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Copper-Catalyzed Intramolecular C–H Amination: A New Entry to Substituted Xanthine Derivatives

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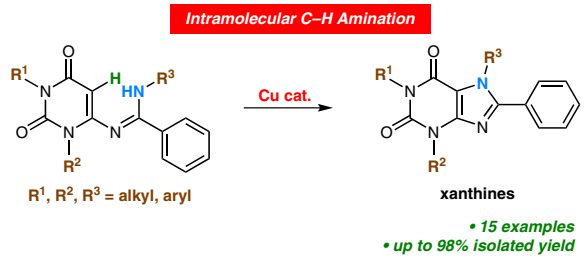

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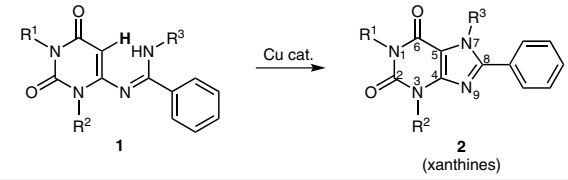
Abstract Catalytic synthesis of xanthines was achieved in the presence of a copper catalyst. The process involves copper-catalyzed intramolecular C–H amination of benzamidines that possess a uracil moiety and produces variously substituted xanthines generally in good to high yields. This work introduces a new, facile approach to polysubstituted xanthine compounds.

Key words copper, catalysis, C–H functionalization, amination, cyclization, xanthines

Xanthine derivatives constitute a considerably important class of heterocycles, possessing well-established activities as adenosine receptor antagonists and phosphodiesterase inhibitors.[1] The therapeutic application of xanthines includes their use as diuretics and cardiac stimulants as well as in the treatment of bronchial asthma and vascular diseases.[2] Despite their importance in the medicinal area, efficient and applicable synthetic methods for variously substituted xanthines remain considerably scarce. Classical methods used for the construction of the xanthine framework usually rely on the formation of the imidazole ring in the final steps, including Traube purine synthesis starting from 6-aminouracil derivatives.[3] However, they often require lengthy, multi-step reactions with harsh reaction conditions, thus limiting their usefulness in obtaining variously functionalized xanthines.[4] Although several alternate or improved strategies have so far been reported,[5] the development of general methods for the synthesis of xanthines, which would realize wide substrate scope and high functional group tolerance, is still essential. Moreover, catalytic cyclization approaches using transition metals for the construction of the xanthine skeleton, which would provide a more efficient and practical route, are extremely rare in the literature.[6] Herein we report a novel catalytic method for synthesizing variously substituted xanthines. The process involves copper-catalyzed intramolecular C–H amination reaction[7] of benzamidines **1** as cyclization precursors that possess a uracil moiety, which can be prepared readily from commercially available materials. Using the reaction conditions developed, the desired cyclized products are obtained generally in good to high yields, providing a facile, convenient, and practical route to 1,3,7,8-tetrasubstituted xanthines (Scheme 1).[8]



Scheme 1 Intramolecular C–H amination for synthesis of xanthines

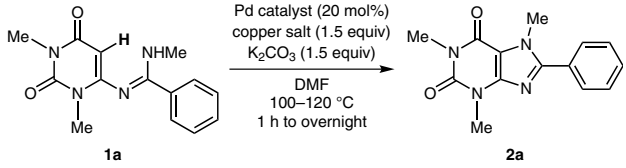
On the basis of our recent fruitful results of the N-heterocycles synthesis via palladium-catalyzed intramolecular C–H amination,[9] the reaction of benzamidine **1a** in the presence of a palladium catalyst along with a copper salt as a reoxidant was first examined (Table 1). The use of 20 mol % of $PdCl_2(PhCN)_2$ and 1.5 equivalents of $Cu(OAc)_2$ as well as 1.5 equivalents of K_2CO_3 base in DMF resulted in the formation of the desired cyclized product **2a** in fairly good yield (Table 1, entry 1). On the other hand, the cyclization did not proceed efficiently without the addition of a copper salt (entry 2). Interestingly, a further screening of reaction conditions revealed that xanthine **2a** did produce even in the absence of a palladium catalyst (entry 3). Intrigued by this apparently copper-mediated C–H amination process, examination of the effect of a copper salt was subsequently performed. A survey of a variety of commercially available copper(I) and copper(II) salts led to the fact that $CuBr_2$ was the

best (entries 3–10 vs. 11). Essentially, the desired cyclization did not proceed efficiently in the absence of K_2CO_3 (entry 12).

As copper salts turned out to be suitable for the xanthine synthesis via intramolecular C–H amination, efforts were next focused on investigation to render the process catalytic. Indeed, the use of a reduced amount (20 mol%) of $CuBr_2$ led to a considerable decrease in yield (Table 2, entry 1). Thus, an effect of the reoxidant was evaluated. Although most of the reoxidants employed were unfortunately ineffective (entries 2–7), we were delighted to find that xanthine **2a** was produced in 51% yield when $PhI(OAc)_2$ was used (entry 8). $PhI(OAc)_2$ itself did not mediate the C–H amination (entry 9).[10] From subsequent systematic solvent screening (entries 10–17), it was found that changing the solvent system from DMF to DMSO/pyridine (1:1) enabled this process to be performed more efficiently, providing **2a** in high yield (entry 17).

With an optimal process in hand, the substrate scope of this newly developed xanthine synthesis was investigated next. The above-obtained optimized reaction conditions were found to be applicable to the synthesis of variously substituted benzamidines **1b–o** (Table 3). A wide range of substrates that has alkyl (Me, *i*-Pr), benzyl, and aryl groups as a substituent R^3 were successfully utilized for the C–H

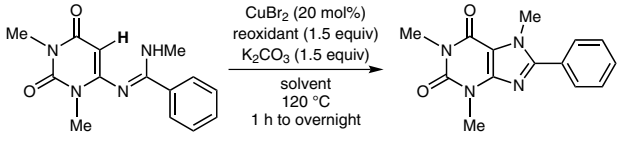
Table 1 Initial Screening of Reaction Parameters[a]



Entry	Pd catalyst	Copper salt	Yield (%)[b]
1	$PdCl_2(PhCN)_2$	$Cu(OAc)_2$	52
2	$PdCl_2(PhCN)_2$	none	trace
3	none	$Cu(OAc)_2$	65
4	none	CuO	0
5	none	CuCl	0
6	none	CuI	0
7	none	CuTC[c]	37
8	none	$Cu(acac)_2$	14
9	none	CuF_2	trace
10	none	$CuCl_2$	11
11	none	$CuBr_2$	70
12[d]	none	$CuBr_2$	2

[a] Reaction was run on a 0.10 mmol scale in DMF (2 mL).
[b] Isolated yield.
[c] CuTC: Copper(I) thiophene-2-carboxylate.
[d] In the absence of K_2CO_3.

