JOC Note

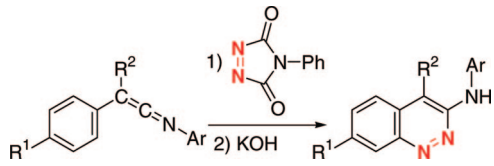
[4 + 2] Cycloaddition Reaction of *C*-Aryl Ketenimines with PTAD as a Synthetic Equivalent of Dinitrogen. Synthesis of Triazolocinnolines and Cinnolines

Mateo Alajarin,*[,†] Baltasar Bonillo,[†] Marta Marin-Luna,[†] Angel Vidal,*[,†] and Raul-Angel Orenes[‡]

Departamento de Quimica Organica, Facultad de Quimica, Universidad de Murcia, Campus de Espinardo, 30100 Murcia, Spain, and Servicio Universitario de Instrumentacion Cientifica, Universidad de Murcia, Campus de Espinardo, 30100 Murcia, Spain

alajarin@um.es

Received February 12, 2009



C,*C*,*N*-Triaryl ketenimines and *C*-alkyl-*C*,*N*-diaryl ketenimines react with 2 equiv of PTAD to provide 1,2,4-triazolo[1,2-*a*]cinnolines with a pendant triazolidindione group by means of a Diels−Alder/ene sequence. The treatment of such adducts with potassium hydroxide affords 3-aminocinnolines.

Ketenimines, a group of organic nitrogen heterocumulenes sharing a common 1-aza-1,2-propadiene system, have served as useful substrates to create structural diversity and complexity in the synthesis of nitrogen heterocycles. The basis of this usefulness lies in the rich chemistry of ketenimines,[1] which may undergo the addition of nucleophiles and carbon-centered radicals[2] to their central carbon atom, and easily participate in pericyclic events: cycloaddition reactions, 6π-electrocyclic ring closures and sigmatropic rearrangements.[3] Among these reactions the [2 + 2] and [4 + 2] cycloaddition processes have attracted the most attention.[4] When participating in Diels−Alder reactions, the role played by ketenimines depends on the reaction partner and the kind of substituents attached to their C and N atoms, more often reacting with remarkable selectivity. Notably, ketenimines can react as dienophiles, with either their N═C or C═C bond getting involved in the cycloaddition process. In addition, ketenimines have the ability to serve as the diene partners, either as 2-azadienes [*N*-vinyl(aryl) ketenimines] or as all-carbon dienes [*C*-vinyl(aryl) ketenimines].

1,2,4-Triazoline-3,5-diones (TADs) are strong electron acceptors and known to be extremely reactive and synthetically useful dienophiles[5] and enophiles.[6] Concerning the dienophilic behavior of TADs, it is worth mentioning that these neutral dienophiles have found application in efficient methods to capture very unstable intermediates,[7] for characterizing dienes,[8] in the isolation of dienes from complex mixtures[9] and for temporarily protecting diene fragments.[10]

The group of Battaglia has reported the periselective Diels−Alder reaction of *C*-vinyl-*N*-(4-methylphenyl) ketenimines with 4-phenyl-1,2,4-triazoline-3,5-dione (PTAD) which gives rise to the monocycloadducts across the diene system formed by the cumulative C═C bond and the adjacent vinyl

[†] Facultad de Quimica.
[‡] Servicio Universitario de Instrumentacion Cientifica.

(1) For reviews in the chemistry of ketenimines, see: (a) Krow, D. R. *Angew., Chem. Int. Ed. Engl.* **1971**, *10*, 435–449. (b) Gambaryan, N. P. *Usp. Khim.* **1976**, *45*, 1251–1268. (c) Dondoni, A. *Heterocycles* **1980**, *14*, 1547–1566. (d) Barker, M. W.; McHenry, W. E. In *The Chemistry of Ketenes, Allenes and Related Compounds*; Patai, S., Ed.; Wiley-Interscience: Chichester, UK, 1980; Part 2, 701. (e) Alajarín, M.; Vidal, A.; Tovar, F. *Targets Heterocycl. Syst.* **2000**, *4*, 293–326. (f) Perst, H. *Sci. Synth.* **2006**, *23*, 781–898.

