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Electrophilicity of 5-Benzylidene-1,3-dimethylbarbituric and -thiobarbituric Acids

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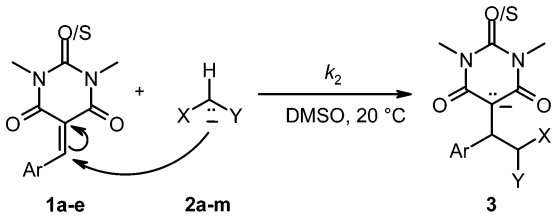

The kinetics of reactions of acceptor-stabilized carbanions **2a**−**m** with benzylidenebarbituric and -thiobarbituric acids **1a**−**e** has been determined in a dimethyl sulfoxide solution at 20 °C. Second-order rate constants were employed to determine the electrophilicity parameters *E* of the benzylidenebarbituric and -thiobarbituric acids **1a**−**e** according to the correlation equation $\log k(20\ °C) = s(N + E)$. With *E* parameters in the range of −10.4 to −13.9, the electrophilicities of **1a**−**e** are comparable to those of analogously substituted benzylidenemalononitriles.

Introduction

Benzylidenebarbituric and thiobarbituric acids are characterized by their strongly polarized exocyclic double bond with a positive partial charge on the arylidene carbon.[1,2] They have been termed as electrically neutral organic Lewis acids[3,4] because they react with typical Lewis bases,[5] such as alkoxides,[3,6] amines,[6−9] thiols,[10] water,[11] and the hydrogensulfite ion.[12] Benzylidenebarbituric and -thiobarbituric acids also react with carbon nucleophiles (e.g., compounds containing an active methylene group,[13,14] isonitriles,[15] phosphacumulene ylids,[16,17] or organo zinc reagents).[18−20] Because of the fact that the active double bond in benzylidenebarbituric acids can easily be reduced,[21−23] these compounds can be used for the synthesis

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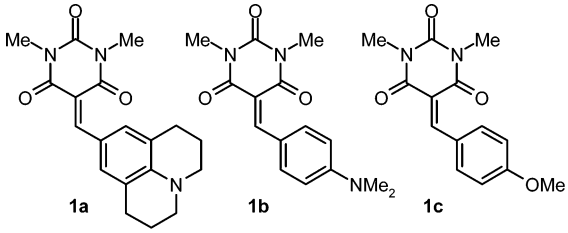
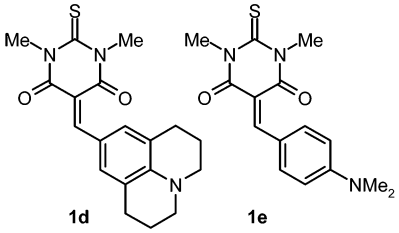
of unsymmetrical disulfides[24,25] and for the mild oxidation of alcohols.[26,27] Furthermore, benzylidenebarbituric and -thiobarbituric acids are important building blocks in the synthesis of pyrazolo-[3,4-*d*]-pyrimidine derivatives,[28,29] which show a broad biological activity.[30−32] Benzylidenethiobarbituric acids also trap radicals and, therefore, can be used as thermal stabilizers in rigid PVC.[33]

Some years ago, we showed that the reactions of diarylcarbenium ions with nucleophiles can be described by the linear free-energy relationship (eq 1) and suggested a set of diarylcarbenium ions and nucleophiles as reference compounds for determining the reactivity of further nucleophiles and electrophiles.[34]

$$\log k_2(20\ ^\circ\mathrm{C}) = s(N + E) \qquad (1)$$

where E is the electrophilicity parameter, N is the nucleophilicity parameter, and s is the nucleophile-specific slope parameter.

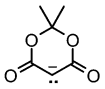
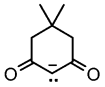




Eq 1 also holds for the reactions of carbanions with quinone methides, which can be considered as uncharged analogues of diarylcarbenium ions,[35,36] and with typical Michael acceptors, such as benzylidenemalononitriles[37] or benzylideneindandiones.[38]

Previously, Bernasconi and Stronach studied the kinetics of the additions of carbanions, alkoxides, and amines to 2-benzylidene-indan-1,3-diones,[39] benzylidene Meldrum's acids,[40,41] and other electrophiles with polarized double bonds in 50% aqueous DMSO.[42] We have now investigated analogous reactions with benzylidenebarbituric and -thiobarbituric acids to examine the scope and limitations of eq 1. For this purpose, we studied the kinetics of the addition reactions of potassium salts of different CH acids (**2a**−**m**, Table 1) to the Michael acceptors **1a**−**e**.

TABLE 1. Reactivity Parameters *N* and *s* of Carbanions 2a−m in DMSO

	X	Y	*N* / *s*
2a			13.91 / 0.86[a]
2b			16.27 / 0.77[a]
2c	4-NC-C_6H_4	SO_2CF_3	16.28 / 0.75[b]
2d	4-NC-C_6H_4	NO_2	16.96 / 0.73[c]
2e	COMe	COMe	17.64 / 0.73[a]
2f	C_6H_5	SO_2CF_3	18.67 / 0.68[b]
2g	COMe	CO_2Et	18.82 / 0.69[a]
2h	CN	CN	19.36 / 0.67[a]
2i	CN	CO_2Et	19.62 / 0.67[a]
2k	CO_2Et	CO_2Et	20.22 / 0.65[a]
2l	H	NO_2	20.71 / 0.60[c]
2m	Me	NO_2	21.54 / 0.62[d]

[a] Reference 36. [b] Reference 43. [c] Reference 44. [d] Reference 37.

Results

Product Studies. When equimolar amounts of the benzylidenebarbituric and -thiobarbituric acids **1a**−**e** and the potassium salts **2** were combined in d_6-DMSO, quantitative formation of the adducts **3** was observed by ^{1}H and ^{13}C NMR spectroscopy (Scheme 1). Because in many cases analogous reaction products can be expected, product studies have not been performed for all reactions that have been studied kinetically. For this paper, the first letter of the adducts identifies the electrophile, while the second letter identifies the nucleophile, for example, **3ah** is an adduct from **1a** and **2h**.

Protons H^a and H^b, which absorb as doublets between δ 4.43−4.81 ppm (H^a) and δ 5.11−6.20 ppm (H^b), are charac-

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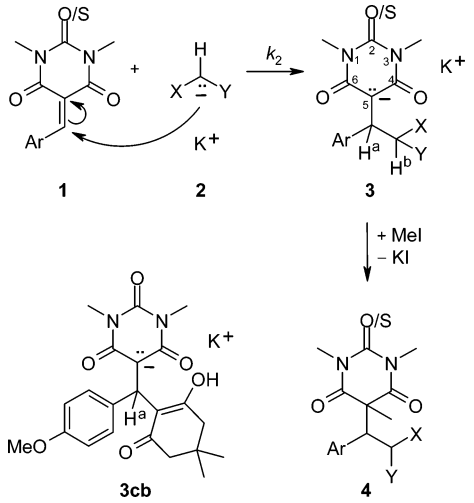
SCHEME 1. Products of Additions of Carbanions 2 to Active Double Bond of Benzylidenebarbituric and -thiobarbituric Acids 1a−e



teristic for the addition products **3**. The high upfield shifts of the ^{1}H NMR signals of the vinylic protons H^a in **1a**−**e** (δ 8.30−8.47 ppm)[45] to δ 4.43−4.81 ppm in products **3** indicate the nucleophilic attack in the β-position of the Michael acceptor.[6] This interpretation is also confirmed by ^{13}C NMR spectra, which show an upfield shift of the benzylidene carbon from δ 159−160 ppm in **1a**−**e** to δ 31−46 ppm in **3** (Table 2). The upfield shift of C-5 by an average of 27 ppm from δ 108−115 ppm in **1a**−**e** to δ 83−86 ppm in **3** reflects the increase of electron density in the pyrimidine rings. The observation of two signal sets in the ^{1}H NMR spectra of **3cg**, **3ci**, and **3cm** indicates the formation of two diastereomers in these cases (**3cg**, 5:3; **3ci**, 2:1; and **3cm**, 9:2).

The enol structure of the dimedone ring of **3cb** (from **1c** and **2b**, Scheme 1) is indicated by its ^{13}C NMR spectrum and the OH signal at δ 14.60 ppm. As a consequence, proton H^a absorbs as a singlet at δ 6.08 ppm.

Treatment of the potassium salts **3ck** and **3cm** with methyl iodide yields **4ck** and **4cm** by methylation of the 5-position of the pyrimidine ring. After separation of the diastereomers (9:2) of **4cm** by crystallization from ethanol, the structure of the major diastereomer was determined by X-ray crystallography (Figure 1).

The anionic adducts **3** obtained from arylidenebarbituric acids **1b**,**c** were also treated with aqueous hydrochloric acid. The adducts **3ce**, **3cg**, **3cm**, and **3bm**, derived from acetylacetone (**2e**), ethyl acetoacetate (**2g**), and nitroethane (**2m**), respectively, yielded the protonated species **5** as depicted in Scheme 2. On the other hand, the protonation of **3cb**, the product from **1c** and dimedone (**2b**), gave **5cb**, where the dimedone group as well as the barbituric acid group adopted an enol structure in $CDCl_3$, as shown by two OH resonances at δ 12.83 (sharp) and δ 11.32 (very broad). This difference is also evident from the ^{13}C NMR spectrum of **5cb**, where C-5 of the barbituric acid group absorbs at δ 92.8, while this carbon absorbs at δ 50.6−52.2 in all other adducts **5**.

The protonation of **3ch** (from malononitrile) and **3ci** (from ethyl cyanoacetate) under the same conditions resulted in retro-

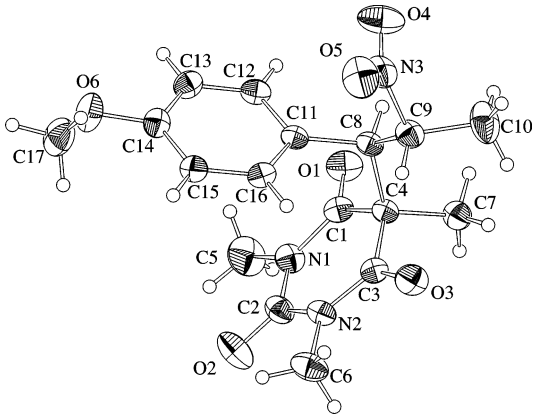


FIGURE 1. X-ray crystal structure (ORTEP projection) of the major diastereomer of **4cm**. Atom numbers refer to the X-ray analysis.

TABLE 2. ^{1}H and ^{13}C NMR Spectroscopic Analysis of Products 3[a]

	δ H^a (ppm)	δ H^b (ppm)	$^3J_{(H^a-H^b)}$ (Hz)	δ (C-H^a) (ppm)	δ (C-5) (ppm)
3ah	4.43	6.02	11.9	43.2	83.7
3bh	4.57	6.08	11.9	43.2	83.6
3cb	6.08	14.60[b]		31.0	89.6
3ce	4.81	5.48	12.3	40.5	86.0
3cg[c]	4.78	5.11	12.6	40.5	85.7
3cg[d]	4.76	5.28	12.2	40.4	86.1
3ch	4.61	6.12	12.2	43.2	83.7
3ci[c]	4.59	5.37	12.3	40.3	85.1
3ci[d]	4.65	5.35	12.2	40.3	83.9
3ck	4.70	5.14	12.3	40.5	85.9
3cm[c]	4.45	6.00	11.4	45.8	85.0
3cm[d]	4.43	6.20	11.4	45.7	83.8
3de	4.67	5.41	12.3	40.3	91.5
3dh	4.43	5.96	12.1	43.2	88.9
3ee	4.78	5.47	12.5	40.4	91.4

[a] For assignment of structures, see Scheme 1 and Table 3; **3ah** means product from **1a** and **2h**. [b] See text. [c] Major diastereomer. [d] Minor diastereomer.

