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Synthesis of 1,3,5-Tricarbonyl Derivatives by Condensation of 1,3-Bis(silyl enol ethers) with Acid Chlorides

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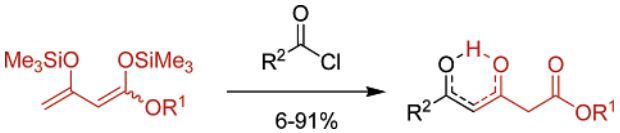

A variety of 1,3,5-tricarbonyl derivatives were prepared by reaction of 1,3-bis(silyl enol ethers) with acid chlorides under mild conditions. This includes reactions of both aromatic and aliphatic acid chlorides and bis(acid chlorides). The yields vary depending on the type of acid chloride employed.

1,3,5-Tricarbonyl derivatives and their higher homologues occur in a variety of pharmacologically important natural products (polyketides) and represent important starting materials for stereoselective syntheses of polyols.[1] 1,3-Dicarbonyl dianions[2] represent versatile building blocks for the synthesis of polyketides. In their pioneering work, Hauser[3] and Weiler[4] reported the reaction of 1,3-dicarbonyl dianions with esters and nitriles. These reactions have been successfully applied to the synthesis of pyran-2-ones.[5] However, reactions of dianions with esters may suffer from proton transfer and O-acylation. In addition, the preparative scope is limited to substrates which tolerate the presence of strong nucleophiles and bases. The reaction of 1,3-dicarbonyl dianions with acid chlorides has been reported to give complex mixtures.[4] In contrast, the condensation of dianions with *N*-acyl-2-methylaziridines[6] and Weinreb amides[7] proved to be very efficient. Harris and co-workers developed elegant biomimetic syntheses of 1,3,5-tricarbonyl compounds, 1,3,5,7-tetracarbonyl compounds, and higher homologues by condensation of 1,3-dicarbonyl dianions or 1,3,5-tricarbonyl trianions with esters and diesters, Weinreb amides, and salts of β-keto esters.[8] Yamaguchi et al. reported the condensation of 1,3-dicarbonyl dianions with ethyl chloroacetate and other acylating agents.[9] 3,5-Diketo esters have been prepared also by other methods—for example, methyl 3,5-dioxohexanoate is available by ring-opening of 3-acetyl-4-hydroxy-6-methylpyran-2-one[10]—and have found various applications in organic synthesis.[11]

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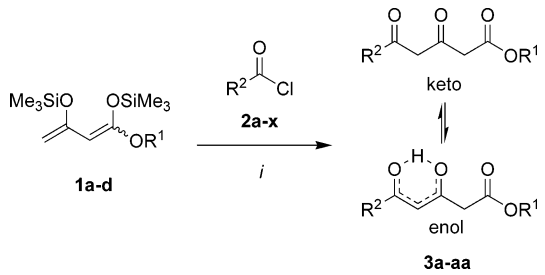
1,3-Bis(silyl enol ethers) can be regarded as electroneutral equivalents of 1,3-dicarbonyl dianions (masked dianions).[12,13] Reactions of 1,3-bis(silyl enol ethers) with acid chlorides have been reported. Chan and co-workers reported the synthesis of methyl 3,5-dioxohexanoate by reaction of 1-methoxy-1,3-bis-(trimethylsiloxy)-1,3-butadiene with acetyl chloride.[14] Chan and Chaly reported[15] the [3 + 3] cyclization of a 1,3-bis(silyl enol ether) with a protected 3-oxooctanoyl chloride. The $TiCl_4$-mediated reaction of a 1,3,5-tris(silyl enol ether) with acid chlorides and imidazolides resulted in the formation of salicylates by attack of the triene onto the acid derivative and subsequent Mukaiyama aldol reaction ([5 + 1] cyclization).[16] We reported the synthesis of 3(2*H*)-furanones by condensation of 1,3-bis(silyl enol ethers) with chloroacetyl chloride and subsequent cyclization.[17] γ-Alkylidenebutenolides are available by cyclization of 1,3-bis(silyl enol ethers) with oxalyl chloride[18,19] or phthaloyl chloride.[20] Recently, we reported the synthesis of 1,3,5-tricarbonyl compounds by condensation of 1,3-bis(silyl enol ethers) with acid chlorides.[21] Herein, we report full details of these reactions which proceed under mild conditions. With regard to our preliminary communication,[21] the preparative scope was considerably extended. Notably, a number of products are not directly available from the corresponding 1,3-dicarbonyl dianions, due to competing side reactions of the highly reactive dianions (metal−halide exchange, competing nucleophilic attack, ring opening, etc.).