(2) (a) Alajarín, M.; Vidal, A.; Ortín, M.-M. *Tetrahedron Lett.* **2003**, *44*, 3027–3030. (b) Alajarín, M.; Vidal, A.; Ortín, M.-M. *Org. Biomol. Chem.* **2003**, *1*, 4282–4292. (c) Alajarín, M.; Vidal, A.; Ortín, M.-M.; Bautista, D. *New J. Chem.* **2004**, *28*, 570–577. (d) Alajarín, M.; Vidal, A.; Ortín, M.-M.; Bautista, D. *Synlett* **2004**, 991–994.

(3) For some recent examples, see: (a) Alajarín, M.; Ortín, M.-M.; Sánchez-Andrada, P.; Vidal, A.; Bautista, D. *Org. Lett.* **2005**, *7*, 5281–5284. (b) Alajarín, M.; Bonillo, B.; Ortín, M.-M.; Sánchez-Andrada, P.; Vidal, A. *Org. Lett.* **2006**, *8*, 5645–5648. (c) Alajarín, M.; Ortín, M.-M.; Sánchez-Andrada, P.; Vidal, A. *J. Org. Chem.* **2006**, *71*, 8126–8139.

(4) For selected examples of [2 + 2] cycloadditions of ketenimines, see: (a) Alajarín, M.; Molina, P.; Vidal, A. *Tetrahedron Lett.* **1996**, *37*, 8945–8948. (b) Alajarín, M.; Vidal, A.; Tovar, F.; Arrieta, A.; Lecea, B.; Cossío, F. P. *Chem.—Eur. J.* **1999**, *5*, 1106–1117. (c) Cossío, F. P.; Arrieta, A.; Lecea, B.; Alajarín, M.; Vidal, A.; Tovar, F. *J. Org. Chem.* **2000**, *65*, 3633–3643. (d) Alajarín, M.; Vidal, A.; Tovar, F.; Ramírez de Arellano, M. C.; Cossío, F. P.; Arrieta, A.; Lecea, B. *J. Org. Chem.* **2000**, *65*, 7512–7515. (e) Alajaŕ; in, M.; Vidal, A.; Tovar, F.; Ramírez de Arellano, M. C. *Tetrahedron: Asymmetry* **2004**, *15*, 489–494. (f) For selected examples of [4 + 2] cycloadditions of ketenimines, see: Alajarín, M.; Vidal, A.; Tovar, F.; Conesa, C. *Tetrahedron Lett.* **1999**, *40*, 6127–6130. (g) Alajarín, M.; Vidal, A.; Tovar, F. *Tetrahedron Lett.* **2000**, *41*, 7029–7032. (h) Alajarín, M.; Vidal, A.; Ortín, M.-M.; Tovar, F. *Synthesis* **2002**, 2393–2398. (i) Lee, K.-J.; Kim, D.-W.; Kim, B.-G. *J. Heterocycl. Chem.* **2003**, *40*, 363–367. (j) Martorell, A.; Inman, G.; Alper, H. *J. Mol. Catal. A: Chem.* **2003**, *204−205*, 91–96. (k) Alajarín, M.; Vidal, A.; Tovar, F.; Sánchez-Andrada, P.; Bautista, D. *Tetrahedron* **2003**, *59*, 9913–9918. (l) Alajarín, M.; Vidal, A.; Ortín, M.-M. *Tetrahedron* **2005**, *61*, 7613–7621. (m) Alajarín, M.; Bonillo, B.; Sánchez-Andrada, P.; Vidal, A.; Bautista, D. *J. Org. Chem.* **2007**, *72*, 5863–5866.

(5) For recent examples of using PTAD as dienophile, see: (a) Kobayashi, S.; Furuya, T.; Otani, T.; Saito, T. *Tetrahedron* **2008**, *64*, 9705–9716. (b) Süennemann, H. W.; Banwell, M. G.; de Meijere, A. *Chem.—Eur. J.* **2008**, *14*, 7236–7249. (c) Kobayashi, S.; Furuya, T.; Otani, T.; Saito, T. *Tetrahedron Lett.* **2008**, *49*, 4513–4515. (d) Alajarín, M.; Cabrera, J.; Pastor, A.; Sánchez-Andrada, P.; Bautista, D. *J. Org. Chem.* **2008**, *73*, 963–973.

