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Synthesis of *N*-Acyl-5-aminopenta-2,4-dienals via Base-Induced Ring-Opening of *N*-Acylated Furfurylamines: Scope and Limitations

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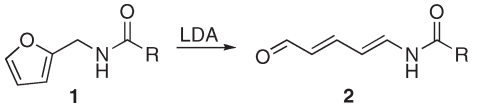
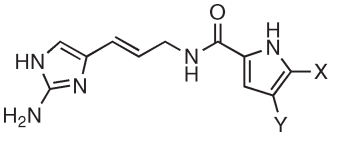


N-Acylation of furfurylamines provided **1**, which on double deprotonation with LDA led to the formation of *N*-acyl-5-aminopenta-2,4-dienals **2** via an isomerization involving opening of the furan ring. The scope and limitations of the procedure were examined by considering the influence of substituents on the carbonyl group and also on the heterocycle moiety. The efficacy of the reaction was shown to be very dependent on the nature of these groups.

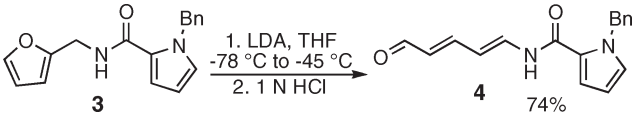
5-Aminopenta-2,4-dienals are regarded as key intermediates in the biomimetic schemes developed in the laboratory toward the manzamine alkaloids.[1] In an attempt to extend these approaches to the pyrrole−imidazole alkaloids such as oroidin,[2] we required a facile entry into *N*-(pyrrole-2-carbonyl)-5-aminopenta-2,4-dienals.



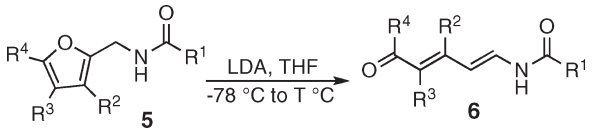
oroidin (X = Y = Br)
hymenidin (X = Y = H)
clathrodin (X = H, Y = Br)

Existing literature methods for the synthesis of 5-aminopenta-2,4-dienals appeared to be unsuitable for our purpose.[3] For example, these compounds are usually obtained from glutaconaldehydes via Zincke salts,[3c] but their acylation is expected to lead to the *O*- rather than the required *N*-acyl derivatives.[4] The ring-opening of pyridiniums salts with sodium hydroxide likewise did not appear to be a convenient preparative method for the *N*-acylaminopentadienals.[5,6] Therefore, we were forced to search for alternative entries to these potentially useful synthons and were attracted by the reported formation of *N*-benzoylaminopentadienal on treatment of *N*-furfurylbenzamide with 2.5−3.0 equiv of LDA in THF between −78 and −30 °C.[7] Here, we report on the scope and limitations of this ring-opening isomerization procedure as it pertains to the preparation of *N*-acylated aminopentadienals.

SCHEME 1. Base-Induced Ring-Opening of *N*-Furfurylpyrrole-2-carboxamide 4



SCHEME 2. Formation of *N*-Acylaminopentadienals 6 from *N*-Acylfurfurylamines 5



The ring-opening of *N*-acylfurfurylamines with a pyrrole-2-carboxamide moiety was first envisaged to probe the feasibility of the process. The amide **3** was prepared by acylation of furfurylamine with *N*-benzyl-2-trichloroacetylpyrrole, and its behavior in the presence of 2.9 equiv of LDA in THF was examined. After deprotonation at −78 °C, increasing the temperature of the reaction mixture from −78 to −45 °C, and quenching with 1 N HCl, the (*E*,*E*)-*N*-acylated aminopentadienal **4** was obtained in 74% yield (Scheme 1).

The success of this base-induced rearrangement with a pyrrole-2-carboxamide prompted us to study this isomerization method further and to probe the scope and limitations of compatible *N*-acylfurfurylamines and their substituents.

The effect of the substituent R^1 on the carbonyl group as well as the possibility of extending the reaction to differently

† Deceased November 12, 2008.