Results and Discussion

Optimal yields for the reaction of 1,3-bis(silyl enol ethers) with acid chlorides were obtained in the absence of any Lewis acid; notably, the use of Me_3SiOTf resulted in decomposition. In addition, the stoichiometry played an important role: the reactions were carried out using 1.0 equiv of the 1,3-bis(silyl enol ethers) and 1.5 equiv of the acid chloride. The yields decreased when 2.0 equiv of the 1,3-bis(silyl enol ethers) and 1.0 equiv. of the acid chloride were employed. The temperature (−78 → +20 °C), the addition procedure (the acid chloride was slowly added to a CH_2Cl_2 solution of the silyl enol ether), and the workup procedure (use of an aqueous solution of $NaHCO_3$) also played an important role.

The reaction of 1,3-bis(silyl enol ethers) **1a** and **1b**, prepared from the respective acetoacetates, with various aromatic acid chlorides afforded the 5-aryl-3,5-dioxopentanoates **3a**−**n** (Scheme 1, Table 1). The condensation of **1a** with phenylacetyl chloride and 1,1-diphenylacetyl chloride afforded the 6-aryl-3,5-dioxohexanoates **3o**,**p**. The reaction of **1a** and **1b** with a variety of aliphatic acid chlorides gave the 3,5-dioxoalkanoates **3q**−**y**. The methoxyethyl and isobutyl 3,5-dioxohexanoates **3z** and **3aa** were prepared from 1,3-bis(silyl enol ethers) **1c**,**d** and acetyl chloride. Surprisingly, all attempts to prepare 3,5-dioxoalkanoates from 4-alkyl-1,3-bis(silyl enol ethers) failed, presumably for steric reasons. Notably, functionalized 3,5-dioxoalkanoates **3e**,**i**−**k** are not directly available from the corresponding 1,3-dicarbonyl dianions due to formation of complex mixtures. In fact, reactions of dianions are often limited by competing side reactions, such as metal−halide exchange, SET processes, elimination, or polymerization.[22] It was previously noted that reactions of

SCHEME 1. Reaction of 1,3-Bis(silyl enol ethers) with Acid Chlorides[a]



[a] Key: (i) (1) CH_2Cl_2, −78 → +20 °C, 8−12 h, (2) $NaHCO_3$ (saturated aqueous solution).