(6) For recent examples of using PTAD as enophile, see: (a) Acevedo, O.; Squillacote, M. E. *J. Org. Chem.* **2008**, *73*, 912–922. (b) Basheer, A.; Rappoport, Z. *J. Org. Chem.* **2008**, *73*, 184–190. (c) Vougioukalakis, G. C.; Roubelakis, M. M.; Alberti, M. N.; Orfanopoulos, M. *Chem.—Eur. J.* **2008**, *14*, 9697–9705.

(7) Anastassiou, A. G.; Yakali, E. *J. Chem. Soc., Chem. Commun.* **1972**, 92–93.

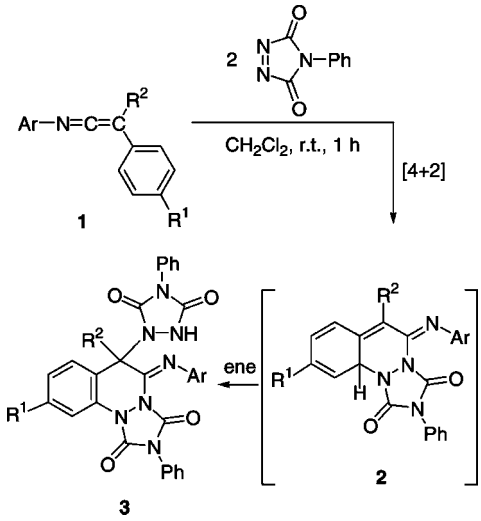
(8) (a) Askani, R.; Chesick, J. P. *Chem. Ber.* **1973**, *106*, 8–19. (b) Imagawa, T.; Sueda, N.; Kawanisi, M. *J. Chem. Soc., Chem. Commun.* **1972**, 388. (c) Kobal, V. M.; Gibson, D. T.; Davies, R. E.; Garza, A. *J. Am. Chem. Soc.* **1973**, *95*, 4420–4421.

(9) (a) Poutsma, M. L.; Ibarbia, P. A. *Tetrahedron Lett.* **1970**, *11*, 4967–4970. (b) Poutsma, M. L.; Ibarbia, P. A. *J. Am. Chem. Soc.* **1971**, *93*, 440–450.

(10) (a) Ochi, K.; Matsunaga, I.; Nagano, H.; Fukushima, M.; Shindo, M.; Kanedo, C.; Ishikawa, M.; DeLuca, H. F. *J. Chem. Soc., Perkin Trans. 1* **1979**, 165–169. (b) Bosworth, N.; Emke, A.; Midgley, J. M.; Moore, C. J.; Whalley, W. B.; Fergurson, G.; Marsh, W. C. *J. Chem. Soc., Perkin Trans. 1* **1977**, 805–809. (c) Barton, D. H. R.; Gunatilaka, A. A. L.; Nakanishi, T.; Patin, H.; Widdowson, D. A.; Worth, B. R. *J. Chem. Soc., Perkin Trans.1* **1976**, 821–826.

10.1021/jo900304a CCC: $40.75
Published on Web 04/03/2009

SCHEME 1. Reaction of Ketenimines 1 with PTAD



group.[11] On the basis of this result and as a part of our research activity on the chemistry of ketenimines, we planned to find out if PTAD would be also reactive toward *C*,*C*,*N*-triaryl and *C*-alkyl-*C*,*N*-diaryl ketenimines to produce similar Diels−Alder reactions, but involving in such case an aryl C═C bond as part of the diene component instead of a vinyl group. However, given the diverse reactivity of ketenimines, we cannot discard either their alternative behavior as 2-azadienes, by involving its C═N bond and one conjugated C═C bond of the *N*-aryl substituent, or their participation in ene reactions (as ene components) when bearing and alkyl group at the terminal carbon atom.

In this note we disclose that the reactions of *C*,*C*,*N*-triaryl and *C*-alkyl-*C*,*N*-diaryl ketenimines with 2 equiv of PTAD afford periselectively adducts resulting from a Diels−Alder/ene sequence in which these heterocumulenes play the role of all-carbon dienes.

