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Formation of 3-Aminophenols from Cyclohexane-1,3-diones

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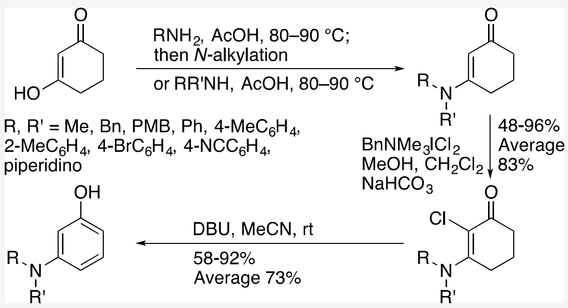
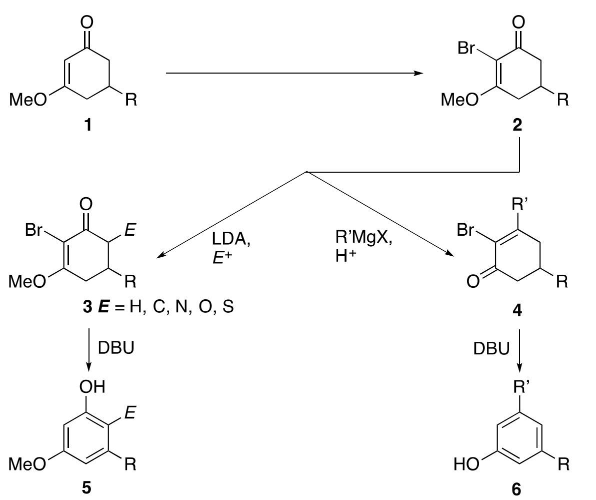
ABSTRACT: *meta*-Aminophenols are formed by the action of DBU on 3-amino-2-chlorocyclohex-2-en-1-ones at room temperature in MeCN. The chloro compounds are generated by treating 3-aminocyclohex-2-en-1-ones with the easily prepared halogenating agent $BnNMe_3 \cdot ICl_2$ in MeOH-CH_2Cl_2. The amino group must carry two substituents, either two aryl, one aryl and one alkyl, or two alkyl groups; 3-aminocyclohex-2-en-1-ones of this type are readily made from cyclohex-2-en-1-one and a primary or secondary amine.



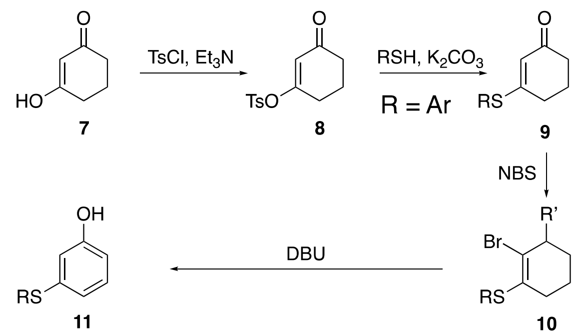
INTRODUCTION

The synthesis of *meta*-substituted phenols (as well as the corresponding ethers) is made difficult by the *ortho-para* directing properties of the phenolic oxygen. In those cases where the *meta* substituent is itself *ortho-para* directing, similar complications thwart the alternative approach of direct *meta*-oxygenation. Solutions to such problems have been addressed in four publications from this laboratory. The first two[1,2] reported procedures along the lines shown in Scheme 1 for converting readily available 3-methoxycyclohex-2-en-1-ones (**1**) into 3-methoxyphenols (**5**) that can carry a variety of carbon, nitrogen, sulfur, or oxygen substituents (*E*). The third publication[3] explained how to introduce a carbon unit, either aliphatic or aromatic, *meta* to the phenolic oxygen (Scheme 1, **1** → **2** → **4** → **6**), and the last paper[4] dealt with the formation of *meta*-sulfanylphenols (Scheme 2, **7** → **8** → **9** → **10** → **11**). All these transformations were carried out under mild conditions and without metal catalysis.

Scheme 1. Formation of *meta*-Substituted Phenols



Scheme 2. Formation of *meta*-Sulfanylphenols



We have now incorporated the above principles into a procedure for making *meta*-aminophenols (Scheme 3, *A* and *B* = aryl or alkyl groups). As indicated in this generic scheme, cyclohexane-1,3-dione (**7**) is converted into a 3-amino-cyclohex-2-en-1-one (**13**), either directly or in two steps via the secondary enaminone **12**. The tertiary enaminone **13** is then halogenated at C(2) and the product treated with DBU to

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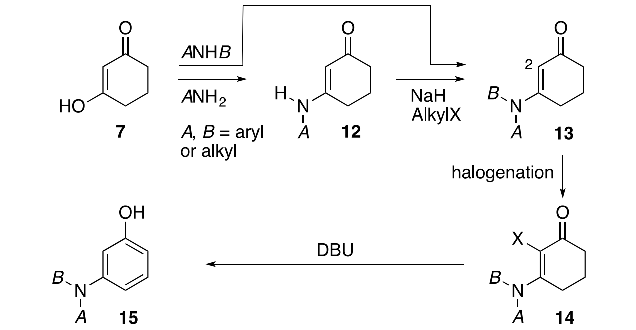
Scheme 3. Our Approach to *meta*-Aminophenols