Michael additions with formation of the cyanostyrenes **7ch** and **7ci** (Scheme 2). Acidification of **3bh** (malononitrile adduct to **1b**) also gave rise to the formation of the corresponding benzylidenemalononitrile **7bh**. Analogous retro-Michael additions have previously been observed by Patai and Rappoport when treating α-cyano-β-phenylacrylates with malononitrile in 95% ethanol[46a] and by us when benzylidenemalononitriles were combined with the carbanion of ethyl cyanoacetate in DMSO.[37] Szántay observed this so-called aryl methylene transfer when methoxy-substituted β-nitro styrenes were treated with ethyl cyanoacetate or malononitrile in the presence of a basic catalyst.[46b]

In addition to the retro-Michael adduct **7ch**, just discussed, the acid hydrolysis of **3ch** (from malononitrile anion **2h** and **1c**) yields 47% of the dihydropyrano[2,3-*d*]-pyrimidine **8ch**. Syntheses of analogous pyrano[2,3-*d*]-pyrimidines via the reaction of benzylidenemalononitriles with 1,3-dimethylbarbituric acid[47] or via microwave irradiation of barbituric acids, benzaldehyde, and cyanoacetates or malononitriles[48] have been reported. In these reactions, the Michael adducts **5** are probably

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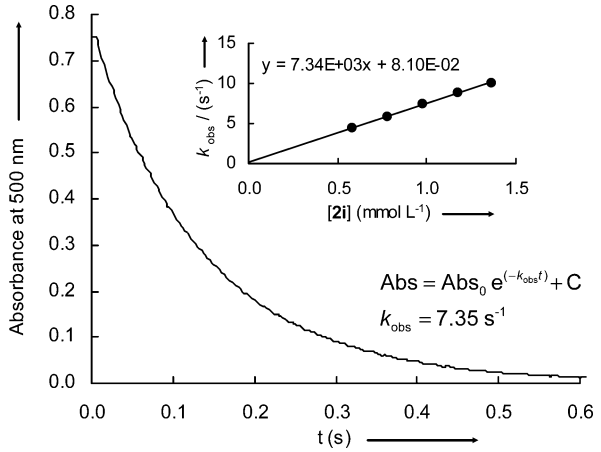
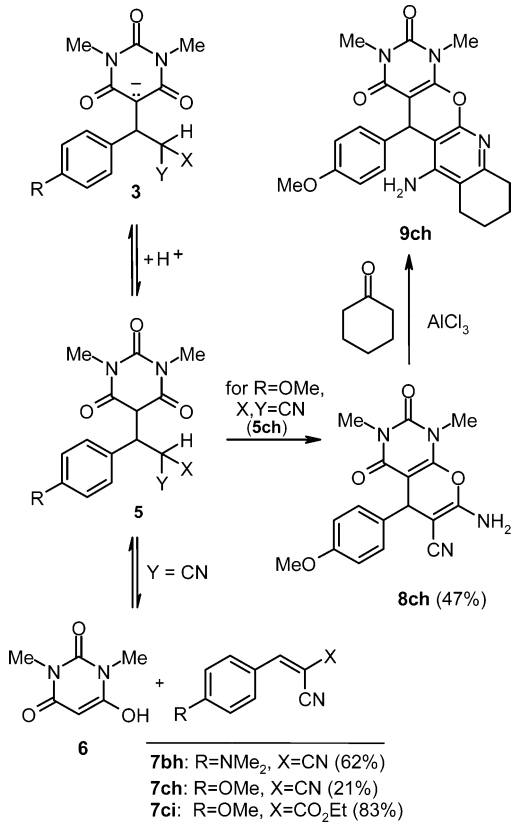


FIGURE 2. Exponential decay of absorbance at 500 nm during the reaction of **1a** ($c_0 = 2.90 \times 10^{-5}$ mol L^{-1}, $\lambda = 500$ nm) with **2i** ($c_0 = 9.78 \times 10^{-4}$ mol L^{-1}) in DMSO at 20 °C.

SCHEME 2. Protonation of Potassium Salts 3 Leads to 5[a]



[a] Salts **3bh**, **3ch**, and **3ci** undergo a retro Michael addition upon protonation to form cyanoolefins **7bh**, **7ch**, and **7ci**. Under these conditions, **5ch** forms also the cyclic dihydropyrano [2,3-*d*]pyrimidine **8ch**, which reacts with cyclohexanone via a Friedländer reaction to pyrano[2,3-*b*]quinoline **9ch**.

formed as intermediates, which then undergo cyclization by attack of an enolic hydroxy group at one of the cyano functions.

Because of the structural analogy to tacrine,[49,50] which is an inhibitor of acetyl cholinesterase and a drug that proved to have a beneficial effect on cognition in patients with Alzheimer's disease,[51,52] dihydropyran **8ch** was used as starting material for the synthesis of a new pyrano[2,3-*b*]-quinoline. In a Friedländer reaction, the acid catalyzed condensation of **8ch** with cyclohexanone gave 69% of the tacrine analogue **9ch**.

TABLE 3. Second-Order Rate Constants k_2 (DMSO, 20 °C) and Characterized Products of Reactions of Benzylidenebarbituric and -thiobarbituric Acids 1a−e with Potassium Salts of Different Carbanions 2

elec	nuc	k_2 (L mol^{-1} s^{-1})	products
1a	**2b**	1.49×10^2	
	2c	5.37×10^1	
	2d	1.88×10^2	
	2e	5.45×10^2	
	2f	1.01×10^3	
	2g	3.78×10^3	
	2h	1.27×10^4	**3ah**[a]
	2i	7.34×10^3	
	2k	7.66×10^3	
	2l	1.54×10^4	
	2m	2.98×10^4	
1b	**2b**	1.04×10^3	
	2c	2.18×10^2	
	2e	3.72×10^3	
	2f	5.71×10^3	
	2g	2.03×10^4	
	2h	5.88×10^4	**3bh**,[a] **7bh**[b]
	2i	4.00×10^4	
	2k	3.49×10^4	
	2m		**5bm**[b]
1c	**2a**	1.42×10^3	
	2b	4.83×10^4	**3cb**,[a] **5cb**[b]
	2e	1.44×10^5	**3ce**,[a] **5ce**[b]
	2f	1.97×10^5	
	2g	1.08×10^6	**3cg**,[a] **5cg**[b]
	2h	1.80×10^6	**3ch**,[a] **7ch**[b] **8ch**[b]
	2i	1.49×10^6	**3ci**,[a] **7ci**[b]
	2k	1.41×10^6	**3ck**,[a] **4ck**[b]
	2m		**3cm**,[a] **4cm**[b] **5cm**[b]
1d	**2b**	4.36×10^3	
	2e	1.17×10^4	**3de**[a]
	2g	7.41×10^4	
	2h	1.64×10^5	**3dh**[a]
	2i	1.06×10^5	
	2k	1.13×10^5	
1e	**2a**	4.97×10^2	
	2b	3.72×10^4	
	2e	1.03×10^5	**3ee**[a]
	2g	4.89×10^5	
	2i	7.05×10^5	
	2k	6.71×10^5	

[a] Potassium salts of **3** produced in d_6-DMSO were characterized by ^{1}H and ^{13}C NMR. [b] Characterization of isolated products.

Kinetics. Benzylidenethiobarbituric acids **1a−e** show strong absorption bands in the UV−vis spectra (375−525 nm).[1] By nucleophilic attack at the benzylidene carbon, the chromophore is destroyed, and the reaction can be followed by the decrease of the absorbance. All reactions proceeded quantitatively, so that the solutions were completely decolorized. The kinetic experiments were performed under pseudo-first-order conditions using a high excess of nucleophiles. From the exponential decays of the UV−vis absorbances of the electrophiles, the pseudo-first-order rate constants were obtained (Figure 2). In previous work, we have demonstrated that the potassium salts of the carbanions studied in this work are not paired under the conditions used for the kinetic experiments.[35,43,44] The second-

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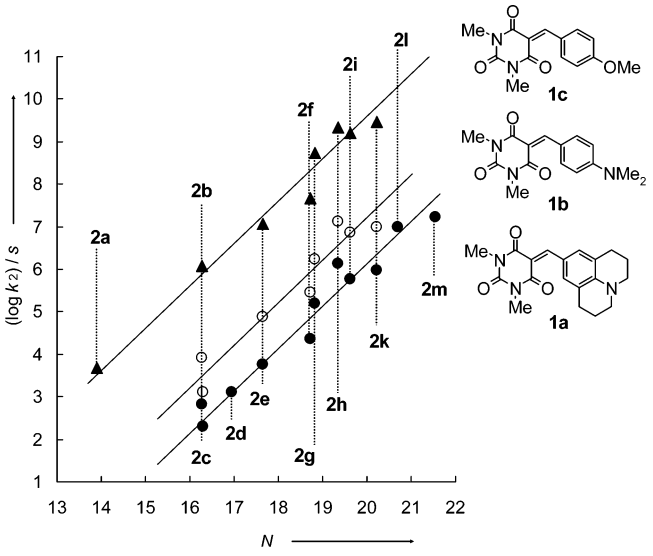


FIGURE 3. Plot of (log k_2)/s vs N for reactions of **1a**−**c** with selected carbanions **2**. Correlation lines are fixed at a slope of 1.0, as required by eq 1.

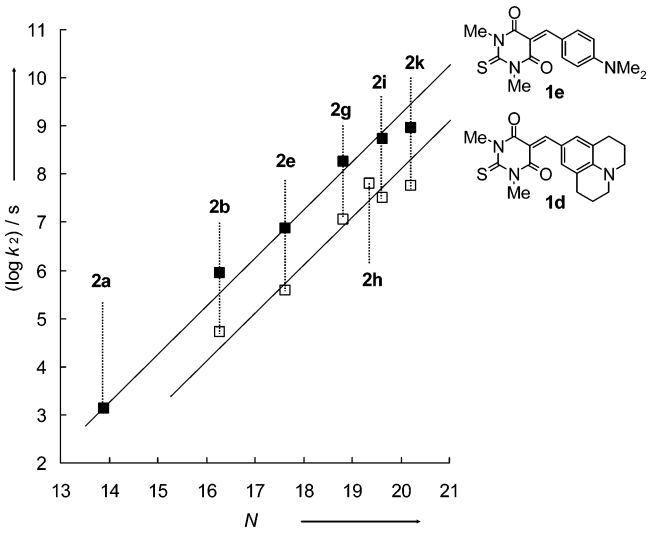


FIGURE 4. Plot of (log k_2)/s vs N for reactions of **1d**,**e** with different carbanions **2**. Correlation lines are fixed at a slope of 1.0, as required by eq 1.

order rate constants k_2 (Table 3), which are obtained as the slopes of $k_{1\Psi}$ versus [**2**] correlations (Figure 2, inset), can therefore be considered to reflect the reactivities of free carbanions.