Our investigations started by reacting *C*,*C*-diphenyl-*N*-(4-methylphenyl)ketenimine **1a** with PTAD. When a solution of compound **1a** in dichloromethane was treated, at room temperature, with a stoichiometric amount of PTAD the reaction seemed to be very fast as the deep pink color of PTAD disappeared in a few seconds. However, the IR spectrum of a small sample aliquot of the reaction mixture still showed the strong absorption band near 2000 cm^{-1} associated with the N═C═C grouping of the starting heterocumulene. Ketenimine **1a** was totally consumed after the addition of a second equivalent of PTAD, and a crystalline solid precipitated out from the reaction medium.

The structure of the reaction product was determined to be that of the Diels−Alder/ene double adduct **3a**, showing a 1,2,4-triazolo[1,2-*a*]cinnoline heterocyclic nucleus bearing a pendant *N*-linked triazolidinone group (Scheme 1). An X-ray structure determination of a monocrystal of **3a** (see Supporting Information) was crucial for its precise structural elucidation, also showing that the exocyclic iminic C═N bond was (*Z*)-configured. It seems clear that this configuration minimizes the steric repulsion between the imine aryl and the phenyl and triazoline rings attached to the C6 carbon atom of the triazolocinnoline skeleton.

(11) Barbaro, G.; Battaglia, A.; Giorgianni, P. *J. Org. Chem.* **1987**, *52*, 3289–3296.

TABLE 1. Triazolocinnolines 3

compd	R^1	R^2	Ar	yield[a] (%)
3a	H	C_6H_5	4-CH_3−C_6H_4	71
3b	H	C_6H_5	2-[$(CH_3)_2CH$]−C_6H_4	64
3c	H	C_6H_5	3-CH_3−C_6H_4	72
3d	Cl	4-Cl−C_6H_4	3-CH_3−C_6H_4	80
3e	H	C_6H_5	2-CH_3−C_6H_4	67
3f	H	C_6H_5	4-CH_3O−C_6H_4	66
3g	H	C_6H_5	4-[$(CH_3)_2CH$]−C_6H_4	66
3h	H	C_6H_5	2,6-$(CH_3)_2$−C_6H_3	70
3i	H	C_6H_5	2-[(4-CH_3O−$C_6H_4)_2CH$]-C_6H_4	51
3j	H	CH_3CH_2	4-[$(CH_3)_2CH$]−C_6H_4	50

[a] Isolated yield.

Next we submitted ketenimines **1b**−**j** to reaction with 2 equiv of PTAD obtaining the same type of double adducts, in moderate to good isolated yields (50−80%) (Scheme 1, Table 1).

Due to the high reactivity of PTAD as dienophile and enophile, some of its reported Diels−Alder reactions have been shown to yield 1:1 diene/PTAD double adducts. These double adducts resulted from either a two sequential [4 + 2] cycloaddition processes[12] or a Diels−Alder/ene sequence[13] comparable with that leading to compounds **3**. In a few cases both types of sequential processes occur simultaneously.[14]

In the present case, the first step of the periselective conversion (**1** + PTAD) → **3** is a [4 + 2] cycloaddition reaction, where the ketenimine acts as all-carbon diene with participation of its cumulative C═C bond and leads to the formation of the monoadduct **2**. Subsequently, this intermediate undergoes an ene process with a second molecule of PTAD to give the triazolocinnoline **3** (Scheme 1).

Besides of testing the reactivity of *C*-aryl ketenimines as all-carbon dienes versus PTAD one of our aims at the start of this project was to be able of removing the O═C═N(Ph)═C═O moiety of the presumed cycloadducts in order to use the dienophile as a synthetic equivalent of molecular dinitrogen. The oxidative hydrolysis of such moiety has been claimed by Adam and De Lucchi to be a notably difficult reaction,[15] in the context of the synthesis of azoalkanes. However, Adam and co-workers eventually succeeded in this task by sequential treatment of the PTAD cycloadducts with KOH and $CuCl_2$.[16] We were pleased to find out that the simple treatment of triazolocinnolines **3** with a methanolic KOH solution at room temperature caused not only the desired hydrolysis of the urazole fragment but also the removal of the pendant triazolidinedione group with the concurrent oxidative aromatization of the cinnoline ring system. This remarkable and unprecedented one-pot reaction provided the corresponding 3-arylamino-4-substituted cinnolines **4** in excellent isolated yields (80−98%) (Scheme 2, Table 2). We assume that the exocyclic imino

(12) Lai, Y.-C.; Mallakpour, S. E.; Butler, G. B. *J. Org. Chem.* **1985**, *50*, 4378–4381.