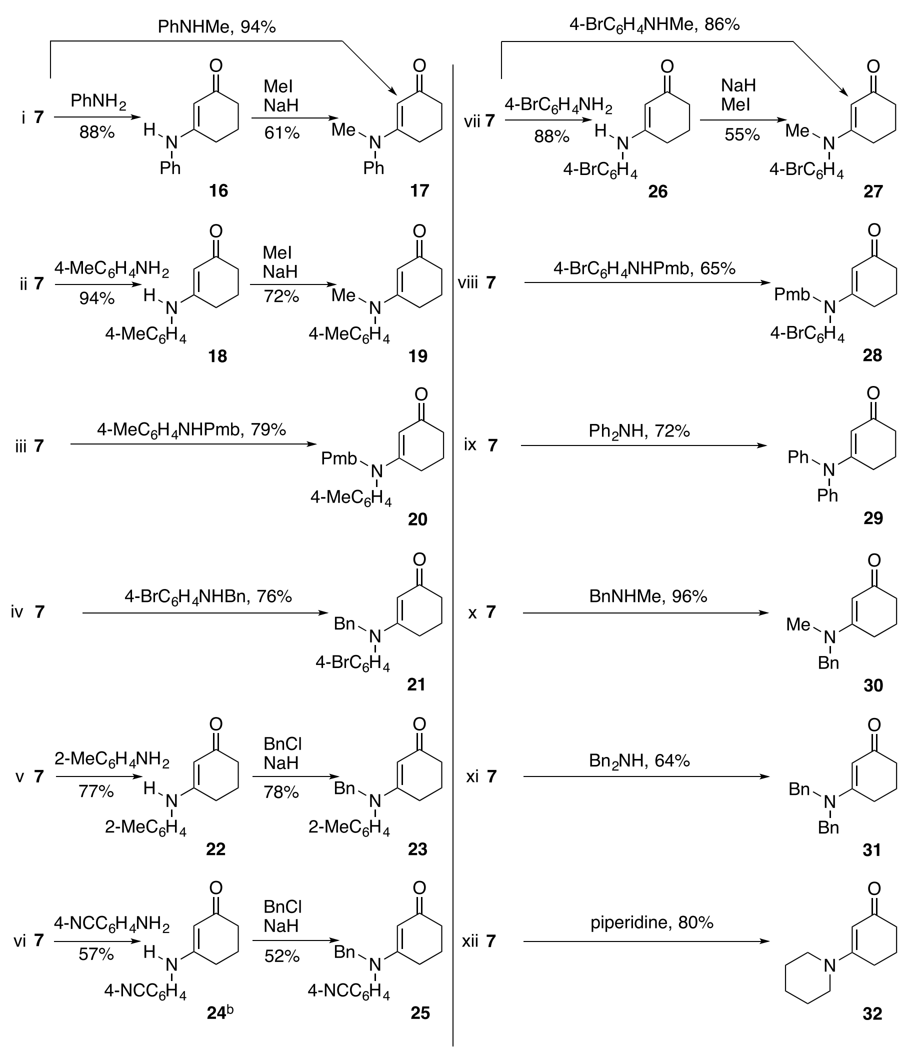
effect elimination of HX and form the *meta*-aminophenol **15**. Simple *meta*-aminophenols of therapeutic or agrochemical value are phentolamine[5] (an anti-hypertensive), demecarium bromide (formally used in treating glaucoma),[6] phenmedipham (a herbicide),[7] and formetanate (a miticide and insecticide).[8] Benzene rings with oxygen and nitrogen substitution in a 1,3 relationship are subunits of quinolinone alkaloids[9] and some carbazole alkaloids,[10] and they are used as precursors of dyes.[11]

RESULTS AND DISCUSSION

Preparation of Starting Materials. The required starting materials, 3-aminocyclohex-2-en-1-ones (**13**), were made from cyclohexane-1,3-dione and the appropriate amine. We examined several standard methods[12] for condensing the amine and the dione: the use of refluxing PhH or PhMe and a Dean-Stark apparatus with or without catalytic *p*-TsOH·H_2O, the use of catalytic AcOH in PhMe,[13] and the use of catalytic $Yb(OTf)_3$[14] in MeCN. We find that the most reliable procedure is to use AcOH as the solvent at 80−95 °C; under these conditions, the reaction works with both primary and secondary amines, is usually over in 2−6 h, and does not require removal of water. Diphenylamine was an exception, and a much longer time was needed (ca. 50 h). Diluting the reaction mixture with THF (1:1 AcOH-THF) resulted in a lower yield, 20% versus 65% in the one case we tested (**28**, see Table 1 for structure).

When cyclohexanedione was condensed with a primary amine the next step required *N*-alkylation, and this was

Table 1. Preparation of Tertiary 3-Aminocyclohex-2-en-1-ones[a]



[a]Reaction of the amines with cyclohexane-1,3-dione were done in AcOH, except for the preparation of **30** and **32** where no acid was used. [b]Reaction done without acid gave almost the same yield (59%).

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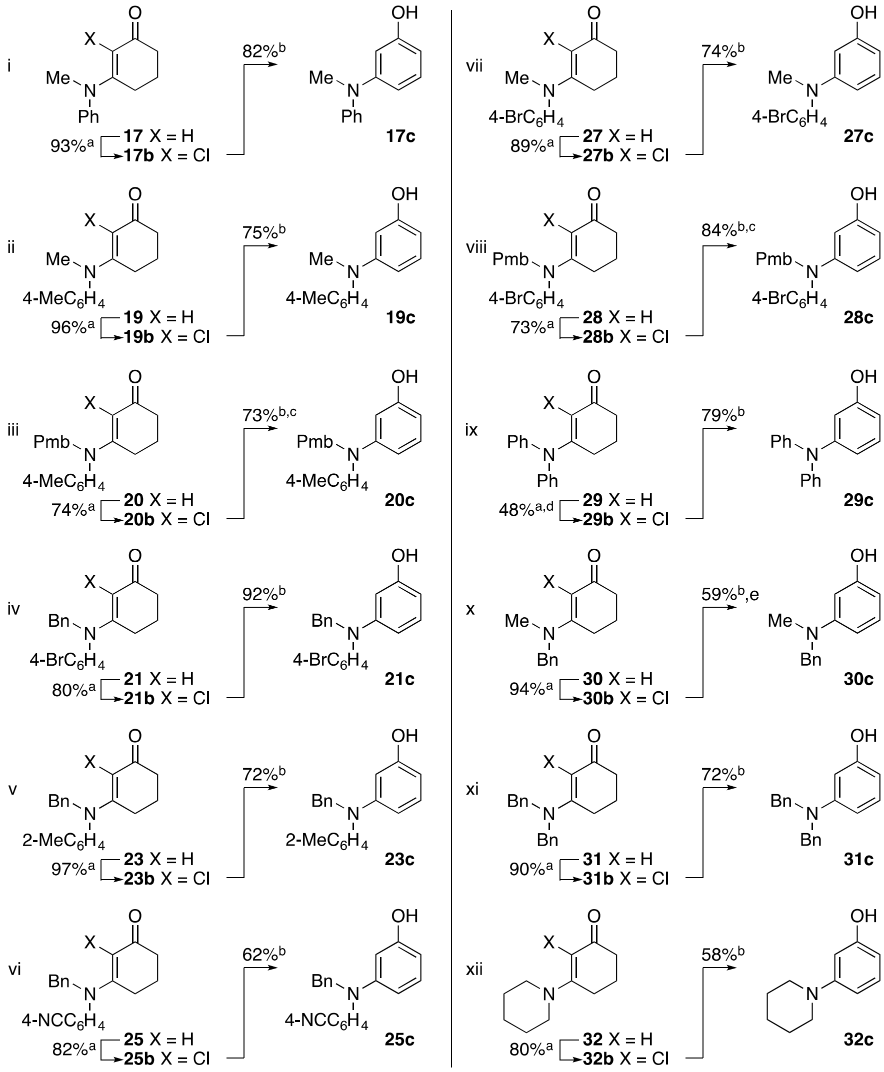
Table 2. Formation of *meta*-Aminophenols

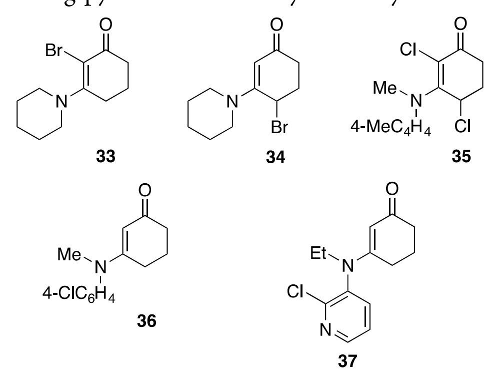


[a]$BnNMe_3ICl_2$, $NaHCO_3$, CH_2Cl_2-MeOH, room temp. [b]DBU, MeCN, room temp. [c]Reaction done in the presence of LiCl. [d]2-Iodo enaminone (12%) and 4-iodo enaminone (31%) also isolated. [e]Reaction at a higher than normal concentration.

achieved by deprotonation with NaH in DMF followed by addition of an alkyl or benzyl halide (MeI, BnCl).[15]

The 3-aminocyclohex-2-en-1-ones we have studied are listed in Table 1. In the two cases where the same product was made by direct use of a secondary amine and also by the two-step method involving a primary amine followed by *N*-alkylation, the single step process gave a higher yield.