TABLE 1. Synthesis of 1,3,5-Tricarbonyl Compounds 3a−aa

1	2	3	R^1	R^2	keto/enol ratio	yield[a] (%)
a	**a**	**a**	Me	2-ClC_6H_4	0:100	59
a	**b**	**b**	Me	2-MeC_6H_4	0:100	48
a	**c**	**c**	Me	4-ClC_6H_4	0:100	54
a	**d**	**d**	Me	2-$(MeO)C_6H_4$	14:86	45
a	**e**	**e**	Me	4-$(ClCH_2)C_6H_4$	0:100	74
a	**f**	**f**	Me	2,6-$(MeO)_2C_6H_3$	29:71	6
a	**g**	**g**	Me	2,4-$(MeO)_2C_6H_3$	20:80	24
a	**h**	**h**	Me	3,4,5-$(MeO)_3C_6H_2$	9:91	68
a	**i**	**i**	Me	4-$(O_2N)C_6H_4$	0:100	65
a	**j**	**j**	Me	C_6F_5	0:100	55
a	**k**	**k**	Me	2-IC_6H_4	0:100	87
b	**l**	**l**	Et	Ph	0:100	66
a	**m**	**m**	Me	1-Naph	0:100	40
a	**n**	**n**	Me	2-Naph	0:100	62
a	**o**	**o**	Me	$PhCH_2$	13:87	87
a	**p**	**p**	Me	$(Ph)_2CH$	11:89	78
a	**q**	**q**	Me	1-Ad	0:100	17
a	**r**	**r**	Me	$H_2C{=}CH(CH_2)_8$	13:87	67
a	**s**	**s**	Me	*t*-Bu	0:100	40
a	**t**	**t**	Me	$MeOCH_2$	17:83	41
a	**u**	**u**	Me	*c*-Pr	17:83	91
a	**v**	**v**	Me	*n*-Pr	17:83	69
b	**w**	**w**	Et	Et	20:80	48
a	**x**	**x**	Me	Me	29:71	34
b	**x**	**y**	Et	Me	33:67	40
c	**x**	**z**	*i*-Bu	Me	33:67	32
d	**x**	**aa**	$(CH_2)_2OMe$	Me	40:60	50

[a] Yields of isolated products.

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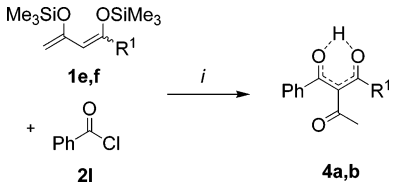
SCHEME 2. Acylation of 1,3-Bis(silyl enol ethers) 1e,f[a]



[a] Key: (i) (1) CH_2Cl_2, −78 → +20 °C, (2) $NaHCO_3$ (saturated aqueous solution).

TABLE 2. Synthesis of Triacylmethanes 4a,b

1	4	R^1	yield[a] (%)
e	**a**	Me	28
f	**b**	Ph	36

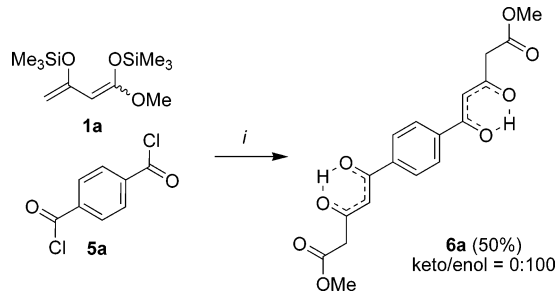
[a] Yields of isolated products.

dilithiated arylacetonitriles and oximes were not compatible with the presence of bromo- or nitroaryl groups in the substrates.[23,24] The yields of compounds **3a**−**aa** vary from excellent to poor, depending on the type of acid chloride. Low yields were obtained for products **3f** and **3q**, which are derived from sterically hindered acid chlorides. On the other hand, the reaction of **1a** with sterically hindered pivaloyl chloride afforded **3s** in 40% yield. There seems to be a trend toward poorer yields for more electron-rich (and thus less reactive) acid chlorides (used for the synthesis of **3d**,**f**,**g**).

All products were characterized by spectroscopic methods and exist (in $CDCl_3$ solution) as mixtures of keto/enol tautomers or exclusively as enol tautomers. Most of the 5-aryl-3,5-dioxopentanoates exclusively exist in their enol tautomeric form. This can be explained by conjugation of the enolic double bond with the arene moiety. In case of **2d**,**f**,**g**, all containing an *o*-methoxy group, some amount of keto tautomer could be detected. This might be explained by orthogonal twisting of the arene moiety (due to steric reasons) which results in a decreased extent of conjugation.