Discussion

Eq 1 was used to calculate the E parameters of **1a**−**e** from the rate constants given in Table 3 and the previously reported N and s parameters of the carbanions **2a**−**m**.[36,37,43,44] A least-squares fit of calculated and experimental rate constants (minimization of $\Delta^2 = \Sigma(\log k - s(N + E))^2$ with the What's*Best!* nonlinear solver) gave the E parameters of the benzylidenebarbituric and -thiobarbituric acids **1a**−**e**, which are close to the arithmetic means of the E values that are calculated from k_2 of the individual electrophile−nucleophile combinations.

However, the reactivities of some carbanions deviate slightly but systematically from the correlation lines. Figure 3 shows that the triflinate-stabilized carbanion **2f** reacts 2−3 times slower

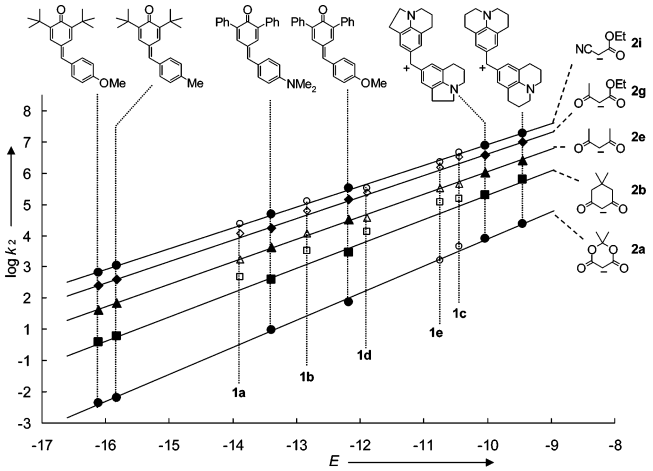


FIGURE 5. Rate constants for reactions of selected carbanions **2** with benzylidenebarbituric and -thiobarbituric acids **1a**−**e** as compared to reactivities toward reference electrophiles. Rate constants for reactions of **1a**−**e** with **2** were not used for the construction of the correlation lines.

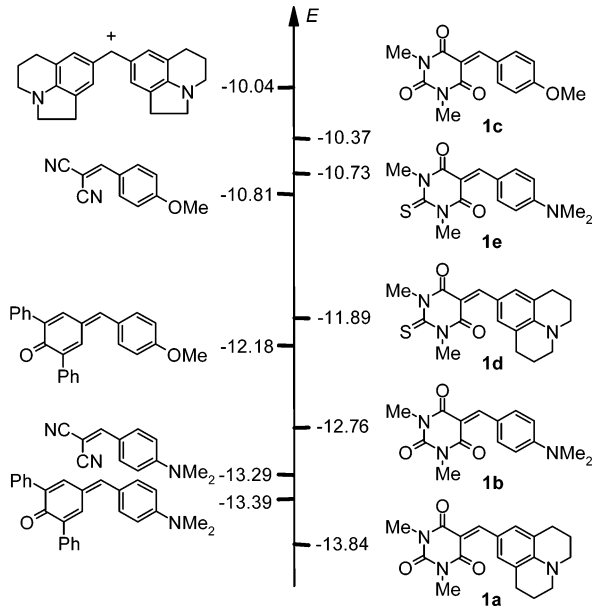
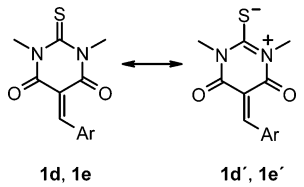


FIGURE 6. Comparison of electrophilicity parameters E of Michael acceptors, quinone methides, and diarylcarbenium ions.

SCHEME 3. Resonance Effects of Benzylidenethiobarbituric Acids 1d,e



with each of the electrophiles **1a**−**c** than expected from its previously published reactivity parameters N and s.[43] On the other hand, the malononitrile anion **2h** reacts 2−4 times faster with electrophiles **1a**−**d** than expected (Figures 3 and 4). A comparison of the electrophilicities of diarylcarbenium ions, quinone methides, and benzylidenebarbituric and -thiobarbituric acids (**1a**−**e**) is given in Figure 5.

The good fit demonstrates that the nucleophilic reactivity order of carbanions that was derived from the rates of their

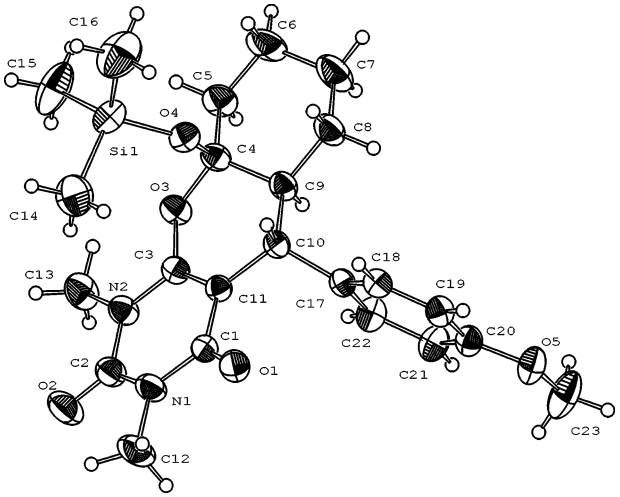


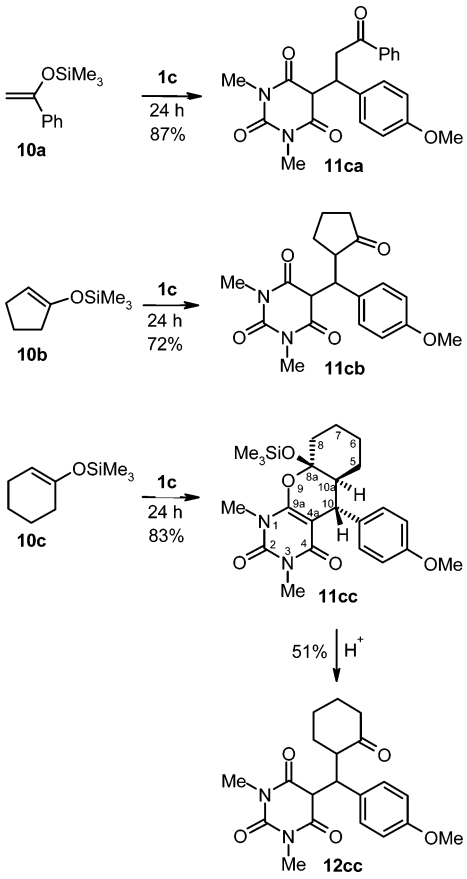
FIGURE 7. X-ray crystal structure (ORTEP projection) of **11cc**. Atom numbers refer to X-ray analysis.

reactions with diarylcarbenium ions and quinone methides in DMSO also holds for the reactions with typical Michael acceptors. In agreement with the conclusions drawn from Figures 3 and 4, Figure 5 also shows that **2b**, the anion of dimedone, reacts faster with the benzylidenebarbituric and -thiobarbituric acids **1a**−**e** than expected from the rates of reactions of **2b** with the reference electrophiles (diarylcarbenium ions and quinone methides).

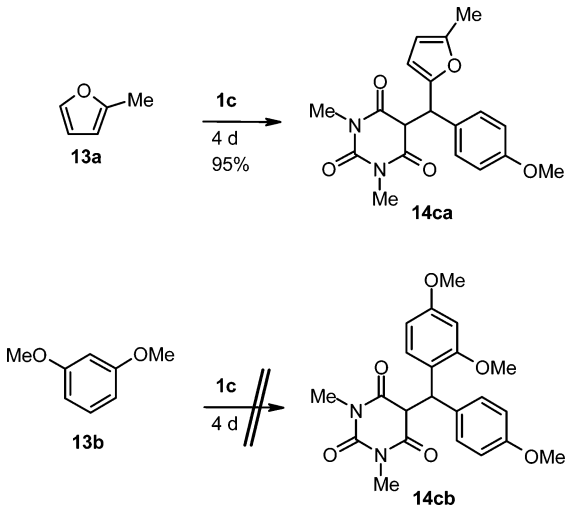
As summarized in Figure 6, benzylidenebarbituric and -thiobarbituric acid derivatives have similar electrophilicities as the corresponding benzylidenemalononitriles. It is found that the thiobarbiturates are more reactive than the corresponding oxa analogues. This observation may be surprising because oxygen is more electronegative than sulfur. Obviously different resonance effects in amides and thioamides are responsible for this ranking of reactivity. It has been reported that thiolactams possess greater dipole moments than lactams.[53] The higher rotational barrier for the C−N bond in thioformamides as compared to formamides also indicates the high contribution of a resonance structure with a C═N double bond.[54] Ab initio MO calculations by Wiberg and Rablen showed that more electron density is transferred from nitrogen to sulfur in thioformamides than from nitrogen to oxygen in formamides.[55] If one assumes that the thioamide structure with a C═N double bond also has a greater importance in the thiobarbituric acids, one can conclude that the positive polarization of nitrogen in the resonance structures **1d′** and **1e′** (Scheme 3) is responsible for the increased electron accepting abilities of the thiobarbituric acids.

Reactions with Other Types of Nucleophiles. From the reactivity parameter of **1c** ($E = -10.37$), one can derive that this electrophile should also be capable of undergoing reactions with electron-rich π-systems with $N > 5$ (e.g., silyl enol ethers or electron-rich arenes). In accord with this conclusion, **1c** was found to react with 1-phenyl-1-(trimethylsiloxy)ethene (**10a**, $N = 6.22$, $s = 0.96$)[56] and 1-(trimethylsiloxy)cyclopentene (**10b**, $N = 6.57$, $s = 0.93$)[56] in DMSO at 20 °C to give **11ca** and **11cb**, respectively, after aqueous workup (Scheme 4). Compound **11ca** has previously been synthesized by the base catalyzed addition of 1,3-dimethylbarbituric acid to 3-(4-methoxyphenyl)-1-phenylprop-2-en-1-one.[57] Attempts to follow the reaction of **1c** with **10b** kinetically were not successful. At $[\mathbf{1c}]_0 = 9.92 \times 10^{-5}$ mol L^{-1} and $[\mathbf{10b}]_0 = 1.08 \times 10^{-2}$ mol

SCHEME 4. Reactions of 1c with Silyl Enol Ethers 10a−c in DMSO at 20 °C



SCHEME 5. Reactions of 1c with Electron-Rich Arenes 13a,b in DMSO at 20 °C



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SCHEME 6. Reactions of 1b,c with Amines in DMSO at 20 °C

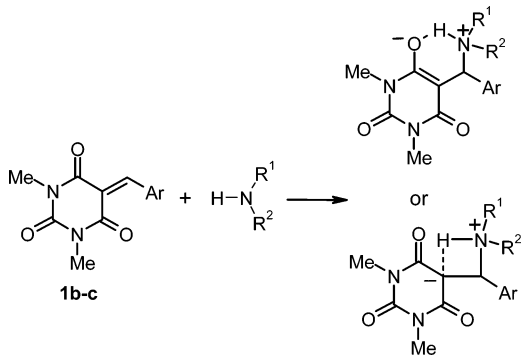


TABLE 4. Experimental and Calculated (eq 1) Second-Order Rate Constants k_2 for Reactions of Amines with 1b,c in Comparison with Literature Data

	nucleophile	$N/s^{a,b}$	exptl k_2 (L mol^{-1} s^{-1})^b	calcd k_2 (L mol^{-1} s^{-1})^b	k_2 (L mol^{-1} s^{-1})^{c,d}
1b	propyl amine	15.70/0.64	2.12×10^3	7.61×10^1	
	morpholine	16.96/0.67	2.01×10^4	6.52×10^2	
	piperidine	17.19/0.71		1.40×10^3	2.9×10^4
1c	propyl amine	15.70/0.64	3.13×10^4	2.58×10^3	
	morpholine	16.96/0.67	2.02×10^5	2.60×10^4	
	piperidine	17.19/0.71		6.95×10^4	3.2×10^5

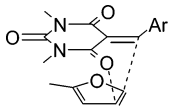
[a] Reference 65. [b] DMSO, 20 °C. [c] MeCN, 25 °C. [d] Reference 7.

