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One-Pot Synthesis of Functionalized Carbazoles via a CAN-Catalyzed Multicomponent Process Comprising a C−H Activation Step

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Supporting Information

ABSTRACT: The microwave-promoted three-component reaction between *o*-nitrochalcones, primary amines and *β*-dicarbonyl compounds in the presence of Ce(IV) ammonium nitrate constitutes the first example of a multicomponent carbazole synthesis. This reaction furnishes highly substituted and functionalized carbazole derivatives via a double annulation process that generates two C−C and two C−N bonds, with water as the only side product. Mechanistically, this transformation has some unusual features that include an intramolecular coupled hydrogenation-dehydrogenation process, the functionalization of a C−H group by direct attack onto a nitrogen function and a CAN-catalyzed reduction via hydride transfer from ethanol. The mechanisms of these reactions were studied with the aid of computational techniques.

INTRODUCTION

Carbazoles are widespread in nature and are very important in medicinal chemistry and functional materials science. Thus, carbazole is the central core of a large family of alkaloids,[1] with both natural and unnatural carbazoles exhibiting a variety of interesting biological activities including antibacterial, anti-fungal, antitumor, anti-inflammatory and neuroprotective properties.[2] In recent years, the carbazole moiety is being widely investigated as a privileged building block for the synthesis of polymers of relevance in organic electronics[3] and materials science, in general.[4] Some representative carbazole derivatives are shown in Figure 1.

Because of its importance, synthetic methodology leading to the carbazole framework has been widely investigated,[5,6] with most known methods creating the carbazole framework from two pre-existing aromatic rings (Scheme 1a). The traditional Borsche−Drechsel reaction (disconnection A) relies on the adaptation of the Fischer indole synthesis and involves an additional dehydrogenation step. A second approach involves the construction of carbazole from biphenyls bearing an *ortho* nitrogen substituent. Reductive cyclization of nitroaromatic compounds (disconnection B) is known as the Cadogan synthesis and is usually achieved by deoxygenative cyclization of the starting material at high temperature in the presence of triethyl phosphite or triphenylphosphine involving the exhaustive deoxygenation of the nitro group to a singlet nitrene, which then undergoes the N-annulation step.[7] A milder transition metal-catalyzed version of this reaction has been developed using stoichiometric CO as an alternative reducing agent, but yields are often moderate due to the formation of side products arising from over-reduction and CO insertion.[8] In another approach to the same overall transformation, carbazoles have been prepared by treating 2-nitrobiphenyls with 3 equiv of phenylmagnesium bromide.[9] The cyclization of 2-azidobiphenyls to carbazoles via insertion of transition metal

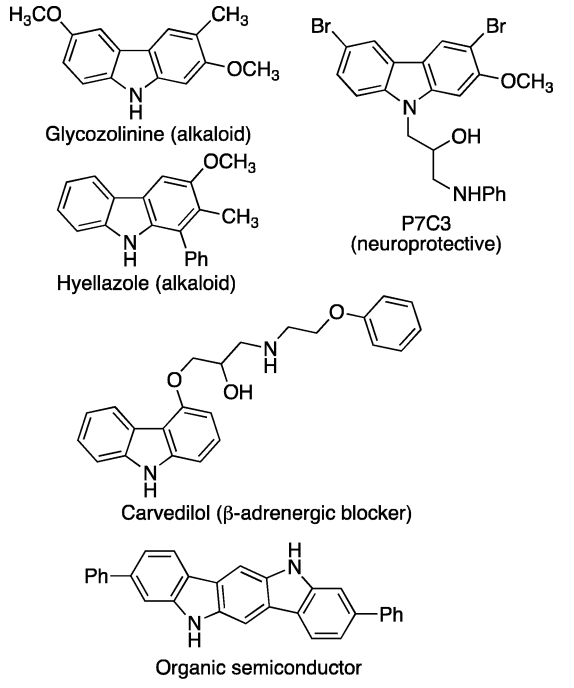

Figure 1. Some carbazoles with scientific and technical relevance.

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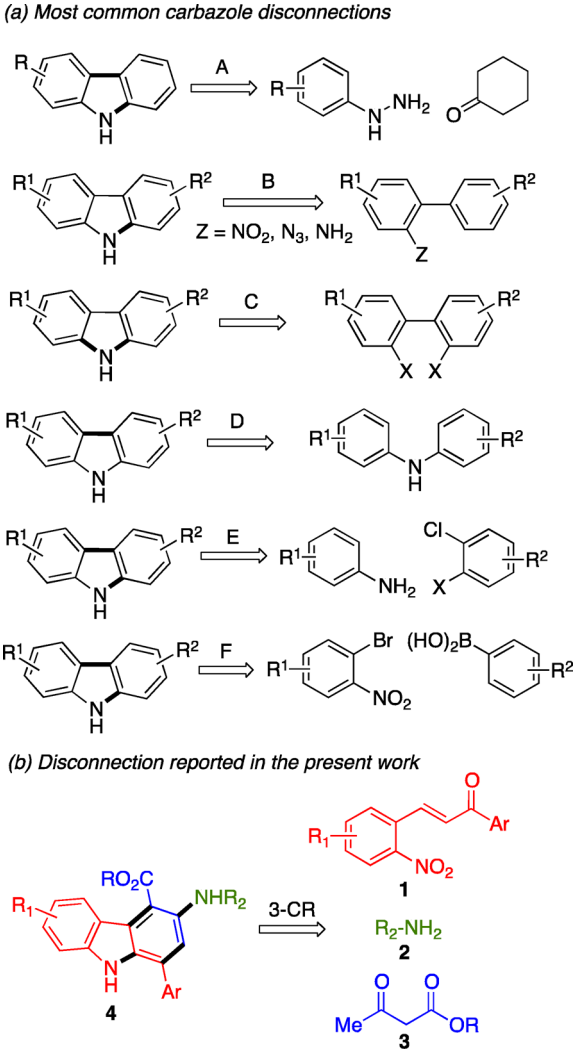
Scheme 1. Main Disconnections of the Carbazole System, Compared with the One Reported Here



nitrenoids generated at high temperatures from the azido group in the presence of different metal catalysts[10] and the Pd or Rh-catalyzed oxidative intramolecular aromatic amination reactions starting from 2-aminobiphenyls[11] or from their amides[12] provide alternative ways to create the carbazole 8a−9 bond. The oxidative cyclization of arylamine-substituted tricarbonyl-(η^4- cyclohexadiene)iron complexes[1c] corresponds also to this disconnection. Double C−N bond formation strategies are also known (disconnection C), via Pd-catalyzed double amination reactions of 2,2′-dihalo-1,1′-biaryls.[13] The dehydrogenative intramolecular cross-coupling oxidative cyclization of diarylamines (disconnection D) was originally reported using stoichiometric palladium(II),[14] although later several alternative co-oxidants have allowed recycling palladium (0), and thus the use of catalytic amounts of Pd(II).[15] A palladium-catalyzed one-pot sequence comprising an intermolecular Buchwald−Hartwig amination and an intramolecular arylation via C−H activation allows the regioselective syntheses of carbazoles from anilines and 1,2-dihaloarenes (disconnection E)[16] or anilines and aromatic triflates.[17] A similar disconnection (F) is achieved by means of one-pot Suzuki-Cadogan sequences in the presence of palladium acetate and triphenylphosphine.[18] The generation of carbazole by creation of one of its aromatic rings has also received some attention and has been achieved by cyclization of indole-tethered propargyl alcohol precursors[19] or by 6π electrocyclic ring closure of 2,3-divinylindoles[20] or (Z)-2-(enynyl)indoles.[21] On the other hand, disconnections involving the generation of two of the carbazole rings in the same operation have received very little attention,[22] in spite of their potential to create the target framework with the highest efficiency from simple starting materials.

In spite of the plethora of known methods for carbazole synthesis, there is still much room for improvement since most of them lack generality regarding the positions to which substituents can be attached, and few of the available methodologies lead to polysubstituted and functionalized carbazoles. One area that is key in terms of synthetic efficiency but has been neglected so far is the use of multicomponent reactions for the construction of the carbazole framework, in spite of the fact that they are widely accepted to constitute a step toward achieving the ideal synthesis.[23] In this context, we describe in this article a synthetic method that affords densely substituted and functionalized carbazole derivatives (compounds **4**) containing a synthetically and biologically relevant β-aminoester unit.[24] These carbazoles were obtained in a fully regioselective fashion via a three-component reaction that generates four new bonds and two rings from 2-nitrochalcones **1**, primary amines **2** and β-dicarbonyl compounds **3** (Scheme 1b). Besides being, to our knowledge, the first multicomponent synthesis of carbazole derivatives, the method includes the functionalization of a C−H group by direct attack onto a nitrogen function, a transformation that is very rare in contrast to the direct functionalization of C−H fragments in the *ortho*-position relative to the nitro group of nitroarenes.[25]

RESULTS AND DISCUSSION

In the context of our work in the synthesis of nitrogen heterocycles by multiple bond-forming reactions,[26] we became interested in the possibility to synthesize carbazole derivatives by cyclization of a suitable nitrogen function onto an adjacent aromatic CH bond. Some years back, we reported a CAN-catalyzed three-component reaction starting from alkylamines, β-ketoesters and chalcones that affords *cis*-4,6-disubstituted 2-alkylaminocyclohexene-1-carboxylic esters,[27] which we subsequently found to spontaneously dehydrate to the corresponding cyclohexadiene derivatives when the reaction is performed under microwave irradiation.[28] We envisioned the possibility to generate a carbazole ring by coupling the aromatization of the cyclohexadiene ring with the generation of the carbazole 8a−9 bond. To this end, the experiments summarized in Scheme 2 and Table 1 were performed. The starting cyclohexadiene derivative **5a** was synthesized by our previously reported MCR strategy, from (2-nitrobenzylidene)acetophenone, ethyl acetoacetate and butylamine in the presence of CAN. An experiment involving exposure of **5a** to microwave irradiation at 100 °C in ethanol as solvent and in the presence of 30% CAN was promising in that it led directly to a carbazole derivative **4a** albeit in only 7% yield, along with recovered starting material (Table 1, entry 1). An increase in temperature to 140 °C considerably improved the yield of the target compound **4a**, accompanied by **6a**, the product from the aromatization of the starting material; a 30% catalyst load was still considered necessary at this stage (entries 2−4). The presence of the catalyst was proved to be essential, since only recovered starting material was isolated in its absence (entry 5), and replacement of CAN by $InCl_3$, even in equimolecular amounts, was not

