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Synthesis and cycloadditions of 1-[(*tert*-butyldimethylsilyl)oxy]alkenyl isocyanates

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Summary — 1-[(*tert*-Butyldimethylsilyl)oxy]alkenyl isocyanates **1a** and **1b** have been conveniently prepared from acetyl or propionyl chloride, silver cyanate and *tert*-butyldimethylsilyl triflate in the presence of triethylamine. They react with electron-deficient acetylenic dienophiles or with tosyl cyanide to give highly functionalised pyridines or derivatives of uracil or thymine in moderate yields. They also cycloadd with 1-(diethylamino)prop-1-yne, an electron-rich dienophile, to yield glutaconimides and pyridine derivatives.

alkenyl isocyanate / Diels–Alder reaction / pyridine / uracil / thymine / glutaconimide

Résumé — Synthèse et cycloadditions d'isocyanates de 1-[(*tert*-butyldiméthylsilyl)oxy]alcényle. Les isocyanates de 1-[(*tert*-butyldiméthylsilyl)oxy]alcényle **1a** and **1b** sont facilement préparés à partir de chlorure d'acétyle ou de propionyle, de cyanate d'argent et de triflate de *tert*-butyldiméthylsilyle en présence de triéthylamine. Ils réagissent avec les diénophiles acétyléniques déficients en électrons ou avec le cyanure de tosyle pour donner des pyridines hautement fonctionnalisées et des dérivés de l'uracile ou de la thymine avec des rendements moyens. Ils réagissent également avec le 1-(diéthylamino)prop-1-yne, un diénophile riche en électrons, pour donner des glutaconimides et des dérivés de la pyridine.

isocyanate d'alcényle / réaction de Diels–Alder / pyridine / uracile / thymine / glutaconimide

Introduction

The hetero Diels–Alder reaction has become a powerful tool for the synthesis of six-membered heterocycles as a consequence of the ready availability of many reactive heterodienes [1, 2]. Vinyl isocyanates have been considered by several groups as potentially interesting azadiene partners for hetero Diels–Alder reactions. These studies have shown that alkenyl isocyanates behave as electron-deficient azadienes, reacting with dienophiles such as ynamines [3, 4], enamines [5–8] and β-ketoester enolates [9, 10]. A reaction with benzyne has also been described [11, 12].

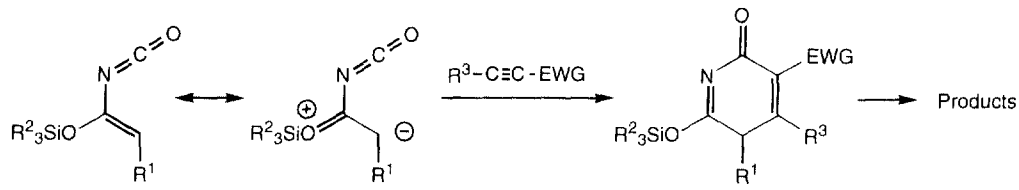
In the context of our studies on 1- and 2-azadienes [13–17], we have considered the possibility of reversing the reactivity of alkenyl isocyanates by the introduction of the electron-releasing trialkylsilyloxy group on the carbon atom bearing the isocyanate group (scheme 1). We present here a study of the synthesis and Diels–Alder reactions of 1-[(*tert*-butyldimethylsilyl)oxy]alkenyl isocyanates **1a** and **1b**.

Synthesis of 1-[(*tert*-butyldimethylsilyl)oxy]-alkenyl isocyanates

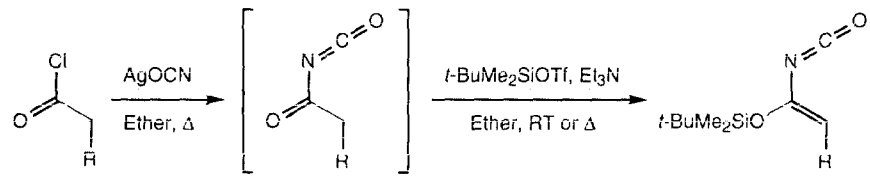
Compounds **1a** and **1b** have been conveniently prepared by a *one-pot* procedure involving (a) the reaction of silver cyanate with acid chlorides **2a** or **2b** to yield the corresponding acyl isocyanates **3a** or **3b**, (b) the silylation of crude **3** with *tert*-butyldimethylsilyl triflate in the presence of triethylamine (scheme 2). This procedure avoids the distillation of the intermediate acyl isocyanate which always led to extensive decomposition and drop of yields.