L^{-1}, 50% of **1c** was consumed after 3.5 h, but the decay of **1c** was not monoexponential.

The reaction of **1c** with 1-(trimethylsiloxy)cyclohexene (**10c**, $N = 5.21$, $s = 1.00$)[56] did not give the expected cyclohexanone **12cc**. When the solution of the reaction product in DMSO was diluted with water and extracted with ethyl acetate, the hetero-Diels−Alder adduct **11cc** was isolated as the only product. X-ray analysis of **11cc** revealed the trans fusion of the cyclohexane and the tetrahydropyran ring with a pseudo-equatorial position of the anisyl group and a pseudo-axial orientation of the trimethylsiloxy group (Figure 7).

The trans diaxial coupling of the vicinal protons 10-H and 10a-H ($^3J_{10-10a} = 10.8$ Hz) is in accord with this structure. The trans fusion of the two rings of the chromene fragment excludes a concerted Diels−Alder reaction.[58] Because the product has not been exposed to acidic conditions, epimerization of the acetal center appears unlikely,[59−61] and we assume a stepwise mechanism via a dipolar intermediate.[62] Treatment of **11cc** with 1 M aqueous HCl cleaves the silylated acetal and yields the initially expected cyclohexanone **12cc** as a 7:1 mixture of two diastereomers.

As predicted by eq 1, 1,3-dimethoxybenzene (**13b**, $N = 2.48$, $s = 1.09$)[56] does not react with **1c** ($E = -10.37$) in DMSO; after 4 days at room temperature, we did not observe any conversion (Scheme 5). Analogously, eq 1 predicts a very slow reaction ($k_2 = 3.14 \times 10^{-8}$ L mol^{-1} s^{-1}) of **1c** with 2-methylfuran (**13a**, $N = 3.61$, $s = 1.11$).[34] While this rate constant refers to a half reaction time of 10 years for a 0.1 M solution in dichloromethane, the electrophilic substitution product **14ca** was obtained in 95% yield after 4 days in DMSO. The kinetic investigation of this reaction yields a rate constant of $k_2 = 1.24 \times 10^{-4}$ L mol^{-1} s^{-1} (DMSO, 20 °C) (i.e., almost 4 orders of magnitude faster than calculated by eq 1). Although reactions of neutral reactants via dipolar intermediates can be expected to show a large dependence on solvent polarity,[63] we cannot explain at present why calculated and observed rate constants for the reaction of **1c** with **13a** differ so much. Possibly, secondary orbital interactions as indicated in transition state **15** account for the high reactivity of 2-methylfuran (**13a**).



15

To check the applicability of the *E* parameters of the benzylidenebarbituric and -thiobarbituric acids listed in Table 3 for reactions with other types of nucleophiles, we have also studied the rates of the reactions of **1b**,**c** with propyl amine and morpholine.

Because alkyl ammonium ions have higher pK_a values than 5-alkyl-substituted barbituric acids,[64] the additions of primary and secondary amines to **1b**,**c** yield zwitterionic adducts in DMSO as shown in Scheme 6. While the additions of propyl amines proceeded quantitatively, the reactions with morpholine were incomplete, and the absorbances of the electrophiles **1b**,**c** did not disappear completely.

Table 4 compares calculated and experimental rate constants for the additions of amines and shows that eq 1 predicts rate constants for the additions of propyl amine and morpholine to **1c** with an accuracy of 1 order of magnitude. The corresponding reactions of **1b** proceed 28 and 31 times faster than predicted.

The reported rate constants for the additions of piperidine to **1b**,**c** in acetonitrile at 25 °C are 20 and 5 times greater than the calculated rate constants for these reactions in DMSO at 20 °C, again showing qualitative agreement. For the reactions of secondary amines with benzylidene Meldrum's acids in aqueous DMSO, Bernasconi postulated an early development of hydrogen bonding on the reaction coordinate that was supposed to be responsible for enhanced intrinsic rate constants k_0.[66,67] Furthermore, Oh et al. proposed that the additions of benzyl amines to dicarbonyl activated olefins in acetonitrile proceed through cyclic transition states with four- or six-membered rings, where the amine proton forms a hydrogen bond to C_α of the Michael acceptor or to a carbonyl oxygen.[68−71] As a conse-

(58) For an intramolecular hetero-Diels−Alder reaction of a benzylidenebarbituric acid derivative under high pressure, see: Tietze, L. F.; Ott, C.; Gerke, K.; Buback, M. *Angew. Chem.* **1993**, *105*, 1536−1538. Tietze, L. F.; Ott, C.; Gerke, K.; Buback, M. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 1485−1486.

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quence, it is possible that the constant higher reactivity of amines in reactions with benzylidenebarbituric acids is due to interactions of the N−H bonds with the developing negative charge on C_α or one of the carbonyl oxygens of the Michael acceptor.

However, because the deviation between calculated and experimental rate constants for the reactions of **1a**−**e** with amines is within the previously suggested confidence limit of eq 1 (1−2 orders of magnitude),[72] these deviations shall not be overinterpreted.

Conclusion

The linear free-energy relationship $\log k_2(20\ °C) = s(N + E)$ (eq 1) has been found to be suitable for the calculation of the rates of reactions of the benzylidenebarbituric and -thiobarbituric acids **1a**−**e** with carbanions and amines from the *E* parameters of **1a**−**e** determined in this work and the nucleophile-specific parameters *N* and *s* reported earlier.[36,37,43,44] The agreement between calculated and experimental data is within 1 order of magnitude for carbanions, while the few amines examined react 10−30 times faster than calculated. 2-Methylfuran (**13a**), the only π-nucleophile that was kinetically investigated, reacted 4 orders of magnitude faster than predicted. It is speculated as to whether stabilizing secondary orbital interactions are responsible for the failure of eq 1 to predict this rate constant.

Experimental Section

All reactions were performed under an atmosphere of dry nitrogen. Benzylidenebarbituric and -thiobarbituric acids (**1a**−**e**) were synthesized from the corresponding barbituric and thiobarbituric acids and *p*-substituted benzaldehydes according to ref 73.

1,3-Dimethyl-5-(2,3,6,7-tetrahydro-1*H*,5*H*-pyrido[3,2,1-*ij*]-quinolin-9-ylmethylene)pyrimidine-2,4,6(1*H*,3*H*,5*H*)-trione (1a). Red crystals, 90% yield, mp 197−198 °C (EtOH). ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.98 (quint, $^3J = 6.3$ Hz, 4H, 2 × CH_2), 2.78 (t, $^3J = 6.0$ Hz, 4H, 2 × CH_2), 3.35−3.39 (m, 10H, 2 × NCH_3 + 2 × CH_2), 8.07 (s, 2H, Ar), 8.30 (s, 1H, CH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 21.3 (CH_2), 27.8 (CH_2), 28.4 (NCH_3), 29.0 (NCH_3), 50.7 (CH_2), 107.9 ($C(COR)_2$), 120.6 (C_{Ar}-H), 120.7 (C_{Ar}), 137.6 (C_{Ar}), 149.4 (C_{Ar}-N), 152.2 (CO), 158.4 (CH), 162.0 (CO), 164.5 (CO). $C_{19}H_{21}N_3O_3$ (339.4): calcd C 67.77, H 6.24, N 12.38; found C 67.26, H 6.21, N 12.38. HR-MS (EI) [M^+]: calcd 339.1583; found 339.1556.

1,3-Dimethyl-5-(2,3,6,7-tetrahydro-1*H*,5*H*-pyrido[3,2,1-*ij*]-quinolin-9-ylmethylene)-2-thioxo-dihydropyrimidine-4,6(1*H*,5*H*)-dione (1d). Red crystals, 99% yield, mp 193−194 °C (EtOH). ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.99 (quint, $^3J = 6.3$ Hz, 4H, 2 × CH_2), 2.79 (t, $^3J = 6.3$ Hz, 4H, 2 × CH_2), 3.40 (t, $^3J = 5.7$ Hz, 4H, 2 × CH_2), 3.81 (s, 6H, 2 × NCH_3), 8.09 (s, 2H, Ar), 8.30 (s, 1H, CH). ^{13}C NMR (150.8 MHz, $CDCl_3$): δ 21.5 (CH_2), 27.9 (CH_2), 36.0 (NCH_3), 36.6 (NCH_3), 51.1 (CH_2), 108.3 ($C(COR)_2$), 121.1 (C_{Ar}-H), 121.7 (C_{Ar}), 138.4 (C_{Ar}), 150.5 (C_{Ar}-N), 159.7 (CH), 160.5 (CO), 163.6 (CO), 180.4 (CS). HR-MS (ESI) [MH^+]: calcd 356.1433; found 356.1428.

General Procedure A for the Characterization of Potassium Salts 3 by NMR Spectroscopy. Under an argon atmosphere, potassium salt **2** (0.090 mmol) and electrophile **1** (0.090 mmol) were dissolved in 0.7 mL of dry d_6-DMSO. The resulting mixture was investigated by NMR spectroscopy. Explicit formula drawings are given in the Supporting Information.

General Procedure B for the Synthesis of 4, 5, 7, and 8. Under a nitrogen atmosphere, potassium salt **2** (0.44 mmol) was added to a stirred solution of electrophile **1** (0.36 mmol) in dry DMSO (4 mL). For the products of series **4** methyl iodide (0.2 mL, 3.21 mmol) and for the products **5**, **7**, and **8**, concd HCl (0.1 mL) was added after 10 min. The resultant mixture was stirred for additional 2 h and then poured into water (30 mL). After extraction with ethyl acetate (3 × 20 mL) and removal of the solvent in vacuo, the solid residue was recrystallized from ethanol.

General Procedure C for the Synthesis of 11 and 14. Under a nitrogen atmosphere, **10** or **13** (0.54 mmol) were added to a stirred solution of electrophile **1** (0.36 mmol) in dry DMSO (5 mL). After 24 h, the reaction mixture was poured into water (30 mL). After extraction with ethyl acetate (3 × 20 mL) and removal of the solvent in vacuo, the residue was recrystallized from ethanol.

Reactions of 1 with 2 to the Corresponding Potassium Salts 3 According to General Procedure A: 1,3-Dimethyl-2,4,6-trioxo-5-[1-(2,3,6,7-tetrahydro-1*H*,5*H*-pyrido[3,2,1-*ij*]-quinoline-9-yl)-2,2′-dicyanoethyl]-hexahydropyrimidine-5-yl Potassium (3ah). ^{1}H NMR (400 MHz, d_6-DMSO): δ 1.85 (quint, $^3J = 5.7$ Hz, 4H, 2 × CH_2), 2.61 (t, $^3J = 6.5$ Hz, 4H, 2 × CH_2), 3.04 (t, $^3J = 5.7$ Hz, 4H, 2 × CH_2), 3.06 (s, 6H, 2 × NCH_3), 4.43 (d, $^3J = 11.9$ Hz, 1H, CH), 6.02 (d, $^3J = 11.9$ Hz, 1H, CH), 6.85 (s, 2H, Ar). ^{13}C NMR (100 MHz, d_6-DMSO): δ 21.6 (CH_2), 25.8 ($CH(CN)_2$), 26.5, 27.1, 43.2 (CH), 49.2 (CH_2), 83.7 (C-5), 115.0 (CN), 115.3 (CN), 120.0 (2 × C_{Ar}), 125.9 (2 × C_{Ar}-H), 128.7 (C_{Ar}), 141.3 (C_{Ar}-N), 152.5 (CO), 161.5 (2 × CO).