(1) (a) Kaiser, A.; Billot, X.; Gateau-Olesker, A.; Marazano, C.; Das, B. C. *J. Am. Chem. Soc.* **1998**, *120*, 8026–8034. (b) Jakubowicz, K.; Ben Abdeljelil, K.; Herdemann, M.; Martin, M.-T.; Gateau-Olesker, A.; Al Mourabit, A.; Marazano, C.; Das, B. C. *J. Org. Chem.* **1999**, *64*, 7381–7387. (c) Wypych, J.-C.; Nguyen, T. M.; Nuhant, P.; Bénéchie, M.; Marazano, C. *Angew. Chem., Int. Ed.* **2008**, *47*, 5418–5421.

(2) (a) For reviews on the synthesis of these compounds, see: Feldman, K. S.; Fodor, M. D.; Skoumbourdis, A. P. *Synthesis* **2009**, 3162–3173. Weinreb, S. M. *Nat. Prod. Rep.* **2007**, *24*, 931–948. Hoffmann, H.; Lindel, T. *Synthesis* **2003**, 1753–1783. (b) For biosynthetic proposals, see: Al Mourabit, A.; Potier, P. *Eur. J. Org. Chem.* **2001**, 237–243.

(3) (a) For a review on aminopentadienals, see: Becher, J. *Synthesis* **1980**, 589–612. (b) The parent compound is rather unstable: Reinehr, D.; Winkler, T. *Angew. Chem., Int. Ed.* **1981**, *20*, 881–882. (c) Nguyen, T. M.; Peixoto, S.; Ouairy, C.; Nguyen, T. D.; Bénéchie, M.; Marazano, C.; Michel, P. *Synthesis* **2010**, 103–109. (d) For a recent use of aminopentadienals in alkaloid synthesis, see: Martin, D. B. C.; Vanderwal, C. D. *J. Am. Chem. Soc.* **2009**, *131*, 3472–3473.

(4) Nuhant, P.; Raikar, S. B.; Wypych, J.-C.; Delpech, B.; Marazano, C. *J. Org. Chem.* **2009**, *74*, 9413–9421.

(5) *N*-Acylpyridiniums are acylating reagents, and to the best of our knowledge, only a *N*,*N*-dimethylcarbamoyl derivative has been used for such a reaction: (a) Johnson, S. L.; Rumon, K. A. *Tetrahedron Lett.* **1966**, 1721–1726. (b) Johnson, S. L.; Rumon, K. A. *Biochemistry* **1970**, *9*, 847–857. (c) Colabroy, K. L.; Begley, T. P. *J. Am. Chem. Soc.* **2005**, *127*, 840–841.

(6) The *N*-benzoyl derivative of 5-aminopenta-2,4-dienal was formed via a pyridinium salt in a colorimetric Fujiwara reaction (pyridine and α,α,α-trichlorotoluene in aqueous sodium hydroxide): Uno, T.; Okumura, K.; Kuroda, Y. *J. Org. Chem.* **1981**, *46*, 3175–3178.

(7) Ohno, K.; Machida, M. *Tetrahedron Lett.* **1981**, *22*, 4487–4488.

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TABLE 1. Yields of *N*-Acylaminopentadienals 6 from Ring Opening of Furans 5

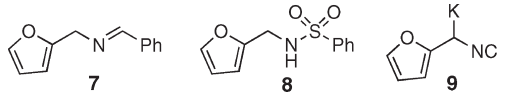
entry	furan	R^1	R^2	R^3	R^4	T (°C)[a]	product	yield (%)
1	**5a**	CH_3	H	H	H	0	**6a**[b]	6
2	**5b**	$C(CH_3)_3$	H	H	H	−50	**6b**	47
3	**5c**	4-$CH_3OC_6H_4$	H	H	H	−55	**6c**	66
4	**5d**	4-$O_2NC_6H_4$	H	H	H	0	*b*	
5	**5e**	pyrrole-2-yl	H	H	H	0	*b*	
6	**5f**	*N*-methylpyrrole-2-yl	H	H	H	−45	**6f**	43
7	**5g** (**3**)	*N*-benzylpyrrole-2-yl	H	H	H	−45	**6g** (**4**)	74
8	**5h**	CF_3	H	H	H	0	*b*	
9	**5i**	$OC(CH_3)_3$	H	H	H	0	*b*	
10	**5j**	$N(CH_3)_2$	H	H	H	0	**6j**	44
11	**5k**	Ph	CH_3	H	H	−45	**6k**[c]	75
12	**5l**	Ph	H	4-ClC_6H_4	H	0	*b*	
13	**5m**	Ph	H	H	CH_3	−55	**6m**	69