Halogenation Studies. The initial halogenation studies were attempts at bromination because our prior experience[1−4] was based on the introduction of bromine.[16] A suitable test appeared to be the preparation of bromide **33**, which was reported to be available as a hydrobromide by treatment of 3-(piperidin-1-yl)cyclohex-2-en-1-one (**32**, Table 1)[17] with Br_2.[18] It turns out that the compound is not a 2-bromo derivative but the hydrobromide of the structural isomer **34**. This assignment was clear from the ^1H NMR spectrum, and an X-ray structure determination indicated that the material is best regarded as the bromide salt[19] of an *O*-protonated enaminone. The compound readily gives the expected phenol (90% yield) on treatment with DBU in MeCN at room temperature, but, unfortunately, the smooth C(4) bromination of **32** is not a general reaction and did not work with the corresponding pyrrolidino or diethylamino cyclohexenones.



Consequently, other halogenation methods were tested on a variety of enaminones. The action of NBS[20] or Br_2[19] (both in CH_2Cl_2) on **30** (see Table 1 for structure) gave a complex mixture in both cases, as did I_2 in MeCN.[21] *t*-BuOCl[22] failed to afford the desired chloride with 3-(pyrrolidin-1-yl)cyclohex-2-en-1-one, and the use of NCS, tried with **19** (see Table 1), was also unsatisfactory; it led to the desired product in 59% yield as

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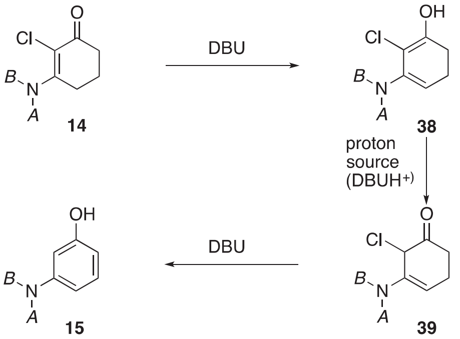
well as the byproduct **35** (27%). It is not clear whether the formation of **35** is the result of an ionic reaction via an extended enolate or is the product of a free radical allylic chlorination. However, $BrCH(CN)_2$,[23] which is known to work well with secondary enaminones,[24] seemed promising (68% yield) when tried with **36** in DMF. We soon found, however, that the yields of the required bromides were lower and erratic with other tertiary enaminones. Finally, we turned to the easily prepared and crystalline reagent $BnNMe_3·ICl_2$,[25] which had been reported to convert **17** into the corresponding 2-chloro compound under very mild conditions and in good yield (83%).[26] Likewise, the tertiary enaminone **37** had also been chlorinated[27] (no yield given). The generality of this chlorination of tertiary enaminones was unestablished as these were the only examples. The reagent has the curious property of iodinating secondary enaminones.[26,28] In the event, $BnNMe_3·ICl_2$ proved to be satisfactory for the chlorinations we needed, although we have found one case, the *N*,*N*-diphenyl enaminone **29** (see Table 2), where iodination is a competing reaction and we isolated (see the Experimental Section) the 2-iodo compound **29b′** (12% yield), the desired chloro compound **29b** (48%), and the 4-iodo compound **29b″** (31%). All three of these products were again formed when the halogenation of **29** was done with protection from light. Presumably, the electron density on the nitrogen or the conformation about the N−C(3) bond are factors responsible for this behavior. In general, the optimum conditions for chlorination with $BnNMe_3·ICl_2$ are the use of 1.2−1.5 equiv of the reagent and a reaction time of 1−12 h; with this procedure, the average yield for the chlorination of our 12 examples (Table 1) is 83%.

All the 2-chloro enaminones should be used promptly after isolation; those that were not solids turned black at room temperature after about 1 week.

Aromatization by Base Treatment. For the aromatization step, we examined several bases (pyridine, Et_3N, *i*-Pr_2NEt, DBN, and DBU) but only DBU was satisfactory. The slightly less basic[29] analog DBN was less effective (26% in a test with **19b**, Table 2). There appeared to be little if any reaction with *i*-Pr_2NEt in the case of **19b**. The action of DBU was examined in several solvents (PhMe, THF, and MeCN), and we established that DBU in MeCN at room temperature is the best, as judged by isolated yields from **30b**. Generally, we use 2 equiv DBU and arbitrarily leave the reaction mixtures for 24 h. In a few cases, e.g., **20c** (48 h), **21c** (48 h), **23c** (70 h), and **30c** (42 h) (Table 2), a longer time was required. Our results for the complete sequence of halogenation and aromatization are listed in Table 2. With the formation of **19c** as a test case, the yield was 63% with 1.2 equiv DBU after 22 h (concentration of **19b** = 0.21 mmol/mL) and 75% with 2 equiv DBU after 20 h (concentration of **19b** = 0.15 mmol/mL). In the case of **30c**, the yield was improved by running the aromatization at a concentration of 0.25 molar in starting chloro enaminone (59%) rather than 0.11 molar (36%), a reaction time of 42 h being used for both experiments.

In the aromatization of **17b**, **19b**, and **27b**, we noticed by TLC examination of the reaction mixtures that two products were formed; these were eluted from the flash chromatography column in successive fractions, but the NMR spectra of the content of these fractions were identical, as was their TLC behavior. Clearly, one of the initial products changes into the desired *meta*-aminophenol during the chromatography. Possibly, this compound is the intermediate enamine **39** (Scheme 4), but we were unable to isolate it for characterization. In an attempt to clarify what was happening, we

Scheme 4. Reaction Mechanism



evaporated the reaction mixture from **19b** and kept the residue under oil pump vacuum (ca. 0.005 mmHg) overnight to remove DBU and then ran NMR spectra in THF-d_8, but at that stage, all the material was the aminophenol **19c**.

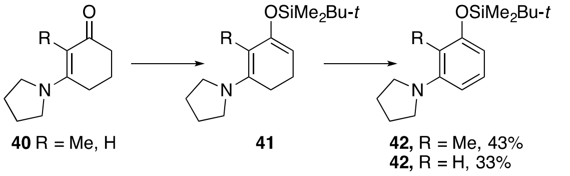
In early experiments aimed at optimizing the conditions for aromatization of **20b**, we arbitrarily added the weak Lewis acid LiCl to the reaction mixture in the hope that it might facilitate an enolization step (see Scheme 4), and we observed an improvement in the yield of the phenol from 38% to 73%. LiCl was again used for aromatization of **28b**, giving a yield of 84% after a reaction period of 48 h; in the absence of LiCl, the yield was 74%, again after 48 h.