1,3-Dimethyl-2,4,6-trioxo-5-[1-(4-dimethylaminophenyl)-2,2′-dicyano-ethyl]-hexahydropyrimidine-5-yl Potassium (3bh). ^{1}H NMR (400 MHz, d_6-DMSO): δ 2.84 (s, 6H, $N(CH_3)_2$), 3.07 (s, 6H, 2 × NCH_3), 4.57 (d, $^3J = 11.9$ Hz, 1H, CH), 6.08 (d, $^3J = 11.9$ Hz, 1H, CH), 6.60 (d, $^3J = 8.8$ Hz, 2H, Ar), 7.33 (d, $^3J = 8.8$ Hz, 2H, Ar). ^{13}C NMR (100 MHz, d_6-DMSO): δ 25.9 ($CH(CN)_2$), 26.5 (2 × NCH_3), 40.0 ($N(CH_3)_2$), 43.2 (CH), 83.6 (C-5), 111.9 (2 × C_{Ar}-H), 114.9 (CN), 115.1 (CN), 128.3 (2 × C_{Ar}-H), 129.7, 149.2 (C_{Ar}), 152.5 (CO), 161.6 (CO).

1,3-Dimethyl-2,4,6-trioxo-5-[1-(4,4′-dimethyl-2,6-dioxocyclohexyl)-1′-(4-methoxyphenyl)-methyl]-hexahydropyrimidine-5-yl Potassium (3cb). ^{1}H NMR (400 MHz, d_6-DMSO): δ 0.99 (s, 3H, CH_3), 1.04 (s, 3H, CH_3), 2.04−2.33 (m, CH_2, 4H), 3.00 (s, 3H, NCH_3), 3.08 (s, br, 3H, NCH_3), 3.67 (s, 3H, OCH_3), 6.08 (s, 1H, CH), 6.68 (d, $^3J = 8.8$ Hz, 2H, Ar), 6.90 (d, $^3J = 8.8$ Hz, 2H, Ar), 14.60 (s, 1H, OH). ^{13}C NMR (75.5 MHz, d_6-DMSO): δ 26.5 (NCH_3), 27.0 (CH_3), 27.4 (NCH_3), 29.4 (CH_3), 31.0 (CH), 44.8 (CH_2), 50.6 (CH_2), 54.8 (OCH_3), 89.6 (C-5), 112.7 (C_{Ar}-H), 114.6, 116.1, 127.6 (C_{Ar}-H), 136.6, 152.1, 156.2, 163.2, 174.1, 196.2.

1,3-Dimethyl-2,4,6-trioxo-5-[1-(4-methoxyphenyl)-2-acetyl-3-oxo-butyl]-hexahydropyrimidine-5-yl Potassium (3ce). ^{1}H NMR (300 MHz, d_6-DMSO): δ 1.92 (s, 3H, CH_3), 2.05 (s, 3H, CH_3), 2.99 (s, 6H, 2 × NCH_3), 3.66 (s, 3H, OCH_3), 4.81 (d, $^3J = 12.3$ Hz, 1H, CH), 5.48 (d, $^3J = 12.3$ Hz, 1H, CH), 6.67 (d, $^3J = 8.4$ Hz, 2H, Ar), 7.32 (d, $^3J = 8.4$ Hz, 2H, Ar). ^{13}C NMR (75.5 MHz, d_6-DMSO): δ 26.8 (NCH_3), 28.3, 30.5 (CH_3), 40.5 (CH), 54.8 (OCH_3), 69.9 (CH), 86.0 (C-5), 112.7 (C_{Ar}-H), 128.7 (C_{Ar}-H), 137.6, 152.8, 156.8, 161.6, 204.1 (CO), 204.7 (CO).

1,3-Dimethyl-2,4,6-trioxo-5-[1-(4-methoxyphenyl)-2-acetyl-2′-ethoxy-carbonylethyl]-hexahydropyrimidine-5-yl Potassium (3cg). Mixture of diastereomers (5:3). Major diastereomer: ^{1}H NMR (400 MHz, d_6-DMSO): δ 0.94 (t, $^3J = 7.2$ Hz, 3H, CH_2CH_3), 2.11 (s, 3H, CH_3), 2.99 (s, 6H, 2 × NCH_3), 3.66 (s, 3H, OCH_3), 3.83 (q, $^3J = 7.2$ Hz, 2H, CH_2), 4.78 (d, $^3J = 12.8$ Hz, 1H, CH), 5.11 (d, $^3J = 12.4$ Hz, 1H, CH), 6.67 (d, $^3J = 8.8$ Hz, 2H, Ar), 7.32 (d, $^3J = 8.8$ Hz, Ar). ^{13}C NMR (100 MHz, d_6-DMSO): δ 13.8 (CH_2CH_3), 26.8 (NCH_3), 27.8 ($COCH_3$), 40.5 (CH), 54.8 (OCH_3), 59.9 (CH_2), 61.7 (CH), 85.7 (C-5), 112.5 (C_{Ar}-H), 128.8 (C_{Ar}-H), 137.5, 152.8, 156.8, 168.6, 169.3, 203.4 ($COCH_3$). Minor diastereomer: ^{1}H NMR (400 MHz, d_6-DMSO): δ 0.99 (t, $^3J = 7.2$ Hz, 3H, CH_2CH_3), 1.94 (s, 3H, CH_3), 2.99 (s, 6H, 2 × NCH_3), 3.66 (s, 3H, OCH_3), 3.90−3.98 (m, 2H, CH_2), 4.76 (d, $^3J = 12.0$ Hz 1H, CH), 5.28 (d, $^3J =$

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12.4 Hz 1H, CH), 6.67 (d, ^3J = 8.8 Hz, 2H, Ar), 7.32 (d, ^3J = 8.8 Hz, Ar). ^{13}C NMR (100 MHz, d_6-DMSO): δ 13.7 (CH_2CH_3), 26.8 (NCH_3), 29.3 ($COCH_3$), 40.4 (CH), 54.8 (OCH_3), 59.7 (CH_2), 61.6 (CH), 86.1 (C-5), 112.6 (C_{Ar}-H), 128.9 (C_{Ar}-H), 137.3, 152.8, 156.8, 168.6, 169.3, 204.2 (*C*OCH_3).

1,3-Dimethyl-2,4,6-trioxo-5-[1-(4-methoxyphenyl)-2,2′-dicyanoethyl]-hexahydropyrimidine-5-yl Potassium (3ch). ^{1}H NMR (400 MHz, d_6-DMSO): δ 3.05 (s, 6H, 2 × NCH_3), 3.70 (s, 3H, OCH_3), 4.61 (d, ^3J = 12.0 Hz, 1H, CH), 6.12 (d, ^3J = 12.4 Hz, 1H, CH), 6.80 (d, ^3J = 8.8 Hz, 2H, Ar), 7.42 (d, ^3J = 8.8 Hz, 2H, Ar). ^{13}C NMR (100 MHz, d_6-DMSO): δ 26.1 (*C*H($CN)_2$), 26.9 (NCH_3), 43.2 (CH), 55.0 (OCH_3), 83.7 (C-5), 113.3 (Ar), 115.1 (CN), 115.4 (CN), 129.0, 134.0, 152.7 (Ar), 158.1, 161.8 (CO).

1,3-Dimethyl-2,4,6-trioxo-5-[1-(4-methoxyphenyl)-2-cyano-2′-ethoxy-carbonylethyl]-hexahydropyrimidine-5-yl Potassium (3ci). Mixture of diastereomers (2:1). Major diastereomer: ^{1}H NMR (300 MHz, d_6-DMSO): δ 0.92 (t, ^3J = 6.9 Hz, 3H, CH_3), 3.05 (s, 6H, 2 × NCH_3), 3.66 (s, 3H, OCH_3), 3.91 (q, ^3J = 6.9 Hz, 2H, CH_2), 4.59 (d, ^3J = 12.3 Hz, 1H, CH), 5.37 (d, ^3J = 12.3 Hz, 1H, CH), 6.71 (d, ^3J = 8.7 Hz, 2H, Ar), 7.34 (d, ^3J = 8.7 Hz, 2H, Ar). ^{13}C NMR (75.5 MHz, d_6-DMSO): δ 13.5 (CH_3), 26.8 (NCH_3), 40.3 (CH), 42.3 (CH), 54.8 (OCH_3), 61.3 (CH_2), 85.1 (C-5), 112.9 (C_{Ar}-H), 118.0 (CN), 129.0 (C_{Ar}-H), 135.3, 152.7, 157.6, 161.8, 166.8. Minor diastereomer: ^{1}H NMR (300 MHz, d_6-DMSO): δ 1.01 (t, ^3J = 7.2 Hz, 3H, CH_3), 3.00 (s, 6H, 2 × NCH_3), 3.70 (s, 3H, OCH_3), 3.97−3.14 (m, 2H, CH_2), 4.65 (d, ^3J = 12.3 Hz, 1H, CH), 5.35 (d, ^3J = 12.0 Hz, 1H, CH), 6.78 (d, ^3J = 8.4 Hz, 2H, Ar), 7.44 (d, ^3J = 8.7 Hz, 2H, Ar). ^{13}C NMR (75.5 MHz, d_6-DMSO): δ 13.5 (CH_3), 26.7 (NCH_3), 40.3 (CH), 42.3 (CH), 54.8 (OCH_3), 61.0 (CH_2), 83.9 (C-5), 112.9 (C_{Ar}-H), 118.4 (CN), 129.1 (C_{Ar}-H), 135.6, 152.7, 157.5, 161.5, 166.3.

1,3-Dimethyl-2,4,6-trioxo-5-[1-(4-methoxyphenyl)-2,2′-diethoxy-carbonylethyl]-hexahydropyrimidine-5-yl Potassium (3ck). ^{1}H NMR (300 MHz, d_6-DMSO): δ 0.92 (t, ^3J = 7.2 Hz, 3H, CH_3), 0.99 (t, ^3J = 6.9 Hz, 3H, CH_3), 2.99 (s, 6H, 2 × NCH_3), 3.65 (s, 3H, OCH_3), 3.83 (q, ^3J = 6.9 Hz, 2H, CH_2), 3.94 (q, ^3J = 6.9 Hz, 2H, CH_2), 4.70 (d, ^3J = 12.3 Hz, 1H, CH), 5.14 (d, ^3J = 12.3 Hz, 1H, CH), 6.66 (d, ^3J = 8.7 Hz, 2H, Ar), 7.33 (d, ^3J = 8.7 Hz, 2H, Ar). ^{13}C NMR (75.5 MHz, d_6-DMSO): δ 13.7 (CH_3), 26.7 (NCH_3), 40.5 (CH), 53.7 (CH), 54.8 (OCH_3), 59.7, 59.8 (CH_2), 85.9 (C-5), 112.4, 128.9, 137.5, 152.8 (Ar), 156.8, 161.5 (CO), 168.4, 169.0 (*C*O_2Et).