Compounds **1a** and **1b** are moisture sensitive and must be kept under inert atmosphere in the refrigerator. The IR spectra of **1** show an absorption band at 2260–2240 cm^{-1} indicative of the presence of an N=C=O group. The vinyl protons of **1a** give rise to two doublets at 3.96 (J = 1.6 Hz) and 3.78 ppm (J = 1.6 Hz). The presence of only one quadruplet at 4.42 ppm (J = 6.9 Hz) and one doublet at 1.55 ppm (J = 6.9 Hz) in the ^1H NMR spectrum of **1b** indicates the presence of a single stereoisomer. It was tentatively assigned the (Z)-configuration by analogy with our earlier work on the silylation of N-acyl iminoethers [16].

* Correspondence and reprints



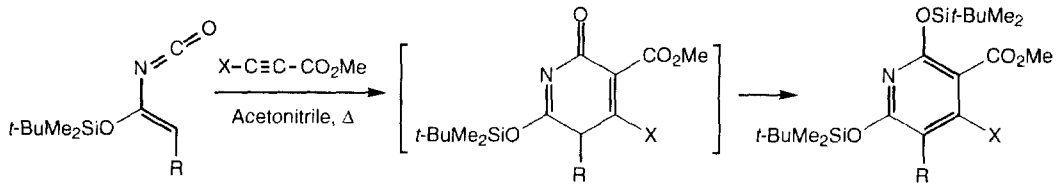
Scheme 1



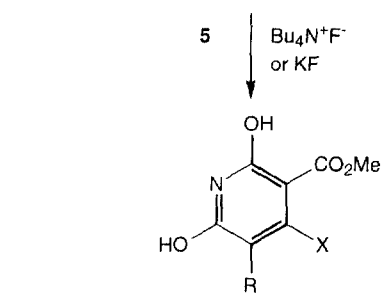
2a or 2b — 3a or 3b

1a, R=H 49%
1b, R=Me 72%

Scheme 2



1a or 1b — 4 — 5

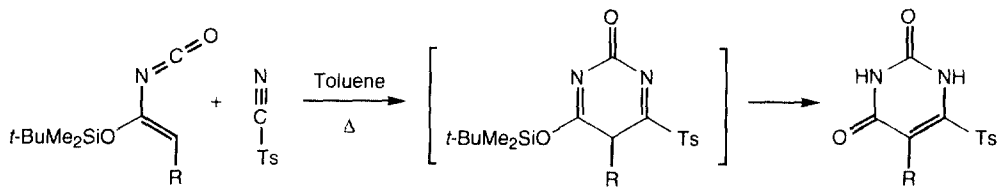


	R	X	5 (%)[1]	6 (%)[1]
a	H	H or CO_2CH_3	-	-
b	CH_3	H	**5b** (23%)[2]	**6b** (39%)
c	CH_3	CO_2CH_3	**5c** (32%)[3]	**6c** (99%)

[1] yields of isolated pure compounds ; [2] from 2 equiv of diene ; [3] from 1 equiv of diene

6

Scheme 3



1a or 1b — 8a or 8b

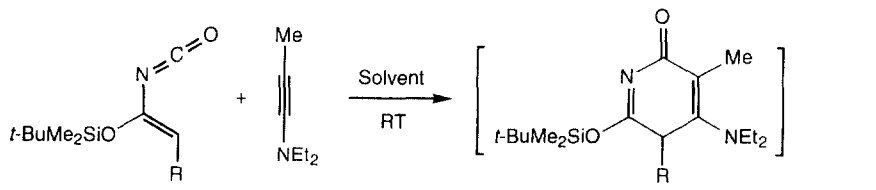
7a, R=H 35%
7b, R=Me 47%

Scheme 4

Cycloadditions with electron-deficient dienophiles

Both alkenyl isocyanates **1a** and **1b** quickly disappeared in the presence of methyl propiolate or dimethyl acetylenedicarboxylate. No Diels–Alder adducts could be isolated from the complex mixtures obtained from **1a** (scheme 3). Compound **1b** gave low yields of **5b** and **5c**. The formation of these heterocycles can be explained by the reaction of a primary adduct **4b** or **4c** with any silylating agent present in the mixture. However, yields were only slightly increased by using an excess of diene. Both compounds **5b** and **5c** could be desilylated in the presence of a source of fluoride ions to yield dihydroxypyridines **6b** and **6c**.

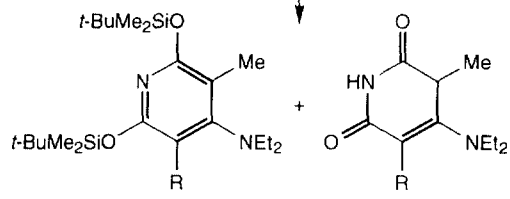
Moderate yields of uracil **7a** and thymine **7b** derivatives were obtained from the reaction of tosyl cyanide with both **1a** and **1b** (scheme 4). They were formed by desilylation of the primary adducts **8a** and **8b** under the work-up conditions. Reaction of **1a** and **1b** with phenylvinyl sulfone and 1,2-difluorovinylphenyl sulfone [18, 19] gave an untractable mixture of products.