[a]See Scheme 2. [b]Starting material recovered. [c]Mixture of isomers E/Z = 2/1.

substituted furans were examined (Scheme 2). The *N*-acylamines **5** were generally prepared by acylation of the corresponding furfurylamines (see the Supporting Information). Compounds **5** were treated in the presence of 2.9 equiv of LDA in THF at −78 °C, and the reaction mixture was allowed to warm until disappearance of the starting material (when the ring-opening was effective), as estimated by TLC. This reaction was accompanied by a color change,[6,7] whose nature depends on the type of compound. Quenching was carried out either with 1 N HCl or saturated NH_4Cl, and the results are reported in Table 1. Except for entry 1, the behavior of the furfuryl compounds was clear-cut since either a ring-opening was observed or the starting furan was recovered. The aminopentadienals **6** were obtained as clean (*E*,*E*) isomers, except in the case of compound **6k** whose trisubstituted double bond was obtained as a 2/1 mixture of geometric isomers.

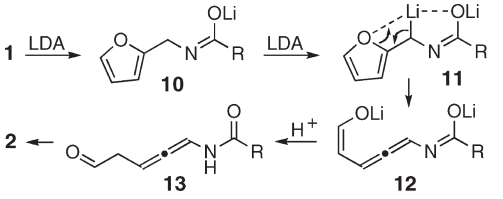
From Table 1, it appears that the ring opening generally affords the desired *N*-acylaminopentadienals when R^1 is a phenyl ring[7] or an electron-donating group. However, it seems that with an electron-withdrawing substituent on the carbonyl group capable of stabilizing a negative charge (entries 4 and 8), the opening of the heterocycle is prevented.

The same observation was also made for the imine **7** and for the sulfonamide **8**, which were recovered after treatment with LDA. This behavior recalls the observation of Schöllkopf whereby the potassium derivative **9**, obtained by deprotonation of the corresponding isocyanide with *t*-BuOK, was stable in THF up to −10 °C.[8]



For the acetamide **5a** (entry 1), the yield was very low probably due to competitive deprotonation of the methyl group and to the aqueous solubility of the aminopentadienal (compare with the pivalamide **5b** of entry 2). The pyrrole-2-carboxamide must be *N*-protected for efficient ring-opening

SCHEME 3. Possible Mechanism for the Formation of *N*-Acylminopentadienals



(compare entry 5 with entries 6 and 7). The case of the Boc derivative **5i** (entry 9) is particular since the *tert*-butoxy group is an electron-donating one; failure is probably due to difficulties in deprotonating α to nitrogen.[9]

For the benzamides substituted on the heterocycle moiety (entries 11−13), the base-induced ring-opening was effective with the compounds possessing a methyl group at C-3 and C-5 (furan numbering, entries 11 and 13, respectively) but not with the C-4-substituted derivatives (entry 12). In the case of the formation of the *N*-benzoylaminopentadienal **6k** (entry 11), the product was isolated as a 2/1 mixture of *E* and *Z* isomers for the trisubstituted double bond. It is emphasized that the procedure is also useful for the preparation of *N*-acylaminopentadienones, as exemplified by the formation of **6m** (entry 13).