1,3-Dimethyl-2,4,6-trioxo-5-[1-(4-methoxyphenyl)-2-nitropropyl]-hexahydropyrimidine-5-yl Potassium (3cm). Mixture of diastereomers (9:2). Major diastereomer: ^{1}H NMR (300 MHz, d_6-DMSO): δ 1.37 (d, ^3J = 6.3 Hz, 3H, CH_3), 3.03 (s, 6H, NCH_3), 3.66 (s, 3H, OCH_3), 4.45 (d, ^3J = 11.4, 1H, CH), 6.00 (m, 1H, C*H*CH_3), 6.69, (d, ^3J = 8.7 Hz, 2H, Ar), 7.34 (d, ^3J = 8.7 Hz 2H, Ar). ^{13}C NMR (75.5 MHz, d_6-DMSO): δ 18.9 (CH_3), 26.9 (NCH_3), 45.8 (CH), 54.8 (OCH_3), 85.0 (C-5), 86.8 (*C*-CH_3), 112.8 (C_{Ar}-H), 128.8 (C_{Ar}-H), 136.2, 152.7, 157.3, 161.5, 161.6. Minor diastereomer: ^{1}H NMR (300 MHz, d_6-DMSO): δ 1.21 (d, ^3J = 6.6 Hz, 3H, CH_3), 2.99 (s, 6H, NCH_3), 3.69 (s, 3H, OCH_3), 4.43 (d, ^3J = 11.4, 1H, CH), 6.20 (m, 1H, C*H*CH_3), 6.75 (d, ^3J = 8.7 Hz, 2H, Ar), 7.45 (d, ^3J = 8.7 Hz 2H, Ar). ^{13}C NMR (75.5 MHz, d_6-DMSO): δ 18.9 (CH_3), 27.2 (NCH_3), 45.7 (CH), 55.0 (OCH_3), 83.8 (C-5), 88.3 (*C*-CH_3), 113.0 (C_{Ar}-H), 129.6 (C_{Ar}-H), 137.3, 152.6, 157.3, 161.7, 161.7.

5-[2-Acetyl-1-(2,3,6,7-tetrahydro-1*H*,5*H*-pyrido[3,2,1-*ij*]-quinoline-9-yl)-3-oxobutyl]-1,3-dimethyl-2-thioxodihydropyrimidine-4,6(1*H*,5*H*)-dione-5-yl Potassium (3de). ^{1}H NMR (300 MHz, d_6-DMSO): δ 1.82 (quint, ^3J = 5.4 Hz, 4H, 2 × CH_2), 1.96, 2.02 (2s, 6H, 2 × CH_3-CO), 2.57 (t, ^3J = 6.3 Hz, 4H, 2 × CH_2), 2.97 (t, ^3J = 5.1 Hz, 4H, CH_2), 3.46 (s, 6H, 2 × NCH_3), 4.67 (d, ^3J = 12.3 Hz, 1H, CH), 5.41 (d, ^3J = 12.3 Hz, 1H, CH), 6.73 (s, 2H, Ar). ^{13}C NMR (100 MHz, d_6-DMSO): δ 22.0 (CH_2), 27.3 (CH_2), 28.4 (*C*H_3−CO), 30.6 (*C*H_3-CO), 34.5 (2 × NCH_3), 40.3 (CH), 49.5 (CH_2), 69.7 (*C*H($COCH_3)_2$), 91.5 (C-5), 120.0 (2 × C_{Ar}), 126.2 (2 × C_{Ar}-H), 131.7 (C_{Ar}), 140.6 (C_{Ar}-N), 160.2 (2 × CO), 174.9 (CS), 203.9 (*C*O-CH_3), 204.6 (*C*O-CH_3).

1,3-Dimethyl-5-[1-(2,3,6,7-tetrahydro-1*H*,5*H*-pyrido[3,2,1-*ij*]-quinoline-9-yl)-2,2′-dicyano-ethyl]-2-thioxodihydropyrimidine-4,6(1*H*,5*H*)-dione-5-yl Potassium (3dh). ^{1}H NMR (300 MHz, d_6-DMSO): δ 1.83 (quint, ^3J = 5.4 Hz, 4H, 2 × CH_2), 2.60 (t, ^3J = 6.3 Hz, 4H, 2 × CH_2), 3.03 (t, ^3J = 5.4 Hz, 4H, 2 × CH_2), 3.51 (s, 6H, 2 × NCH_3), 4.43 (d, ^3J = 12.1 Hz, 1H, CH), 5.96 (d, ^3J = 12.1 Hz, 1H, CH), 6.82 (s, 2H, Ar). ^{13}C NMR (75.5 MHz, d_6-DMSO): δ 21.7 (CH_2), 26.1 (*C*H($CN)_2$), 27.3 (CH_2), 34.4 (2 × NCH_3), 43.2 (CH), 49.3 (CH_2), 88.9 (C-5), 115.0 (CN), 115.3 (CN), 120.3 (2 × C_{Ar}), 126.1 (2 × C_{Ar}-H), 127.8 (C_{Ar}), 141.7 (C_{Ar}-N), 160.4 (2 × CO), 175.6 (C═S).

5-[2-Acetyl-1-(4-dimethylaminophenyl)-3-oxobutyl]-1,3-dimethyl-2-thioxodihydropyrimidine-4,6(1*H*,5*H*)-dione-5-yl Potassium (3ee). ^{1}H NMR (400 MHz, d_6-DMSO): δ 1.93, 2.05 (2s, 2 × 3H, 2 × CH_3-CO), 2.78 (s, 6H, $N(CH_3)_2$), 3.46 (s, 6H, 2 × NCH_3), 4.78 (d, ^3J = 12.5 Hz, 1H, CH), 5.47 (d, ^3J = 12.4 Hz, 1H, CH), 6.52 (d, ^3J = 8.7 Hz, 2H, Ar), 7.22 (d, ^3J = 8.6 Hz, 2H, Ar). ^{13}C NMR (100 MHz, d_6-DMSO): δ 28.4 (*C*H_3-CO), 30.4 (*C*H_3-CO), 34.4 (NCH_3), 40.4 ($N(CH_3)_2$), 40.4 (CH), 69.8 (*C*H-$(COCH_3)_2$), 91.4 (C-5), 112.0 (C_{Ar}-H), 128.3 (C_{Ar}-H), 132.6 (C_{Ar}-N), 148.5 (C_{Ar}), 160.3 (2 × CO), 174.9 (CS), 203.8 (*C*O-CH_3), 204.5 (*C*O-CH_3).

Reactions of 1 with 2 Followed by Methylation to the Corresponding Compounds 4 According to General Procedure B: Diethyl [4-Methoxyphenyl(1,3,5-trimethyl-2,4,6-trioxohexahydropyr-imidine-5-yl)methyl]-malonate (4ck). Colorless oil, 74% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.84, 1.23 (2t, ^3J = 7.2 Hz, 2 × 3H, 2 × CH_3), 1.32 (s, 3H, 5-CH_3), 3.06, 3.18, (2s, 6H, 2 × NCH_3), 3.71 (s, 3H, OCH_3), 3.72−3.80 (m, 2H, CH_2), 4.14 (q, ^3J = 7.2 Hz, 2H, CH_2), 4.32 (d, ^3J = 11.7 Hz, 1H, CH), 4.43 (d, ^3J = 11.4 Hz, 1H, CH), 6.71 (d, ^3J = 9.0 Hz, 2H, Ar), 7.09 (d, ^3J = 8.7 Hz, 2H, Ar). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 13.7 (CH_2CH_3), 14.0 (CH_2CH_3), 23.6 (CH_3-5), 28.5 (NCH_3), 28.7 (NCH_3), 50.0 (CH), 53.6 (CH), 54.5 (C-5), 55.2 (OCH_3), 61.4 (CH_2), 62.1 (CH_2), 113.5 (C_{Ar}-H), 128.3 (C_{Ar}), 130.7 (C_{Ar}-H), 150.7 (CO), 159.3 (C_{Ar}-OCH_3), 167.3 (CO_2), 169.0 (CO_2), 171.8 (2 × CO). IR (KBr): $\tilde{\nu}$ = 2983, 2840, 1734, 1679, 1612, 1583, 1514, 1449, 1422, 1383, 1294, 1253, 1217, 1182, 1152, 1118, 1096, 1070, 1033 cm^{-1}. MS (EI) *m*/*z* (%) = 448.2 (3) [M^+], 279 (98), 233 (33), 207 (17), 206 (12), 170 (10), 165 (49), 162 (12), 161 (100), 133 (14).

5-[1-(4-Methoxyphenyl)-2-nitropropyl]-1,3,5-trimethylpyrimidine-2,4,6(1*H*,3*H*,5*H*)-trione (4cm). Colorless crystals, 98% yield, isolated as mixture of diastereomers (9:2). Major diastereomer: ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.59 (s, 3H, 5-CH_3), 1.76 (d, ^3J = 6.4 Hz, 3H, CH_3), 2.97, 3.27 (2s, 6H, 2 × NCH_3), 3.71 (s, 3H, OCH_3), 3.93 (d, ^3J = 10.8 Hz, 1H, CH), 5.39 (qd, 1H, ^3J = 6.5 Hz, ^3J = 10.8 Hz, 1H, CH), 6.72 (d, ^3J = 8.8 Hz, 2H, Ar), 7.01 (d, ^3J = 8.4 Hz, 2H, Ar). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 20.7 (CH_3), 25.4 (CH_3-5), 28.6, 28.8 (NCH_3), 54.3 (C-5), 54.5 (CH), 55.2 (OCH_3), 86.3 (CH), 114.0 (C_{Ar}-H), 126.9, 130.1 (C_{Ar}-H), 150.2, 159.7, 171.0, 171.3. Minor diastereomer: ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.22 (d, ^3J = 6.4 Hz, 3H, CH_3), 1.38 (s, 3H, 5-CH_3), 3.07, 3.22 (2s, 6H, 2 × NCH_3), 3.75 (s, 3H, OCH_3), 4.14 (d, ^3J = 10.8 Hz, 1H, CH), 5.56 (qd, 1H, ^3J = 6.7 Hz, ^3J = 10.5 Hz, 1H, CH), 6.79 (d, ^3J = 8.8 Hz, 2H, Ar), 7.06 (d, ^3J = 8.8 Hz, 2H, Ar). $C_{17}H_{21}N_3O_6$ (363.3): calcd C 56.19, H 5.82, N 11.56; found C 56.03, H 5.82, N 11.53.

Reactions of 1 with 2 Followed by Protonation to the Corresponding Compounds 5, 7, and 8 According to General Procedure B: 5-[1-(4-Dimethylaminophenyl)-2-nitropropyl]-1,3-dimethylpyrimidine-2,4,6(1*H*,3*H*,5*H*)-trione (5bm). Colorless crystals, 74% yield, isolated as mixture of diastereomers (10:1). Major diastereomer: ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.39, (d, ^3J = 6.9 Hz, 3H, CH_3), 2.92 (s, 6H, $N(CH_3)_2$), 3.05, 3.17 (2s, 6H, 2 × NCH_3), 3.68 (d, ^3J = 3.3 Hz, 1H, 5-H), 4.02 (dd, ^3J = 11.4 Hz, ^3J = 3.6 Hz, 1H, CH), 5.55 (m, 1H, CH), 6.55 (d, ^3J = 9.0 Hz, 2H, Ar), 6.82 (d, ^3J = 8.7 Hz, 2H, Ar). ^{13}C NMR (75.5 MHz,

$CDCl_3$): δ 19.7 (CH_3), 28.4, 28.5 (NCH_3), 40.3, 51.2, 51.7, 83.5, (CH), 112.5 (C_{Ar}-H), 119.9, 129.0 (C_{Ar}-H), 150.7, 151.0, 167.2, 167.4. $C_{17}H_{22}N_4O_5$ (362.4): calcd C 56.35, H 6.12, N 15.46; found C 56.17, H 6.14, N 15.16. HR-MS (EI) [M^+]: calcd 362.1590; found 362.1565.