Table 2 Development of Catalytic Process[a]



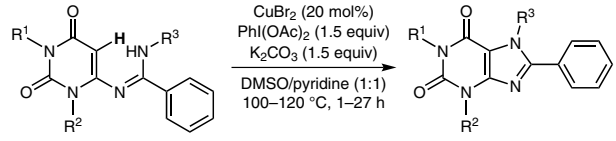
Entry	Reoxidant	Solvent	Yield (%)[b]
1	none	DMF	9
2	O_2	DMF	17
3	Ag_3PO_4	DMF	19
4	Ag_3PO_4, O_2	DMF	14
5	CF_3CO_2Ag	DMF	3
6	DTBP	DMF	26
7	TBHP	DMF	13
8	$PhI(OAc)_2$	DMF	51
9[c]	$PhI(OAc)_2$	DMF	0
10	$PhI(OAc)_2$	DMSO	63
11	$PhI(OAc)_2$	MeCN	38
12	$PhI(OAc)_2$	1,4-dioxane	39
13	$PhI(OAc)_2$	toluene	7
14	$PhI(OAc)_2$	pyridine	57
15	$PhI(OAc)_2$	DMF/DMSO (1:1)	41
16	$PhI(OAc)_2$	DMF/pyridine (1:1)	61
17	$PhI(OAc)_2$	DMSO/pyridine (1:1)	74

[a] Reaction was run on a 0.10 mmol scale in solvent (2 mL).
[b] Isolated yield.
[c] In the absence of $CuBr_2$.

cyclization, affording the corresponding xanthines generally in good to high yields. Halogen atoms such as F, Cl, and Br were all compatible with this transformation (Table 3, entries 5–7 and 12). In addition to 1,3-dialkylxanthines **2a–n**, 1,3-diphenylxanthine **2o** could also be prepared in good yield, indicating the wide substrate scope of the catalytic system (entry 15).[11]

In conclusion, we have developed a copper-based catalytic system that successfully effects intramolecular C–H amination of benzamidines possessing a uracil moiety, leading to a novel method for the construction of xanthine scaffolds. Variously substituted benzamidines, which can be readily prepared from commercially available materials, were smoothly reacted in the presence of a $CuBr_2$ catalyst along with $PhI(OAc)_2$ as the reoxidant. Studies to improve the catalytic efficiency of the process as well as to further broaden the substrate scope are currently under way.

Table 3 Substrate Scope[a]



1a–o 2a–o

Entry	2	R^1	R^2	R^3	Yield (%)[b]
1	**2a**	Me	Me	Me	74
2	**2b**	Me	Me	*i*-Pr	42
3	**2c**	Me	Me	Bn	51
4	**2d**	Me	Me	Ph	78
5	**2e**	Me	Me	4-FC_6H_4	77
6	**2f**	Me	Me	4-ClC_6H_4	98
7	**2g**	Me	Me	4-BrC_6H_4	89
8	**2h**	Me	Me	4-$MeOC_6H_4$	78
9	**2i**	Me	Me	2-$MeOC_6H_4$	80
10	**2j**	Me	Me	3-MeC_6H_4	89
11	**2k**	Me	Me	3,4,5-$(MeO)_3C_6H_2$	96
12	**2l**	Me	Me	3-Cl-4-$MeOC_6H_3$	98
13	**2m**	Pr	Pr	Me	61
14	**2n**	Hex	Hex	Me	58
15	**2o**	Ph	Ph	Me	77

[a] Reaction was run on a 0.10 mmol scale in solvent (2 mL).
[b] Isolated yield.

All reactions were carried out under an argon atmosphere unless otherwise noted. Anhydrous solvents, including DMSO and pyridine, were purchased from Sigma-Aldrich. All other commercially available materials were purchased from Sigma-Aldrich, Tokyo Chemical Industry Co., and Wako Pure Chemical Industries, and were used as received. Melting points were measured with a Yanaco micro melting point apparatus and are uncorrected. IR spectra were recorded on a Shimadzu IRAffinity-1 spectrophotometer. ^{1}H NMR spectra were recorded on a Jeol JNM-ECP400 (400 MHz) spectrometer. Chemical shifts (δ) are given from TMS (0 ppm) in $CDCl_3$ and coupling constants are expressed in hertz (Hz). Standard abbreviations are used to denote signal multiplicities. ^{13}C NMR spectra were recorded on a Jeol JNM-ECP400 (100 MHz) spectrometer. Chemical shifts (δ) are given from $^{13}CDCl_3$ (77.0 ppm). Mass spectra and high-resolution mass spectra were recorded on a Jeol JMS-700 instrument.

Benzamidines 1a–e,h,k–o; General Procedure A

The required amine (20.0 mmol) was added dropwise at 0 °C to a solution of ethyl benzimidate hydrochloride (10.0 mmol) in EtOH (15 mL) and the reaction mixture was stirred at r.t. to reflux overnight. EtOH was removed under a reduced pressure and 1 M aq NaOH (15 mL) was added. The mixture was extracted with $CHCl_3$ (3 × 10 mL) and the combined organic phases were dried ($MgSO_4$): The solvent was removed under a reduced pressure and the crude N-substituted benzamidine obtained was used for the next reaction without further purification.

A solution of the above crude N-substituted benzamidine (10.0 mmol) in DMF (5 mL) was added dropwise at 0 °C to a solution of NaH (20.0 mmol) in DMF (5 mL) and stirred for 30 min. A solution of 1,3-dimethyl-6-chlorouracil (5.0 mmol) in DMF (5 mL) was added dropwise at 0 °C and the reaction mixture was stirred at 80 °C overnight. Sat. aq NH_4Cl (20 mL) was added at 0 °C and the mixture was extracted with EtOAc (5 × 10 mL). The combined organic phases were washed with H_2O (2 × 10 mL) and brine (1 × 10 mL), and dried ($MgSO_4$). The solvent was removed under reduced pressure and the crude material was purified by silica gel column chromatography to give **1a–e**,**h**,**k–o**.