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Scheme 2. Initial Optimization of the Synthesis of Carbazoles from Cyclohexadiene Derivatives

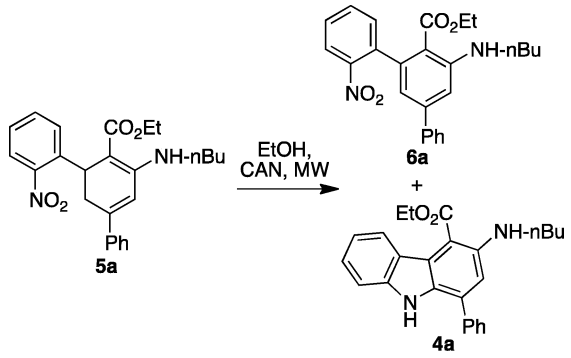


Table 1. Optimization of the Synthesis of Carbazole 4a[a]

entry	time (min)	catalyst (equiv)	T (°C)[b]	6a (%)[c]	4a (%)[c]
1	60	0.3	100	–	7
2	30	0.1	140	35	35
3	60	0.1	140	32	42
4	60	0.3	140	32	61
5	60	0	140	–	–
6	60	1[d]	140	30	42
7	90	0.1	140	13	72
8	150	0.1	140	5	85

[a]Conditions: **5a** (1 equiv) was dissolved in EtOH and the catalyst (normally CAN) was added. [b]Microwave irradiation heating to the indicated temperature. [c]Yield of isolated products. [d]The reaction was carried out in the presence of $InCl_3$.

satisfactory (entry 6). Finally, in an effort to decrease the amount of aromatized starting material, we resorted to the use of 10% of the CAN catalyst, at 140 °C, but with longer reaction times (entries 7 and 8). Indeed, carrying out the reaction for 2.5 h under these conditions provided **4a** in 85% yield, with only 5% of the aromatic product **6a** being recovered (entry 8).

The fact that both the initial multicomponent reaction leading to the cyclohexadiene derivative and the transformation of the latter into a carbazole could be performed with the same catalyst encouraged us to investigate whether the synthesis of carbazole derivatives would proceed in a one-pot process from acyclic precursors. Optimization studies revealed that heating an equimolecular mixture of nitrochalcone **1a**, ethyl acetoacetate, butylamine and catalytic CAN (10%) in a 0.2 M ethanol solution, at 100 °C for 2.5 h, followed by an increase of the temperature to 140 °C for additional 2.5 h afforded **4a** in 85% yield (entry 1, Table 2).

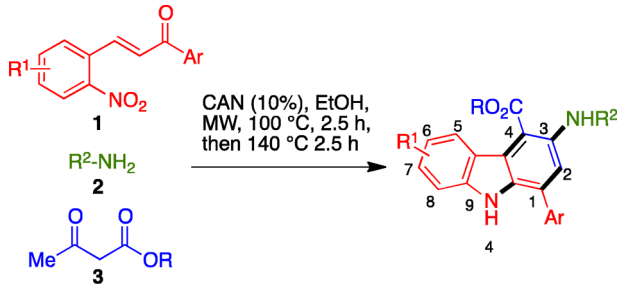
To further probe the scope of the one-pot protocol, a variety of chalcones **1**, primary amines **2** and *β*-ketoesters **3** were next subjected to the optimal conditions, with the results shown in Scheme 3 and Table 2. The reaction worked well for all kinds of substitution in the C5–C8 part of the carbazole framework, allowing the preparation of all-hydrogen derivatives (entries 1, 2, 4, 8 and 12–15), as well as compounds bearing electron-releasing substituents (entries 9–11) and electron acceptors, in particular halogens (entries 3 and 5–7). The latter are interesting for their potential to generate further structural complexity via cross-coupling reactions. The phenyl substituent at C-1 is also amenable to varied types of substitution, including all-hydrogen (entries 1, 3, 9, 13 and 15), electron-releasing groups (entries 2, 7, 8 and 11) and electron-withdrawing substituents (entries 4–6, 10, 12 and 14). Steric hindrance

Table 2. Scope and Yields of the Carbazole Synthesis

entry	R	R^1	R^2	Ar	product	yield (%)[a]
1	Et	H	Bu	Ph	**4a**	85
2	Et	H	Bu	4-MeC_6H_4	**4b**	82
3	Et	6-Cl	Bu	Ph	**4c**	78
4	Et	H	Bu	2-$NO_2C_6H_4$	**4d**	83
5	Et	6-Br	Bu	4-BrC_6H_4	**4e**	72
6	Et	6-Br	Bu	4-Br-2-$NO_2C_6H_3$	**4f**	76
7	Et	6-Br	Bu	4-MeC_6H_4	**4g**	87
8	Et	H	Bu	2-furyl	**4h**	82
9	Et	6,7-$(MeO)_2$	Bu	Ph	**4i**	81
10	Et	6,7-(OCH_2O)	Bu	2-$NO_2C_6H_4$	**4j**	78
11	Et	6,7-$(MeO)_2$	Bu	4-MeC_6H_4	**4k**	74
12	Et	H	Bu	4-ClC_6H_4	**4l**	71
13	^{t}Bu	H	Bu	Ph	**4m**	90
14	^{t}Bu	H	Bu	2-$NO_2C_6H_4$	**4n**	88
15	Et	H	Ph	Ph	**4o**	65[b]

[a]Yield of isolated products. [b]In this case, the starting mixture was heated in a microwave reactor at 100 °C, for 4 h, and then the temperature was increased to 140 °C for additional 2.5 h.

Scheme 3. One-Pot, Three Component Carbazole Synthesis



caused by ortho substituents was also well tolerated (entries 4, 6, 10 and 14). Aromatic substituents different from phenyl were also readily introduced, as shown by the preparation of a 1-(2-furyl)carbazole (entry 8). The substituent at C-3 was normally an alkylamino, but arylamino groups could also be introduced, albeit in slightly lower yields (entry 15). Some variations in the ester group at C-4 were also examined (entries 13 and 14). The presence of amino and ester functional groups at C-3 and C-4, respectively, is potentially useful for conjugation reactions in both biology- and materials-oriented synthetic projects. It is noteworthy that the reactions starting from doubly ortho-nitrated chalcones proceeded in full regioselectivity, giving only cyclizations para with respect to the alkylamino substituent (entries 4, 6, 10 and 14). This observation has mechanistic relevance, as will be discussed below.

The structure of the carbazole derivatives was derived from spectral data (see the Supporting Information for a summary of the 2D-NMR study of compound **4l**) and confirmed by single crystal X-ray diffraction of **4f** (see the corresponding ORTEP diagram in the Supporting Information).

The carbazole synthesis described above raises some points of mechanistic interest. The overall process can be viewed as the combination of the initial three-component reaction that generates a cyclohexadiene derivative with a second domino transformation involving a Lewis acid-catalyzed heterocyclization. The MCR can be assumed to take place by the mechanism summarized in Scheme 4, involving the formation of a *β*-

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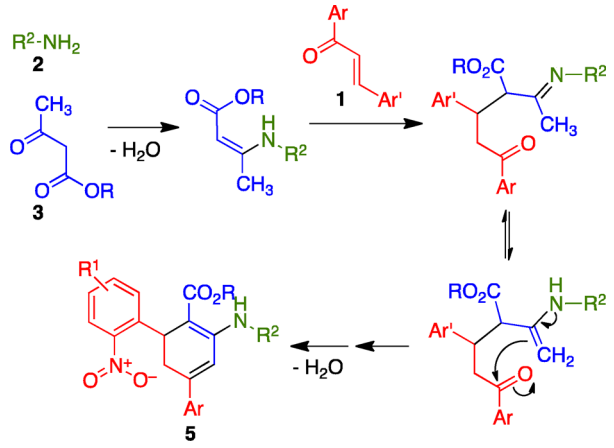
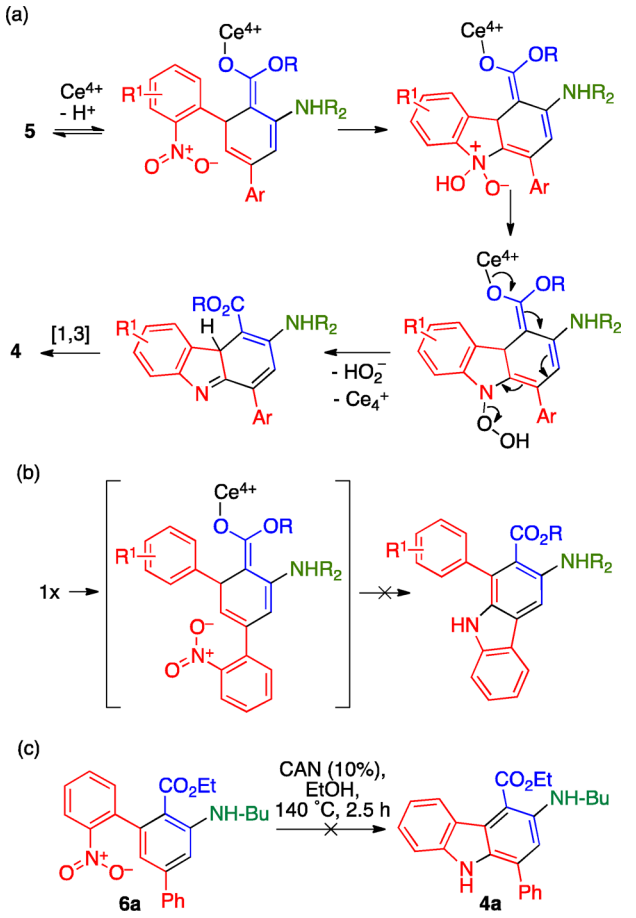
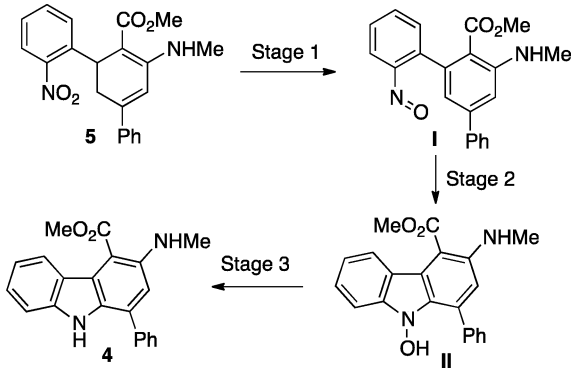
Scheme 4. Literature-Based Mechanistic Proposal for the Initial Three-Component Reaction



Scheme 5. (a) Initial Mechanistic Proposal, Based on Reference 22 and Initiated by the Enolization of the Ester Group in Intermediate 5; This Proposal Was Subsequently Discarded on the Basis of Experimental Evidence (b and c)



Scheme 6. Three Stages Proposed for the Transformation of Intermediate 5 into Carbazole 4



enaminone from the primary amine and β-dicarbonyl components followed by a Michael addition to the chalcone, imine-enamine tautomerism and a final cyclocondensation step. The intermediacy of a β-enaminone in this mechanism has been proved previously.[26]

A mechanism for the transformation of compounds **5** into the observed carbazoles **4** based on an initial enolization (Scheme 5a) may be feasible in principle, and indeed this pathway is similar to the one proposed in the closest literature precedent to our reaction, involving the synthesis of 3-hydroxycarbazoles from *o*-nitrochalcones and β-dicarbonyl compounds in the presence of Cs_2CO_3.[22] However, this mechanism can be discarded in our case because it is not compatible with the experimental observation that the reaction does not take place when the *ortho*-nitro substituent is at the aromatic ring adjacent to the chalcone carbonyl, as in the case of compound **1x** (Scheme 5b). The possibility of a cyclization of an aromatic nitro derivative was also discarded, since the chalcone **6a** failed to afford the corresponding carbazole **4a** under our reaction conditions (Scheme 5c).