(13) (a) Mallakpouk, S. E.; Hajipour, A.-R.; Mahdavian, A.-R.; Khoee, S. *J. Appl. Polym. Sci.* **2000**, *76*, 240–248. (b) Mallakpour, S. E.; Hajipour, A.-R.; Roohipour-Fard, R. *J. Appl. Polym. Sci.* **2001**, *79*, 1716–1725. (c) Mallakpour, S.; Hajipour, A.-R.; Vahabi, R. *J. Appl. Polym. Sci.* **2003**, *89*, 1942–1951.

(14) (a) Seguchi, K.; Tanaka, S. *J. Chem. Soc., Chem. Commun.* **1991**, 89–90. (b) Seguchi, K.; Tanaka, S. *Bull. Chem. Soc. Jpn.* **1991**, *64*, 3188–3190. (c) Tanaka, S.; Seguchi, K.; Itoh, K.; Sera, A. *J. Chem. Soc., Perkin Trans. 1* **1994**, 2335–2339. (d) Mallakpour, S. E.; Asghari, J. *Polym. Int.* **1996**, *41*, 43–52.

(15) Adam, W.; De Lucchi, O. *Angew. Chem., Int. Ed. Engl.* **1980**, *19*, 762–779.

(16) (a) Adam, W.; De Lucchi, O.; Erden, I. *Angew. Chem., Int. Ed. Engl.* **1979**, *18*, 468–469. (b) Adam, W.; De Lucchi, O.; Erden, I. *J. Am. Chem. Soc.* **1980**, *102*, 4806–4809. (c) Adam, W.; De Lucchi, O.; Peters, K.; Peters, E. M.; Von Schnering, H. G. *J. Am. Chem. Soc.* **1982**, *104*, 161–166.

SCHEME 2. Preparation of Cinnolines 4

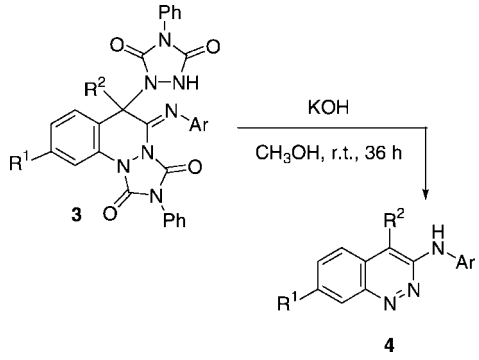


TABLE 2. 3-Aminocinnolines 4

compd	R^1	R^2	Ar	yield[a] (%)
4a	H	C_6H_5	4-CH_3−C_6H_4	91
4b	H	C_6H_5	2-[$(CH_3)_2CH$]−C_6H_4	89
4c	Cl	4-Cl−C_6H_4	3-CH_3−C_6H_4	91
4d	H	C_6H_5	2-CH_3−C_6H_4	97
4e	H	C_6H_5	4-CH_3O−C_6H_4	98
4f	H	C_6H_5	4-[$(CH_3)_2CH$]−C_6H_4	95
4g	H	C_6H_5	2,6-$(CH_3)_2$−C_6H_3	98
4h	H	C_6H_5	2-[(4-CH_3O−C_6H_4)$_2$CH]-C_6H_4	93
4i	H	CH_3CH_2	4-[$(CH_3)_2CH$]−C_6H_4	80

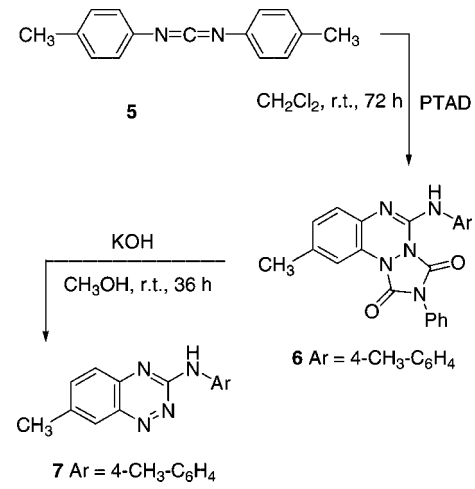
[a] Isolated yield.

function of **3** may cooperate with the external base in promoting a β-elimination process along the N═N bond of the pendant fragment, by stabilizing the negative charge originated at C-4 of the cinnoline nucleus. The PTAD resulting from such elimination would probably become hydrolyzed in the reaction medium.