Concerning the mechanism of the reaction (Scheme 3), deprotonation of **1** at nitrogen followed by lateral lithiation of intermediate **10** should lead to the dilithiated species **11**, which we hypothesize then undergoes opening of the furan ring into an *N*-substituted lithium penta-1,3,4-trien-1-olate **12**. The thermodynamic balance of this step is expected to be favorable (lithium carbanion for **11** vs conjugated lithium enolate for **12**), even though the resonance energy of furan is lost. However, it could be a reversible process (5-*exo*-*dig* cyclization).[10] This mechanism is analogous to that proposed for the ring-opening of furfuryl carbanions stabilized by a dithiane,[11] a phenyl, or a trimethylsilyl group[12] and from which allenyl derivatives have been isolated after

(8) Schöllkopf, U.; Frieben, W. *Liebigs Ann. Chem.* **1980**, 1722–1727.

(9) Treatment of **5i** with 2.2 equiv of BuLi in THF from −78 to −10 °C led to recovery of the starting material. This base has been used for *N*-silylation of **5i** and for *C*-lithiation of the resulting product to achieve a reverse aza-Brook rearrangement: Liu, G.; Sieburth, S. McN. *Org. Lett.* **2005**, *7*, 665–668. However, double deprotonation of *tert*-butyl benzylcarbamate required 3 equiv of *s*-BuLi in the presence of 2.1 equiv of TMEDA: Kanazawa, A. M.; Correa, A.; Denis, J.-N.; Luche, M.-J.; Greene, A. E. *J. Org. Chem.* **1993**, *58*, 255–257.

(10) (a) Marshall, J. A.; DuBay, W. J. *J. Org. Chem.* **1993**, *58*, 3435–3443. (b) Sherry, B. D.; Maus, L.; Laforteza, B. N.; Toste, F. D. *J. Am. Chem. Soc.* **2006**, *128*, 8132–8133. (c) For the formation of a furan by intramolecular cyclization of an enol onto an allene, see: Mageswaran, S.; Ollis, W. D.; Southam, D. A.; Sutherland, I. O.; Thebtaranonth, Y. *J. Chem. Soc, Perkin Trans. 1* **1981**, 1969–1980. (d) For cyclization reactions of allenes, see: Ma, S. *Acc. Chem. Res.* **2009**, *42*, 1679–1688. and references therein.

(11) Taschner, M. J.; Kraus, G. A. *J. Org. Chem.* **1978**, *43*, 4235–4236.

(12) (a) Atsumi, K.; Kuwajima, I. *Chem. Lett.* **1978**, 387–390. (b) Atsumi, K.; Kuwajima, I. *J. Am. Chem. Soc.* **1979**, *101*, 2208–2210.

quenching with trimethylsilyl chloride. After the hydrolytic treatment, a sequence of prototropy−isomerization should lead, via intermediate **13**, to the most stable form (*N*-acylaminopentadienal) and isomer (*E*,*E*) of the product **2**.[13]

The fact that ring-opening was not observed with an electron-withdrawing group R (4-$O_2NC_6H_4$ and CF_3, respectively, for **5d** and **5h**) could be imputed to the increased stability of the dilithiated species **11**, which likely renders the passage from **11** to **12** thermodynamically unfavorable. A similar argument can also be used to explain the lack of reactivity of compounds **7** and **8**. In the case of the Boc derivative **5i**, the failure of the reaction might be attributed to the ineffectiveness of the *C*-lithiation (slowed formation of **11** with R = *t*-BuO).[9] For the urea **5j**, the formation of the corresponding aminopentadienal **6j** needs a higher temperature (0 °C, entry 10 of Table 1), perhaps owing to a more difficult lateral lithiation with a more electron-rich species **10** with R = NMe_2.

For the heterocycle-substituted compounds **5k**−**m**, the ring-opening presumably proceeds with an increase in strain in the transition state (C−C/C−H 1,2-interactions), due to the increase of internal bond angles of the opening heterocycle as the C−O bond breaks. This strain is expected to be more important for **5l** (two interactions) than for **5k** or **5m** (one interaction) and might hinder the opening step in the former cases.