The commonly accepted mechanism for the reductive cyclization of nitroaromatics involves the formation of nitrenes. However, Houk and Davies have presented computational evidence for the existence of oxygenated intermediates considering a nitroso derivative as starting point.[29] Consequently, an alternative process initiated by reduction of the nitro group to nitroso and concomitant aromatization of the cyclohexadiene ring was considered with the help of computational DFT methods (for details, see the SI). For convenience, this mechanism has been divided into three stages (Scheme 6): (i) transformation of **5** into intermediate **I**; (ii) transformation of intermediate **I** into *N*-hydroxycarbazole **II** and (iii) reductive loss of the hydroxy group, leading to the final product **4**.

Stage 1. Our hypothesis is based on the initial nitro to nitroso transformation driven by CAN, with the requirement of an accessible proton. The whole catalytic process involves a coupled hydrogenation-dehydrogenation within the same molecule. Coupled dehydrogenation/hydrogenation processes are known in the literature and include the traditional Skraup quinoline synthesis, in which nitrobenzene acts as a hydrogen acceptor with concomitant dehydrogenation of another molecule. These transformations have been performed in the presence of a number of catalysts,[30] but intramolecular examples are rare.[31] Scheme 7 illustrates the catalytic cycle proposed for stage 1, and the optimized geometries for all intermediates can be found in the Supporting Information (Figure S1). The catalytic species **III**, generated initially from CAN, coordinates the nitro group in **5** to give intermediate **IV.** Hydride transfer of H_a to the nitro group to give **V** is promoted by cerium by transferring the positive charge from the nitro nitrogen toward the amine nitrogen even though it will be delocalized by the whole conjugated system. The charge of the amine nitrogen is essentially the same throughout the process. In fact, the displaced charge is delocalized by the whole

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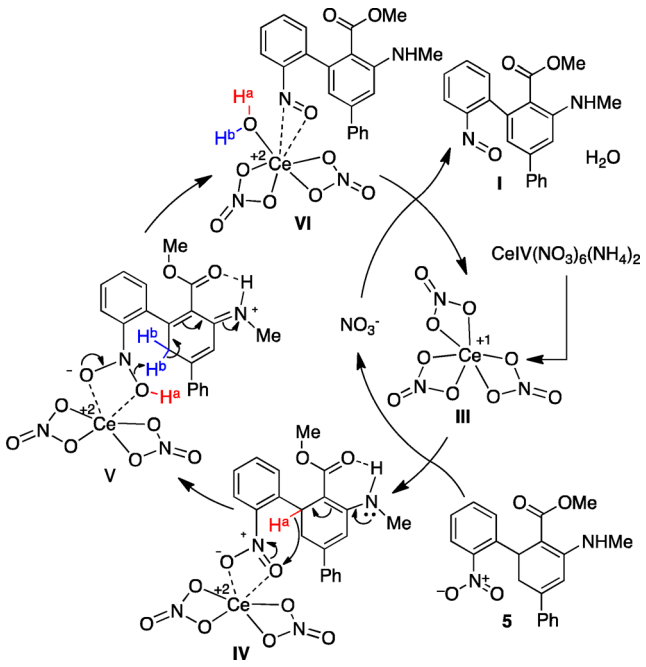
Scheme 7. Catalytic Cycle Proposed to Explain Stage 1 of Our Mechanism



conjugated system, the representation **V** in Scheme 7 being a resonant form.

The H-transfer elongates the corresponding N−O bond facilitating its cleavage in the next step. Further aromatization by loss of one H_b proton to form water gives rise to **VI** in which the nitroso group is formed. The subsequent release of nitroso intermediate **I** and water regenerates **III**, which continues the cycle. Minima **I**, **III**, **IV** and **V** have been located and the geometrical parameters are in agreement with the formation of **V** and **VI**, the nitroso group being already formed in the latter (Figure 2). After the first hydride transfer both N−O bonds are

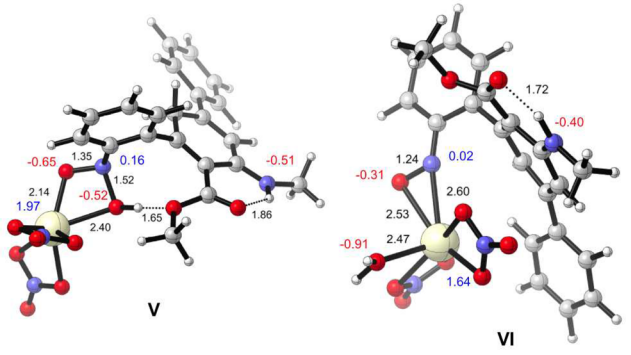
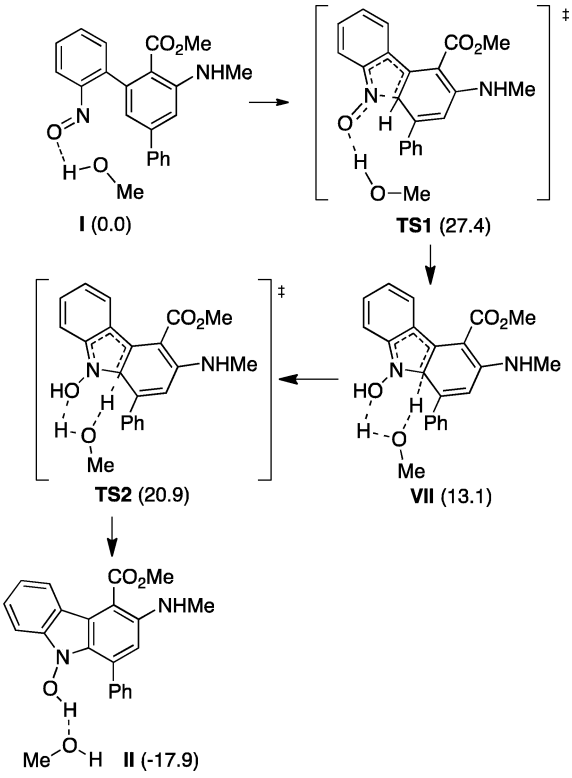


Figure 2. Geometrical parameters in angstroms (black) and selected NBO charges (red for negative and blue for positive) for intermediates **V** and **VI**.

different (1.35 Å for that coordinated to cerium and 1.52 Å for that to which hydride has been transferred). The N═O distance in **VI** is reduced to 1.24 Å, in agreement with a N═O double bond that is further away from cerium than in **V**. The thermodynamics of the transformation of **IV** into **VI** is highly favorable (ca. −90 kcal/mol) as well as the transformation of **5** into **I** + H_2O (ΔG = −11.8 kcal/mol).

Stage 2. Once the nitroso intermediate **I** is formed, the reaction proceeds following the mechanism suggested by Davies and Houk (Scheme 8).[29] We have carried out a

Scheme 8. Formation of Hydroxycarbazole II from the Nitroso Intermediate I (Relative Free-Energies Are Given in kcal/mol)



complete DFT analysis of the process and all stationary points have been located. Since it is well-known that proton transfers usually are bimolecular processes and the reaction is carried out in EtOH, we added a discrete molecule of MeOH to calculations. The first step is the formation of intermediate nitrone **VII** from **I** through transition state **TS1**. A further 1,3-H shift promoted by a molecule of solvent would afford hydroxylamine **II** through **TS2**. The rate-limiting step of the process is the formation of **VII** from **I**, with a barrier of 27.4 kcal/mol. The whole transformation from **I** to **II** is exergonic by 17.9 kcal/mol (Figures S2 and S3, Supporting Information). The geometries of **TS1** and **TS2** are given in Figure 3.

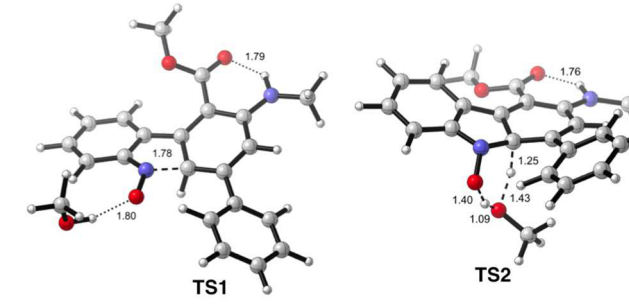


Figure 3. Transition states for the transformation of **I** into **II** (distances are in angstroms).