Benzamidines 1f,g,i,j; General Procedure B

A mixture of benzamidine hydrochloride (5.0 mmol), aryl iodide (7.5 mmol), CuI (1.0 mmol), and Cs_2CO_3 (15.0 mmol) in DMF (10 mL) was stirred at 90 °C overnight. H_2O (10 mL) was added and the mixture was extracted with EtOAc (3 × 10 mL). The combined organic phases were washed with H_2O (3 × 10 mL) and brine (1 × 10 mL), and dried (Na_2SO_4). The solvent was removed under a reduced pressure and the crude material was purified by silica gel column chromatography to give the intermediate N-substituted benzamidine.

A solution of the above N-substituted benzamidine (1.0 mmol) in DMF (5 mL) was added dropwise at 0 °C to a solution of NaH (4.0 mmol) in DMF (5 mL) and stirred for 30 min. A solution of 1,3-dimethyl-6-chlorouracil (2.0 mmol) in DMF (5 mL) was added dropwise at 0 °C and the reaction mixture was stirred at 80 °C overnight. Sat. aq NH_4Cl (10 mL) was added at 0 °C and the mixture was extracted with EtOAc (5 × 10 mL). The combined organic phases were washed with H_2O (2 × 10 mL) and brine (1 × 10 mL), and dried ($MgSO_4$). The solvent was removed under a reduced pressure and the crude material was purified by silica gel column chromatography to give **1f**,**g**,**i**,**j**.

N-(1,3-Dimethyl-2,4-dioxo-1,2,3,4-tetrahydropyrimidin-6-yl)-*N*′-methylbenzamidine (1a)

According to General Procedure A, starting from $MeNH_2$; mp 234.5–238.9 °C; colorless needles (hexane/EtOAc).

IR (film): 3252, 1686, 1653, 1630, 1587, 1560, 1474, 1431, 1410, 1277, 1240, 1211 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.42 (1 H, t, *J* = 7.6 Hz), 7.35 (2 H, t, *J* = 7.6 Hz), 7.20 (2 H, d, *J* = 7.6 Hz), 5.72 (1 H, br), 4.43 (1 H, s), 3.49 (3 H, s), 3.20 (3 H, s), 3.06 (3 H, d, *J* = 4.8 Hz).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 163.2, 161.3, 158.2, 152.7, 132.7, 131.0, 129.1, 127.2, 88.2, 30.4, 29.1, 27.6.

MS (EI): *m*/*z* (%) = 272 (83) [M$^+$], 271 (100).

HRMS: *m*/*z* calcd for $C_{14}H_{16}N_4O_2$: 272.1273; found: 272.1274.

N-Isopropyl-*N*′-(1,3-dimethyl-2,4-dioxo-1,2,3,4-tetrahydropyrimidin-6-yl)benzamidine (1b)

According to General Procedure A, starting from *i*-$PrNH_2$; mp 216.6–219.1 °C; colorless needles (hexane/EtOAc).

IR (film): 3265, 1690, 1630, 1605, 1585, 1541, 1528, 1431, 1375, 1277, 1236, 1167, 1101 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.43 (1 H, t, *J* = 7.6 Hz), 7.36 (2 H, t, *J* = 7.3 Hz), 7.20 (2 H, d, *J* = 7.3 Hz), 5.21 (1 H, br), 4.43 (1 H, s), 4.29–4.21 (1 H, m), 3.49 (3 H, s), 3.23 (3 H, s), 1.31 (6 H, d, *J* = 6.4 Hz).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 163.2, 159.8, 158.1, 152.8, 133.0, 131.0, 129.1, 127.2, 88.2, 44.1, 30.5, 27.6, 22.4.

MS (EI): *m*/*z* (%) = 300 (100) [M$^+$].

HRMS: *m*/*z* calcd for $C_{16}H_{20}N_4O_2$: 300.1586; found: 300.1586.

_N_-Benzyl-_N′_-(1,3-dimethyl-2,4-dioxo-1,2,3,4-tetrahydropyrimidin-6-yl)benzamidine (1c)

According to General Procedure A, starting from benzylamine; mp 227.5–229.0 °C; colorless needles (hexane/EtOAc).

IR (film): 3275, 1686, 1630, 1609, 1589, 1541, 1528, 1431, 1329, 1279, 1209, 1163, 1128 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.46–7.32 (8 H, m), 7.24 (2 H, d, *J* = 8.0 Hz), 5.66 (1 H, br), 4.68 (2 H, d, *J* = 5.6 Hz), 4.49 (1 H, s), 3.39 (3 H, s), 3.23 (3 H, s).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 163.2, 160.2, 157.9, 152.7, 137.4, 132.5, 131.3, 129.3, 129.0, 127.9, 127.7, 127.2, 88.5, 46.4, 30.4, 27.6.

MS (EI): *m*/*z* (%) = 348 (100) [M$^+$].

HRMS: *m*/*z* calcd for $C_{20}H_{20}N_4O_2$: 348.1586; found: 348.1583.

_N_-(1,3-Dimethyl-2,4-dioxo-1,2,3,4-tetrahydropyrimidin-6-yl)-_N′_-phenylbenzamidine (1d)

According to General Procedure A, starting from aniline; mp 107.7–110.2 °C; colorless needles (hexane/EtOAc).

IR (film): 3275, 1695, 1628, 1585, 1541, 1528, 1508, 1499, 1491, 1474, 1466, 1458, 1431, 1375, 1340, 1204, 1094 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.59 (2 H, d, *J* = 7.7 Hz), 7.52 (1 H, br), 7.45 (1 H, d, *J* = 7.7 Hz), 7.40–7.34 (4 H, m), 7.29 (2 H, d, *J* = 7.7 Hz), 7.18 (1 H, t, *J* = 7.7 Hz), 4.54 (1 H, s), 3.45 (3 H, s), 3.16 (3 H, s).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 163.1, 157.6 (2 C), 152.5, 138.5, 132.9, 131.3, 129.2, 129.0, 127.4, 125.0, 120.9, 88.5, 30.7, 27.6.