The structural determination of the previously unknown 3-aminocinnolines **4** was easily accomplished following their analytical and spectral data. Cinnolines are known to show a broad spectrum of pharmacological activities,[17] the most representative drug belonging to this class of compounds is Cinoxacin.[18] As far as we know, only a limited number of 3-aminocinnolines have been reported.[19]

Following the experiments with ketenimines we carried out the treatment of *N*,*N*′-bis(4-methylphenyl)carbodiimide **5** with PTAD. In this case, the starting carbodiimide **5** behaved as a 2-azadiene, by involving one of the cumulated N═C bonds.[20] Then, only 1 equiv of the dienophile PTAD was added to **5**, providing the [1,2,4]triazolo[1,2-*a*][1,2,4]-benzotriazine **6** (93% isolated yield), a new type of fused heterocyclic system (Scheme 3). No 1:2 diaddition products were formed, although this transformation required an excess of PTAD for the total consumption of the carbodiimide **5**. By treatment of compound **6** with methanolic KOH at room temperature, it smoothly converted into the 3-arylamino-1,2,4-benzotriazine **7** (59% yield). Thus, this sequence opens a new route for the synthesis

SCHEME 3. Reaction of Carbodiimides with PTAD



of 3-arylamino-1,2,4-benzotriazines,[21] compounds structurally related with the anticancer agent tirapazamine.[22]

In summary, *C*-aryl ketenimines participate as dienes in [4 + 2] cycloaddition reactions with PTAD, which are followed by in situ ene reactions of the primary cycloadducts with a second equivalent of enophile. The Diels−Alder/ene double adducts obtained are converted into 3-aminocinnolines in an easy and efficient way. In this global sequence PTAD behaves as a synthetic equivalent of molecular nitrogen reacting as dienophile in a [4 + 2] cycloaddition with the starting ketenimines. A diarylcarbodiimide displays a similar sequence, lacking in the ene process, and leads to a 3-aminobenzotriazine.

Experimental Section

Sample Procedure for the Preparation of Triazolocinnolines 3. To a solution of the corresponding ketenimine **1** (1 mmol) in anhydrous dichloromethane (10 mL) was added solid PTAD (0.35 g, 2 mmol) at once. The reaction mixture was stirred at room temperature for 1 h. The precipitated solid was filtered and air-dried.

Triazolocinnoline 3a (R = H; Ar = 4-CH_3−C_6H_4): Yield 71%; mp 267−268 °C (colorless prisms, dichloromethane); IR (Nujol) 3250 (w), 1778 (s), 1724 (vs), 1707 (vs), 1503 (s), 1492 (s), 1406 (vs), 1235 (s), 1150 (m), 835 (m), 763 (s), 744 (m), 713 (s), 638 (s) cm^{-1}; ^1H NMR (DMSO-d_6; 300 MHz) δ 2.24 (s, 3 H), 7.09 (s, 4 H), 7.19−7.64 (m, 17 H), 7.91 (d, 1 H, J = 7.5 Hz), 8.10 (d, 1 H, J = 7.5 Hz), 9.84 (br s, 1 H); ^{13}C NMR (DMSO-d_6, 75 MHz) δ 20.7, 71.5 (s), 118.6, 121.7, 126.2, 126.3, 126.5, 127.5 (s), 128.1, 128.2, 128.5 (s), 128.8, 129.0, 129.1, 129.2, 129.8, 130.1 (s), 131.5 (s), 134.4 (s), 134.5 (s), 135.6 (s), 143.1 (s), 143.7 (s), 144.2 (s), 153.3 (s), 155.3 (s); exact mass (EI) *m*/*z* calcd for $C_{37}H_{27}N_7O_4$ $[M]^+$ 633.2124, found 633.2132.