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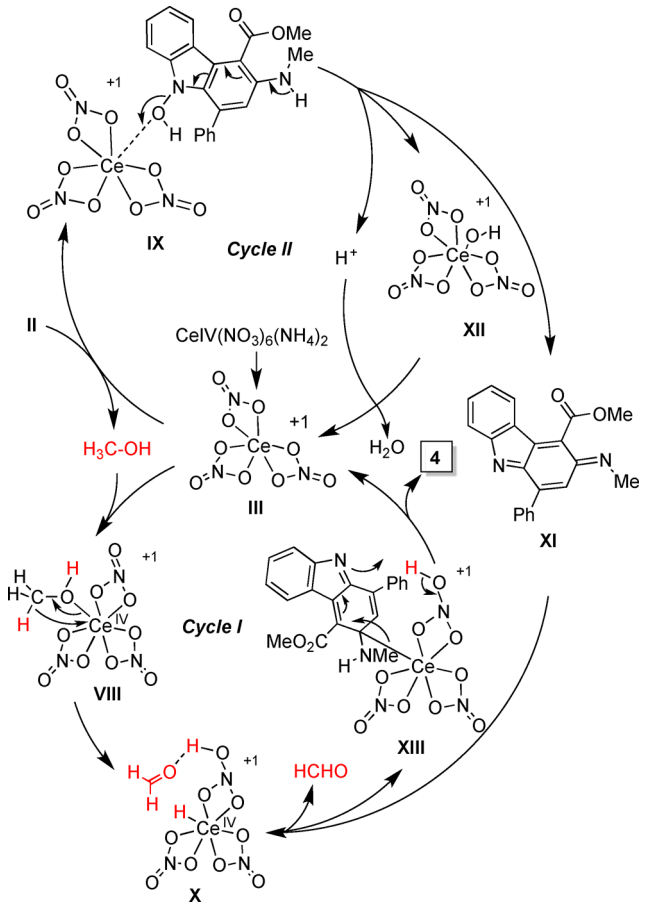
In some instances, it has been reported that 1,3-H shifts take place through two consecutive 1,2-H shifts. Although such a process is not possible for **VII**, we have studied an alternative transformation of **VII** into **II** through an initial 1,2-H shift followed by a MeOH-assisted 1,4-H shift (Figure S4, Supporting Information). However, the rate-limiting step for this route is higher (37.9 kcal/mol) than the direct 1,3-H shift shown in Scheme 8 and Figure 3.

Stage 3. The final stage consists of a deoxygenation from **II** to yield the final product **4**. This transformation is proposed to be also catalyzed by CAN via the catalytic cycle outlined in Scheme 9, formed by two internal cycles and taking place at the

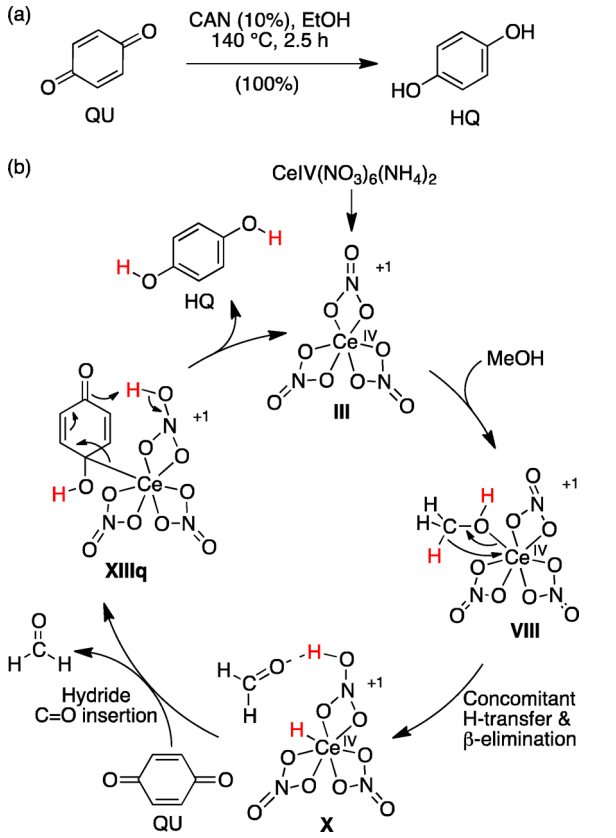
Scheme 9. Catalytic Cycles for Stage 3



expense of the oxidation of methanol into formaldehyde. First, CAN forms the catalytic species **III** which takes the MeOH molecule from **II** to form **VIII** and **IX**. **VIII** is converted into **X** were the methanol has been oxidized to acetaldehyde (cycle I). Loss of the NH proton in **IX** (cycle II) furnishes quinoid intermediate **XI** together with **XII** which, upon release of a water molecule, regenerates the catalytic species **III**. Intermediate **XI** then enters cycle I and forms **XIII** by reaction with **X**, with release of formaldehyde (the oxidized species). Proton transfer in **XIII** regenerates **III** and releases the final reduced species, the final product **4**. The global balance for this stage 3 is the transformation of **II** + MeOH into **4** + HCHO mediated by CAN, with an overall ΔG = −14.3 kcal/mol. Since both oxidized and reduced species come from the system, CAN does not act as a typical oxidizing agent but as an electron transporter,[33] and can be employed in catalytic amounts.[34]

Catalytic transfer hydrogenation from alcohols is known in the literature, and it has been performed in the presence of catalysts such as magnesium oxide, zirconium oxide, MgO−B_2O_3, Al_2O_3−$AlPO_4$ and several ruthenium species.[32] In order to obtain experimental support for the reduction of quinoid systems by primary alcohols in the presence of CAN, we exposed benzoquinone to our usual reaction conditions, and found that it was transformed into hydroquinone in quantitative yield (Scheme 10a). Thus, computational support

Scheme 10. Experimental Support for the Reduction of a Simple Quinone System under Our Reaction Conditions and Its Mechanistic Explanation



for catalytic cycles I and II given in Scheme 9 has been obtained by studying the quinone/hydroquinone model system, as illustrated in Scheme 10b. We have located all the minima and demonstrated the ability of CAN to promote electron transfer from methanol to quinone **QU** to form formaldehyde and hydroquinone **HQ**. The catalytic species in all cases is **III** which forms **VIII** leading to a concomitant H-transfer and *β*-elimination yielding **X**. A typical hydride C═O insertion releasing formaldehyde forms intermediate **XIIIq** which upon a second H-transfer regenerates the catalytic species **III** and produces hydroquinone **HQ**. The overall process was thermodynamically favorable (ΔG = −14.7 kcal/mol). The optimized geometries for the intermediates of this catalytic cycle can be found in the Supporting Information (Figure S5).

Finally, in order to underscore the synthetic applicability of the carbazole derivatives obtained by our method, we undertook a brief study of the synthesis of indolocarbazoles. This ring system represents an important class of nitrogen heterocycles, with a broad array of applications, especially in the fields of cancer chemotherapy and the chemistry of new

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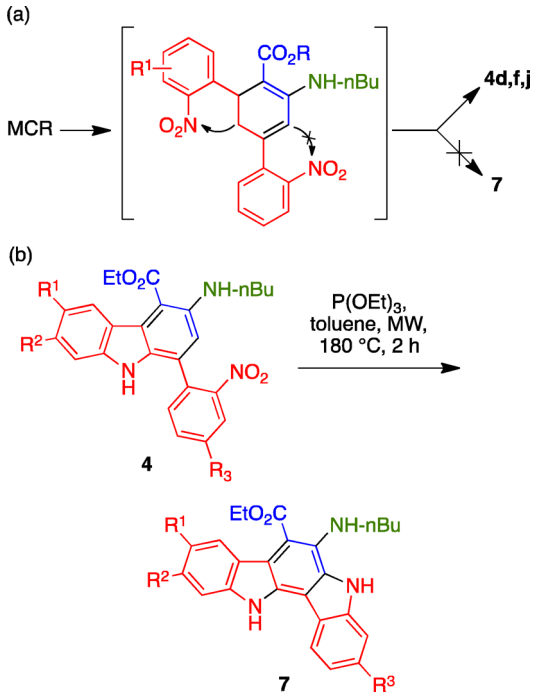
materials.[35] Among the possible indolocarbazole regioisomers, the indolo[3,2-*a*]carbazole framework has received the least attention because of the absence of efficient and selective methods for its synthesis. With these ideas in mind, we briefly examined the preparation of indolo[3,2-*a*]carbazoles based on the chemistry described in this article. While, in agreement with our initial data discussed above (Table 2), one-pot double cyclizations from chalcones bearing two *ortho* substituents were not feasible (Scheme 11a), the second carbazole unit was

Scheme 11. Synthesis of Some Indolo[3,2-*a*]carbazoles by Application of the Cadogan Reaction to Compounds 4



readily generated using a microwave-promoted Cadogan reaction in the presence of triethyl phosphite in toluene, as shown by the preparation of three representative derivatives of framework **7** from the corresponding carbazoles **4** (Scheme 11b and Table 3).

Table 3. Results Obtained in the Synthesis of Indolo[3,2-*a*]carbazoles

entry	R^1	R^2	R^3	product	yield (%)
1	H	H	H	**7a**	67
2	H	Br	Br	**7b**	58
3	−O−CH_2−O−		H	**7c**	62

CONCLUSIONS

Both target-oriented and property-oriented synthesis require tools that allow the rapid generation of molecular diversity and complexity from simple building blocks. In this context, we disclose in this article a method for the synthesis of highly substituted and functionalized carbazole derivatives via a three-component reaction between *o*-nitrochalcones, primary amines and *β*-dicarbonyl compounds. This reaction involves the generation of two rings and four new bonds (two C−C and two C−N) and proceeds in high atom economy, with water as the only side product. Mechanistically, it involves an intramolecular hydrogenation-dehydrogenation process driven by CAN, the functionalization of a C−H group by direct attack onto a nitrogen function and a CAN-catalyzed reduction via hydride transfer from ethanol. The proposed mechanism was based on experimental observations and computational studies.

EXPERIMENTAL SECTION

General Experimental Details. All reagents and solvents were of commercial quality and were used as received. Reactions were monitored by thin layer chromatography on aluminum plates coated with silica gel and fluorescent indicator. Separations by flash chromatography were performed on silica gel (40−63 mm particle size). Melting points were determined in capillary tubes using an immersion apparatus and are uncorrected. Separations by flash chromatography were performed on silica gel columns, either manually or using an automated flash chromatograph. A CEM-Discover focused microwave synthesizer with microwave power maximum level of 300 W and microwave frequency of 2455 MHz was employed for the microwave-assisted reactions, which were performed in sealed vessels controlling the reaction temperature with an internal temperature probe. Infrared spectra were recorded with a FTIR spectrophotometer working by attenuated total reflection (ATR), with a diamond accesory for solid and liquid samples. NMR spectroscopic data were recorded using a spectrometer operating at 250 MHz for ^{1}H NMR and 63 MHz for ^{13}C NMR; chemical shifts are given in ppm and coupling constants in Hertz. Elemental analyses were determined using a microanalyzer based on the flash combustion technique.