1a or **1b**

	R	Solvent	**9** (%)[1]	**10** (%)[1]
a	H	Toluene	**9a** (33%)	**10a** (10%)
b	H	Acetonitrile	**9a** (71%)[2]	**10a** (0%)[2]
c	CH_3	Benzene	**9b** (18%)	**10b** (44%)

[1] yields of isolated pure compounds ; [2] from 2 equiv of diene



9a, R=H
9b, R=Me

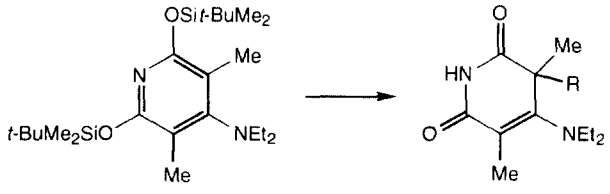
10a, R=H
10b, R=Me

Scheme 5

Cycloadditions with electron-rich dienophiles

The reaction of **1a** and **1b** with 3-pyrrolidinopent-2-ene and 1-pyrrolidinocyclohexene gave no cycloadducts but an unseparable mixture of products. However, both **1a** and **1b** rapidly reacted with 1-(diethylamino)prop-1-yne to give compounds **9** and **10** (scheme 5). Compound **10a** resulted from the desilylation of **9a** during the purification by chromatography on silica gel whereas **10b** was already present in the crude reaction mixture.

Treatment of **9b** with methanol yielded heterocycle **10b** (scheme 6). Interestingly, when the desilylation was performed in the presence of potassium fluoride, α'-hydroxyglutaconimide **11** was isolated in excellent yield. By analogy with earlier examples of autoxidation of enolates [20–23], the formation of **11** can be explained by the mechanism outlined in scheme 7.



9b

10b, R=H
11, R=OH

	Conditions	Desilylated compound (%)
a	MeOH/$CHCl_3$, 60°C, 2 days	**10b** (79%)
b	KF, MeOH/$CHCl_3$, RT, 1 day	**11** (81%)

Scheme 6

Conclusion

In this paper we have reported the first examples of Diels–Alder reactions of an α,β-unsaturated isocyanate with electron-deficient dienophiles. The natural electrophilic reactivity of the 4π system of a vinyl isocyanate can thus be reversed by the introduction of a trialkylsilyloxy substituent at C-3. Nevertheless these highly reactive dienes are of limited synthetic value. In many cases, complex mixtures were formed. This could be the result of the formation of dipolar intermediates which could further react instead of undergoing the ring closure yielding the expected Diels–Alder adduct. Still the above reactions provide highly functionalised aza-heterocycles which would otherwise be difficult to prepare. Interestingly, both isocyanates **1a** and **1b** still reacted with an electron-rich dienophile such as 1-(diethylamino)prop-1-yne.