MS (EI): *m*/*z* (%) = 334 (93) [M$^+$], 333 (100).

HRMS: *m*/*z* calcd for $C_{19}H_{18}N_4O_2$: 334.1430; found: 334.1428.

_N_-(4-Fluorophenyl)-_N′_-(1,3-dimethyl-2,4-dioxo-1,2,3,4-tetrahydropyrimidin-6-yl)benzamidine (1e)

According to General Procedure A, starting from 4-fluoroaniline; mp 225.9–226.8 °C; colorless scales (hexane/EtOAc).

IR (film): 3283, 1695, 1630, 1609, 1593, 1541, 1528, 1508, 1437, 1408, 1375, 1340, 1277, 1200, 1092, 1001 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.54–7.47 (3 H, m), 7.43 (2 H, t, *J* = 7.3 Hz), 7.32 (2 H, d, *J* = 7.3 Hz), 7.09–7.04 (3 H, m), 4.61 (1 H, s), 3.46 (3 H, s), 3.23 (3H, s).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 163.1, 159.9 (*J* = 244.0 Hz), 157.7, 157.4, 152.6, 134.3 (*J* = 3.2 Hz), 132.7, 131.6, 129.5, 127.3, 122.9 (*J* = 8.0 Hz), 115.9 (*J* = 22.2 Hz), 88.8, 30.8, 27.7.

MS (EI): *m*/*z* (%) = 352 (88) [M$^+$], 351 (100).

HRMS: *m*/*z* calcd for $C_{19}H_{17}FN_4O_2$: 352.1336; found: 352.1336.

_N_-(4-Chlorophenyl)-_N′_-(1,3-dimethyl-2,4-dioxo-1,2,3,4-tetrahydropyrimidin-6-yl)benzamidine (1f)

According to General Procedure B, starting from 1-chloro-4-iodobenzene; mp 253.6–256.2 °C; yellow scales (hexane/EtOAc).

IR (film): 3279, 1695, 1632, 1584, 1533, 1491, 1437, 1400, 1375, 1341, 1277, 1204, 1088, 1013, 1001 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.56–7.54 (3 H, m), 7.47 (1 H, t, *J* = 7.4 Hz), 7.41–7.37 (2 H, m), 7.33–7.26 (4 H, m), 4.53 (1 H, s), 3.44 (3 H, s), 3.16 (3 H, s).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 163.1, 157.6, 157.5, 152.5, 137.0, 132.6, 131.5, 130.1, 129.3, 129.1, 127.3, 122.1, 88.6, 30.8, 27.6.

MS (EI): *m*/*z* (%) = 368 (86) [M$^+$], 367 (100).

HRMS: *m*/*z* calcd for $C_{19}H_{17}{}^{35}ClN_4O_2$: 368.1040; found: 368.1041.

_N_-(4-Bromophenyl)-_N′_-(1,3-dimethyl-2,4-dioxo-1,2,3,4-tetrahydropyrimidin-6-yl)benzamidine (1g)

According to General Procedure B, starting from 1-bromo-4-iodobenzene; mp 264.3–268.1 °C; pale yellow scales (hexane/EtOAc).

IR (film): 3275, 1701, 1630, 1582, 1528, 1489, 1429, 1395, 1375, 1340, 1277, 1202, 1094, 1072, 1007 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.50–7.46 (5 H, m), 7.40 (2 H, t, *J* = 7.6 Hz), 7.34 (1 H, br), 7.29 (2 H, d, *J* = 7.6 Hz), 4.56 (1 H, s), 3.45 (3 H, s), 3.19 (3 H, s).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 163.0, 157.5, 157.4, 152.5, 137.5, 132.6, 132.1, 131.5, 129.4, 127.3, 122.4, 117.8, 88.7, 30.8, 27.7.

MS (EI): *m*/*z* (%) = 413 (100), 412 (78) [M$^+$].

HRMS: *m*/*z* calcd for $C_{19}H_{17}{}^{79}BrN_4O_2$: 412.0535; found: 412.0461.

_N_-(4-Methoxyphenyl)-_N′_-(1,3-dimethyl-2,4-dioxo-1,2,3,4-tetrahydropyrimidin-6-yl)benzamidine (1h)

According to General Procedure A, starting from 4-methoxyaniline; mp 180.6–182.4 °C; pale yellow needles (hexane/EtOAc).

IR (film): 3280, 1692, 1632, 1589, 1541, 1535, 1510, 1437, 1414, 1375, 1344,1292, 1248, 1204, 1093, 10332, 1001 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.48–7.38 (5 H, m), 7.32 (2 H, d, *J* = 7.2 Hz), 7.10 (1 H, br), 6.89 (2 H, d, *J* = 8.8 Hz), 4.58 (1 H, s), 3.82 (3 H, s), 3.45 (3 H, s), 3.22 (3 H, s).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 163.1, 157.7, 157.1, 152.6, 133.0, 131.3, 129.3, 127.4, 122.9, 114.3, 88.5, 55.5, 30.7, 27.6.

MS (EI): *m*/*z* (%) = 364 (100) [M$^+$].

HRMS: *m*/*z* calcd for $C_{20}H_{20}N_4O_3$: 364.1535; found: 364.1533.

_N_-(2-Methoxyphenyl)-_N′_-(1,3-dimethyl-2,4-dioxo-1,2,3,4-tetrahydropyrimidin-6-yl)benzamidine (1i)

According to General Procedure B, starting from 2-iodoanisole; mp 221.5–222.7 °C; pale yellow prisms (hexane/EtOAc).

IR (film): 3390, 1695, 1641, 1628, 1618, 1587, 1533, 1458, 1429, 1371, 1288, 1250, 1202, 1115, 1026 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.38 (1 H, d, *J* = 7.9 Hz), 7.60 (1 H, br), 7.51–7.42 (3 H, m), 7.35 (2 H, d, *J* = 7.6 Hz), 7.12 (1 H, t, *J* = 7.9 Hz), 7.00 (1 H, t, *J* = 7.9 Hz), 6.94 (1 H, d, *J* = 7.9 Hz), 4.62 (1 H, s), 3.90 (3 H, s), 3.51 (3 H, s), 3.27 (3 H, s).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 163.1, 157.6, 157.1, 152.7, 148.7, 133.4, 131.4, 129.4, 128.1, 127.4, 124.6, 121.0, 120.3, 110.2, 88.7, 55.9, 30.8, 27.7.