General Procedure for the Preparation of Chalcones 1. To a solution of the suitable acetophenone (30 mmol) and *o*-nitrobenzaldehyde (30 mmol) in ethanol (30 mL) was added 6 M aqueous sodium hydroxide solution. The reaction was stirred at room temperature and monitored by TLC for completion. The precipitated solid was filtered and purified by recrystallization from ethanol, affording chalcones **1**. For characterization data of these compounds, see the Supporting Information.

General Procedure for the Preparation of 5,6-Dihydroanthranilates 5. A tube containing a mixture of butylamine (1.3 equiv), ethyl acetoacetate (1 equiv), the suitable *o*-nitrochalcone **1** (1.1 equiv) and CAN (0.1 equiv) in EtOH (2 mL) was sealed and placed in a CEM Discover microwave oven. The tube was subjected to microwave irradiation, programmed at 100 °C and 200 W. After a period of 2−3 min, the temperature remained constant at 100 °C. After completion of the reaction (2.5 h), the tube was cooled to room temperature and the solvent was removed in vacuum to dryness and the residue was purified by column chromatography on silica gel, eluting with petroleum ether/EtOAc (9/1) to give compounds **5**.

Ethyl-6-butylamino-2-(4-nitrophenyl)-4-phenyl-2,3-dihydrobenzoate (5a). Prepared from (*E*)-3-(2-nitrophenyl)-1-phenyl-2-propen-1-one **1a** (0.55 g, 2.2 mmol) according to the general procedure, and obtained as a pale brown oil (665 mg, 72%). Elemental analysis (%) calcd for $C_{25}H_{28}N_2O_4$ (M = 420.50): C, 71.41; H, 6.71; N, 6.66; found: C, 71.37; H, 6.73; N, 6.62. IR (film) ν_{max} 3266, 2957, 1646 cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$) δ 9.11 (s, 1H), 8.09 (d, J = 8.8 Hz, 2H), 7.49−7.30 (m, 8H), 6.69 (d, J = 2.8 Hz, 1H), 4.37 (d, J = 7.3 Hz, 1H), 4.18−3.97 (m, 2H), 3.51−3.35 (m, 2H), 3.24 (ddd, J = 16.9, 8.6, 2.9 Hz, 1H), 2.91 (dd, J = 16.9, 1.7 Hz, 1H), 1.78−1.63 (m, 2H), 1.59−1.44 (m, 2H), 1.16 (t, J = 7.1 Hz, 3H), 1.01 (t, J = 7.2 Hz, 3H); ^{13}C NMR (63 MHz, $CDCl_3$) δ 169.9, 155.2, 154.0, 146.3, 145.9, 139.7, 128.9, 128.7, 128.0, 125.7, 123.3, 116.2, 87.8, 58.8, 42.7, 37.0, 34.6, 32.6, 20.1, 14.5, 13.8.

Ethyl-6-butylamino-2-phenyl-4-(4-nitrophenyl)-2,3-dihydrobenzoate (5b). Prepared from (*E*)-1-(2-nitrophenyl)-3-phenyl-2-propen-1-one **1m** (1000 mg, 3.95 mmol), ethyl acetoacetate (0.45 mL, 3.59 mmol) and butylamine (0.46 mL, 4.67 mmol). Yield: 1253 mg (83%), as a pale brown oil. Elemental analysis (%) calcd for $C_{25}H_{28}N_2O_4$ (M = 420.50): C, 71.41; H, 6.71; N, 6.66; found: C, 71.37; H, 6.73; N, 6.62. IR ν_{max} (film) 2957, 2925, 2868, 1675, 1586, 1524 cm^{-1}. ^{1}H NMR (250 MHz, $CDCl_3$) δ 9.05 (s, J = 5.2 Hz, 1H), 7.88 (dd, J = 7.8, 1.6 Hz, 1H), 7.54−7.35 (m, 3H), 7.34−7.30 (m, 2H), 7.27−7.18 (m,

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2H), 6.83 (dd, J = 7.4, 1.7 Hz, 1H), 6.35 (d, J = 3.0 Hz, 1H), 4.29 (dd, J = 8.2, 1.5 Hz, 1H), 4.22−3.98 (m, 2H), 3.44−3.23 (m, 3H), 2.56 (dd, J = 16.6, 1.7 Hz, 1H), 1.77−1.58 (m, 2H), 1.58−1.40 (m, 2H), 1.19 (t, J = 7.1 Hz, 3H), 1.02 (t, J = 7.2 Hz, 3H). ^{13}C NMR (63 MHz, $CDCl_3$) δ 170.4, 154.5, 148.0, 145.2, 143.7, 137.0, 132.9, 129.9, 128.6, 128.1, 127.5, 126.1, 124.1, 119.3, 89.6, 58.9, 43.0, 37.2, 36.8, 32.9, 20.2, 14.6, 14.0.

Ethyl-6-butylamino-2,4-bis(2-nitrophenyl)-2,3-dihydrobenzoate ***(5c)***. Prepared from (*E*)-1,3-bis(2-nitrophenyl)-2-propen-1-one **1d** (1000 mg, 3.35 mmol), ethyl acetoacetate (0.39 mL, 3.05 mmol) and butylamine (0.39 mL, 3.96 mmol). Yield: 880 mg (62%), as a pale brown solid. Mp: 139−140 °C. Elemental analysis (%) calcd for $C_{25}H_{27}N_3O_6$ (M = 465.50): C, 64.50; H, 5.85; N, 9.03; found: C, 64.47; H, 5.85; N, 9.06. IR ν_{max} (film) 2957, 2930, 2868, 1653, 1577, 1519 cm^{-1}. ^{1}H NMR (250 MHz, $CDCl_3$) δ 9.00 (s, 1H), 8.10 (dd, J = 8.2, 1.0 Hz, 1H), 7.84 (dd, J = 8.0, 1.3 Hz, 1H), 7.79−7.68 (m, 2H), 7.65−7.56 (m, 1H), 7.55−7.37 (m, 5H), 7.35−7.27 (m, 1H), 7.04 (dd, J = 7.6, 1.5 Hz, 1H), 6.35 (d, J = 3.0 Hz, 1H), 4.68 (dd, J = 9.9, 1.3 Hz, 1H), 4.01−3.75 (m, 2H), 3.43−3.21 (m, 3H), 2.66 (dd, J = 17.8, 1.5 Hz, 1H), 1.68−1.51 (m, 4H), 1.51−1.34 (m, 3H), 1.07−0.89 (m, 7H). ^{13}C NMR (63 MHz, $CDCl_3$) δ 169.9, 154.5, 149.4, 148.0, 144.1, 140.4, 136.5, 133.0, 132.4, 130.3, 129.9, 129.0, 127.1, 124.5, 124.0, 118.8, 88.8, 59.1, 42.9, 35.5, 32.8, 32.1, 30.4, 20.2, 14.0.

General Procedure for the Preparation of Carbazoles 4. A tube containing a mixture of the suitable primary amine (1 equiv), the suitable β-ketoester (1 equiv), the suitable nitrochalcone (1 equiv), CAN (0.1 equiv) in absolute EtOH (2 mL) was sealed and placed in the cavity of a CEM Discover microwave reactor. The tube was subjected to microwave irradiation, programmed at 100 °C and 200 W. After a period of 2−3 min, the temperature was kept constant at 100 °C for 2.5 h. Then the reaction mixture was irradiated for an additional period of 2.5 h at 140 °C. The tube was cooled to room temperature, the solvent was removed in vacuo to dryness and the residue was purified by flash column chromatography on silica gel eluting with petroleum ether/ethyl acetate (95/5), to give compounds **4**.

Ethyl 3-(butylamino)-1-phenyl-9H-carbazole-4-carboxylate ***(4a)***. Prepared from (*E*)-3-(2-nitrophenyl)-1-phenyl-2-propen-1-one **1a** (507 mg, 2.0 mmol), ethyl acetoacetate (0.25 mL, 2.0 mmol) and butylamine (0.20 mL, 2.0 mmol). Yield: 657 mg (85%), as a pale brown oil. Elemental analysis (%) calcd for $C_{25}H_{26}N_2O_2$ (M = 386.49): C, 77.69; H, 6.78; N, 7.25; found: C, 77.73; H, 6.82; N, 7.21. IR (neat) ν_{max} 3379, 1674, 1524, 1236 cm^{-1}. ^{1}H NMR (250 MHz, $CDCl_3$) δ 8.25 (d, J = 8.2 Hz, 1H), 8.08 (s, 1H), 7.68 (dd, J = 8.2, 1.4 Hz, 2H), 7.61−7.53 (m, 2H), 7.52−7.47 (m, 1H), 7.38−7.32 (m, 2H), 7.19−7.09 (m, 1H), 6.90 (s, 1H), 4.60 (q, J = 7.2 Hz, 2H), 3.27 (t, J = 7.0 Hz, 2H), 1.71 (q, J = 7.4, 7.0 Hz, 2H), 1.61−1.54 (m, 2H), 1.49 (t, J = 7.2 Hz, 3H), 0.98 (t, J = 7.3 Hz, 3H). ^{13}C NMR (63 MHz, $CDCl_3$) δ 169.5, 140.6, 138.7, 130.9, 129.6, 129.4, 128.6, 128.4, 126.0, 124.7, 122.8, 122.2, 118.7, 111.9, 110.9, 60.9, 44.4, 31.8, 20.6, 14.5, 14.1.

Ethyl 3-(butylamino)-1-(p-tolyl)-9H-carbazole-4-carboxylate ***(4b)***. Prepared from (*E*)-3-(2-nitrophenyl)-1-(*p*-tolyl)-2-propen-1-one **1b** (535 mg, 2.0 mmol), ethyl acetoacetate (0.25 mL, 2.0 mmol) and butylamine (0.20 mL, 2.0 mmol). Yield: 657 mg (82%), as a pale yellow oil. Elemental analysis (%) calcd for $C_{26}H_{28}N_2O_2$ (M = 400.51): C, 77.97; H, 7.05; N, 6.99; found: C, 77.92; H, 7.08; N, 7.02. IR (neat) ν_{max} 3385, 2958, 1667, 1524, 1237 cm^{-1}. ^{1}H NMR (250 MHz, $CDCl_3$) δ 8.26 (d, J = 7.7 Hz, 1H), 8.11 (s, 1H), 7.57 (d, J = 8.1 Hz, 2H), 7.42−7.32 (m, 5H), 7.19−7.08 (m, 1H), 6.92 (s, 1H), 4.60 (q, J = 7.2 Hz, 2H), 3.27 (t, J = 7.0 Hz, 2H), 2.47 (s, 3H), 1.81−1.62 (m, 2H), 1.64−1.53 (m, 2H), 1.49 (t, J = 7.2 Hz, 3H), 0.98 (t, J = 7.3 Hz, 3H). ^{13}C NMR (63 MHz, $CDCl_3$) δ 169.5, 140.6, 138.3, 135.7, 131.0, 130.2, 130.1, 128.4, 125.9, 124.7, 122.8, 122.1, 118.7, 110.9, 60.9, 31.7, 21.5, 20.5, 14.5, 14.1.