In conclusion, the ring-opening of *N*-acylfurfurylamines with LDA provides a convenient entry into the *N*-acyl-5-aminopenta-2,4-dienals when there is a phenyl or an electron-donating substituent on the carbonyl group. The fine-tuning observed between the nature of the substituents and the facility of the isomerization depends on a combination of electronic and steric effects. This procedure allows the preparation of compounds not easily available by other methods, and can be extended to the formation of *N*-acylaminopentadienones. These products might be useful to achieve Diels−Alder reactions,[14] and reduction to the corresponding alcohols with a dienamide moiety,[15] followed by linking to a dienophile, could allow intramolecular cycloadditions.[16,17]

Experimental Section

General Procedure for the Base-Induced Ring-Opening of *N*-Acylated Furfurylamines. To a stirred solution of diisopropylamine (2.80 equiv) in THF (ca. 0.3 M), under an argon atmosphere between −10 and −20 °C, was added BuLi (2.95 equiv). The resulting reaction mixture was stirred for 20 min between −10 and −20 °C and then cooled to −78 °C. A ca. 0.3 M solution of the *N*-acylated furfurylamine **5** (see the Supporting Information for its preparation) in THF was then added, and the mixture was allowed to stir while slowly warming until disappearance of the starting material (up to the temperature indicated in Table 1). A color change, depending on the type of compound, was also observed during this period. Diethyl ether and 1 N HCl (A), or CH_2Cl_2 and saturated NH_4Cl (B), were then added. The organic layer was separated, dried ($MgSO_4$), concentrated in vacuo, and purified by silica gel column chromatography to afford the *N*-acylated aminopentadienal **7**.

***N*-((1*E*,3*E*)-5-Oxopenta-1,3-dienyl)pivalamide (6b).** The general procedure was followed with diisopropylamine (540 μL, 3.85 mmol, 2.80 equiv), BuLi (1.6 M/hexanes) (2.50 mL, 4.00 mmol, 2.90 equiv), and 250 mg (1.38 mmol) of *N*-(furan-2-ylmethyl)-pivalamide **5b**. The reaction mixture was allowed to warm from −78 to −50 °C and turned from yellow to red. After treatment B and chromatography on silica gel (CH_2Cl_2/acetone 90/10), **6b** (118 mg, 47%) was obtained as a yellow powder: mp 138.9−140.2 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 9.51 (d, *J* = 8.2 Hz, 1 H), 7.61 (br s, 1 H), 7.48 (t, *J* = 12.5 Hz, 1 H), 7.14 (dd, *J* = 12.5, 15.0 Hz 1 H), 6.07 (m, 2 H), 1.27 (s, 9 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 193.4 (C), 176.1 (C), 151.7 (CH), 134.9 (CH), 129.2 (CH), 110.5 (CH), 39.3 (C), 27.4 (3 CH_3); FTIR 3275, 1695, 1667, 1596, 983 cm^{-1}; MS (ESI$^+$) *m*/*z* 182.1 $(M + H)^+$, 204.1 $(M + Na)^+$, 220.1 $(M + K)^+$, 236.1 $(M + Na + MeOH)^+$; HRMS (ESI$^+$) calcd for $C_{10}H_{15}NNaO_2$ $(M + Na)^+$ 204.1000, found 204.0994.