MS (EI): *m*/*z* (%) = 364 (42) [M$^+$], 333 (100).

HRMS: *m*/*z* calcd for $C_{20}H_{20}N_4O_3$: 364.1535; found: 364.1537.

_N_-(1,3-Dimethyl-2,4-dioxo-1,2,3,4-tetrahydropyrimidin-6-yl)-_N′_-(3-methylphenyl)benzamidine (1j)

According to General Procedure B, starting from 3-iodotoluene; mp 215.1–217.2 °C; colorless needles (hexane/EtOAc).

IR (film): 3273, 1692, 1630, 1609, 1585, 1545, 1533, 1489, 1429, 1375, 1339, 1277, 1261, 1225, 1209, 1169, 1098, 1026 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.47–7.22 (9 H, m), 6.99 (1 H, d, *J* = 7.2 Hz), 4.57 (1 H, s), 3.45 (3 H, s), 3.19 (3 H, s), 2.36 (3 H, s).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 163.1, 157.6 (2 C), 152.6, 139.0, 138.3, 133.0, 131.3, 129.2, 128.9, 127.3, 125.9, 121.5, 118.0, 88.5, 30.7, 27.6, 21.5.

MS (EI): *m*/*z* (%) = 348 (100) [M^+].

HRMS: *m*/*z* calcd for $C_{20}H_{20}N_4O_2$: 348.1586; found: 348.1588.

N-(3,4,5-Trimethoxyphenyl)-*N*′-(1,3-dimethyl-2,4-dioxo-1,2,3,4-tetrahydropyrimidin-6-yl)benzamidine (1k)

According to General Procedure A, starting from 3,4,5-trimethoxyaniline; mp 220.8–222.2 °C; white scales (hexane/EtOAc).

IR (film): 3289, 1701, 1630, 1589, 1541, 1505, 1431, 1412, 1375, 1323, 1229, 1126, 1098, 1003 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.48 (1 H, t, *J* = 7.3 Hz), 7.42 (2 H, t, *J* = 7.3 Hz), 7.32 (2 H, d, *J* = 7.3 Hz), 7.11 (1 H, br), 6.89 (2 H, s), 4.60 (1 H, s), 3.84 (3 H, s), 3.82 (6 H, s), 3.51 (3 H, s), 3.23 (3 H, s).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 163.0, 157.6, 157.3, 153.4, 152.6, 135.6, 134.3, 133.0, 131.4, 129.4, 127.3, 98.8, 88.8, 61.0, 56.2, 30.7, 27.7.

MS (EI): *m*/*z* (%) = 424 (100) [M^+].

HRMS: *m*/*z* calcd for $C_{22}H_{24}N_4O_5$: 424.1747; found: 424.1743.

N-(3-Chloro-4-methoxyphenyl)-*N*′-(1,3-dimethyl-2,4-dioxo-1,2,3,4-tetrahydropyrimidin-6-yl)benzamidine (1l)

According to General Procedure A, starting from 3-chloro-4-methoxyaniline; mp 244.9–246.9 °C; colorless needles (hexane/EtOAc).

IR (film): 3267, 1701, 1628, 1611, 1585, 1501, 1429, 1400, 1375, 1279, 1261, 1202, 1096, 1063, 1022, 1001 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.66 (1 H, d, *J* = 2.0 Hz), 7.49–7.38 (4 H, m), 7.29 (2 H, d, *J* = 8.0 Hz), 7.23 (1 H, br), 6.92 (1 H, d, *J* = 8.8 Hz), 4.55 (1 H, s), 3.91 (3 H, s), 3.45 (3 H, s), 3.20 (3 H, s).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 163.1, 157.6, 157.5, 152.6, 132.7, 131.8, 131.5, 129.3, 127.3, 123.6, 122.7, 120.7, 112.2, 88.7, 56.4, 30.8, 27.7.

MS (EI): *m*/*z* (%) = 398 (100) [M^+].

HRMS: *m*/*z* calcd for $C_{20}H_{19}{}^{35}ClN_4O_3$: 398.1146; found: 398.1140.

N-Methyl-*N*′-(1,3-Dipropyl-2,4-dioxo-1,2,3,4-tetrahydropyrimidin-6-yl)benzamidine (1m)

According to General Procedure A using 1,3-dipropyl-6-chlorouracil instead of 1,3-dimethyl-6-chlorouracil, and starting from $MeNH_2$; mp 189.1–191.2 °C; pale yellow needles (hexane/EtOAc).

IR (film): 3237, 1686, 1630, 1584, 1545, 1533, 1437, 1420, 1398, 1379, 1364, 1341, 1323, 1279, 1260, 1153, 1051 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.43 (1 H, t, *J* = 7.2 Hz), 7.36 (2 H, t, *J* = 7.2 Hz), 7.24 (2 H, d, *J* = 7.2 Hz), 5.57 (1 H, br), 4.35 (1 H, s), 3.99 (2 H, t, *J* = 7.4 Hz), 3.78 (2 H, t, *J* = 7.4 Hz), 3.04 (3 H, d, *J* = 4.8 Hz), 1.80 (2 H, sext, *J* = 7.4 Hz), 1.58 (2 H, sext, *J* = 7.4 Hz), 1.00 (3 H, t, *J* = 7.4 Hz), 0.87 (3 H, t, *J* = 7.4 Hz).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 163.1, 161.1, 157.6, 152.3, 132.6, 131.0, 129.1, 127.2, 88.3, 45.2, 42.4, 29.2, 22.0, 21.0, 11.3, 11.2.

MS (EI): *m*/*z* (%) = 328 (100) [M^+].

HRMS: *m*/*z* calcd for $C_{18}H_{24}N_4O_2$: 328.1899; found: 328.1893.

N-(1,3-Dihexyl-2,4-dioxo-1,2,3,4-tetrahydropyrimidin-6-yl)-*N*′-methylbenzamidine (1n)

According to General Procedure A using 1,3-dihexyl-6-chlorouracil instead of 1,3-dimethyl-6-chlorouracil, and starting from $MeNH_2$; mp 98.5–102.6 °C; brown scales (hexane/EtOAc).