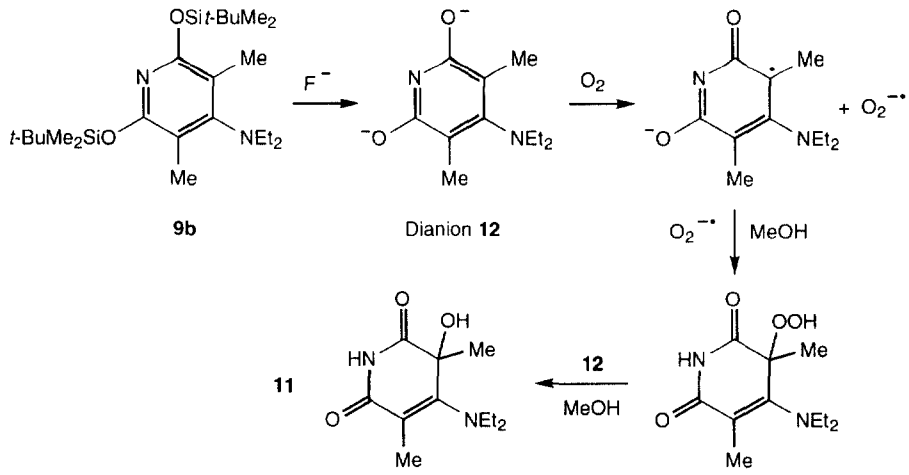
Experimental section

Melting points were measured on a Leitz-Wetzlar HM-LUX apparatus and are uncorrected. IR spectra were recorded on a Perkin-Elmer 681 spectrophotometer. ^1H and ^{13}C NMR spectra were recorded, if not specified, in $CDCl_3$ at 200 and 50 MHz on Gemini-200 and VRX-200, at 300 and 75 MHz on Gemini-300 and at 500 and 125 MHz on Bruker AM-500 spectrometers. Chemical shifts are quoted as δ values from TMS as internal reference. Mass spectra were measured on Finnigan-MAT TSQ-700 (electronic impact 70 eV) and TSQ-7000 (atmospheric pressure chemical ionisation, capillary temperature 250 °C, spray voltage 5.5 kV, sheath gas N_2 50 Psi, auxiliary gas N_2 10 Psi) spectrometers. Microanalyses were performed by the laboratory of Dr Stones, University College of London (UK). HRMS (EI) were performed by the laboratory of Prof Flammang, Université de Mons-Hainaut (Belgium).

All dry solvents were distilled under argon. Diethyl ether, benzene and toluene were distilled from sodium-benzophenone ketyl. Acetonitrile, dichloromethane and triethylamine were distilled from calcium hydride. Acid chlorides were freshly distilled prior to use. All reactions requiring anhydrous or inert conditions were run under a positive pressure of argon. *t*-Butyldimethylsilyl triflate has been prepared according to the procedure described in the literature [24]. The acetylenic dienophiles are commercially available and are used as received.

Synthesis of the dienes

• *1-[(t-Butyldimethylsilyl)oxy]vinyl isocyanate* **1a**
Acetyl chloride (948 μL, 13.33 mmol, 1 equiv) was added dropwise to a suspension of silver cyanate (2.50 g,



Scheme 7

16.68 mmol, 1.25 equiv) in diethyl ether (10 mL). The mixture was refluxed for 2 h 30 min until the IR absorption of the acid chloride had disappeared. The suspension was quickly filtered to remove the silver chloride and the salts were washed with diethyl ether. To this solution were added successively a solution of triethylamine (2.23 mL, 16.00 mmol, 1.2 equiv) in diethyl ether (15 mL) and a solution of *t*-butyldimethylsilyl triflate (3.06 mL, 13.33 mmol, 1 equiv) in diethyl ether (15 mL). The mixture was stirred at room temperature for 2 h. Two layers were formed. The upper layer was removed and the lower layer washed twice with diethyl ether. The combined ethereal fractions were carefully concentrated under vacuum to give crude vinyl isocyanate **1a** (1.99 g, 75% from acetyl chloride). This diene was pure enough to be used as such in the Diels–Alder reactions. It can be further purified by bulb-to-bulb distillation under vacuum to yield **1a** (1.30 g, 49% from acetyl chloride) as a colourless liquid. Bp: 35 °C/0.08 mm Hg.

IR (ether): 2 240, 1 650 cm^{-1}.

^1H NMR (200 MHz): 3.96 (d, J = 1.6, 1H), 3.78 (d, J = 1.6, 1H), 0.93 (s, 9H), 0.21 (s, 6H).

^{13}C NMR: no satisfactory spectrum could be obtained (degradation of **1a** during the analysis).

• *1-[(t-Butyldimethylsilyl)oxy]prop-1-enyl isocyanate* ***1b***

Propionyl chloride (2.48 mL, 28.54 mmol, 1 equiv) was added dropwise to a suspension of silver cyanate (5.35 g, 35.68 mmol, 1.25 equiv) in diethyl ether (25 mL). The mixture was refluxed for 2 h 30 min until the IR absorption of the acid chloride had disappeared. The suspension was then quickly filtered to remove the silver chloride and the salts were washed with diethyl ether. To this solution were added successively a solution of triethylamine (4.77 mL, 34.25 mmol, 1.2 equiv) in diethyl ether (30 mL) and a solution of *t*-butyldimethylsilyl triflate (6.55 mL, 28.54 mmol, 1 equiv) in diethyl ether (30 mL). The mixture was refluxed for 2 h. Two layers were formed. The upper layer was removed and the lower layer washed twice with diethyl ether. The combined ethereal fractions were carefully concentrated under vacuum to give crude vinyl isocyanate **1b** (5.98 g, 98% from propionyl chloride). This diene was pure enough to be used as such in the Diels–Alder reactions. It can be further purified by bulb-to-bulb under vacuum to yield **1b** as a colourless liquid (4.39 g, 72%). Bp: 35 °C/0.04 mm Hg.

IR (ether): 2 960, 2 260, 1 660 cm^{-1}.

^1H NMR (200 MHz): 4.42 (q, J = 6.90, 1H), 1.55 (d, J = 6.90, 3H), 0.95 (s, 9H), 0.20 (s, 6H).

^{13}C NMR (50 MHz): 135.01, 124.57, 96.27, 25.46, 17.94, 10.56, −4.65.