4-Methoxy-*N*-((1*E*,3*E*)-5-oxopenta-1,3-dienyl)benzamide (6c). The general procedure was followed with diisopropylamine (425 μL, 3.03 mmol, 2.78 equiv), BuLi (1.6 M/hexanes) (2.00 mL, 3.20 mmol, 2.94 equiv), and 252 mg (1.09 mmol) of *N*-(furan-2-ylmethyl)-4-methoxybenzamide **5c**. The reaction mixture was allowed to warm from −78 to −55 °C and turned from blue to green. After treatment B and chromatography on silica gel (CH_2Cl_2/acetone 90/10), **6c** (167 mg, 66%) was obtained as a beige powder: mp 170.0−171.7 °C; ^{1}H NMR (DMSO-d_6, 300 MHz) δ 10.92 (d, *J* = 10.2 Hz, 1 H), 9.45 (d, *J* = 8.2 Hz, 1 H), 7.97 (d, *J* = 8.9 Hz, 2 H), 7.71 (dd, *J* = 13.6, 10.2 Hz, 1 H), 7.51 (dd, *J* = 14.6, 11.4 Hz, 1 H), 7.08 (d, *J* = 8.9 Hz, 2 H), 6.38 (dd, *J* = 13.6, 11.4 Hz, 1 H), 6.09 (dd, *J* = 14.6, 8.2 Hz, 1 H), 3.85 (s, 3 H); ^{13}C NMR (DMSO-d_6, 75 MHz) δ 193.2 (C), 174.5 (C), 163.8 (C), 154.0 (CH), 137.3 (CH), 130.0 (2 CH), 127.6 (CH), 124.6 (C), 113.9 (2 CH), 110.7 (CH), 55.5 (CH_3); FTIR: 3306, 1678, 1633, 1604, 1530, 1494, 1254, 1024, 972 cm^{-1}; MS (ESI$^+$) *m*/*z* 232.1 $(M + H)^+$, 254.1 $(M + Na)^+$, 270.1 $(M + K)^+$, 286.1 $(M + Na + MeOH)^+$; HRMS (ESI$^+$) calcd for $C_{13}H_{13}NNaO_3$ $(M + Na)^+$ 254.0793, found 254.0793.

1-Benzyl-*N*-((1*E*,3*E*)-5-oxopenta-1,3-dienyl)-1*H*-pyrrole-2-carboxamide (6g) (4). The general procedure was followed with diisopropylamine (420 μL, 3.00 mmol, 2.80 equiv), BuLi (2.5 M/hexanes) (1.25 mL, 3.12 mmol, 2.92 equiv), and 302 mg (1.07 mmol) of *N*-(furan-2-ylmethyl)-1-benzyl-1*H*-pyrrole-2-carboxamide **5g** (**3**). The reaction mixture was allowed to warm from −78 to −45 °C and turned from red to orange. After treatment A and chromatography on silica gel (AcOEt/pentane 30/70 to AcOEt), **6g** (222 mg, 74%) was obtained as a red powder: mp 164.2−165.2 °C; ^{1}H NMR (DMSO-d_6, 300 MHz) δ 10.61 (d, *J* = 10.5 Hz, 1 H), 9.41 (d, *J* = 8.2 Hz 1 H), 7.61 (dd, *J* = 13.4, 10.5 Hz, 1 H), 7.45 (t, *J* = 11.3 Hz, 1 H), 7.29 (m, 3 H), 7.23 (m, 1 H), 7.17 (dd, *J* = 4.1, 1.7 Hz, 1 H), 7.09 (d, *J* = 8.3 Hz, 2 H), 6.29 (dd, *J* = 13.4 Hz, 11.3 Hz, 1 H), 6.22 (m, 1 H), 6.04 (dd, *J* = 14.9, 8.2 Hz, 1H), 5.60 (s, 2 H); ^{13}C NMR (DMSO-d_6, 75 MHz) δ 193.0 (C), 158.1 (C), 154.2 (CH), 139.1 (C), 137.1 (CH), 130.3 (C), 128.4 (2 CH), 127.1 (CH), 127.0 (CH), 126.6 (2 CH), 123.2 (CH), 116.0 (CH), 109.6 (CH), 108.2 (CH), 51.1 (CH_2); FTIR 3310, 1668, 1652, 1592, 1530, 1493, 1159, 1073, 995, 742 cm^{-1}; MS (ESI$^+$) *m*/*z* 303.1 $[M + Na]^+$; HRMS (ESI$^+$) calcd for $C_{17}H_{16}N_2NaO_2$ $(M + Na)^+$ 303.1109, found 303.1105.

1,1-Dimethyl-3-(1*E*,3*E*)-5-oxopenta-1,3-dienyl)urea (6j). The general procedure was followed with diisopropylamine (585 μL, 4.17 mmol, 2.80 equiv), BuLi (2.5 M/hexanes) (1.75 mL,

(13) A sigmatropic [1,5] hydrogen shift from the enol corresponding to **12**, followed by *Z*−*E* isomerization, could also account for the formation of **2**. See, for example: Maynard, D. F.; Okamura, W. H. *J. Org. Chem.* **1995**, *60*, 1763–1771.