We have also examined the possibility of aromatizing an enaminone having one hydrogen on the nitrogen since halogenation is then very easy.[19] The compound used was 2-bromo-3-[(4-chlorophenyl)amino]cyclohex-2-en-1-one, but the action of DBU failed to produce the aromatic system, probably because of preferential deprotonation of the nitrogen. In two experiments,[30] *N*-acylation of the nitrogen with Boc_2O or AcCl after chlorination was also unpromising.[31]

The mechanism of the aromatization presumably occurs via the process summarized in Scheme 4,[1,32] but we were unable to isolate what may be the enamine **39** in the one case we examined (**19b**) where TLC monitoring of the aromatization revealed the formation of a precursor to the aminophenol.

Related Approaches to *meta*-Aminophenols. *meta*-Aminophenols can be prepared from cyclohexanone systems by several methods reported in the literature. Heating a 3-aminocyclohex-2-en-1-one with Pd/C to 150−220 °C effects aromatization.[33] The two enaminones **40** (Scheme 5), on

Scheme 5. Silylation Route



silylation and heating (50 °C) with stoichiometric $PdCl_2(MeCN)_2$, affording the corresponding *O*-silylated *meta*-aminophenols **42** in poor yield.[34] The action of palladium(II) on 3-(arylamino)cyclohex-2-en-1-ones does not seem to lead to aromatization however.[35] Another palladium-based method involves in situ dehydrogenation of cyclo-

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hexanone at 100 °C in the presence of an amine, Cu_2O, I_2, TEMPO, *t*-BuOOH, and air to afford the *meta*-aminophenols resulting from sequential conjugate addition of the amine to the intermediate cyclohexenone followed by dehydrogenation.[36] In the few examples reported for this method, yields varied from 40% to 51%.

The closest procedure to our own approach is the report that secondary 3-aminocyclohex-2-en-1-ones react with aryliododiacetates $[Ar(I(OAc)_2]$ in the presence of K_2CO_3 to give *meta*-aminophenols in which the nitrogen now carries the aryl group that was initially part of the hypervalent iodine reagent.[37] The reaction proceeds at 100 °C via an intermediate 3-amino-2-iodocyclohex-2-en-1-one, and yields in this process were generally very high.[38]

The *meta*-aminophenol unit has been generated at 130 °C in the form of hydroxyphenanthridinones by aromatization of 3-aminocyclohex-2-en-1-ones in the presence of stoichiometric $Cu(OAc)_2$ and air.[40]

meta-Aminophenols are formed (32−78% yield) when 3-aminocyclohex-2-en-1-ones are treated with 1 equiv (or more) of $Hg(OAc)_2$ in refluxing MeCN or AcOH for 1−20 h.[41,42]

Two 3-aminocyclohex-2-en-1-ones have been aromatized at 150 °C in the presence of both Pd/C and H_2 (0.2 atm).[43] Several secondary 3-aminocyclohex-2-en-1-ones have been aromatized by heating with Pd/C at 210−300 °C for 12 to 48 h,[10,44] and 3-aminophenol itself can be obtained by heating 3-aminocyclohex-2-en-1-one with 5% Pd/C and AcOK in refluxing *N*-methylpyrrolidinone.[45]

Halogenated *meta*-aminophenols are available by successive reaction of 3-aminocyclohex-2-en-1-ones with $(Me_3Si)_2NLi$ and TsCl (or TsBr) and again with $(Me_3Si)_2NLi$.[46,47]

Certain 3-aminocyclohex-2-en-1-ones have been deprotonated regioselectively and silylated to generate a diene system that undergoes Diels−Alder cycloaddition followed by retro-Diels−Alder reaction to afford *O*-silyl derivatives of *meta*-aminophenols.[48]

■ CONCLUSIONS

Cyclohexane-1,3-dione is readily converted into 3-aminocyclohex-2-en-1-ones in which the nitrogen carries two substituents, which are both aryl or alkyl units, or one of each type. Such compounds can be chlorinated at C(2) with the crystalline reagent $BnNMe_3{\cdot}ICl_2$, and the resulting chloro enaminones undergo aromatization at room temperature on treatment with DBU in MeCN. The average yield for the chlorination was 83% (12 examples); the average yield for the aromatization was 73%.

■ EXPERIMENTAL SECTION

Solvents used for chromatography were distilled before use. Commercial thin layer chromatography plates (silica gel, Merck 60F-254) were used. Silica gel for flash chromatography was Merck type 60 (230−400 mesh). Dry solvents were prepared under an inert atmosphere (N_2) and transferred by a syringe or cannula. The symbols s, d, t, and q used for $^{13}C\{^1H\}$ NMR spectra indicate zero, one, two, or three attached hydrogens, respectively, the assignments being made from APT spectra. Solutions were evaporated under water pump vacuum, and the residue was then kept under oil pump vacuum. In the formation of enaminones, a heating mantle was used; in all other cases, the heat source was a temperature-controlled oil bath.

High-resolution electrospray mass spectrometric analyses were done with an orthogonal time-of-flight analyzer, and electron ionization mass spectra were measured with a double-focusing sector mass spectrometer.

3-(Phenylamino)cyclohex-2-en-1-one (16).[13] Aniline (0.4549 mL, 15 mmol) was added to AcOH (6 mL) followed by cyclohexane-1,3-dione (560 mg, 5.0 mmol), and the mixture was stirred at 90 °C (N_2 atmosphere) for 6 h. The solvent was then evaporated at 40 °C, and the residue was dissolved in the minimum of EtOAc and applied to the top of a chromatography column made up with silica gel (2 × 20 cm) and hexane. Flash chromatography, using first hexane (ca. 250 mL) and then 1:9 hexane-EtOAc, gave **16** (830 mg, 88%) as a yellow solid: mp 179−181 °C; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.36 (t, J = 7.59 Hz, 2 H), 7.22−7.16 (m, 3 H), 6.13 (br s, 1 H), 5.61 (s, 1 H), 2.52 (t, J = 6.24 Hz, 2 H), 2.39 (t, J = 7.12 Hz, 2 H), 2.07 (quint, J = 6.6 Hz, 2 H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 175 MHz) δ 198.2 (s), 162.5 (s), 138.1 (s), 129.2 (d), 125.5 (d), 123.9 (d), 99.6 (d), 36.4 (t), 29.6 (t), 21.8 (t).

3-[Methyl(phenyl)amino]cyclohex-2-en-1-one (17).[35] Dry DMF (30 mL) was injected into a flask containing the enaminone **16** (2.02 g, 10.8 mmol) (N_2 atmosphere), and the stirred mixture was cooled in an ice bath. NaH (60% w/w dispersion in oil, 968 mg, 24.3 mmol) was tipped into the resulting solution under a stream on N_2, the ice bath was removed, and stirring was continued for 2 h. MeI (1.7 mL, 27.3 mmol) was then injected dropwise over about 2 min, and stirring was continued overnight. The mixture was poured into water (300 mL) and extracted with EtOAc (5 × 50 mL). The combined organic extracts were washed with brine (2 × 50 mL), dried (Na_2SO_4), and evaporated. Flash chromatography of the residue over silica gel (3 × 15 cm), using 19:1 CH_2Cl_2-MeOH, gave **17** (1.33 g, 61%) as a beige solid. For characterization data, see the next experiment.