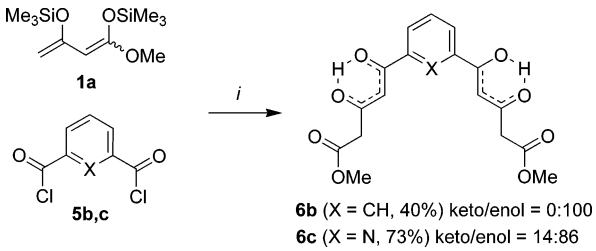
1,3-Bis(silyl enol ethers) **1e** and **1f** are available from acetylacetone and benzoylacetone, respectively. Unexpectedly, the reaction of **1e** and **1f** with benzoyl chloride (**2l**) resulted in acylation of the central rather than the terminal carbon atom of the 1,3-bis(silyl enol ether) to give products **4a** and **4b**, respectively (Scheme 2, Table 2). The yields are relatively low, due to substantial losses of material during chromatographic purification. The formation of the regioisomer, which was formed by attack of the terminal carbon atom of the bis(silyl enol ether) onto the acid chloride, was not observed. A related unusual regiochemical behavior was recently observed for the reaction of **1e** and **1f** with phthaloyl dichloride.[18] On the other hand, the reactions of **1e** and **1f** with oxalyl chloride, 1,1-dimethoxy-2-azidoethane, and 1-chloro-2,2-dimethoxyethane take a regular path and proceed by attack of the terminal carbon atom of the 1,3-bis(silyl enol ether) onto the electrophile. The reaction of **1e** and **1f** with chloroacetyl chloride proved to be unsuccessful.[17] The formation of **4a**,**b** can be explained by the lower reactivity of **1e**,**f** compared to β-ketoester-derived 1,3-bis(silyl enol ethers) which are more electron rich, due to the influence of the π-donating effect of the ester alkoxy group. The regioselectivity of **1e**,**f** strongly depends on the type of electrophile employed. The configurations of the double bonds of 1,3-bis(silyl enol ethers) are, in many cases, known and vary depending on the substituents.[25] On the basis of the literature,

SCHEME 3. Synthesis of 6a[a]



[a] Key: (i) (1) CH_2Cl_2, −78 → +20 °C, (2) $NaHCO_3$ (saturated aqueous solution).

SCHEME 4. Synthesis of 6b and 6c[a]



[a] Key: (i) (1) CH_2Cl_2, −78 → +20 °C, (2) $NaHCO_3$ (saturated aqueous solution).

a relationship between configuration and regioselectivity would not be expected and is indeed not seen.

The reaction of 1,3-bis(silyl enol ether) **1a** with 1,4-benzenedicarboxylic dichloride (**5a**) proceeded with 2:1 stoichiometry and afforded condensation product **6a** in 50% yield (Scheme 3). The structure of **6a** was independently confirmed by crystal structure analysis (see the Supporting Information). It completely exists in the enol tautomeric form (both in a $CDCl_3$ solution and in the solid state). The reaction of **1a** with 1,3-benzenedicarboxylic dichloride (**5b**) afforded **6b**, which also completely exists in its enol tautomeric form (Scheme 4). Pyridine derivative **6c** was prepared from 1,3-pyridinedicarboxylic dichloride (**5c**). Recently, we reported[20] the synthesis of benzo-annulated γ-(2,4-dioxobut-1-ylidene)butenolide **6d** by reaction of 1,3-bis(silyl enol ether) **1b** with phthaloyl dichloride (**5d**) (Scheme 5). The formation of **6d** can be explained by formation of isophthaloyl dichloride and subsequent attack of the terminal carbon atom of **1b** onto the dichloride moiety. The reaction of 1,3-bis(silyl enol ether) **1e** with 1,3-benzenedicarboxylic dichloride (**5b**) afforded **6e** by acylation of the central rather than the terminal carbon atom of the 1,3-bis(silyl enol ether) (Scheme 6). As noted above, a related unusual regiochemical behavior was previously observed for the reaction of **1e** and **1f** with phthaloyl dichloride (**5d**).[20]

