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 191.2, 163.7, 132.9, 127.4, 122.5, 40.6, 25.7, 25.6, 17.7, 17.5. IR (neat, cm^{-1}): 1675, 1632, 1611. MS m/z: 152 (M^+), 69 (100%). HRMS (EI) calcd for $C_{10}H_{16}O$: 152.1201, found 152.1199.

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3-Cyclohexene-1-carboxaldehyde (54). ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.70 (d, J = 0.97 Hz, 1H), 5.74−5.68 (m, 2H), 2.55−2.48 (m, 1H), 2.25−2.23 (m, 2H), 2.13−2.08 (m, 2H), 2.03−1.96 (m, 1H), 1.72−1.62 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 204.4, 127.2, 124.7, 46.0, 24.3, 23.7, 22.1. IR (neat, cm^{-1}): 1729, 1652. MS m/z: 110 (M^+), 79 (100%). HRMS (EI) calcd for $C_7H_{10}O$: 110.0732, found 110.0725.

Phenylpropynal (55). ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.43 (s, 1H), 7.62−7.59 (m, 2H), 7.51−7.47 (m, 1H), 7.43−7.39 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 176.7, 133.3, 131.3, 128.7, 119.5, 95.1, 88.4. IR (neat, cm^{-1}): 2188, 1660, 759. MS m/z: 130 (M^+), 130 (100%). HRMS (EI) calcd for C_9H_6O: 130.0419, found 130.0405.

Benzoine (56). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.93−5.54 (m, 2H), 7.52−7.40 (m, 1H), 7.38−7.23 (m, 7H), 5.95 (d, J = 6.3 Hz, 1H), 4.55 (d, J = 6.3 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 198.9, 139.0, 133.8, 133.5, 129.1, 129.1, 128.6, 128.5, 127.7, 76.2. IR (neat, cm^{-1}): 3414, 1679. MS m/z: 212 (M^+), 105 (100%). HRMS (EI) calcd for $C_{14}H_{12}O_2$: 212.0837, found 212.0829.

Benzil (57). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.99−7.96 (m, 4H), 7.68−7.63 (m, 2H), 7.53−7.49 (t, J = 7.7 Hz, 4H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 194.5, 134.9, 133.0, 129.9, 129.0. IR ($CHCl_3$, cm^{-1}): 1660. MS m/z: 210 (M^+), 105 (100%). HRMS (EI) calcd for $C_{14}H_{10}O_2$: 210.0681, found 210.0679.

5,6-Dodecandion (58). ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.75−2.71 (m, 4H), 1.60−1.53 (m, 4H), 1.37−1.29 (m, 8H), 0.93−0.86 (m, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 200.2, 200.2, 36.1, 35.8, 31.5, 28.8, 25.1, 23.0, 22.4, 22.3, 24.0, 13.8. IR ($CHCl_3$, cm^{-1}): 1711. MS m/z: 199 (M^+ + H), 199 (100%). HRMS (EI) calcd for $C_{12}H_{23}O_2$: 199.1698 (M^+ + H), found 199.1700.

3-Hydroxy-2,2,4-trimethylpentanal (59). ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.62 (s, 1H), 3.55 (dd, J = 5.1, 4.1 Hz, 1H), 2.07 (br d, J = 5.4 Hz, 1H), 1.92−1.84 (m, 1H), 1.12 (d, J = 4.4 Hz, 6H), 0.97 (d, J = 6.8 Hz, 3H), 0.90 (d, J = 6.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 206.7, 80.3, 50.5, 29.9, 21.7, 19.8, 18.6, 17.2. IR (neat, cm^{-1}): 3479, 1714. MS m/z: 145 (M^+ + H), 72 (100%). HRMS (EI) calcd for $C_8H_{17}O_2$: 145.1229 (M^+ + H), found 145.1204.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Copy of NMR spectra This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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(9) We also tested other stronger acids such as trifluoroacetic acid and methansulfonic acid. They were found to be less effective, resulting in lower yields.

(10) The reaction proceeded only when DPAD was used; however, the yield was low (20%) because of unwanted side reactions.

(11) We tested the oxidation of **47** by Nor-AZADO (1 mol%) and BAIB (1.5 equiv) in CH_2Cl_2 at room temperature. This reaction posed an oxidative cleavage of 1,2-diol and afforded benzaldehyde in 60% yield. For examples of oxidative cleavage of 1,2-diol by hypervalent iodine, see: (a) Mu, R.; Liu, Z.; Yang, Z.; Liu, Z.; Wu, L.; Liu, Z.-L. *Adv. Synth. Catal.* **2005**, *347*, 1333−1336. (b) Barton, D. H. R.; Godfrey, C. R. A.; Morzycki, J. W.; Motherwell, W. B.; Stobie, A. *Tetrahedron Lett.* **1982**, *23*, 957−960.

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(13) We observed the generation of oxoammonium ion and hydroxyl amine by acid-catalyzed disproportionation of AZADO by ESI-MS measurement (see Supporting Information).