3-[Methyl(phenyl)amino]cyclohex-2-en-1-one (17).[35] *N*-Methylaniline (0.54 mL, 5.0 mmol) was added to AcOH (6.5 mL) followed by cyclohexane-1,3-dione (560 mg, 5.0 mmol), and the mixture was stirred at 85 °C (N_2 atmosphere) for 6 h. The solvent was then evaporated at 40 °C, and the residue was dissolved in the minimum of EtOAc and applied to the top of a chromatography column made up with silica gel (2 × 15 cm) and hexane. Flash chromatography, using first hexane (ca. 250 mL) and then 1:9 hexane-EtOAc, gave **17** (950 mg, 94%) as an oil, which slowly solidified: mp 81−83 °C; ^1H NMR ($CDCl_3$, 500 MHz) δ 7.42 (t, J = 7.36 Hz, 2 H), 7.36−7.31 (m, 1 H), 7.15 (d, J = 7.42 Hz, 2 H), 5.34 (s, 1 H), 3.25 (s, 3 H), 2.32 (t, J = 5.0 Hz, 2 H), 2.23 (t, J = 6.23 Hz, 2 H), 1.91 (quint, J = 8.15 Hz, 2 H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 175 MHz) δ 197.5 (s), 164.9 (s), 145.3 (s), 129.6 (d), 127.4 (d), 127.1 (d), 100.5 (d), 40.7 (q), 36.0 (t), 28.4 (t), 22.4 (t).

2-Chloro-3-[methyl(phenyl)amino]cyclohex-2-en-1-one (17b).[26] $BnNMe_3{\cdot}ICl_2$ (450 mg, 1.29 mmol) was tipped into a stirred solution of **17** (217 mg, 1.08 mmol) in a mixture of dry CH_2Cl_2 (8 mL) and dry MeOH (4 mL) followed immediately by $NaHCO_3$ (634 mg, 7.54 mmol), which was also added in one portion (N_2 atmosphere). Stirring was continued for 45 min, and the mixture was then filtered through a sintered disc. Evaporation of the filtrate and flash chromatography of the residue over silica gel (2 × 15 cm), using 19:1 CH_2Cl_2-MeOH, gave **17b** (236 mg, 93%) as an oil containing trace impurities (^1H NMR): FTIR ($CDCl_3$, cast film) 2949, 2825, 1647, 1596, 1584, 1543, 1293, 1188, 1035, 769 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 7.42−7.34 (m, 2 H), 7.26−7.17 (m, 1 H), 7.12−7.06 (m, 2 H), 3.55 (s, 3 H), 2.592−2.52 (m, 4 H), 1.94 (quint, J = 6.5 Hz, 2 H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 176 MHz) δ 191.1 (s), 160.6 (s), 146.4 (s), 129.4 (d), 125.3 (d), 124.2 (d), 42.8 (q), 37.6 (t), 31.8 (t), 20.7 (t); exact mass (ESI) *m/z* calcd for $C_{13}H_{14}ClNO$ $(M + Na)^+$ 258.0656, found 258.0656.

3-[Methyl(phenyl)amino]phenol (17c).[49] DBU (0.1257 mL, 0.840 mmol) was injected at a fast dropwise rate into a stirred solution of **17b** (98.8 mg, 0.420 mmol) in dry MeCN (3 mL) (N_2 atmosphere), and stirring was continued for 16 h. At this stage, examination of the reaction mixture by TLC (silica, 99:1 CH_2Cl_2-MeOH) showed two new spots and examination in two dimensions suggested that the less polar material was decomposing into the more polar on the silica. Evaporation of the solvent and flash chromatography of the residue over silica gel (2 × 15 cm), using 99:1 CH_2Cl_2-MeOH, gave **17c** (68.6 mg, 82%) as a yellow liquid: ^1H

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NMR ($CDCl_3$, 500 MHz) δ 7.33 (t, J = 7.24 Hz, 2 H), 7.16−7.09 (m, 3 H), 7.06 (t, J = 7.47 Hz, 1 H), 6.56 (dd, J = 8.15, 2.11 Hz, 1 H), 6.45 (t, J = 2.29 Hz, 1 H), 6.39 (ddd, J = 7.99, 2.40, 0.78 Hz, 1 H), 4.63 (br d, J = 15.75 Hz, 1 H), 3.32 (s, 3 H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz) δ 156.3 (s), 150.6 (s), 148.7 (s), 130.0 (d), 129.3 (d), 122.60 (d), 122.58 (d), 111.2 (d), 107.1 (d), 105.5 (d), 40.2 (q).

3-[(4-Methylphenyl)amino]cyclohex-2-en-1-one (18).[13] 4-$MeC_6H_4NH_2$ (330 mg, 2.924 mmol) was added to AcOH (6 mL) followed by cyclohexane-1,3-dione (327 mg, 2.92 mmol), and the mixture was stirred at 88−90 °C (N_2 atmosphere) for 4 h. The solvent was then evaporated at 40 °C, and the residue was dissolved in the minimum of EtOAc and applied to the top of a chromatography column made up with silica gel (2 × 22 cm) and hexane. Flash chromatography, using first hexane (ca. 250 mL) and then 1:9 hexane-EtOAc, gave **18** (557 mg, 94%) as a yellow solid: mp 139−141 °C; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.15 (d, J = 8.22 Hz, 2 H), 7.06 (d, J = 8.36 Hz, 2 H), 6.19 (br s, 1 H), 5.53 (s, 1 H), 2.50 (t, J = 6.24 Hz, 2 H), 2.39−2.33 (m including a singlet, 5 H), 2.05 (quint, J = 6.31 Hz, 2 H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 175 MHz) δ 198.0 (s), 162.3 (s), 135.55 (s), 135.32 (s), 129.8 (d), 124.1 (d), 99.7 (d), 36.4 (t), 29.7 (t), 21.8 (t), 20.9 (q).