The reaction of 1,3-bis(silyl enol ether) **1a** with bis(acid chlorides) **7a**−**c** afforded the tetraoxodioates **8a**−**c** which mainly

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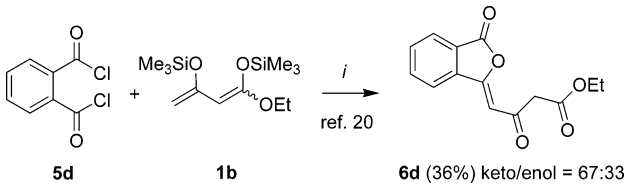
TABLE 3. Antibacterial Properties of Selected Compounds[a]

3	*B. subtilis* ATCC 6051	*E. coli* ATCC 11229	*C. maltosa* ATCC 200	*S. aureus* ATCC 6538	*P. aeruginosa* ATCC 27853
a	10	10	12	10	r
b	14	16	20	R	r
c	17	19	22	14	r
d	r	r	r	r	r
e	12	12	14	11	r
f	r	r	r	r	r
g	r	r	r	r	r
h	r	r	r	r	r
i	r	r	r	r	r
j	14	10	r	14	r
ampicillin	33	25	n.t.	35	20
gentamicin	n.t.	n.t.	35	n.t.	n.t.

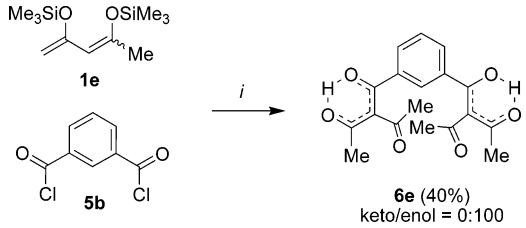
[a] Key: diameter of inhibition zones in mm; including test plate 6 mm, all test plates were soaked with 0.1 μmol of test substance; r = resistant; n.t. = not tested.

SCHEME 5. Reaction of 1,3-Bis(silyl enol ether) 1b with Phthaloyl Dichloride[a]



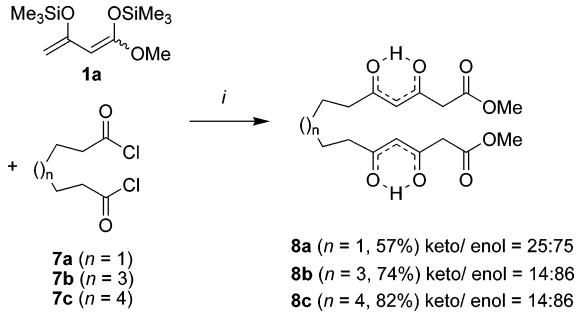
[a] Key: (i) CH_2Cl_2, −78 → 20 °C (ref 20).

SCHEME 6. Synthesis of 6e[a]



[a] Key: (i) (1) CH_2Cl_2, −78 → +20 °C, (2) $NaHCO_3$ (saturated aqueous solution).

SCHEME 7. Reaction of 1,3-Bis(silyl enol ether) 1a with Bis(acid chlorides) 7a−c[a]



[a] Key: (i) (1) CH_2Cl_2, −78 → +20 °C, 8−12 h; (2) $NaHCO_3$ (saturated aqueous solution).

exist in their enol tautomeric form (Scheme 7). Notably, the reactions of **1a** with the dichlorides of malonic and succinic acid were unsuccessful and resulted in the formation of complex mixtures.