Cycloadditions with electron-deficient dienophiles

• *General procedure for the cycloadditions*

The dienophile was added at room temperature to a solution of the diene. The mixture was refluxed for several hours. Evaporation of the solvent and chromatography on silica gel gave the corresponding adduct.

• *2,6-Bis[(tert-butyldimethylsilyl)oxy]-3-(methoxycarbonyl)-5-methylpyridine* ***5b***

The cycloaddition of diene **1b** (115 mg, 0.54 mmol, 2 equiv) with methyl propiolate (26 μL, 0.27 mmol, 1 equiv) in acetonitrile (1 mL) (Δ, 26 h) yielded after chromatography (SiO_2, dichloromethane/cyclohexane 35:10) **5b** (25 mg, 23%) as a white solid.

IR (CH_2Cl_2): 2 900–2 840, 1 720, 1 610, 1 570, 1 430 cm^{-1}.

^1H NMR (200 MHz): 7.95 (s, 1H), 3.84 (s, 3H), 2.11 (s, 3H), 1.02 (s, 9H), 1.00 (s, 9H), 0.35 (s, 12H).

^{13}C NMR (50 MHz): 166.31 (m), 161.83 (dq, ^3J = 10.90 and 4.30), 158.78 (d, ^3J = 9.30), 144.20 (Dq, ^1J = 160.50, ^3J = 4.70), 114.20 (q, ^2J = 6.30), 104.57 (s), 51.47 (Q, ^1J = 146.61), 25.57 (Qhept, ^1J = 125.33, ^3J = 5.41), 25.38 (Qhept, ^1J = 125.24, ^3J = 5.55), 18.00 (m), 15.33 (Qd, ^1J = 127.84, ^3J = 4.65), −4.37 (Q, ^1J = 119.36), −4.47 (Q, ^1J = 119.80).

MS (EI): m/z = 411 ($M^{+\bullet}$), 396, 380, 354.

• *Desilylation of 2,6-bis[(t-butyldimethylsilyl)oxy]-3-(methoxycarbonyl)-5-methylpyridine* ***5b***

Tetrabutylammonium fluoride (1 M in THF) (1.46 mL, 1.46 mmol, 3 equiv) was added to a solution of **5b** (200 mg, 0.49 mmol, 1 equiv) in dichloromethane (1 mL). The reaction mixture was stirred at room temperature for 1 h 15 min then diluted in 7 mL of dichloromethane and washed with 1% HCl (10 mL). The organic phase was dried over magnesium sulfate and concentrated. The residue was washed with ethyl acetate (15 mL) yielding 2,6-dihydroxy-3-(methoxycarbonyl)-5-methylpyridine **6b** (35 mg, 39%) as a white solid.

Mp: 214–215 °C.

IR (KBr): 2 900–2 820, 1 660 cm^{-1}.

^1H NMR (200 MHz, DMSO-d_6): 12.38 (broad s, 2H), 7.54 (s, 1H), 3.81 (s, 3H), 1.88 (s, 3H).

^{13}C NMR (125 MHz, DMSO-d_6): 168.84, 163.10, 161.37, 135.95, 117.95, 87.94, 52.05, 15.12.

MS (EI): m/z = 183 ($M^{+\cdot}$), 151, 123, 95.

HRMS calc for $C_8H_9NO_4$: 183.0532. Found: 183.0539 (Δ −4.1 ppm).

• *2,6-Bis[(t-butyldimethylsilyl)oxy]-3,4-di(methoxycarbonyl)-5-methylpyridine* **5c**

The reaction of diene **1b** (451 mg, 2.11 mmol, 1 equiv) with dimethyl acetylenedicarboxylate (293 μL, 2.39 mmol, 1.1 equiv) in acetonitrile (5 mL) (Δ, 17 h) yielded after chromatography (SiO_2, dichloromethane) **5c** (320 mg, 32%) as a white solid. Mp: 100.6–101.9 °C.

IR (CH_2Cl_2): 2 955–2 860, 1 740, 1 710, 1 575, 1 440, 1 410 cm^{-1}.

^{1}H NMR (500 MHz): 3.87 (s, 3H), 3.78 (s, 3H), 2.05 (s, 3H), 0.96 (s, 9H), 0.95 (s, 9H), 0.32 (s, 6H), 0.30 (s, 6H).

^{13}C NMR (125 MHz): 167.86 (q, ^3J = 4.10), 166.21 (q, ^3J = 3.90), 161.37 (q, ^3J = 3.90), 157.70 (s), 146.59 (q, ^3J = 4.60), 112.21 (q, ^2J = 6.20), 106.56 (s), 52.44 (Q, ^1J = 147.46), 51.95 (Q, ^1J = 147.16), 25.49 (Qhept, ^1J = 147.46, ^3J = 5.44), 25.23 (Qhept, ^1J = 125.28, ^3J = 5.45), 17.94 (m), 17.88 (m), 12.45 (Q, ^1J = 128.90), −4.48 (Qm, ^1J = 119.78), −4.56 (Qm, ^1J = 119.80).