3-[Methyl(4-methylphenyl)amino]cyclohex-2-en-1-one (19).[35] Dry DMF (15 mL) was injected into a flask containing enaminone **18** (1.02 g, 5.51 mmol) (N_2 atmosphere), and the stirred mixture was cooled in an ice bath. NaH (60% w/w dispersion in oil, 530 mg, 13.3 mmol) was tipped into the resulting solution under a stream of N_2, the ice bath was removed, and stirring was continued for 2 h. MeI (0.86 mL, 13.8 mmol) was then injected dropwise over about 2 min, and stirring was continued overnight. The mixture was poured into water (125 mL) and extracted with EtOAc (4 × 25 mL). The combined organic extracts were washed with brine (2 × 25 mL), dried (Na_2SO_4), and evaporated. Flash chromatography of the residue over silica gel (2 × 15 cm), using 19:1 CH_2Cl_2-MeOH, gave **19** (78.7 mg, 72%) as a beige solid: ^1H NMR ($CDCl_3$, 600 MHz) δ 7.25−7.20 (m, 2 H), 7.05−7.01 (m, 2 H), 5.33 (s, 1 H), 3.23 (s, 3 H), 2.39 (s, 3 H), 2.32 (dd, J = 7.1, 5.9 Hz, 2 H), 2.22 (t, J = 6.2 Hz, 2 H), 1.90 (quint, J = 6.4 Hz, 2 H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 176 MHz,) δ 197.5 (s), 165.2 (s), 142.8 (s), 137.4 (s), 130.2 (d), 126.9 (d), 100.3 (d), 40.8 (d), 36.1 (t), 28.5 (t), 22.5 (t), 21.0 (q).

2-Chloro-3-[methyl(4-methylphenyl)amino]cyclohex-2-en-1-one (19b). $BnNMe_3·ICl_2$ (333.8 mg, 0.959 mmol) was tipped into a stirred solution of **19** (137 mg, 0.636 mmol) in a mixture of dry CH_2Cl_2 (8 mL) and dry MeOH (4 mL) followed immediately by $NaHCO_3$ (381.9 mg, 4.55 mmol), which was also added in one portion (N_2 atmosphere). Stirring was continued for 45 min, and the mixture was then filtered through a sintered disc. Evaporation of the filtrate and flash chromatography of the residue over silica gel (2 × 15 cm), using 1:1 hexane-EtOAc, gave **19b** (151.9 mg, 96%) as an oil: FTIR (CH_2Cl_2, cast film) 2921, 1649, 1545, 1452, 1275, 1188, 1135, 1110, 1001, 825 cm^{-1}; ^1H NMR ($CDCl_3$, 600 MHz) δ 7.21−7.16 (m, 2 H), 7.03−6.99 (m, 2 H), 3.55 (s, 3 H), 2.56−2.48 (m, 4 H), 2.37 (s, 3 H), 1.90 (tt, J = 6.6, 5.6 Hz, 2 H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 176 MHz) δ 191.0 (s), 160.8 (s), 144.0 (s), 135.8 (s), 130.1 (d), 124.9 (d), 110.0 (s), 43.6 (q), 37.5 (t), 32.0 (t), 20.9 (t), 20.7 (q); exact mass (ESI) m/z calcd for $C_{14}H_{16}ClNO$ $(M + Na)^+$ 272.0813, found 272.0815.

3-[Methyl(4-methylphenyl)amino]phenol (19c). DBU (0.0427 mL, 0.2859 mmol) was injected at a fast dropwise rate into a stirred solution of **19b** (35.7 mg, 0.143 mmol) in dry MeCN (4 mL) (N_2 atmosphere), and stirring was continued for 24 h. At this point, TLC (silica, 99:1 CH_2Cl_2-MeOH) showed two spots but no **19b**. Evaporation of the solvent and flash chromatography of the residue over silica gel (2 × 25 cm), using 99:1 CH_2Cl_2-MeOH, gave **19c** as two successive fractions with identical NMR spectra (20.4 mg in total, 67%) as clear, viscous liquids. The two fractions now had the same TLC R_f values and the same NMR spectra and were combined.

When this experiment was repeated on a larger scale (by a different experimentalist), the development of two fractions in the flash chromatography was not observed: DBU (93 μL, 0.623 mmol) was added dropwise to a stirred solution of **19b** (77.7 mg, 0.278 mmol) in dry MeCN (2 mL) (N_2 atmosphere), and stirring was continued overnight. Evaporation of the solvent and flash chromatography of the residue over silica gel (1 × 15 cm), using EtOAc, gave **19c** (50.3 mg, 75%) as an oil: FTIR (CH_2Cl_2, cast film) 3369, 2919, 2874, 2813, 1602, 1510, 1349, 1129, 956, 819 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.20−7.12 (m, 2 H), 7.12−7.02 (m, 3 H), 6.46 (ddd, J = 8.2, 2.3, 0.8 Hz, 1 H), 6.37−6.28 (m, 2 H), 4.53 (s, 1 H), 3.28 (s, 3 H), 2.36 (s, 3 H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 176 MHz) δ 156.2 (s), 150.9 (s), 146.2 (s), 133.3 (s), 130.0 (d), 129.8 (d), 124.2 (d), 109.3 (d), 105.8 (d), 103.6 (d), 40.3 (q), 20.8 (q); exact mass (ESI) m/z calcd for $C_{14}H_{15}NO$ $(M - H)^-$ 212.1081, found 212.1079.

***N*-[(4-Methoxyphenyl)methyl]-4-methylaniline.**[50−52] 4-$MeOC_6H_4CHO$ (27.4 μL, 2.25 mmol) was added dropwise to a stirred solution of 4-methylaniline (290 mg, 2.7 mmol) in anhydrous EtOH (18 mL). $CeCl_3·7H_2O$ (16 mg, 0.045 mmol) was added, the reaction flask was stoppered, and stirring was continued for an arbitrary period of 2 h. At that stage, $NaBH_4$ (170 mg, 4.50 mmol) was added in one portion. Immediate bubbling was observed, and stirring was continued overnight with the flask open to the atmosphere. Evaporation of EtOH gave a residue, which was partitioned between EtOAc and water. The aqueous phase was washed twice with EtOAc, and the combined organic extracts were dried (Na_2SO_4) and evaporated. Flash chromatography of the residue over silica gel (2 × 15 cm), using 19:1 hexane-EtOAc, gave *N*-[(4-methoxyphenyl)methyl]-4-methylaniline (410 mg, 80%) as a pale yellow solid: ^1H NMR ($CDCl_3$, 400 MHz) δ 7.31 (d, J = 8.66 Hz, 2 H), 7.01 (d, J = 8.07 Hz, 2 H), 6.92−6.88 (m, 2 H), 6.59 (d, J = 7.53 Hz, 2 H), 4.26 (s, 2 H), 3.85 (br s, 1 H), 3.82 (s, 3 H), 2.26 (s, 3 H).