(14) Gauvry, N.; Huet, F. *J. Org. Chem.* **2001**, *66*, 583–588. (b) Aït Youcef, R.; Boucheron, C.; Guillarme, S.; Legoupy, S.; Dubreuil, D.; Huet, F. *Synthesis* **2006**, 633–636.

(15) Aït Youcef, R.; Boucheron, C.; Guillarme, S.; Legoupy, S.; Dubreuil, D.; Huet, F. *Synthesis* **2006**, 633–636.

(16) For reviews, see: (a) Petrzilka, M.; Grayson, J. I. *Synthesis* **1981**, 753–786. (b) Campbell, A. L.; Lenz, G. R. *Synthesis* **1987**, 421–452.

(17) This type of approach has been reported with *O*-acyl glutaconaldehydes, principally by Becher's group: (a) Ingedoh, A.; Becher, J.; Clausen, H.; Nielsen, H. C. *Tetrahedron Lett.* **1985**, *26*, 1249–1252. (b) Becher, J.; Nielsen, H. C.; Jacobsen, J. P.; Simonsen, O.; Clausen, H. *J. Org. Chem.* **1998**, *53*, 1862–1871. (c) Jørgensen, T.; Nielsen, H. C.; Malhotra, N.; Becher, J.; Begtrup, M. *J. Heterocycl. Chem.* **1992**, *29*, 1841–1845. (d) Berthon, L.; Tahri, A.; Ugen, D. *Tetrahedron Lett.* **1994**, *35*, 3937–3940.

4.38 mmol, 2.94 equiv), and 250 mg (1.49 mmol) of *N*-(furan-2-ylmethyl)-1,1-dimethylurea (**5j**). The reaction mixture was allowed to warm from −78 to 0 °C and turned from pale pink to yellow. After treatment A and chromatography on silica gel (CH_2Cl_2/MeOH 95/5), **6j**[18] (109 mg, 44%) was obtained as a yellow powder: mp 113.0−113.7 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 9.39 (d, J = 8.2 Hz, 1 H), 8.23 (d, J = 10.9 Hz, 1 H), 7.52 (dd, J = 13.5, 10.9 Hz, 1 H), 7.15 (dd, J = 14.5, 11.4 Hz 1 H), 5.94 (m, 2 H,), 2.99 (s, 6 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 193.8 (C), 154.8 (C), 154.1 (CH), 139.9 (CH), 126.2 (CH), 107.2 (CH), 36.5 (2 CH_3); FTIR 3277, 1657, 1599, 1244, 861 cm^{-1}; MS (ESI$^+$) m/z 191.1 (M + Na)$^+$, 223.1 [M + Na + MeOH]$^+$; HRMS (ESI$^+$) calcd for $C_8H_{12}N_2NaO_2$ (M + Na)$^+$ 191.0796, found 191.0788.