MS (APCI): m/z = 470 ($(M + H)^+$), 454, 438.

HRMS calc for $C_{18}H_{30}NO_6Si_2$ (M − t-Bu): 412.1612. Found: 412.1619 (Δ −1.8 ppm).

• *Desilylation of 2,6-bis[(t-butyldimethylsilyl)oxy]-3,4-di(methoxycarbonyl)-5-methylpyridine* **5c**

Potassium fluoride (48 mg, 0.84 mmol, 3 equiv) was added to a solution of **5c** (130 mg, 0.28 mmol, 1 equiv) in chloroform (1 mL) and methanol (1 mL). The reaction mixture was stirred at room temperature for 1 h 30 min then poured into 1 N HCl (10 mL) and extracted with two portions of dichloromethane (10 mL). The combined organic extracts were dried over magnesium sulfate and concentrated to yield 2,6-dihydroxy-3,4-di(methoxycarbonyl)-5-methylpyridine **6c** (66 mg, 99%) as a white solid. Mp: 178.5–180.1 °C.

IR (CH_2Cl_2): 1 740, 1 660, 1 640, 1 450 cm^{-1}.

^{1}H NMR (300 MHz): 12.30 (broad s, 2H), 3.91 (s, 3H), 3.88 (s, 3H), 2.00 (s, 3H).

^{13}C NMR (50 MHz): 169.09 (q, ^3J = 3.99), 167.23 (q, ^3J = 3.99), 164.16 (q, ^3J = 3.59), 161.95 (s), 141.97 (q, ^3J = 5.18), 116.76 (q, ^2J = 6.39), 86.62 (s), 53.09 (Q, ^1J = 148.80), 52.61 (Q, ^1J = 148.01), 12.37 (Q, ^1J = 129.26).

MS (APCI): m/z = 242 ($(M + H)^+$), 210, 178.

Anal calc for $C_{10}H_{11}NO_6$: C 49.80, H 4.60, N 5.81. Found: C 49.73, H 4.53, N 5.52.

• *6-Tosyluracil* **7a**

The reaction of diene **1a** (255 mg, 1.28 mmol, 2 equiv) with tosyl cyanide (122 mg, 0.64 mmol, 1 equiv) in toluene (2 mL) (Δ, 19 h) yielded after precipitation in diethyl ether from the crude mixture **7a** (60 mg, 35%) as a white solid. Mp: >300 °C.

IR (KBr): 3 400–3 200, 1 715, 1 660, 1 345, 1 160 cm^{-1}.

^{1}H NMR (200 MHz, DMSO-d_6): 11.95 (broad s, 1H), 11.53 (broad s, 1H), 7.98 (d, J = 7.98, 2H), 7.52 (d, J = 8.06, 2H), 6.15 (s, 1H), 2.42 (s, 3H).

^{13}C NMR (125 MHz, DMSO-d_6): 162.50 (s), 151.83 (s), 150.53 (s), 146.54 (sext, ^2J = ^3J = 6.60), 133.73 (t, ^3J = 8.90), 130.34 (Dm, ^1J = 163.90), 128.89 (Dd, ^1J = 167.75, ^3J = 5.25), 102.52 (D, ^1J = 180.45), 21.19 (Qt, ^1J = 125.66, ^3J = 3.51).

MS (EI): m/z = 266 ($M^{+\cdot}$), 155, 139, 91.

HRMS calc for $C_{11}H_{10}N_2O_4S$: 266.0361. Found: 266.0356 (Δ 2.0 ppm).

• *6-Tosylthymine* **7b**

The reaction of diene **1b** (312 mg, 1.46 mmol, 2 equiv) with tosyl cyanide (132 mg, 0.73 mmol, 1 equiv) in toluene (2 mL) (Δ, 19 h) yielded after precipitation in diethyl ether from the crude mixture **7b** (96 mg, 47%) as a white solid. Mp: >320 °C.

IR (KBr): 3 300, 1 740, 1 680, 1 595, 1 330, 1 150 cm^{-1}.

^{1}H NMR (200 MHz, DMSO-d_6): 11.59 (broad s, 1H), 11.00 (broad s, 1H), 8.06 (d, J = 7.98, 2H), 7.53 (d, J = 7.88, 2H), 2.42 (s, 3H), 2.00 (s, 3H).