IR (film): 3273, 1692, 1636, 1587, 1553, 1437, 1420, 1400, 1368, 1315, 1263, 1155, 1123, 1067, 1032 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.42 (1 H, t, *J* = 7.3 Hz), 7.35 (2 H, t, *J* = 7.3 Hz), 7.24 (2 H, d, *J* = 7.3 Hz), 5.58 (1 H, br), 4.35 (1 H, s), 4.02 (2 H, t, *J* = 7.3 Hz), 3.80 (2 H, t, *J* = 7.3 Hz), 3.04 (3 H, s), 1.77 (2 H, quint, *J* = 7.3 Hz), 1.56–1.53 (2 H, m), 1.42–1.27 (12 H, m), 0.90 (3 H, t, *J* = 7.3 Hz), 0.86 (3 H, t, *J* = 7.3 Hz).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 163.0, 161.1, 157.6, 152.2, 132.6, 131.0, 129.1, 127.2, 88.4, 43.8, 41.0, 31.53, 31.50, 29.1, 28.6, 27.7, 26.61, 26.58, 22.6, 22.5, 14.0.

MS (EI): *m*/*z* (%) = 412 (99) [M^+], 395 (100)

HRMS: *m*/*z* calcd for $C_{24}H_{36}N_4O_2$: 412.2838; found: 412.2840.

N-(1,3-Diphenyl-2,4-dioxo-1,2,3,4-tetrahydropyrimidin-6-yl)-*N*′-methylbenzamidine (1o)

According to General Procedure A using 1,3-diphenyl-6-chlorouracil instead of 1,3-dimethyl-6-chlorouracil, and starting from $MeNH_2$; mp 259.7–262.8 °C; yellow scales (hexane/EtOAc).

IR (film): 3302, 1707, 1647, 1630, 1585, 1560, 1545, 1533, 1491, 1381, 1333, 1285, 1217, 1155, 1111, 1072, 1011 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.49–7.20 (15 H, m), 5.23 (1 H, br), 4.72 (1 H, s), 2.64 (3 H, d, *J* = 4.8 Hz).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 163.2, 160.0, 158.2, 152.3, 136.9, 135.6, 132.5, 131.1, 129.2, 129.1, 128.9, 128.7, 128.6, 128.2, 128.1, 127.2, 88.6, 28.9.

MS (EI): *m*/*z* (%) = 396 (61) [M^+], 276 (100).

HRMS: *m*/*z* calcd for $C_{24}H_{20}N_4O_2$: 396.1586; found: 396.1585.

Cu-Catalyzed Xanthine Synthesis; 1,3,7-Trimethyl-8-phenylxanthine (2a); Typical Procedure (Table 2, Entry 17)

A mixture of **1a** (27.2 mg, 0.10 mmol), $CuBr_2$ (4.5 mg, 0.020 mmol), $PhI(OAc)_2$ (48.3 mg, 0.15 mmol), and K_2CO_3 (20.7 mg, 0.15 mmol) in DMSO (1 mL) and pyridine (1 mL) was stirred at 120 °C for 4 h. Sat. aq NH_4Cl (5 mL) was added and the mixture was filtered through a pad of Celite. The filtrate was extracted with $CHCl_3$ (3 × 10 mL) and the combined organic phases were washed with H_2O (2 × 10 mL) and brine (1 × 10 mL), and dried (Na_2SO_4). The solvent was removed under reduced pressure and the crude material was purified by silica gel column chromatography using hexane/EtOAc (1:1) as an eluent to give xanthine **2a**; yield: 20.0 mg (74%); colorless solid.

IR (film): 1701, 1655, 1630, 1605, 1541, 1458, 1427, 1377, 1341, 1290, 1233, 1080, 1036 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.71–7.68 (2 H, m), 7.55–7.51 (3 H, m), 4.06 (3 H, s), 3.63 (3 H, s), 3.44 (3 H, s).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 155.6, 152.1, 151.7, 148.3, 130.3, 129.2, 128.9, 128.5, 108.6, 33.8, 29.7, 27.9.

MS (EI): *m*/*z* (%) = 270 (100) [M^+].

HRMS: *m*/*z* calcd for $C_{14}H_{14}N_4O_2$: 270.1117; found: 270.1119.

7-Isopropyl-1,3-dimethyl-8-phenylxanthine (2b)

Reaction conditions: 120 °C, 27 h; colorless solid; yield: 12.4 mg (42%).

IR (film): 1701, 1663, 1543, 1518, 1452, 1395, 1225, 1211, 1036, 1022 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.58–7.52 (5 H, m), 4.69 (1 H, sept, *J* = 6.9 Hz), 3.63 (3 H, s) 3.47 (3 H, s), 1.65 (6 H, d, *J* = 6.8 Hz).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 154.6, 152.1, 151.7, 149.7, 130.3, 129.7, 129.4, 128.9, 107.6, 50.9, 29.9, 28.6, 21.8.

MS (EI): *m*/*z* (%) = 298 (60) [M^+], 256 (100).

HRMS: *m*/*z* calcd for $C_{16}H_{18}N_4O_2$: 298.1430; found: 298.1434.

7-Benzyl-1,3-dimethyl-8-phenylxanthine (2c)

Reaction conditions: 120 °C, 23 h; colorless solid; yield: 17.5 mg (51%).

IR (film): 1701, 1660, 1605, 1541, 1514, 1497, 1452, 1433, 1389, 1346, 1288, 1227, 1219, 1125, 1076, 1038, 1001 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.58 (2 H, d, *J* = 7.8 Hz), 7.50–7.43 (3 H, m), 7.30–7.25 (3 H, m), 7.04 (2 H, d, *J* = 7.8 Hz), 5.64 (2 H, s), 3.65 (3 H, s), 3.41 (3 H, s).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 155.2, 152.6, 151.7, 148.6, 136.6, 130.5, 129.2, 128.94, 128.86, 128.6, 127.9, 126.5, 108.0, 49.4, 29.8, 28.0.

MS (EI): *m*/*z* (%) = 346 (100) [M^+].

HRMS: *m*/*z* calcd for $C_{20}H_{18}N_4O_2$: 346.1430; found: 346.1424.