Biological Evaluation. A number of 3,5-dioxoalkanoates **3** were tested for their antibiotic properties. Some of the tested compounds showed antibiotic activity against the Gram-positive bacteria *Bacillus subtilis* and *Staphylococcus aureus*. Growth inhibition was observed also for the Gram-negative bacteria *Escherichia coli* and for the yeast *Candida maltosa*. However, no growth inhibition was observed for the Gram-negative bacteria *Pseudomonas aeruginosa*. The results of the screenings are summarized in Table 3. The antimicrobial activity of the test compounds was only moderate (compared to ampicillin and gentamicin which are antibiotics in clinical use and were included for reasons of comparison). In our tests, similar concentrations of compounds **3**, ampicillin, and gentamicin were applied. The activity clearly depends on the substitution pattern of the aromatic residue R^1. The presence of halide substituents improved the activity (compounds **3a**, **3c**, and **3e**). The presence of methoxy groups attached to the arene moiety completely removed any activity. This observation is in agreement with our previous work (using a different type of molecule) and may depend on the mode of action of the tested compounds.[26] The level of antibiotic activity is below the activity of common antibiotics.

Conclusions

In conclusion, we have reported the condensation of 1,3-bis(silyl enol ethers) with acid chlorides. These reactions allow for a convenient synthetic approach to a variety of 1,3,5-tricarbonyl compounds under mild conditions. The best results were obtained for reactions of 1,3-bis(silyl enol ethers) derived from methyl acetoacetate. The use of 1,3-diketone-derived 1,3-bis(silyl enol ethers) resulted in functionalization of the central rather than the terminal carbon atom of the bis(silyl enol ethers). A variety of acid chlorides were successfully employed which include aromatic, aliphatic, and difunctional substrates. The yields vary depending on the type of acid chloride employed.

Experimental Section

General Procedure A for Synthesis of 3,5-Dioxoalkanoates 3a−k,m−v,x, 6a−c, and 8a−c. To a CH_2Cl_2 solution of 1,3-bis(silyl enol ether) **1** (1.0 equiv) was slowly added the acid chloride **2** (1.5 equiv) at −78 °C. The reaction mixture was slowly warmed to 20 °C during 6 h, and the solution was stirred at 20 °C for a further 6−8 h. To the solution was added a saturated aqueous solution of $NaHCO_3$ (50 mL). The organic layer and the aqueous layer were separated, and the latter was extracted with CH_2Cl_2 (3

(26) (a) Albrecht, U.; Lalk, M.; Langer, P. *Biorg. Med. Chem.* **2005**, *13*, 1531. (b) Albrecht, U.; Gördes, D.; Schmidt, E.; Thurow, K.; Lalk, M.; Langer, P. *Biorg. Med. Chem.* **2005**, *13*, 4402.

× 20 mL). The combined organic layers were dried (Na_2SO_4) and filtered, and the filtrate was concentrated in vacuo. The residue was purified by column chromatography (silica gel, *n*-heptane/EtOAc = 10:1) to give the respective products.

General Procedure B for the Synthesis of 3,5-Dioxoalkanoates 3l,w,y−aa and 6e. To a CH_2Cl_2 solution of 1,3-bis(silyl enol ether) **1** (1.0 equiv) was slowly added the acid chloride **2** (1.5 equiv) at −78 °C. The reaction mixture was slowly warmed to 20 °C during 8−12 h. To the solution was added a saturated aqueous solution of $NaHCO_3$. The organic and the aqueous layer were separated, and the latter was extracted with CH_2Cl_2 (3 × 100 mL). The combined organic layers were dried (Na_2SO_4) and filtered, and the filtrate was concentrated in vacuo. The residue was purified by column chromatography (silica gel, *n*-hexane/EtOAc).