Sample Procedure for the Preparation of 3-Aminocinnolines 4. KOH (0.56 g, 10 mmol) was dissolved in methanol (15 mL) and the corresponding triazolocinnoline **3** (1 mmol) was

(17) For reviews in the synthesis of cinnolines, see: (a) Haider, N.; Holzer, W. *Sci. Synth.* **2004**, *16*, 251–313. (b) Vinogradova, O. V.; Balova, I. A. *Chem. Heterocycl. Compd.* **2008**, *44*, 501–522. (c) For a review dealing with the bioactivity of cinnolines, see: Lewgowd, W.; Stanczak, A. *Arch. Pharm.* **2007**, *340*, 65–80.

(18) (a) Scavone, J. M.; Gleckman, R. A.; Fraser, D. G. *Pharmacotherapy* **1982**, *2*, 266–271. (b) Sisca, T. S.; Heel, R. C.; Romankiewicz, J. A. *Drugs* **1983**, *25*, 544–569.

(19) (a) Bakthavachalam, V.; D'Alarcao, M.; Leonard, N. J. *J. Org. Chem.* **1984**, *49*, 289–295. (b) Scobie, M.; Tennant, G. *J. Chem. Soc., Chem. Commun.* **1994**, 2451–2452.

(20) (a) Molina, P.; Alajarín, M.; Vidal, A. *J. Chem. Soc., Chem. Commun.* **1990**, 1277–1279. (b) Molina, P.; Alajarín, M.; Vidal, A.; Sánchez-Andrada, P. *J. Org. Chem.* **1992**, *57*, 929–939. (c) Saito, T.; Ohkubo, T.; Murayama, K.; Kuboki, H.; Motoki, S. *Chem. Lett.* **1993**, 1127–1130.

(21) For reviews concerning 1,2,4-triazines and their benzo derivatives, see: (a) Neunhoeffer, H. In *1,2,4-Triazines and their Benzo Derivatives*; Boulton, A. J., Ed.; Comprehensive Heterocyclic Chemistry II; Elsevier: Oxford, 1996; Vol. 6, pp 507−573; 1177−1307. (b) Lindsley, C. W.; Layton, M. E. *Sci. Synth.* **2004**, *17*, 357–447.

(22) (a) Rischin, D.; Peters, L.; Hicks, R.; Hughes, P.; Fisher, R.; Hart, R.; Sexton, M.; D'Costa, I.; von Roemeling, R. *J. Clin. Oncol.* **2001**, *19*, 535–542. (b) Marcu, L.; Olver, I. *Curr. Clin. Oncol.* **2006**, *1*, 71–79.

added. The reaction mixture was stirred at room temperature for 36 h. The solvent was removed to dryness under reduced pressure, and the solid residue was triturated with water. The precipitated yellow solid was filtered and dried.

3-(4-Methylphenyl)amino-4-phenylcinnoline 4a: Yield 91%; mp 200 °C (yellow prisms, diethylether); IR (Nujol) 3404 (s), 1610 (vs), 1570 (vs), 1534 (vs), 1493 (vs), 1334 (s), 1177 (m), 1121 (m), 1102 (m), 1089 (s), 1065 (w), 1015 (w), 870 (m), 837 (s), 780 (s) cm^{-1}; ^1H NMR ($CDCl_3$; 400 MHz) δ 2.31 (s, 3 H), 6.23 (s, 1 H), 7.11 (d, 2 H, $J = 7.2$ Hz), 7.33−7.35 (m, 1 H), 7.43−7.50 (m, 6 H), 7.57−7.63 (m, 3 H), 8.36 (d, 1 H, $J = 8.0$ Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 20.8, 117.9 (s), 119.6, 123.7, 126.5, 126.9 (s), 129.3, 129.4, 129.9, 130.0, 130.9, 131.7 (s), 131.8 (s), 137.9 (s), 147.5 (s), 151.5 (s); exact mass (ESI) *m*/*z* calcd for $C_{21}H_{18}N_3$ $[M + H]^+$ 312.1495, found 312.1493.

Acknowledgment. This work was supported by the Ministerio de Educación y Ciencia of Spain and FEDER (Project No. CTQ2008-05827/BQU), and Fundación Séneca-CARM (Project No. 08661/PI/08). B.B. also thanks Fundación Séneca-CARM for a fellowship.

Supporting Information Available: Experimental details for the synthesis of compounds **6** and **7**; spectral data (NMR, IR, MS) for compounds **3b**−**j**, **4b**−**i**, **6** and **7**; CIF file of **3a**. This material is available free of charge via the Internet at http://pubs.acs.org.

JO900304A