1,3-Dimethyl-7,8-diphenylxanthine (2d)

Reaction conditions: 120 °C, 1 h; colorless solid; yield: 26.0 mg (78%).

IR (film): 1701, 1663, 1655, 1533, 1508, 1497, 1491, 1458, 1437, 1225 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.49–7.44 (5 H, m), 7.37–7.25 (5 H, m), 3.71 (3 H, s), 3.37 (3 H, s).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 154.5, 151.7, 151.2, 148.7, 135.8, 130.0, 129.4, 129.2, 128.4, 127.7, 109.2, 29.9, 28.0.

MS (EI): *m*/*z* (%) = 332 (100) [M^+].

HRMS: *m*/*z* calcd for $C_{19}H_{16}N_4O_2$: 332.1273; found: 332.1274.

7-(4-Fluorophenyl)-1,3-dimethyl-8-phenylxanthine (2e)

Reaction conditions: 120 °C, 2 h; colorless solid; yield: 26.8 mg (77%).

IR (film): 1701, 1663, 1647, 1605, 1570, 1558, 1533, 1508, 1449, 1368, 1329, 1252, 1221, 1047 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.45 (2 H, d, *J* = 7.7 Hz), 7.38 (1 H, t, *J* = 7.7 Hz), 7.32–7.29 (4 H, m), 7.14 (2 H, t, *J* = 7.7 Hz), 3.78 (3 H, s), 3.71 (3 H, s).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 162.8 (d, *J* = 249.5 Hz), 154.5, 151.6, 151.4, 148.7, 131.8 (d, *J* = 3.2 Hz), 130.2, 129.5 (d, *J* = 8.7 Hz), 129.2, 128.6, 128.2, 116.3 (d, *J* = 23.0 Hz), 109.2, 29.9, 28.0.

MS (EI): *m*/*z* (%) = 350 (25) [M^+], 256 (100).

HRMS: *m*/*z* calcd for $C_{19}H_{15}FN_4O_2$: 350.1179; found: 350.1180.

7-(4-Chlorophenyl)-1,3-dimethyl-8-phenylxanthine (2f)

Reaction conditions: 120 °C, 1 h; colorless solid; yield: 35.9 mg (98%).

IR (film): 1707, 1665, 1647, 1607, 1533, 1508, 1495, 1452, 1398, 1368, 1329, 1225, 1090, 1049 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.45–7.24 (9 H, m), 3.70 (3 H, s), 3.37 (3 H, s).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 154.4, 151.6, 151.3, 148.8, 135.5, 134.1, 130.2, 129.4, 129.2, 129.0, 128.6, 128.0, 109.0, 29.9, 28.0.

MS (EI): *m*/*z* (%) = 366 (100) [M^+].

HRMS: *m*/*z* calcd for $C_{19}H_{15}{}^{35}ClN_4O_2$: 366.0884; found: 366.0873.

7-(4-Bromophenyl)-1,3-dimethyl-8-phenylxanthine (2g)

Reaction conditions: 120 °C, 1 h; colorless solid; yield: 36.4 mg (89%).

IR (film): 1701, 1663, 1605, 1528, 1491, 1445, 1395, 1331, 1225, 1132, 1065, 1047 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.57 (2 H, d, *J* = 8.4 Hz), 7.44 (2 H, d, *J* = 7.5 Hz), 7.39 (1 H, t, *J* = 7.5 Hz), 7.32 (2 H, t, *J* = 7.5 Hz), 7.20 (2 H, d, *J* = 8.4 Hz), 3.70 (3 H, s), 3.37 (3 H, s).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 154.5, 151.6, 151.3, 148.8, 134.7, 132.4, 130.3, 129.3, 129.2, 128.6, 128.1, 123.5, 109.0, 29.9, 28.0.

MS (EI): *m*/*z* (%) = 410 (100) [M^+].

HRMS: *m*/*z* calcd for $C_{19}H_{15}{}^{79}BrN_4O_2$: 410.0378; found: 410.0375.

7-(4-Methoxyphenyl)-1,3-dimethyl-8-phenylxanthine (2h)

Reaction conditions: 120 °C, 4 h; colorless solid; yield: 28.2 mg (78%).

IR (film): 1734, 1701, 1663, 1609, 1533, 1508, 1458, 1298, 1250, 1173, 1049, 1030 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.48 (2 H, d, *J* = 6.8 Hz), 7.37–7.22 (5 H, m), 6.95 (2 H, d, *J* = 8.8 Hz), 3.85 (3 H, s), 3.70 (3 H, s), 3.37 (3 H, s).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 160.1, 154.5, 151.7, 151.3, 148.6, 129.9, 129.2, 128.7, 128.5, 128.4, 114.4, 109.4, 55.5, 29.8, 28.0.

MS (EI): *m*/*z* (%) = 362 (100) [M^+].

HRMS: *m*/*z* calcd for $C_{20}H_{18}N_4O_3$: 362.1379; found: 362.1381.

7-(2-Methoxyphenyl)-1,3-dimethyl-8-phenylxanthine (2i)

Reaction conditions: 120 °C, 1 h; yellow solid; yield: 29.1 mg (80%).

IR (film): 1705, 1665, 1535, 1504, 1452, 1445, 1396, 1283, 1265, 1242, 1223, 1184, 1161, 1125, 1090, 1043, 1024 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.50–7.43 (3 H, m), 7.33 (1 H, t, *J* = 7.4 Hz), 7.29–7.25 (3 H, m), 7.05–6.98 (2 H, m), 3.71 (3 H, s), 3.63 (3 H, s), 3.36 (3 H, s).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 154.8, 154.4, 151.8, 151.7, 148.6, 131.1, 129.9, 129.1, 128.9, 128.5, 128.3, 125.0, 120.8, 112.2, 109.3, 55.7, 29.8, 27.9.

MS (EI): *m*/*z* (%) = 362 (100) [M^+].

HRMS: *m*/*z* calcd for $C_{20}H_{18}N_4O_3$: 362.1379; found: 362.1382.

7-(3-Methylphenyl)-1,3-dimethyl-8-phenylxanthine (2j)

Reaction conditions: 120 °C, 1 h; colorless solid; yield: 30.9 mg (89%).