Ethyl 3-(butylamino)-6-chloro-1-phenyl-9H-carbazole-4-carboxylate ***(4c)***. Prepared from (*E*)-3-(5-chloro-2-nitrophenyl)-1-phenyl-2-propen-1-one **1c** (575 mg, 2.0 mmol), ethyl acetoacetate (0.25 mL, 2.0 mmol) and butylamine (0.20 mL, 2.0 mmol). Yield: 657 mg (78%), as a brown oil. Elemental analysis (%) calcd for $C_{25}H_{25}ClN_2O_2$ (M = 420.93): C, 71.33; H, 5.99; N, 6.66; found: C, 71.32; H, 6.03; N, 6.62. IR (neat) ν_{max} 3372, 2957, 1668, 1236 cm^{-1}. ^{1}H NMR (250 MHz, $CDCl_3$) δ 8.31 (d, J = 1.9 Hz, 1H), 8.12 (s, 1H), 7.69−7.62 (m, 2H), 7.61−7.55 (m, 2H), 7.54−7.47 (m, 1H), 7.30 (d, J = 1.9 Hz, 1H), 7.26 (d, J = 8.7 Hz, 1H), 6.94 (s, 1H), 4.61 (q, J = 7.2 Hz, 2H), 3.27 (t, J = 7.0 Hz, 2H), 1.80−1.66 (m, 2H), 1.54 (t, J = 7.2 Hz, 3H), 1.52−1.39 (m, 2H), 0.98 (t, J = 7.3 Hz, 3H). ^{13}C NMR (63 MHz, $CDCl_3$) δ 169.1, 138.7, 138.3, 131.4, 129.5, 128.6, 128.5, 126.0, 124.7, 124.0, 123.9, 121.3, 111.8, 61.2, 44.5, 31.6, 20.5, 14.4, 14.1.

Ethyl 3-(butylamino)-1-(2-nitrophenyl)-9H-carbazole-4-carboxylate ***(4d)***. Prepared from (*E*)-1,3-bis(2-nitrophenyl)-2-propen-1-one **1d** (597 mg, 2.0 mmol), ethyl acetoacetate (0.25 mL, 2.0 mmol) and butylamine (0.20 mL, 2.0 mmol). Yield: 716 mg (83%), as a red oil. Elemental analysis (%) calcd for $C_{25}H_{25}N_3O_4$ (M = 431.48): C, 69.59; H, 5.84; N, 9.74; found: C, 69.63; H, 5.86; N, 9.77. IR (neat) ν_{max} 3377, 2959, 1668, 1526 1236 cm^{-1}. ^{1}H NMR (250 MHz, $CDCl_3$) δ 8.25 (d, J = 8.3 Hz, 1H), 8.03 (d, J = 8.1 Hz, 1H), 7.78−7.67 (m, 2H), 7.65−7.54 (m, 2H), 7.36 (ddd, J = 7.8, 6.6, 1.1 Hz, 1H), 7.32−7.27 (m, 1H), 7.15 (ddd, J = 8.2, 6.6, 1.6 Hz, 1H), 6.72 (s, 1H), 4.60 (q, J = 7.2 Hz, 2H), 3.17 (t, J = 7.0 Hz, 2H), 1.75−1.61 (m, 2H), 1.50 (t, J = 7.2 Hz, 3H), 1.48−1.36 (m, 2H), 0.97 (t, J = 7.3 Hz, 3H). ^{13}C NMR (63 MHz, $CDCl_3$) δ 169.3, 149.7, 140.8, 133.1, 132.6, 132.3, 130.5, 129.5, 126.3, 126.1, 124.8, 124.7, 122.8, 122.6, 119.0, 111.5, 111.1, 61.0, 44.3, 31.6, 20.5, 14.5, 14.1.

Ethyl 6-bromo-1-(4-bromophenyl)-3-(butylamino)-9H-carbazole-4-carboxylate ***(4e)***. Prepared from (*E*)-3-(5-bromo-2-nitrophenyl)-1-(4-bromophenyl)-2-propen-1-one **1e** (822 mg, 2.0 mmol), ethyl acetoacetate (0.25 mL, 2.0 mmol) and butylamine (0.20 mL, 2.0 mmol). Yield: 784 mg (72%), as a brown oil. Elemental analysis (%) calcd for $C_{25}H_{24}Br_2N_2O_2$ (M = 544.28): C, 55.17; H, 4.44; N, 5.15; found: C, 55.23; H, 4.47; N, 5.21. IR (neat) ν_{max} 3439, 3377, 2930, 1668, 1525, 1236 cm^{-1}. ^{1}H NMR (250 MHz, $CDCl_3$) δ 8.46 (d, J = 1.9 Hz, 1H), 8.01 (s, 1H), 7.68 (d, J = 8.4 Hz, 2H), 7.50 (d, J = 8.4 Hz, 2H), 7.42 (dd, J = 8.6, 1.9 Hz, 1H), 7.20 (d, J = 8.6 Hz, 1H), 7.00 (s, 1H), 6.84 (s, 1H), 4.59 (q, J = 7.2 Hz, 2H), 3.24 (t, J = 6.9 Hz, 2H), 1.83−1.63 (m, 2H), 1.55 (t, J = 7.2 Hz, 3H), 1.56−1.33 (m, 2H), 0.98 (t, J = 7.3 Hz, 3H). ^{13}C NMR (63 MHz, $CDCl_3$) δ 169.1, 146.5, 139.1, 137.2, 132.6, 130.3, 130.1, 130.1, 128.6, 127.7, 124.5, 122.7, 121.5, 112.3, 111.6, 104.4, 61.2, 44.1, 31.7, 20.5, 14.3, 14.1.

Ethyl 6-bromo-1-(4-bromo-2-nitrophenyl)-3-(butylamino)-9H-carbazole-4-carboxylate ***(4f)***. Prepared from (*E*)-1-(4-bromo-2-nitrophenyl)-3-(5-bromo-2-nitrophenyl)-2-propen-1-one **1f** (912 mg, 2.0 mmol), ethyl acetoacetate (0.25 mL, 2.0 mmol) and butylamine (0.20 mL, 2.0 mmol). Yield: 448 mg (76%), as a dark brown oil. Elemental analysis (%) calcd for $C_{25}H_{23}Br_2N_3O_4$ (M = 589.28): C, 50.96; H, 3.93; N, 7.13; found: C, 50.91; H, 3.89; N, 7.16. IR (neat) ν_{max} 3348, 2931, 1673, 1526, 1234 cm^{-1}. ^{1}H NMR (250 MHz, $CDCl_3$) δ 8.46 (d, J = 1.9 Hz, 1H), 7.95 (d, J = 8.5 Hz, 1H), 7.78 (d, J = 2.1 Hz, 1H), 7.76−7.70 (m, 2H), 7.43 (dd, J = 8.6, 1.9 Hz, 1H), 7.19 (d, J = 8.7 Hz, 1H), 6.70 (s, 1H), 4.60 (q, J = 7.2 Hz, 2H), 3.17 (t, J = 7.0 Hz, 2H), 1.75−1.61 (m, 2H), 1.55 (t, J = 7.2 Hz, 3H), 1.52−1.37 (m, 2H), 0.97 (t, J = 7.3 Hz, 3H). ^{13}C NMR (63 MHz, $CDCl_3$) δ 168.9, 148.2, 139.3, 135.2, 134.3, 132.8, 129.0, 127.8, 126.3, 124.4, 121.8, 112.4, 111.9, 61.3, 44.2, 31.6, 29.8, 20.5, 14.3, 14.1.

Ethyl 6-bromo-3-(butylamino)-1-(p-tolyl)-9H-carbazole-4-carboxylate ***(4g)***. Prepared from (*E*)-3-(5-bromo-2-nitrophenyl)-1-(*p*-tolyl)-2-propen-1-one **1g** (692 mg, 2.0 mmol), ethyl acetoacetate (0.25 mL, 2.0 mmol) and butylamine (0.20 mL, 2.0 mmol). Yield: 834 mg (87%), as an orange oil. Elemental analysis (%) calcd for $C_{26}H_{27}BrN_2O_2$ (M = 479.41): C, 65.14; H, 5.68; N, 5.84; found: C, 65.26; H, 5.61; N, 5.87. IR (neat) ν_{max} 3383, 2927, 1668, 1525, 1463, 1236 cm^{-1}. ^{1}H NMR (250 MHz, $CDCl_3$) δ 8.48 (d, J = 1.9 Hz, 1H), 8.10 (s, 1H), 7.54 (d, J = 8.1 Hz, 2H), 7.42 (dd, J = 8.6, 2.0 Hz, 1H), 7.37 (d, J = 7.8 Hz, 2H), 7.21 (d, J = 8.6 Hz, 1H), 6.89 (s, 1H), 4.59 (q, J = 7.2 Hz, 2H), 3.26 (t, J = 7.0 Hz, 2H), 2.47 (s, 3H), 1.79−1.64 (m, 2H), 1.55 (t, J = 7.2 Hz, 3H), 1.53−1.39 (m, 2H), 0.98 (t, J = 7.3 Hz, 3H). ^{13}C NMR (63 MHz, $CDCl_3$) δ 169.2, 146.7, 139.0, 138.5, 135.4, 131.5, 130.7, 130.2, 128.4, 127.7, 124.6, 121.1, 112.5, 112.2, 111.4, 61.1, 44.2, 31.8, 29.8, 21.5, 20.5, 14.4, 14.1.