^{13}C NMR (125 MHz, DMSO-d_6): 164.06 (q, ^3J = 4.30), 149.11 (s), 146.30 (m), 145.13 (q, ^3J = 5.30), 135.17 (t, ^3J = 8.75), 130.44 (Dm, ^1J = 164.30), 127.90 (Dd, ^1J = 167.30, ^3J = 5.10), 111.56 (m), 21.17 (Qm, ^1J = 127.27), 9.67 (Q, ^1J = 130.50).

MS (EI): m/z = 280 ($M^{+\cdot}$), 215, 157, 139, 91.

HRMS calc for $C_{12}H_{12}N_2O_4S$: 280.0518. Found: 280.0522 (Δ −1.5 ppm).

Cycloadditions with 1-(diethylamino)prop-1-yne

• *General procedure for the cycloadditions*

1-(Diethylamino)prop-1-yne was added at room temperature to a solution of the diene. The mixture was stirred at room temperature. Then, the solvent was evaporated and the residue was purified by chromatography on silica gel.

• *2,6-Bis[(t-butyldimethylsilyl)oxy]-4-(diethylamino)-3-methylpyridine* **9a** *and 4-(diethylamino)-3-methylpyridine-2,6(1H,3H)-dione* **10a**

The reaction of diene **1a** (395 mg, 1.98 mmol, 1 equiv) with 1-(diethylamino)prop-1-yne (279 μL, 1.98 mmol, 1 equiv) in toluene (4 mL) for 15 min yielded after chromatography (SiO_2, dichloromethane/ethyl acetate 1:4 then ethyl acetate) **9a** (277 mg, 33%) and **10a** (40 mg, 10%).

■ ***9a*** *(white solid)*

IR (CH_2Cl_2): 2 960–2 880, 1 590, 1 550, 1 460 cm^{-1}.

^{1}H NMR (200 MHz): 5.89 (s, 1H), 3.00 (q, J = 6.91, 4H), 1.98 (s, 3H), 1.01 (t, J = 7.00, 6H), 0.97 (s, 9H), 0.94 (s, 9H), 0.30 (s, 6H), 0.27 (s, 6H).

^{13}C NMR (50 MHz): 161.59 (m), 159.85 (q, ^3J = 4.20), 158.90 (d, ^2J = 2.60), 106.98 (m), 97.39 (D, ^1J = 161.70), 45.36 (Tsext, ^1J = 134.00, ^2J = ^3J = 3.90), 25.75 (Qhept, ^1J = 124.40, ^3J = 5.33), 18.00 (m), 12.25 (Qt, ^1J = 126.20, ^2J = 2.60), 11.87 (Q, ^1J = 127.50), −4.33 (Qm, ^1J = 119.40).

MS (EI): m/z = 424 ($M^{+\cdot}$), 409, 395, 381, 367, 73.

■ ***10a*** *(pink solid)*

Mp: 136.3–137.9 °C.

IR (CH_2Cl_2): 3 380, 2 970–2 930, 1 700, 1 650, 1 570 cm^{-1}.

^{1}H NMR (500 MHz): 9.39 (s, 1H), 4.91 (s, 1H), 3.42–3.19 (m, 5H), 1.57 (d, J = 7.24, 3H), 1.21 (t, J = 7.12, 6H).

^{13}C NMR (125 MHz): 174.08 (m), 166.88 (m), 161.36 (m), 84.29 (Dt, ^1J = 163.80, ^3J = 3.30), 43.44 (Tm, ^1J = 136.96), 39.05 (Dm, ^1J = 132.62), 21.85 (Qd, ^1J = 132.02, ^2J = 6.31), 12.53 (Qm, ^1J = 120.74).

MS (EI): m/z = 196 ($M^{+\cdot}$), 181, 167, 153, 124.

Anal calc for $C_{10}H_{16}N_2O_2$: C 61.20, H 8.22, N 14.27. Found: C 61.11, H 8.25, N 14.29.

• *2,6-Bis[(t-butyldimethylsilyl)oxy]-4-(diethylamino)-3,5-dimethylpyridine* **9b** *and 4-(diethylamino)-3,5-dimethylpyridine-2,6(1H,5H)-dione* **10b**

The reaction of diene **1b** (650 mg, 3.05 mmol, 1 equiv) with 1-(diethylamino)prop-1-yne (421 μL, 3.05 mmol, 1 equiv) in benzene (6 mL) for 1 h 15 min yielded after chromatography (SiO_2, dichloromethane/cyclohexane 1:1 then ethyl acetate) **9b** (235 mg, 18%) and **10b** (280 mg, 44%).

■ ***9b*** *(white solid)*

Mp: 110.3–111.7 °C.

IR (CH_2Cl_2): 2 960–2 860, 1 580, 1 464 cm^{-1}.