Methyl 5-(*o*-Chlorophenyl)-3,5-dioxopentanoate (3a). Following procedure A and starting with **2a** (1.01 g, 5.76 mmol) and **1a** (3.00 g, 11.52 mmol), dissolved in CH_2Cl_2 (10 mL), **3a** was isolated as a yellow oil (0.86 g, 59%). ^{1}H NMR (300 MHz, $CDCl_3$, keto/enol = 0:100): δ = 3.31 (s, 2H, CH_2), 3.59 (s, 3H, OCH_3), 6.02 (s, 1H, CH), 7.13 − 7.28 (m, 3H, Ar), 7.43 (dd, ^3J = 7.4 Hz, ^4J = 1.9 Hz, 1H, Ar), 15.19 (s, 1H, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 45.7, 52.9, 102.4, 127.3, 130.5, 131.1, 132.3, 132.3, 134.8, 168.1, 183.6, 188.6. IR (neat, cm^{-1}): $\tilde{\nu}$ = 2954 (w), 1744 (s), 1605 (s), 1472 (m), 1437 (s), 1264 (br, s), 1160 (m), 1098 (m) 1045 (m), 1015 (m), 954 (w), 766 (m), 743 (m). MS (EI, 70 eV): *m*/*z* = 256 (M^+, ^{37}Cl, 1), 254 (M^+, ^{35}Cl, 4), 222 (19), 220 (43), 219 (99), 194 (21), 187 (80), 183 (39), 181 (89), 141 (76) 139 (100), 131 (11), 113 (18), 111 (65), 101 (22), 89 (16), 77 (12), 75 (31), 69 (71). Anal. Calcd for $C_{12}H_{11}ClO_4$ (254.67): C, 56.59; H, 4.35. Found: C, 56.30; H, 4.31.

Ethyl 5-Phenyl-3,5-dioxopentanoate (3l). Following procedure B and starting with **1b** (6.0 mmol, 1.646 g) and benzoyl chloride (7.2 mmol, 0.807 g), dissolved in 15 mL of CH_2Cl_2, **3l** was isolated by column chromatography (*n*-hexane/EtOAc = 20:1 → 10:1 → 5:1) as a yellow oil (0.920 g, 66%). ^{1}H NMR (300 MHz, $CDCl_3$, keto/enol = 0:100): δ = 1.28 (t, *J* = 7.2 Hz, 3 H, OCH_2CH_3), 3.48 (s, 2 H, CH_2), 4.24 (q, *J* = 7.1 Hz, 2 H, OCH_2CH_3), 6.29 (s, 1 H, CH), 7.43−7.56 (m, 3 H, Ar), 7.87−7.89 (m, 1 H, Ar), 15.79 (s, 1 H, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.0, 45.8, 61.4, 96.7, 127.0, 128.6, 132.6, 134.0, 167.5, 182.5, 189.2. MS (EI, 70 eV): *m*/*z* = 234 (M^+, 0.4), 160 (1), 146.5 (2), 105 (3), 85 (2), 58 (3), 32 (25), 28 (100). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 2984 (m), 1739 (s), 1607 (s), 1460 (m), 1268 (s), 1180 (m), 1150 (m), 1030 (m), 765 (m), 696 (m). UV−vis (CH_3CN, nm): λ_{max} (log ϵ) = 247.6 (3.73), 312.5 (4.12). Anal. Calcd for $C_{13}H_{14}O_4$: C, 66.65; H, 6.02. Found: C, 66.93; H, 6.65.

1,4-Bis(6-methoxy-2,4,6-trioxohex-1-yl)benzene (6a). Following procedure A and starting with **5a** (0.22 g, 1.10 mmol) and **1a** (1.15 g, 4.42 mmol), dissolved in CH_2Cl_2 (3 mL), **6a** was isolated as a yellow solid (0.20 g, 50%). Mp: 120−121 °C. ^{1}H NMR (300 MHz, $CDCl_3$, keto/enol = 0:100): δ = 3.53 (s, 2H, CH_2), 3.79 (s, 3H, OCH_3), 6.34 (s, 1H, CH), 7.95 (s, 2H, Ar), 15.60 (s, 1H, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 45.3, 51.9, 96.8, 126.6, 136.8, 167.1, 179.5, 189.8. IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3447 (br, m), 3112 (m), 3023 (w), 2964 (w), 2938 (m), 1736 (s), 1618 (br, s), 1507 (s), 1438 (s), 1402 (s), 1338 (s), 1275 (br, s), 1185 (m), 1141 (s), 1121 (s), 1082 (s), 1016 (m), 1004 (s), 949 (m), 897 (m), 873 (m), 858 (w), 834 (m), 816 (s), 782 (m). MS (EI, 70 eV): *m*/*z* = 362 (M^+, 11), 330 (14), 289 (29), 271 (13), 257 (15), 247 (42), 215 (44), 173 (100), 147 (12), 69 (22). HRMS (EI, 70 eV): calcd for $C_{18}H_{18}O_8$ (M^+) 362.0996, found 362.0984.