Ethyl 3-(butylamino)-1-(furan-2-yl)-9H-carbazole-4-carboxylate ***(4h)***. Prepared from (*E*)-1-(furan-2-yl)-3-(2-nitrophenyl)-2-propen-1-

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one **1h** (486 mg, 2.0 mmol), ethyl acetoacetate (0.25 mL, 2.0 mmol) and butylamine (0.20 mL, 2.0 mmol). Yield: 617 mg (82%), as a red oil. Elemental analysis (%) calcd for $C_{23}H_{24}N_2O_3$ (M = 376.45): C, 73.38; H, 6.43; N, 7.44; found: C, 73.41; H, 6.47; N, 7.46. IR (neat) ν_{max} 3380, 2926, 1713, 1682, 1524 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ 9.15 (s, 1H), 8.25 (d, J = 8.2 Hz, 1H), 7.73 (s, 1H), 7.49 (d, J = 8.0 Hz, 1H), 7.46−7.40 (m, 1H), 7.21−7.12 (m, 2H), 6.94 (d, J = 3.4 Hz, 1H), 6.65 (dd, J = 3.4, 1.8 Hz, 1H), 4.61 (q, J = 7.2 Hz, 2H), 3.31 (t, J = 7.0 Hz, 2H), 1.80−1.72 (m, 2H), 1.57−1.53 (m, 2H), 1.51 (t, J = 7.2 Hz, 3H), 1.03 (t, J = 7.4 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 169.3, 142.7, 141.9, 140.8, 137.9, 127.7, 126.3, 124.6, 123.4, 122.1, 118.7, 118.7, 117.3, 114.8, 112.1, 111.0, 107.6, 61.0, 31.7, 29.9, 20.6, 14.5, 14.1.

Ethyl 3-(butylamino)-6,7-dimethoxy-1-phenyl-9H-carbazole-4-carboxylate ***(4i)***. Prepared from (*E*)-3-(4,5-dimethoxy-2-nitrophenyl)-1-phenyl-2-propen-1-one **1i** (627 mg, 2.0 mmol), ethyl acetoacetate (0.25 mL, 2.0 mmol) and butylamine (0.20 mL, 2.0 mmol). Yield: 723 mg (81%), as a brown oil. Elemental analysis (%) calcd for $C_{27}H_{30}N_2O_4$ (M = 446.54): C, 72.62; H, 6.77; N, 6.27; found: C, 72.65; H, 6.74; N, 6.29. IR (neat) ν_{max} 3364, 2853, 1673 cm^{-1}. ^1H RMN (250 MHz, $CDCl_3$) δ 8.03 (s, 1H), 7.80 (s, 1H), 7.70 (dd, J = 8.2, 1.4 Hz, 2H), 7.62−7.52 (m, 2H), 7.52−7.44 (m, 1H), 6.85 (s, 1H), 6.83 (s, 1H), 4.64 (q, J = 7.1 Hz, 2H), 4.00 (s, 3H), 3.94 (s, J = 2.0 Hz, 3H), 3.29 (t, J = 7.0 Hz, 2H), 1.75 (dt, J = 14.4, 7.0 Hz, 2H), 1.64−1.40 (m, 5H), 1.01 (t, J = 7.3 Hz, 3H). ^{13}C NMR (63 MHz, $CDCl_3$) δ 169.4, 149.8, 145.9, 143.4, 138.8, 136.2, 130.8, 130.4, 129.3, 128.6, 128.5, 122.7, 115.1, 110.2, 107.2, 104.2, 93.6, 60.7, 56.6, 56.0, 44.4, 31.8, 20.5, 14.7, 14.1.

Ethyl 8-(butylamino)-6-(2-nitrophenyl)-5H-[1,3]dioxolo[4,5-b]-carbazole-9-carboxylate ***(4j)***. Prepared from (*E*)-3-(6-nitrobenzo[*d*]-[1,3]dioxol-5-yl)-1-(2-nitrophenyl)-2-propen-1-one **1j** (685 mg, 2.0 mmol), ethyl acetoacetate (0.25 mL, 2.0 mmol) and butylamine (0.20 mL, 2.0 mmol). Yield: 742 mg (78%), as a brown oil. Elemental analysis (%) calcd for $C_{26}H_{25}N_3O_6$ (M = 475.49): C, 65.67; H, 5.30; N, 8.84; found: C, 65.64; H, 5.33; N, 8.85. IR (neat) ν_{max} 3376, 2925, 1673 cm^{-1}. ^1H RMN (250 MHz, $CDCl_3$) δ 8.08−7.99 (m, 1H), 7.78−7.56 (m, 5H), 6.68 (d, J = 32.0 Hz, 2H), 6.00 (s, 2H), 4.60 (q, J = 7.1 Hz, 2H), 3.23−3.14 (m, J = 7.0 Hz, 2H), 1.77−1.62 (m, 2H), 1.52 (t, J = 7.2 Hz, 3H), 1.48−1.38 (m, 2H), 0.99 (t, J = 7.3 Hz, 3H). ^{13}C NMR (63 MHz, $CDCl_3$) δ 169.2, 149.7, 147.6, 145.6, 142.2, 136.9, 133.0, 132.6, 132.3, 130.5, 129.4, 126.0, 124.7, 122.9, 116.0, 109.8, 104.9, 103.5, 101.2, 91.7, 60.9, 44.2, 31.7, 20.5, 14.5, 14.1

Ethyl 3-(butylamino)-6,7-dimethoxy-1-(p-tolyl)-9H-carbazole-4-carboxylate ***(4k)***. Prepared from (*E*)-3-(4,5-dimethoxy-2-nitrophenyl)-1-(*p*-tolyl)-2-propen-1-one **1k** (655 mg, 2.0 mmol), ethyl acetoacetate (0.25 mL, 2.0 mmol) and butylamine (0.20 mL, 2.0 mmol). Yield: 682 mg (74%), as a brown oil. Elemental analysis (%) calcd for $C_{28}H_{32}N_2O_4$ (M = 460.56): C, 73.02; H, 7.00; N, 6.08; found: C, 73.07; H, 7.04; N, 6.05. IR (neat) ν_{max} 3363, 2925, 1673 cm^{-1}. ^1H RMN (250 MHz, $CDCl_3$) δ 8.06 (s, 1H), 7.79 (s, 1H), 7.58 (d, J = 8.1 Hz, 2H), 7.38 (d, J = 7.8 Hz, 2H), 6.89 (d, J = 7.9 Hz, 1H), 6.86 (s, 1H), 4.64 (q, J = 7.1 Hz, 2H), 4.00 (s, 3H), 3.95 (s, 3H), 3.30 (t, J = 7.0 Hz, 2H), 2.48 (s, 3H), 1.84−1.68 (m, 2H), 1.60−1.39 (m, 5H), 1.00 (t, J = 7.3 Hz, 3H). ^{13}C NMR (63 MHz, $CDCl_3$) δ 169.3, 149.9, 143.5, 138.3, 136.2, 130.9, 130.0, 128.4, 122.6, 115.1, 107.2, 93.6, 60.9, 56.7, 56.1, 45.2, 31.5, 21.4, 20.5, 14.7, 14.0.

Ethyl 3-(butylamino)-1-(4-chlorophenyl)-9H-carbazole-4-carboxylate ***(4l)***. Prepared from (*E*)-3-(2-nitrophenyl)-1-(4-chlorophenyl)-2-propen-1-one **1l** (575 mg, 2.0 mmol), ethyl acetoacetate (0.25 mL, 2.0 mmol) and butylamine (0.20 mL, 2.0 mmol). Yield: 598 mg (71%), as a yellow solid. Mp: 108−109 °C. Elemental analysis (%) calcd for $C_{25}H_{25}ClN_2O_2$ (M = 420.93): C, 71.33; H, 5.99; N, 6.66; found: C, 71.32; H, 5.97; N, 6.64. IR (neat) ν_{max} 2955, 2918, 2850, 1677, 1600 cm^{-1}. ^1H RMN (250 MHz, $CDCl_3$) δ 8.31−8.24 (m, 1H), 8.05 (bs, 1H), 7.67−7.60 (m, 2H), 7.59−7.52 (m, 2H), 7.42−7.36 (m, 2H), 7.23−7.13 (m, 1H), 6.87 (s, 1H), 4.63 (q, J = 7.2 Hz, 2H), 3.28 (t, J = 7.0 Hz, 2H), 1.83−1.68 (m, 2H), 1.61−1.46 (m, 5H), 1.02 (t, J = 7.3 Hz, 3H). ^{13}C NMR (63 MHz, $CDCl_3$) δ 169.4, 145.8, 140.7, 137.1, 134.3, 130.1, 129.9, 129.6, 129.5, 126.1, 124.7, 122.7, 122.4, 118.8, 111.6, 110.9, 105.3, 61.0, 44.2, 31.7, 20.5, 14.5, 14.1.

tert-Butyl 3-(butylamino)-1-phenyl-9H-carbazole-4-carboxylate ***(4m)***. Prepared from (*E*)-3-(2-nitrophenyl)-1-phenyl-2-propen-1-one **1m** (507 mg, 2.0 mmol), *tert*-butyl acetoacetate (0.33 mL, 2.0 mmol) and butylamine (0.20 mL, 2.0 mmol). Yield: 746 mg (90%), as a brown oil. Elemental analysis (%) calcd for $C_{27}H_{30}N_2O_2$ (M = 414.54): C, 78.23; H, 7.29; N, 6.76; found: C, 78.27; H, 7.34; N, 6.73. IR ν_{max} (film) 3382, 2852, 1674 cm^{-1}. ^1H RMN (250 MHz, $CDCl_3$) δ 8.42 (d, J = 8.1 Hz, 1H), 8.14 (s, 1H), 7.72 (d, J = 6.8 Hz, 2H), 7.60 (t, J = 7.3 Hz, 2H), 7.52 (d, J = 7.3 Hz, 1H), 7.44−7.34 (m, 2H), 7.20 (ddd, J = 8.2, 6.0, 2.2 Hz, 1H), 6.97 (s, 1H), 3.31 (t, J = 6.9 Hz, 2H), 1.81 (s, 9H), 1.79−1.65 (m, 2H), 1.63−1.43 (m, 2H), 1.03 (t, J = 7.3 Hz, 3H). ^{13}C NMR (63 MHz, $CDCl_3$) δ 168.6, 144.0, 140.6, 138.8, 130.7, 129.7, 129.4, 128.6, 128.2, 126.0, 124.7, 122.7, 122.0, 118.5, 112.3, 110.8, 108.5, 82.2, 44.8, 31.8, 28.7, 20.5, 14.1.