^1H NMR (200 MHz): 3.08 (q, J = 7.11, 4H), 2.02 (s, 6H), 1.00 (t, J = 7.11, 6H), 0.99 (s, 18H), 0.32 (s, 12H).

^{13}C NMR (125 MHz): 159.64 (m), 157.23 (q, J = 4.30), 112.52 (q, J = 6.10), 46.62 (Tsext, ^1J = 133.19, $^2J = {}^3J$ = 4.05), 25.84 (Qhept, ^1J = 125.05, ^3J = 5.59), 18.14 (m), 14.48 (Qt, ^1J = 125.56, ^2J = 2.64), 12.36 (Q, ^1J = 127.33), −4.24 (Qm, ^1J = 119.30).

MS (EI): m/z = 438 ($M^{+\cdot}$), 381, 73.

Anal calc for $C_{23}H_{46}N_2O_2Si_2$: C 62.96, H 10.57, N 6.38, O 7.29. Found: C 63.05, H 10.55, N 6.42, O 7.39.

■ ***10b*** *(white solid)*

Mp: 139.1–142.7 °C.

IR (CH_2Cl_2): 3 380, 2 990–2 880, 1 710, 1 665, 1 600 cm^{-1}.

^1H NMR (300 MHz): 8.46 (s, 1H), 3.39 (q, J = 7.35, 1H), 3.37–3.12 (m, 4H), 1.50 (d, J = 7.39, 3H), 1.15 (t, J = 7.13, 6H).

^{13}C NMR (75 MHz): 174.02 (t, ^2J = 4.90), 167.78 (q, ^3J = 3.96), 160.71 (m), 102.11 (m), 45.02 (Tsext, ^1J = 136.08, $^2J = {}^3J$ = 4.07), 40.73 (Dpent, ^1J = 132.40, $^2J = {}^3J$ = 3.90), 21.53 (Qd, ^1J = 131.61, ^2J = 6.78), 14.54 (Qt, ^1J = 126.60, ^2J = 2.95), 13.30 (Q, ^1J = 128.43).

MS (EI): m/z = 210 ($M^{+\cdot}$), 195, 181, 138.

HRMS calc for $C_{11}H_{18}N_2O_2$: 210.1368. Found: 210.1371 (Δ −1.3 ppm).

• *Desilylation of 2,6-bis[(tert-butyldimethylsilyl)oxy]-4-(diethylamino)-3,5-dimethylpyridine* **9b** *with methanol*

Methanol (1 mL) was added to a solution of **9b** (180 mg, 0.41 mmol) in chloroform (2 mL). The mixture was heated at 60 °C for 2 days. Then, the solvent was evaporated and the residue was purified by chromatography on silica gel (ethyl acetate) to yield **10b** (68 mg, 79%).

• *Desilylation of 2,6-bis[(tert-butyldimethylsilyl)oxy]-4-(diethylamino)-3,5-dimethylpyridine* **9b** *in the presence of potassium fluoride*

Potassium fluoride (88 mg, 1.51 mmol, 4 equiv) was added to a solution of **9b** (166 mg, 0.38 mmol, 1 equiv) in chloroform (1 mL) and methanol (1 mL). The mixture was stirred at room temperature for one day then poured into 10% HCl (10 mL) and extracted with two portions of chloroform (10 mL). The combined organic extracts were dried over magnesium sulfate and concentrated to yield 4-(diethylamino)-3-hydroxy-3,5-dimethylpyridine-2,6(1*H*,5*H*)-dione **11** (70 mg, 81%) as a white solid. Mp: 175.8–177.8 °C.

IR (KBr): 3 460–3 420, 3 170–2 820, 1 700, 1 650, 1 570 cm^{-1}.

^1H NMR (300 MHz, DMSO-d_6): 10.55 (s, 1H), 5.87 (s, 1H), 3.36–3.22 (m, 4H), 1.70 (s, 3H), 1.48 (s, 3H), 1.10 (t, J = 7.08, 6H).

^{13}C NMR (125 MHz, DMSO-d_6): 175.82 (q, ^3J = 3.90), 166.28 (q, ^3J = 3.60), 162.59 (m), 103.05 (q, ^2J = 5.90), 72.28 (m), 45.13 (Tsext, ^1J = 136.85, $^2J = {}^3J$ = 4.15), 29.32 (Q, ^1J = 129.74), 13.80 (Q, ^1J = 127.98), 13.78 (Qt, ^1J = 125.93, ^2J = 2.86).

MS (EI): m/z = 226 ($M^{+\cdot}$), 211, 209, 183.

HRMS calc for $C_{11}H_{18}N_2O_3$: 226.1317. Found: 226.1310 (Δ 3.3 ppm).

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