***N*-((1*E*,3*E*/*Z*)-3-Methyl-5-oxopenta-1,3-dienyl)benzamide (2/1) (6k).** The general procedure was followed with diisopropylamine (355 μL, 2.55 mmol, 2.80 equiv), BuLi (2.5 M/hexanes) (1.25 mL, 3.12 mmol, 2.92 equiv), and 195 mg (0.906 mmol) of *N*-((3-methylfuran-2-yl)methyl)benzamide **5k**. The reaction mixture was allowed to warm from −78 to −45 °C and turned from blue to orange. After treatment B with $CHCl_3$, instead of CH_2Cl_2, and chromatography on silica gel (pentane/AcOEt 80/20), **6k** (146 mg, 75%) was obtained as a yellow oil and as a 2/1 (*E*/*Z*) mixture: ^{1}H NMR ($CDCl_3$, 300 MHz) δ for the major isomer 10.06 (d, J = 8.4 Hz, 1 H), 8.46 (d, J = 11.3 Hz, 1 H), 7.90 (m, 2 H), 7.80 (dd, J = 14.4, 11.3 Hz, 1 H), 7.50 (m, 3 H), 6.11 (d, J = 14.4 Hz, 1 H), 5.89 (d, J = 8.4 Hz, 1 H), 2.33 (s, 3 H); for the minor isomer 9.98 (d, J = 6.8 Hz, 1 H), 8.63 (d, J = 11.3 Hz, 1 H), 8.09 (dd, J = 8.1, 1.6 Hz, 2 H), 7.74 (dd, J = 14.4, 11.3 Hz, 1 H), 7.60 (m, 3 H), 7.18 (d, J = 14.4 Hz, 1 H), 5.83 (d, J = 6.8 Hz, 1 H), 2.15 (s, 3 H); ^{13}C NMR (DMSO-d_6, 75 MHz) δ for the major isomer 191.0 (C), 164.5 (C), 141.3 (C), 132.7 (C), 131.1 (CH), 128.6 (2 CH), 128.4 (CH), 127.8 (2 CH), 126.7 (CH), 115.7 (CH), 20.4 (CH_3); for the minor isomer 189.1 (C), 155.4 (C), 140.6 (C), 132.4 (C), 129.2 (CH), 128.6 (2 CH), 128.3 (CH), 127.8 (2 CH), 125.2 (CH), 108.5 (CH), 12.6 (CH_3); FTIR 3311, 1679,1593, 1514, 1485, 1139, 1175, 689 cm^{-1}; MS (ESI$^+$) m/z 238.1 (M + Na)$^+$; HRMS (ESI$^+$) calcd for $C_{13}H_{13}NNaO_2$ (M + Na)$^+$ 238.0844, found 238.0833.

***N*-((1*E*,3*E*)-5-Oxohexa-1,3-dienyl)benzamide (6m).** The general procedure was followed with diisopropylamine (455 μL, 3.25 mmol, 2.80 equiv), BuLi (1.6 M/hexanes) (2.70 mL, 4.32 mmol, 3.70 equiv), and 250 mg (1.16 mmol) of *N*-((5-methylfuran-2-yl)methyl)benzamide (**5m**). The reaction mixture was allowed to warm from −78 to −55 °C and turned from blue to orange. After treatment B and chromatography on silica gel (CH_2Cl_2/acetone 95/5), **6m** (174 mg, 69%) was obtained as a yellow powder: mp 172.4−173.0 °C; ^{1}H NMR (DMSO-d_6, 300 MHz) δ 10.92 (d, J = 10.4 Hz, 1 H), 7.96 (dd, J = 7.2, 1.7 Hz, 2 H), 7.67 (dd, J = 13.5, 10.4 Hz, 1 H), 7.57 (m, 3 H), 7.44 (dd, J = 11.4, 15.1 Hz, 1 H), 6.29 (dd, J = 11.4, 13.5 Hz, 1 H), 6.04 (d, J = 15.1 Hz, 1 H), 2.20 (s, 3 H); ^{13}C NMR (DMSO-d_6, 75 MHz) δ 197.4 (C), 164.3 (C), 144.3 (CH), 135.5 (CH), 132.7 (C), 132.3 (CH), 128.6 (2 CH), 127.8 (2 CH), 127.1 (CH), 111.6 (CH), 26.6 (CH_3); FTIR 3297, 1680, 1595, 1506, 1484, 1248, 1001, 699 cm^{-1}; MS (ESI$^+$) m/z 238.1 (M + Na)$^+$, 270.1 (M + Na + MeOH)$^+$; HRMS (ESI$^+$) calcd for $C_{13}H_{13}NNaO_2$ (M + Na)$^+$ 238.0844, found 238.0835.

Supporting Information Available: Experimental details for the preparation of **3**, **5a**−**m**, **6a**,**f**, **7**, and **8** and copies of ^{1}H and ^{13}C NMR spectra for all compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

(18) Compound **6j** has been obtained in D_2O solution, as a mixture with the enolic tautomer, and the ^{1}H NMR spectra and chemical shifts of these compounds in this solvent are reported in ref 5c.