tert-Butyl 3-(butylamino)-1-(2-nitrophenyl)-9H-carbazole-4-carboxylate ***(4n)***. Prepared from (*E*)-1,3-bis(2-nitrophenyl)-2-propen-1-one **1d** (597 mg, 2.0 mmol), *tert*-butyl acetoacetate (0.33 mL, 2.0 mmol) and butylamine (0.20 mL, 2.0 mmol). Yield: 809 mg (88%), as a brown oil. Elemental analysis (%) calcd for $C_{27}H_{29}N_3O_4$ (M = 459.54): C, 70.57; H, 6.36; N, 9.14; found: C, 70.54; H, 6.32; N, 9.18. IR ν_{max} (film) 3374, 2854, 1707 cm^{-1}. ^1H RMN (250 MHz, $CDCl_3$) δ 8.38 (d, J = 8.1 Hz, 1H), 8.06 (dd, J = 7.9, 1.1 Hz, 1H), 7.80−7.71 (m, 2H), 7.69−7.58 (m, 2H), 7.43−7.30 (m, 2H), 7.23−7.13 (m, 1H), 6.84 (bs, 1H), 3.20 (t, J = 7.0 Hz, 2H), 1.78 (s, 9H), 1.76−1.65 (m, 3H), 1.59−1.41 (m, 3H), 0.99 (t, J = 7.3 Hz, 3H). ^{13}C NMR (63 MHz, $CDCl_3$) δ 168.4, 167.0, 149.8, 140.8, 133.3, 132.7, 132.4, 130.9, 129.4, 126.3, 124.8, 124.7, 124.7, 122.7, 122.4, 118.9, 111.8, 110.9, 82.4, 44.7, 31.7, 28.7, 20.5, 14.1.

Ethyl 1-phenyl-3-(phenylamino)-9H-carbazol-4-carboxylate ***(4o)***. Prepared from (*E*)-3-(2-nitrophenyl)-1-phenyl-2-propen-1-one **1a** (507 mg, 2.0 mmol), ethyl acetoacetate (0.25 mL, 2.0 mmol) and aniline (0.18 mL, 2.0 mmol). Yield: 529 mg (65%), as a pale brown oil. Elemental analysis (%) calcd for $C_{27}H_{22}N_2O_2$ (M = 406.48): C, 79.78; H, 5.46; N, 6.89; found: C, 79.82; H, 5.48; N, 6.91. IR ν_{max} (film) 3385, 2925, 1711 cm^{-1}. ^1H RMN (250 MHz, $CDCl_3$) δ 8.28 (s, 1H), 8.17 (d, J = 8.1 Hz, 1H), 7.82 (s, 1H), 7.67−7.61 (m, 2H), 7.59−7.50 (m, 4H), 7.44−7.37 (m, 4H), 7.23 (s, 1H), 7.17−7.11 (m, 3H), 6.91 (t, J = 7.2 Hz, 1H), 4.60 (q, J = 7.2 Hz, 2H), 1.48 (t, J = 7.2 Hz, 3H). ^{13}C NMR (63 MHz, $CDCl_3$) δ 168.2, 143.4, 139.8, 137.4, 136.9, 132.2, 128.9, 128.8, 128.6, 127.9, 127.8, 127.7, 125.7, 123.1, 121.7, 120.2, 118.7, 117.6, 117.4, 110.4, 60.9, 13.7.

Ethyl-6-butylamino-2-(2-nitrophenyl)-4-phenyl benzoate ***(6)***. Isolated during the optimization studies leading to **4a** as a pale brown oil. Elemental analysis (%) calcd for $C_{25}H_{26}N_2O_4$ (M = 418.48): C, 71.75; H, 6.26; N, 6.69; found: C, 71.79; H, 6.24; N, 6.65. IR ν_{max} (film) 2925, 2854, 1656, 1595, 1522 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$) δ 8.06 (dd, J = 8.1, 1.2 Hz, 1H), 7.76−7.55 (m, 3H), 7.54−7.31 (m, 6H), 6.94 (d, J = 1.6 Hz, 1H), 6.60 (d, J = 1.7 Hz, 1H), 3.91 (q, J = 7.2 Hz, 2H), 3.31 (q, J = 6.8 Hz, 2H), 1.84−1.67 (m, 2H), 1.66−1.35 (m, 2H), 1.02 (t, J = 7.3 Hz, 3H), 0.72 (t, J = 7.2 Hz, 3H). ^{13}C NMR (63 MHz, $CDCl_3$) δ 168.1, 151.1, 147.4, 144.9, 141.3, 140.0, 139.7, 131.8, 130.7, 128.3, 127.8, 126.9, 123.4, 115.6, 109.1, 108.0, 59.6, 42.7, 30.9, 20.1, 13.6, 12.8.

General Procedure for the Microwave-Assisted Cadogan Reaction for the Synthesis of Indolocarbazoles 7a−7c. A microwave tube containing a solution of suitable starting carbazole (1 equiv) and triethyl phosphite (3 equiv) in dry toluene (0.1 M), was closed and placed in the cavity of a CEM Discover focused microwave oven. The reaction mixture was irradiated with microwaves for 2 h, at 180 °C. The reaction mixture was allowed to cool to room temperature and was diluted with AcOEt (20 mL). The organic phase was washed with water (10 mL) and brine (10 mL), dried over anhydrous Na_2SO_4, filtered and evaporated under reduced pressure to give a residue that was purified by column chromatography on silica gel, eluting with petroleum ether/EtOAc.

Ethyl 6-(butylamino)-5,12-dihydroindolo[3,2-a]carbazole-7-carboxylate ***(7a)***. Prepared from ethyl 3-(butylamino)-1-(2-nitrophenyl)-9*H*-carbazole-4-carboxylate **4d** (432 mg, 1.0 mmol). Yield: 268 mg (67%), as a pale brown oil. Elemental analysis (%) calcd for $C_{25}H_{25}N_3O_2$ (M = 399.48): C, 75.16; H, 6.31; N, 10.52; found: C,

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75.21; H, 6.34; N, 10.53. IR ν_{max} (film) 3361, 2927, 1674, 1614, 1524, 1235 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$) δ 8.25 (d, J = 8.2 Hz, 1H), 8.12 (s, 1H), 7.37−7.33 (m, 2H), 7.32−7.27 (m, 2H), 7.18−7.09 (m, 1H), 6.97 (s, 1H), 6.93 (dd, 2H), 6.88 (dd, J = 7.4, 1.2 Hz, 1H), 4.61 (q, J = 7.2 Hz, 2H), 3.25 (t, J = 7.0 Hz, 2H), 1.81−1.62 (m, 2H), 1.50 (t, J = 7.1 Hz, 3H), 1.47−1.42 (m, 2H), 0.97 (t, J = 7.3 Hz, 3H). ^{13}C NMR (63 MHz, $CDCl_3$) δ 169.4, 143.8, 140.8, 131.0, 129.7, 128.0, 126.2, 124.7, 123.5, 122.7, 122.1, 119.1, 118.8, 116.1, 111.1, 61.1, 31.6, 29.8, 20.5, 14.5, 14.1.

Ethyl-2,9-dibromo-6-(butylamino)-5,12-dihydroindolo[3,2-a]-carbazole-7-carboxylate ***(7b)***. Prepared from ethyl 6-bromo-1-(4-bromo-2-nitrophenyl)-3-(butylamino)-9*H*-carbazole-4-carboxylate **4f** (589 mg, 1.0 mmol). Yield: 323 mg, (58%), as a brown oil. Elemental analysis (%) calcd for $C_{25}H_{23}Br_2N_3O_2$ (M = 557.28): C, 53.88; H, 4.16; N, 7.54; found: C, 53.91; H, 4.18; N, 7.57. IR ν_{max} (film) 2924, 2853, 1679 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$) δ 8.51 (d, J = 3.1 Hz, 2H), 8.05 (d, J = 7.8 Hz, 1H), 7.50 (d, J = 8.0 Hz, 1H), 7.43−7.33 (m, 1H), 7.29−7.20 (m, 1H), 7.17 (s, 1H), 6.94 (s, 1H), 4.54 (q, J = 7.2 Hz, 2H), 3.19 (q, J = 6.7, 6.1 Hz, 2H), 1.49−1.36 (m, 5H), 1.27−1.23 (m, 2H), 1.02 (d, J = 7.1 Hz, 3H). ^{13}C NMR (63 MHz, $CDCl_3$) δ 169.1, 146.5, 142.9, 139.2, 133.2, 132.5, 130.5, 128.8, 127.6, 126.9, 125.1, 124.3, 121.4, 117.6, 113.2, 112.4, 111.6, 110.6, 104.9, 61.3, 44.1, 31.7, 20.5, 14.4, 14.1.

Ethyl 6-(butylamino)-7,13-dihydro-[1,3]dioxolo[4,5-b]indolo[2,3-g]carbazole-5-carboxylate ***(7c)***. Prepared from ethyl 8-(butylamino)-6-(2-nitrophenyl)-5*H*-[1,3]dioxolo[4,5-*b*]carbazole-9-carboxylate **4j** (444 mg, 1.0 mmol). Yield: 275 mg, (62%), as a pale brown oil. Elemental analysis (%) calcd for $C_{26}H_{25}N_3O_4$ (M = 443.49): C, 70.41; H, 5.68; N, 9.47; found: C, 70.45; H, 5.62; N, 9.44; IR ν_{max} (film) 3357, 2928,1703 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$) δ 8.51 (d, J = 3.1 Hz, 2H), 8.05 (d, J = 7.8 Hz, 1H), 7.50 (d, J = 8.0 Hz, 1H), 7.43−7.33 (m, 1H), 7.29−7.20 (m, 1H), 7.17 (s, 1H), 6.94 (s, 1H), 4.54 (q, J = 7.2 Hz, 2H), 3.19 (q, J = 6.7, 6.1 Hz, 2H), 1.49−1.36 (m, 5H), 1.27−1.23 (m, 2H), 1.02 (d, J = 7.1 Hz, 3H). ^{13}C NMR (63 MHz, $CDCl_3$) δ 170.6, 146.3, 143.1, 138.9, 137.8, 135.0, 132.3, 125.9, 125.4, 124.1, 122.5, 121.2, 120.1, 116.3, 111.4, 108.4, 101.4, 100.1, 92.8, 62.1, 55.5, 50.0, 31.9, 21.0, 15.0, 14.7.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.7b01199.

Additional synthetic protocols, additional details of DFT calculations and copies of spectra (PDF)

Crystal data (CIF)

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Notes

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