1,3-Dimethyl-5-[(4,4′-dimethyl-2,6-dioxocyclohexyl)(4-methoxyphenyl)methyl]-pyrimidine-2,4,6(1*H*,3*H*,5*H*)-trione (5cb). Colorless crystals, 93% yield, mp 146−147 °C (EtOH). ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.13 (s, 3H, CH_3), 1.26 (s, 3H, CH_3), 2.40 (m, 4H, CH_2), 3.35 (s, 3H, NCH_3), 3.44 (s, 3H, NCH_3), 3.78 (s, 3H, OCH_3), 5.51 (s, 1H, CH), 6.82 (d, ^3J = 8.8 Hz, 2H, Ar), 7.02 (d, ^3J = 8.8 Hz, 2H, Ar), 11.32 (br. s, 1H, OH), 12.82 (s, 1H, 6-OH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 27.3, 29.0, 29.4, 30.2, 31.4, 33.1, 46.2 (CH_2), 47.2 (CH_2), 55.4 (OCH_3), 92.8 (C-5), 113.9 (C_{Ar}-H), 116.8 (C-1), 127.8 (C_{Ar}-H), 129.1, 150.9, 158.1, 162.5, 164.3, 190.9, 191.4. IR (KBr): $\tilde{\nu}$ = 3428, 3055, 3001, 2959, 2839, 2632, 1702, 1609, 1510, 1466, 1421, 1389, 1305, 1264, 1249, 1178, 1154, 1117, 1095, 1031, 938 cm^{-1}. $C_{22}H_{26}N_2O_6$ (414.4): calcd C 63.77, H 6.32, N 6.76; found C 63.50, H 6.33, N 6.55.

5-[2-Acetyl-1-(4-methoxyphenyl)-3-oxobutyl]-1,3-dimethylpyrimidine-2,4,6(1*H*,3*H*,5*H*)-trione (5ce). Colorless crystals, 93% yield, mp 116−118 °C (EtOH). ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.88 (s, 3H, CH_3), 2.36 (s, 3H, CH_3), 2.92 (s, 3H, NCH_3), 3.10 (s, 3H, NCH_3), 3.69 (s, 3H, OCH_3), 3.73 (d, ^3J = 4.4 Hz, 1H, 5-H), 4.28 (dd, ^3J = 12.0 Hz, J = 4.4 Hz, 1H, CH), 4.79 (d, ^3J = 12.4 Hz, 1H, CH), 6.70, (d, ^3J = 8.8 Hz, 2H, Ar), 6.85 (d, ^3J = 8.8 Hz, 2H, Ar). ^{13}C NMR (100 MHz, $CDCl_3$): δ 28.1 (NCH_3), 28.2 (NCH_3), 28.5 (CH_3), 30.6 (CH_3), 46.5 (CH), 51.1 (CH), 55.3 (OCH_3), 70.7 (CH), 114.4 (C_{Ar}-H), 126.5, 129.1 (C_{Ar}-H), 150.8, 158.8, 159.9, 167.6 (2 × CO), 201.4 (*C*OCH_3), 202.4 (*C*OCH_3). IR (KBr): $\tilde{\nu}$ = 3409, 2943, 2843, 1744, 1678, 1611, 1570, 1540, 1514, 1424, 1380, 1363, 1256, 1185, 1140, 1120, 1085, 1022, 994 cm^{-1}. $C_{19}H_{22}N_2O_6$ (374.4): calcd C 60.95, H 5.92, N 7.48; found C 60.90, H 5.86, N 7.57.

Ethyl 2-[(1,3-Dimethyl-2,4,6-trioxohexahydropyrimidine-5-yl)(4-methoxyphenyl)-methyl]-3-oxobutanoate (5cg). Colorless crystals, 88% yield, isolated as mixture of diastereomers (4:3). Major diastereomer: ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.93 (t, ^3J = 7.2 Hz, 3H, CH_2CH_3), 2.42 (s, 3H, CH_3), 2.95, 3.14 (2s, 6H, 2 × NCH_3), 3.72 (s, 3H, OCH_3), 3.83−4.33 (m, 4H, CH_2 + 5-H + CH), 4.64 (d, ^3J = 12.4 Hz, 1H, CH), 6.72 (d, ^3J = 8.8 Hz, 2H, Ar), 6.90 (d, ^3J = 8.8 Hz, 2H, Ar). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 13.9, (CH_2CH_3), 28.2, 28.3 (NCH_3), 30.2 (CH_3), 45.9 (CH), 50.8 (C-5), 55.3 (OCH_3), 61.5 (CH), 61.8 (CH_2), 114.1 (C_{Ar}-H), 127.4, 129.1 (C_{Ar}-H), 150.9, 159.7, 166.9, 167.7, 168.0, 201.6. Minor diastereomer: ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.29 (t, ^3J = 7.2 Hz, 3H, CH_2CH_3), 2.01 (s, 3H, CH_3), 2.99, 3.15 (2s, 6H, 2 × NCH_3), 3.71 (s, 3H, OCH_3), 3.83−4.33 (m, 4H, CH_2 + 5-H + CH), 4.64 (d, ^3J = 12.4 Hz, 1H, CH), 6.71 (d, ^3J = 8.8 Hz, 2H, Ar), 6.91 (d, ^3J = 8.8 Hz, 2H, Ar). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 14.2 (CH_2CH_3), 28.2, 28.3 (NCH_3), 30.9 (CH_3), 46.4 (CH), 51.4 (C-5), 55.3 (OCH_3), 60.6 (CH), 62.1 (CH_2), 114.4 (C_{Ar}-H), 127.4, 129.1 (C_{Ar}-H), 151.0, 159.7, 166.9, 167.7, 167.9, 168.0, 201.3. $C_{20}H_{24}N_2O_7$ (404.4): calcd C 59.40, H 5.98, N 6.93; found C 59.00, H 5.82, N 6.82.

5-[1-(4-Methoxyphenyl)-2-nitropropyl]-1,3-dimethylpyrimidine-2,4,6-(1*H*,3*H*,5*H*)-trione (5cm). Colorless crystals, 74% yield, isolated as mixture of diastereomers (7:2). Major diastereomer: ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.90 (d, ^3J = 6.6 Hz, 3H, CH_3), 3.02, 3.14, (2s, 6H, NCH_3), 3.73 (d, ^3J = 3.3 Hz, 1H, 5-H), 3.72 (s, 3H, OCH_3), 4.01−4.11 (m, 1H, CH), 5.44−5.55 (m, 1H, C*H*CH_3), 6.73 (d, ^3J = 8.7 Hz, 2H, Ar), 6.91 (d, ^3J = 8.7 Hz, 2H, Ar). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 18.9 (CH_3), 28.3, 28.6 (NCH_3), 50.6 (C-5), 51.8 (CH), 55.3 (OCH_3), 84.9 (CH), 114.5 (C_{Ar}-H), 125.2, 128.8 (C_{Ar}-H), 150.5, 160.2, 167.0, 167.3. Minor diastereomer: ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.37 (d, ^3J = 6.6 Hz, 3H, CH_3), 3.04, 3.16 (2s, 6H, NCH_3), 3.68 (d, ^3J = 3.3 Hz, 1H, 5-H), 3.75 (s, 3H, OCH_3), 4.01−4.11 (m, 1H, CH), 5.55−5.64 (m, 1H, C*H*CH_3), 6.79 (d, ^3J = 8.7 Hz, 2H, Ar), 6.93 (d, ^3J = 8.7 Hz, 2H, Ar). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 19.7 (CH_3), 28.3, 28.5 (NCH_3), 50.9 (C-5), 51.3 (CH), 55.3 (OCH_3), 83.4 (CH), 114.8 (C_{Ar}-H), 125.4, 129.5 (C_{Ar}-H), 150.7, 160.1, 167.0, 167.3. $C_{16}H_{19}N_3O_6$ (349.2): calcd C 55.01, H 5.48, N 12.03; found C 54.66, H 5.61, N 11.85.

1-(4-Dimethylaminophenyl)-2,2′-dicyanoethene (7bh). 62% yield, mp 179−180 °C (EtOH, 179 °C).[74] The ^{1}H NMR spectrum is consistent with that reported in ref 74.

1-(4-Methoxyphenyl)-2,2′-dicyanoethene (7ch). 21% yield, mp 113−114 °C (EtOH, 115−116 °C).[76] The ^{1}H NMR spectrum is consistent with that reported in ref 76.

1-(4-Methoxyphenyl)-2-cyano-2-ethoxycarbonylethene (7ci). 83% yield, mp 79−81 °C (EtOH, 81−82 °C).[75] The ^{1}H NMR spectrum is consistent with that reported in ref 75.

7-Amino-5-(4-methoxyphenyl)-1,3-dimethyl-2,4-dioxo-1,3,4,5-tetrahydro-2*H*-pyrano[2,3-*d*]-pyrimidine-6-carbonitrile (8ch). Colorless crystals, 47% yield, mp 225−227 °C (EtOH). ^{1}H NMR (400 MHz, d_6-DMSO): δ 3.08 (s, 3H, NCH_3), 3.34 (s, 3H, NCH_3), 3.72 (s, 3H, OCH_3), 4.27 (s, 1H, CH), 6.83 (d, ^3J = 8.8 Hz, 2H, Ar), 7.15 (d, ^3J = 8.8 Hz, 2H, Ar), 7.30 (br s, 2H, NH_2). ^{13}C NMR (100 MHz, d_6-DMSO): δ 27.7 (NCH_3), 29.1 (NCH_3), 35.8 (CH), 55.0 (OCH_3), 58.9 (*C*-CN), 89.1, 113.6 (C_{Ar}-H), 115.2 (CN), 119.2, 128.4 (C_{Ar}-H), 133.4, 136.2, 150.0, 150.9, 157.6, 158.1, 160.5. IR (KBr): $\tilde{\nu}$ = 3419, 3306, 3190, 2950, 2194, 1687, 1639, 1611, 1511, 1493, 1461, 1388, 1304, 1262, 1244, 1230, 1181, 1037, 970 cm^{-1}. $C_{17}H_{21}N_3O_6$ (340.3): calcd C 59.99, H 4.74, N 16.46; found C 60.18, H 4.73, N 16.65.

Reaction of 8ch with Cyclohexanone to 9ch. Compound **8ch** (0.130 g, 0.382 mmol) and cyclohexanone (0.043 mL, 0.42 mmol) were added to a suspension of $AlCl_3$ (0.056 g, 0.42 mmol) in 5 mL of 1,2-dichloroethane. The mixture was then refluxed for 3.5 h in a nitrogen flow. After cooling, 3 mL of aqueous THF (65%) and 3 mL of sodium hydroxide solution (10%) were added, and the resulting mixture was extracted with ethyl acetate (3 × 50 mL). The combined organic layers were washed with water and dried over $CaCl_2$. After removal of the solvent, the residue was purified by column chromatography (silica gel, $CHCl_3$/EtOH 50:1) and recrystallization from ethanol.