Dimethyl 3,5,9,11-Tetraoxotridecanedioate (8a). Following procedure A and starting with **7a** (0.47 g, 2.40 mmol) and **1a** (2.50 g, 9.60 mmol), dissolved in CH_2Cl_2 (8 mL), **8a** was isolated as a yellow oil (0.49 g, 57%). ^{1}H NMR (300 MHz, $CDCl_3$, keto/enol = 25:75): (keto) δ = 1.35 (m, 6H, CH_2), 2.52 (t,^3J = 5.5 Hz, 4H, $COCH_2CH_2$), 3.56 (s, 4H, $COCH_2CO$), 3.71 (s, 4H, CH_2), 3.72 (s, 6H, CH_3); (enol) 1.61 (m, 6H, CH_2), 2.30 (t,^3J = 5.5 Hz, 4H, $COCH_2CH_2$), 3.34 (s, 4H, $COCH_2CO$), 3.73 (s, 6H, CH_3), 5.58 (s, 2H, CH), 15.10 (s, 2H, OH). ^{13}C NMR (75 MHz, $CDCl_3$): enol: δ = 25.5, 28.9, 37.9, 45.2, 52.8, 100.2, 168.3, 187.3, 193.4. IR (neat, cm^{-1}): $\tilde{\nu}$ = 3466 (w), 2953 (m), 2863 (w), 1743 (s), 1616 (s), 1559 (m), 1541 (w), 1507 (w), 1437 (m), 1409 (w), 1329 (m), 1263 (s), 1202 (m), 1156 (m), 1016 (m), 920 (m), 777 (w). MS (EI, 70 eV): *m*/*z* = 356 (M^+, 4), 293 (41), 292 (15), 223 (38), 222(24), 209 (27), 199 (44), 180 (21), 171 (21) 167 (48), 163 (23), 158 (81), 143 (95), 139 (100), 126 (80), 125 (62), 121 (24), 116 (22), 111 (50), 101 (98), 97 (49), 84 (40), 69 (97). Anal. Calcd for $C_{17}H_{24}O_8$ (356.37): C, 57.30; H, 6.79. Found: C, 57.30; H, 6.66.

Biological Studies. Bacterial cultures were obtained from the ATCC (American Type Culture Collection, 10801 University Blvd., Manassas, VA 20110-2209).

Assay for Antimicrobial and Antifungal Activity. A modified disk diffusion method was used to determine the antimicrobial activity of the compounds. Nutrient agar was used for bacteria and malt agar for *C. maltosa*. A sterile filter disk of 6 mm (B&D research) diameter impregnated with test compound was used for the assay. The paper disk was placed on the agar plate seeded with the respective microorganisms. The plates were kept in the refrigerator at 4 °C for 4 h. Then the plates were turned over to incubate overnight at 37 °C in an inverted position. In contrast, *C. maltosa* was incubated at 28 °C for 72 h. At the end of the incubation period, the clear zones of inhibition around the paper disk were measured. Negative control experiments were performed by using paper disks loaded with an equivalent volume of solvent, and positive control experiments were performed by use of an equivalent amount of ampicillin, and gentamicin in case of *C. maltosa*. The amount of substance of the compounds tested during the experiments was 1000 nmol per paper disk.

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Supporting Information Available: Data for the crystal structure analysis, experimental procedures, spectroscopic data, and copies of NMR spectra. This material is available free of charge via the Internet at http://pubs.acs.org.

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