3-{[(4-Methoxyphenyl)methyl](4-methylphenyl)amino}-cyclohex-2-en-1-one (20). *N*-[4-Methoxybenzyl]-4-methylaniline (prepared as in the previous experiment, 366 mg, 1.61 mmol) was added to AcOH (6 mL) followed by cyclohexane-1,3-dione (180 mg, 1.61 mmol), and the mixture was stirred at 95 °C (N_2 atmosphere) for 2 h (TLC monitoring, silica, EtOAc). At this point, more cyclohexane-1,3-dione (45.0 mg, 0.40 mmol) was added and heating was continued for 2 h. Some starting amine was still present (TLC, silica, EtOAc), and so a further portion of cyclohexane-1,3-dione (46.0 mg, 0.41 mmol) was added. Heating was continued for 1 h, by which stage all the amine had reacted. The solvent was evaporated at 40 °C, and the residue was dissolved in the minimum of EtOAc and applied to the top of a chromatography column made up with silica gel (2 × 15 cm) and hexane. Flash chromatography, using first hexane (ca. 200 mL) and then EtOAc, gave **20** (474 mg, 91%) as a dark yellow, viscous liquid. This material was further purified by flash chromatography over silica gel (1 × 21 cm), using 98.5:1.5 CH_2Cl_2-MeOH, to give **20** (410 mg, 79%) as a solid: mp 124−126 °C; FTIR (CH_2Cl_2 cast film) 3031, 2946, 2835, 1620, 1557, 1248, 727 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 7.17−7.09 (m, 4 H), 6.97 (d, J = 7.46 Hz, 2 H), 6.82 (d, J = 7.69 Hz, 2 H), 5.42 (s, 1 H), 4.73 (s, 2 H), 3.77 (s, 3 H), 2.34 (s, 3 H), 2.31−2.26 (m, 4 H), 1.90 (quint, J = 6.78 Hz, 2 H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz) δ 197.5 (s), 165.1 (s), 158.9 (s), 141.7 (s), 137.4 (s), 130.2 (d), 128.49 (s), 128.43 (d), 127.7 (d), 114.0 (d), 101.1 (d), 56.1 (t), 55.2 (q), 36.1 (t), 28.7 (t), 22.5 (t), 21.0 (q); exact mass (ESI) m/z calcd for $C_{21}H_{23}NNaO_2$ $(M + Na)^+$ 344.1621, found 344.1621.

2-Chloro-3-{[(4-methoxyphenyl)methyl](4-methylphenyl)-amino}cyclohex-2-en-1-one (20b). $NaHCO_3$ (146 mg, 1.74 mmol) and $BnNMe_3·ICl_2$ (129 mg, 0.328 mmol) were tipped into a flask containing **20** (79.9 mg, 0.249 mmol) and a magnetic stir bar. The flask was closed with a septum, flushed with N_2, and kept under a static pressure of N_2. A 2:1 mixture of CH_2Cl_2 and MeOH (4.5 mL in total) was injected, and the mixture was stirred at room temperature for 1 h. At this stage, TLC (silica, 24:1 CH_2Cl_2-MeOH) showed the presence of **20**. Stirring was continued overnight by which time all of the starting enaminone had been consumed. The mixture was filtered through a sintered disc and evaporated. Flash chromatography of the residue over silica gel (2 × 25 cm), using 99:1 CH_2Cl_2-MeOH, gave **20b** (65.9 mg, 74%) as a light brown solid: mp 133−135 °C; FTIR (CH_2Cl_2 cast film) 3030, 2951, 2835, 1652, 1580, 1542, 1510, 1183, 1033, 821 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 7.22 (d, J = 8.61 Hz,

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2 H), 7.11 (d, *J* = 8.15 Hz, 2 H) , 6.94 (d, *J* = 8.33 Hz, 2 H), 6.88 (d, *J* = 8.61 Hz, 2 H), 5.09 (s, 2 H), 3.82 (s, 3 H), 2.61 (t, *J* = 6.09 Hz, 2 H), 2.53 (t, *J* = 6.96 Hz, 2 H), 2.33 (s, 3 H), 1.89 (quint, *J* = 6.34 Hz, 2 H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz) δ 191.1 (s), 159.6 (s), 158.9 (s), 143.8 (s), 134.8 (s), 129.8 (d), 129.7 (s), 127.9 (d), 124.0 (d), 114.1 (d), 112.8 (s), 56.7 (t), 55.2 (q), 37.5 (t), 31.9 (t), 20.9 (q), 20.8 (t); exact mass (ESI) *m*/*z* calcd for $C_{21}H_{23}ClNO_2$ $(M + H)^+$ 356.1412, found 356.1412.

3-{[(4-Methoxyphenyl)methyl](4-methylphenyl)amino}-phenol (20c). DBU (7.31 μL, 0.0489 mmol) was injected at a fast dropwise rate into a stirred mixture of LiCl (1.52 mg, 0.037 mmol), **20b** (8.7 mg, 0.024 mmol), and dry MeCN (2 mL) (N_2 atmosphere), and stirring was continued for 24 h. Examination of the mixture by TLC (silica, 99.5:0.5 CH_2Cl_2-MeOH) showed the presence of **20b**, and so stirring was continued for a further 24 h. The mixture was filtered through a sintered disc, and the filtrate was evaporated. Flash chromatography of the residue over silica gel (1.5 × 15 cm), using 99.5:0.5 CH_2Cl_2-MeOH, gave **20c** (5.7 mg, 73%) as a thick oil: FTIR (CH_2Cl_2 cast film) 3405, 3027, 2919, 2835, 1607, 1511, 1245, 1171, 822 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 7.26 (d, *J* = 8.61 Hz, 2 H), 7.15−7.09 (m, 4 H), 7.04 (t, *J* = 8.15 Hz, 1 H), 6.88−6.84 (m, 2 H), 6.48 (dd, *J* = 8.24, 1.74 Hz, 1 H), 6.36 (t, *J* = 2.33 Hz, 1 H), 6.29 (dd, *J* = 8.01, 1.79 Hz, 1 H), 4.89 (s, 2 H), 4.52 (s, 1 H), 3.80 (s, 3 H), 2.34 (s, 3 H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz) δ 158.4 (s), 156.3 (s), 150.2 (s), 145.2 (s), 133.2 (s), 131.1 (s), 130.1 (d), 129.9 (d), 127.7 (d), 124.4 (d), 114.0 (d), 109.9 (d), 106.1 (d), 104.1 (d), 55.9 (t), 55.3 (q), 20.8 (q); exact mass (ESI) *m*/*z* calcd for $C_{21}H_{22}NO_2$ $(M + H)^+$ 320.1645, found 320.1641. A similar experiment done without LiCl gave a poor yield (38%).

***N*-Benzyl-4-bromoaniline.**[51] 4-Bromoaniline (1.198 g, 7.00 mmol), PhCHO (0.59 mL, 5.84 mmol), and $CeCl_3 \cdot 7H_2O$ (43.5 g, 0.116 mmol) were added in that order to anhydrous EtOH (12 mL). The reaction flask was stoppered, and stirring was continued for 2.5 h (TLC monitoring, silica, 4:1 EtOAc-hexane). At that stage, $NaBH_4$ (441 mg, 11.68 mmol) was added in one portion to cause immediate bubbling. Stirring was continued overnight with the flask open to the atmosphere. Evaporation of EtOH gave a residue, which was partitioned between EtOAc and water. The aqueous phase was washed twice with EtOAc, and the combined organic extracts were dried (Na_2SO_4) and evaporated. Flash chromatography of the residue over silica gel (2 × 15 cm), using first hexane (ca. 200 mL) and then 1:4 hexane-EtOAc, gave *N*-benzyl-4-bromoaniline (1.286 g, 84%) as a solid: ^1H NMR ($CDCl_3$, 400 MHz) δ 7.40−7.25 (m, 7 H), 6.54 (d, *J* = 7.90 Hz, 2 H), 4.33 (d, *J* = 3.89 Hz, 2 H), 4.11 (br s, 1 H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 175 MHz) δ 147.0 (s), 138.5 (s), 131.9 (d), 128.6 (d), 127.38 (d), 127.36 (d), 114.4 (d), 109.1 (s), 48.2 (t).