6-Amino-5-(4-methoxyphenyl)-1,3-dimethyl-1,5,7,8,9,10-hexahydro-12-oxa-1,3,11-triaza-naphthacene-2,4-dione (9ch). Colorless crystals, 69% yield, mp >240 °C (EtOH). ^{1}H NMR (600 MHz, $CDCl_3$): δ 1.83 (m, 4H, 2 × CH_2), 2.30 (m, 2H, CH_2), 2.79 (m, 2H, CH_2), 3.27 (s, 3H, NCH_3), 3.59 (s, 3H, NCH_3), 3.74 (s, 3H, OCH_3), 4.17 (br. s, 2H, NH_2), 4.91 (s, 1H, CH), 6.81 (d, ^3J = 8.4 Hz, 2H, Ar), 7.30 (d, ^3J = 9.0 Hz, 2H, Ar). ^{13}C NMR (150 MHz, $CDCl_3$): δ 22.4 (CH_2), 22.7 (CH_2), 23.1 (CH_2), 28.3 (NCH_3), 29.6 (NCH_3), 32.7 (CH_2), 35.3, 55.4 (OCH_3), 91.0, 99.7, 114.3 (C_{Ar}-H), 115.1, 129.6 (C_{Ar}-H), 134.4, 150.9, 151.2, 152.6, 153.7, 154.5, 159.0, 162.0. IR (KBr): $\tilde{\nu}$ = 3502, 3393, 2937, 1709, 1664, 1627, 1510, 1491, 1447, 1420, 1376, 1320, 1301, 1260, 1237, 1204, 1186, 1084, 1046, 1030, 976 cm^{-1}. $C_{23}H_{24}N_4O_4$ (420.45): calcd C 65.70, H 5.75, N 13.32; found C 65.51, H 5.79, N 13.02.

Reactions of 1c with 10a-c and 13a to the Corresponding Compounds 11 and 14ca according to General Procedure C. 1,3-Dimethyl-5-(4-methoxyphenyl-3-oxo-1-phenylpropyl)pyrimidine-2,4,6(1*H*,3*H*,5*H*)-trione (11ca). Colorless crystals, 87% yield, mp 140−141 °C).[57] ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.07, 3.12 (2s, 2 × 3 H, NCH_3), 3.48 (dd, ^2J = 18.2 Hz, ^3J = 5.8 Hz, 1H, CH_2), 3.75 (s, 3H, OCH_3), 3.96 (d, ^3J = 4.0 Hz, 1H, 5-H), 4.48 (dd, ^2J = 18.2 Hz, ^3J = 9.0 Hz, 1H, CH_2), 4.29−4.34 (m, 1 H, CH), 6.78 (d, ^3J = 8.8 Hz, 2H, Ar-H), 7.01 (d, ^3J = 8.8 Hz, 2H, Ar-H), 7.45−7.59 (m, 3H, Ar-H), 7.99−8.02 (m, 2H, Ar-H). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 28.2, 28.4 (NCH_3), 40.9 (CH_2), 44.0 (CH), 53.3 (C-5), 55.4 (OCH_3), 114.2, 128.2, 128.6, 128.8, 130.2

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(C_{Ar}-H), 133.5, 137.0 (C_{Ar}-H), 152.0, 159.5, 168.1, 168.6, 197.9. IR (KBr): $\tilde{\nu}$ = 2957, 2838, 1746, 1678, 1611, 1598, 1581, 1514, 1449, 1423, 1380, 1252, 1209, 1181, 1117, 1033, 1002, 840 cm^{-1}.

5-[(4-Methoxyphenyl)(2-oxocyclopentyl)methyl]-1,3-dimethylpyrimidine-2,4,6-(1*H*,3*H*,5*H*)-trione (11cb). Colorless crystals, 72% yield, isolated as mixture of diastereomers (5:2). Major diastereomer: ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.23−2.46 (m, 6H, CH_2), 3.11, 3.15 (2s, 6H, 2 × NCH_3), 3.29−3.37 (m, 1H, CH), 3.62−3.69 (m, 1H, CH), 3.76 (s, 3H, OCH_3), 4.81 (d, ^3J = 2.8 Hz, 1H, CH), 6.76 (d, ^3J = 8.8 Hz, 2H, Ar), 7.02 (d, ^3J = 8.8 Hz, 2H, Ar). ^{13}C NMR (150 MHz, $CDCl_3$): δ 20.0 (CH_2), 28.4, 28.4, (NCH_3), 30.5, 39.2 (CH_2), 47.4, 48.0, 51.6 (CH), 55.4 (OCH_3), 114.1 (C_{Ar}-H), 129.3 (C_{Ar}-H), 130.8, 151.4, 159.3, 168.2, 168.7, 220.5 (CO). Minor diastereomer: ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.23−2.46 (m, 6H, CH_2), 3.04, 3.08 (2s, 6H, 2 × NCH_3), 3.29−3.37 (m, 1H, CH), 3.50 (dd, ^3J = 10.8 Hz, ^3J = 4.2 Hz, 1H, CH), 3.62−3.69 (m, 1H, CH), 3.75 (s, 3H, OCH_3), 6.76 (d, ^3J = 8.8 Hz, 2H, Ar), 6.89 (d, ^3J = 8.8 Hz, 2H, Ar). ^{13}C NMR (150 MHz, $CDCl_3$): δ 20.1 (CH_2), 28.2, 28.4 (NCH_3), 29.9, 38.4 (CH_2), 50.6, 50.8, 53.2 (CH), 55.3 (OCH_3), 114.0 (C_{Ar}-H), 128.5 (C_{Ar}-H), 130.8, 151.0, 159.4, 167.5, 168.9, 216.8 (CO). $C_{19}H_{22}N_2O_5$ (358.4): calcd C 63.68, H 6.19, N 7.82; found C 63.46, H 6.20, N 7.75.

10-(4-Methoxyphenyl)-1,3-dimethyl-8a-trimethylsiloxy-1,5,6,7,8,8a,10,10a-octahydro-9-oxa-1,3-diaza-anthracene-2,4-dione (11cc). Colorless crystals, 83% yield, mp 193−195 °C (EtOH). ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.12 ($SiMe_3$), 1.03−1.26 (m, 2H, CH_2), 1.45−1.73 (m, 6H, CH + CH_2), 2.17 (m, 1H, CH_2), 3.21, 3.40 (2s, 6H, 2 × NCH_3), 3.38 (d, ^3J = 10.4 Hz, 1H, 5-H), 3.77 (s, 3H, OCH_3), 6.81 (d, ^3J = 8.8 Hz, 2H, Ar), 7.06 (d, ^3J = 8.4 Hz, 2H, Ar). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 1.5 ($SiMe_3$), 23.3, 25.3, 26.9 (CH_2), 28.1, 29.0 (NCH_3), 37.2 (CH_2), 39.5 (C-5), 49.5, 55.2 (OCH_3), 92.4, 104.5, 113.8 (C_{Ar}-H), 128.8 (C_{Ar}-H), 135.2, 151.6, 154.3, 158.1, 162.0. IR (KBr): $\tilde{\nu}$ = 2941, 1706, 1654, 1613, 1585, 1512, 1461, 1279, 1253, 1172, 1148, 1108, 1070, 1050, 969 cm^{-1}. $C_{23}H_{32}N_2O_5Si$ (444.6): calcd C 62.13, H 7.25, N 6.30; found C 62.00, H 7.25, N 6.26.

Acid Catalyzed Hydrolysis of 11cc to 12cc. Silyl enol ether **10c** (0.54 mmol) was added under a nitrogen atmosphere to **1c** (0.36 mmol) in 5 mL of dry DMSO. After 24 h, the reaction mixture was poured into HCl solution (1 m, 30 mL), stirred for 1 h, and then extracted with ethyl acetate (3 × 20 mL). After removal of the solvent in vacuo, the residue was recrystallized from ethanol.

1,3-Dimethyl-5-[(4-methoxyphenyl)(2-oxocyclohexyl)methyl]-pyrimidine-2,4,6(1*H*,3*H*,5*H*)-trione (12cc). Colorless crystals, 51% yield, isolated as mixture of diastereomers (7:1). Major diastereomer: ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.07−1.19, 1.62−1.77, 2.11−2.60 (3m, 8H, CH_2), 3.00, 3.18 (2s, 2 × 3H, 2 × NCH_3), 3.35−3.45 (m, 1H, CH), 3.69−3.76 (m, 1H, CH), 3.76 (s, 3H, OCH_3), 4.50 (d, ^3J = 3.9 Hz, 1H, CH), 6.77 (d, ^3J = 8.7 Hz, 2H, Ar), 6.92 (d, ^3J = 8.7 Hz, 2H, Ar). ^{13}C NMR (MHz, 75.5 MHz, $CDCl_3$): δ 25.6 (CH_2), 28.1, 28.1 (NCH_3), 29.3, 34.0, 43.1 (CH_2), 48.0, 50.7, 51.4 (CH), 55.2 (OCH_3), 114.1 (C_{Ar}-H), 129.0 (C_{Ar}-H), 129.3, 151.2, 159.2, 168.3, 168.5, 213.5 (CO). Minor diastereomer: ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.07−1.19, 1.62−1.77, 2.11−2.60 (3 m, 8H, CH_2), 3.03, 3.09 (2s, 6H, 2 × NCH_3), 3.35−3.45 (m, 1H, CH), 3.69−3.76 (m, 2H, 2 × CH), 3.72 (s, 3H, OCH_3), 6.71 (d, ^3J = 9.0 Hz, 2H, Ar), 6.88 (d, ^3J = 9.0 Hz, 2H, Ar). $C_{20}H_{24}N_2O_5$ (372.4): calcd C 64.50, H 6.50, N 7.52; found C 64.38, H 6.56, N 7.55.

5-[(4-Methoxyphenyl)(5-methyl-2-furyl)methyl]-1,3-dimethylpyrimidine-2,4,6-(1*H*,3*H*,5*H*)-trione (14ca). In contrast to general procedure C, the reaction mixture was stirred for 4 days. Colorless oil, 95% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.27 (s, 3H, CH_3), 3.13 (s, 6H, NCH_3), 3.78 (s, 3H, OCH_3), 4.21 (d, ^3J = 4.0 Hz, 1H, 5-CH), 4.86 (d, ^3J = 4.0 Hz, 1H, CH), 5.89 (d, ^3J = 3.2 Hz, 1H, Fu), 5.97 (d, ^3J = 3.2 Hz, 1H, Fu), 6.83 (d, ^3J = 8.8 Hz, 2H, Ar), 7.16 (d, ^3J = 8.8 Hz, 2H, Ar). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 13.7 (CH_3), 28.4, 28.4 (NCH_3), 48.9 (CH), 54.3 (5-C), 55.4 (OCH_3), 106.5 (C_{Fur}-H), 109.7 (C_{Fur}-H), 114.1 (C_{Ar}-H), 128.2, 129.8 (C_{Ar}-H), 150.5, 151.4, 152.1, 159.6, 167.2, 167.7. MS (EI): *m*/*z* (%) = 356 (1) [M^+], 202(14), 201 (100).

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Supporting Information Available: Details of the kinetic experiments, crystallographic data, and NMR spectra of all characterized compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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