IR (film): 1705, 1665, 1605, 1533, 1491, 1452, 1395, 1364, 1331, 1225, 1132, 1055 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.48–7.45 (2 H, m), 7.37–7.32 (2 H, m), 7.30–7.28 (3 H, m), 7.13–7.11 (2 H, m), 3.71 (3 H, s), 3.38 (3 H, s), 2.37 (3 H, s).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 154.4, 151.7, 151.1, 148.6, 139.3, 135.7, 130.2, 130.0, 129.1, 129.0, 128.5, 128.4, 128.1, 124.7, 109.3, 29.8, 28.0, 21.3.

MS (EI): *m*/*z* (%) = 346 (100) [M^+].

HRMS: *m*/*z* calcd for $C_{20}H_{18}N_4O_2$: 346.1430; found: 346.1433.

7-(3,4,5-Trimethoxyphenyl)-1,3-dimethyl-8-phenylxanthine (2k)

Reaction conditions: 120 °C, 1 h; colorless solid; yield: 40.6 mg (96%).

IR (film): 1705, 1663, 1601, 1533, 1506, 1452, 1420, 1339, 1312, 1283, 1237, 1236, 1128, 1040, 1007 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.50 (2 H, d, *J* = 8.0 Hz), 7.39–7.28 (3 H, m), 6.54 (2 H, s), 3.90, (3 H, s), 3.74 (6 H, s), 3.70 (3 H, s), 3.39 (3 H, s).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 154.3, 153.3, 151.6, 151.2, 148.6, 138.8, 131.0, 130.1, 129.0, 128.5, 109.2, 105.5, 61.0, 56.3, 29.8, 28.0.

MS (EI): *m*/*z* (%) = 422 (100) [M^+].

HRMS: *m*/*z* calcd for $C_{22}H_{22}N_4O_5$: 422.1590; found: 422.1589.

7-(3-Chloro-4-methoxyphenyl)-1,3-dimethyl-8-phenylxanthine (2l)

Reaction conditions: 120 °C, 1 h; yellow solid; yield: 38.9 mg (98%).

IR (film): 1705, 1665, 1603, 1535, 1503, 1452, 1294, 1265, 1223, 1184, 1150, 1134, 1098, 1065, 1022, 1007 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.48 (2 H, d, *J* = 7.2 Hz), 7.40–7.29 (4 H, m), 7.23 (1 H, dd, *J* = 8.5, 2.6 Hz), 6.97 (1 H, d, *J* = 8.5 Hz), 3.95 (3 H, s), 3.69 (3 H, s), 3.37 (3 H, s).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 155.8, 154.4, 151.6, 151.3, 148.6, 130.2, 129.4, 129.1, 128.6, 128.5, 128.1, 127.1, 122.9, 111.7, 109.2, 56.3, 29.8, 28.0.

MS (EI): *m*/*z* (%) = 396 (100) [M^+].

HRMS: *m*/*z* calcd for $C_{20}H_{17}{}^{35}ClN_4O_3$: 396.0989; found: 396.0988.

7-Methyl-1,3-dipropyl-8-phenylxanthine (2m)

Reaction conditions: 100 °C, 22 h; colorless solid; yield: 20.0 mg (61%).

IR (film): 1701, 1659, 1601, 1539, 1518, 1452, 1429, 1379, 1335, 1263, 1186, 1074, 1061 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.69–7.67 (2 H, m), 7.54–7.51 (3 H, m), 4.12 (2 H, t, *J* = 7.4 Hz), 4.05 (3 H, s), 4.01 (2 H, t, *J* = 7.4 Hz), 1.84 (2 H, sext, *J* = 7.4 Hz), 1.71 (2 H, sext, *J* = 7.4 Hz), 1.01–0.96 (6 H, m).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 155.6, 152.0, 151.2, 148.2, 130.2, 129.2, 128.8, 128.6, 108.6, 44.8, 42.8, 33.8, 21.38, 21.36, 11.3, 11.1.

MS (EI): *m*/*z* (%) = 326 (100) [M^+].

HRMS: *m*/*z* calcd for $C_{18}H_{22}N_4O_2$: 326.1743; found: 326.1741.

1,3-Dihexyl-7-methyl-8-phenylxanthine (2n)

Reaction conditions: 100 °C, 21 h; colorless solid; yield: 23.7 mg (58%).

IR (film): 1701, 1658, 1601, 1537, 1518, 1452, 1429, 1402, 1377, 1337, 1314, 1269, 1240, 1219, 1167, 1080, 1028 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.69–7.67 (2 H, m), 7.53–7.51 (3 H, m), 4.14 (2 H, t, *J* = 8.0 Hz), 4.05 (3 H, s), 4.03 (2 H, t, *J* = 8.0 Hz), 1.80 (2 H, quint, *J* = 7.4 Hz), 1.67 (2 H, quint, *J* = 7.4 Hz), 1.41–1.26 (12 H, m), 0.91–0.86 (6 H, m).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 155.6, 152.0, 151.1, 148.2, 130.2, 129.2, 128.8, 128.6, 108.7, 43.4, 41.4, 33.8, 31.54, 31.46, 29.7, 28.1, 26.7, 26.4, 22.6, 22.5, 14.00, 13.96.

MS (EI): *m*/*z* (%) = 410 (100) [M^+].

HRMS: *m*/*z* calcd for $C_{24}H_{34}N_4O_2$: 410.2682; found: 410.2684.

7-Methyl-1,3,8-triphenylxanthine (2o)

Reaction conditions: 100 °C, 21 h; colorless solid; yield: 14.7 mg (77%).

IR (film): 1713, 1674, 1589, 1526, 1514, 1491, 1450, 1425, 1389, 1375, 1331, 1296, 1146, 1115, 1072 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.64–7.62 (2 H, m), 7.54–7.38 (11 H, m), 7.35–7.33 (2 H, m), 4.07 (3 H, s).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 155.6, 152.5, 151.2, 148.8, 135.5, 134.8, 130.3, 129.33, 129.25, 129.1, 128.83, 128.78, 128.60, 128.58, 128.3, 109.1, 33.9.

MS (EI): *m*/*z* (%) = 394 (100) [M^+].

HRMS: *m*/*z* calcd for $C_{24}H_{18}N_4O_2$: 394.1430; found: 394.1429.

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Supporting Information

Supporting information for this article is available online at https://doi.org/10.1055/s-0036-1588821.

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