3-[Benzyl(4-bromophenyl)amino]cyclohex-2-en-1-one (21). *N*-Benzyl-4-bromoaniline (prepared as in the previous experiment, 1.286 g, 4.90 mmol) was added to AcOH (12 mL) followed by cyclohexane-1,3-dione (550 mg, 4.90 mmol), and the mixture was stirred at 85 °C (N_2 atmosphere) for 4 h (TLC monitoring, silica, EtOAc). At this stage, more cyclohexane-1,3-dione (275 mg, 2.45 mmol) was added and heating was continued for 3 h (TLC monitoring, silica, EtOAc). The solvent was then evaporated at 40 °C, and the residue was dissolved in the minimum of EtOAc and applied to the top of a chromatography column made up with silica gel (2 × 15 cm) and hexane. Flash chromatography, using first hexane (ca. 250 mL) and then 1:9 hexane-EtOAc, gave **21** (1.340 g, 76%) as a solid, together with cyclohexane-1,3-dione (150 mg, 8.6%) and compound (**i**) (15 mg, 0.9%), which was visible as a bright spot on TLC under UV light. Enaminone **21**: mp 90−92 °C; ^1H NMR ($CDCl_3$, 500 MHz) δ 7.50 (d, *J* = 8.52 Hz, 2 H), 7.35−7.27 (m, 3 H), 7.20 (br d, *J* = 7.23 Hz, 2 H), 7.03 (d, *J* = 8.52 Hz, 2 H), 5.42 (s, 1 H), 4.82 (s, 2 H), 2.35−2.32 (m, 4 H), 1.99−1.94 (m, 2 H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz) δ 197.7 (s), 164.4 (s), 143.4 (s), 136.0 (s), 132.8 (d), 129.5 (d), 128.8 (d), 127.6 (d), 126.9 (d), 121.2 (s), 102.3 (d), 56.5 (t), 36.1 (t), 28.6 (t), 22.5 (t); exact mass (ESI) *m*/*z* calcd for $C_{19}H_{18}BrNO$ $(M + Na)^+$ 378.0464, found 378.0461.

10-(4-Bromophenyl)-9-phenyl-1,2,3,4,5,6,7,8,9,10-decahydroacridin-1,8-dione (i).[53] Compound (**i**): mp 262−265 °C; FTIR (CH_2Cl_2 cast film) 3057, 2946, 2866, 1637, 1573, 1488, 1363, 1182, 1011, 749 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.69 (d, *J* = 7.91 Hz, 2 H), 7.41 (d, *J* = 7.04 Hz, 2 H), 7.30−7.25 (m, 2 H), 7.21−7.13 (m, 3 H), 5.41 (s, 1 H), 2.44−2.15 (m, 6 H), 2.10−2.02 (m, 2 H), 1.97−1.75 (m, 4 H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz) δ 195.8 (s), 150.9 (s), 146.2 (s), 138.1 (s), 128.2 (d), 127.7 (d), 126.0 (d), 123.4 (s), 115.8 (s), 36.7 (t), 31.9 (d), 30.9 (d), 28.3 (t), 21.1 (t); exact mass (ESI) *m*/*z* calcd for $C_{25}H_{22}BrNNaO_2$ $(M + Na)^+$ 470.0726, found 470.0728. A sample was recrystallized from chloroform-hexane for X-ray analysis.

3-[Benzyl(4-bromophenyl)amino]-2-chlorocyclohex-2-en-1-one (21b). $BnNMe_3 \cdot ICl_2$ (163 mg, 0.468 mmol) was tipped into a stirred solution of **21** (139.7 mg, 0.392 mmol) in a mixture of dry CH_2Cl_2 (8 mL) and dry MeOH (4 mL) followed immediately by $NaHCO_3$ (239 mg, 2.84 mmol), which was also added in one portion (N_2 atmosphere). Stirring was continued for 80 min, and the mixture was then filtered through a sintered disc. Evaporation of the filtrate and flash chromatography of the residue over silica gel (2 × 15 cm), using 19:1 CH_2Cl_2-MeOH, gave **21b** (123 mg, 80%) as a yellow solid: FTIR ($CDCl_3$, cast film) 3030, 2951, 2870, 1658, 1544, 1487, 1452, 1280, 1185, 733 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 7.41−7.32 (m, 4 H), 7.32−7.21 (m, 3 H), 6.89−6.83 (m, 2 H), 5.06 (s, 2 H), 2.66 (t, *J* = 6.0 Hz, 2 H), 2.54 (dd, *J* = 7.3, 5.9 Hz, 2 H), 1.93 (quint, *J* = 6.3 Hz, 2 H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 126 MHz) δ 191.2 (s), 158.7 (s), 145.3 (s), 137.4 (s), 132.2 (d), 129.0 (d), 127.7 (d), 126.3 (d), 124.1 (d), 117.0 (s), 116.3 (s), 56.5 (t), 37.6 (t), 31.3 (t), 20.8 (t); exact mass (ESI) *m*/*z* calcd for $C_{19}H_{17}BrClNO$ $(M + Na)^+$ 412.0074, found 412.0072.

3-[Benzyl(4-bromophenyl)amino]phenol (21c). DBU (70 μL, 0.469 mmol) was added dropwise to a stirred solution of **21b** (91.6 mg, 0.234 mmol) in dry MeCN (3 mL) (N_2 atmosphere), and stirring was continued for 48 h. Evaporation of the solvent and flash chromatography of the residue over silica gel (1 × 10 cm), using 1:1 hexane-EtOAc, gave **21c** (76.2 mg, 92%) as a purplish oil: FTIR ($CDCl_3$, cast film) 3521, 3390, 3087, 3062, 3029, 2923, 2855, 1585, 1490, 1452 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 7.39−7.31 (m, 6 H), 7.30−7.22 (m, 1 H), 7.13 (t, *J* = 8.1 Hz, 1 H), 7.01−6.94 (m, 2 H), 6.67 (ddd, *J* = 8.2, 2.2, 0.9 Hz, 1 H), 6.56 (t, *J* = 2.3 Hz, 1 H), 6.46 (ddd, *J* = 8.1, 2.4, 0.9 Hz, 1 H), 4.97 (s, 2 H), 4.77−4.73 (m, 1 H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 126 MHz) δ 156.5 (s), 149.3 (s), 146.8 (s), 138.6 (s), 132.2 (d), 130.3 (d), 128.7 (d), 127.0 (d), 126.5 (d), 122.7 (d), 114.1 (s), 113.2 (d), 108.9 (d), 107.6 (d), 56.3 (t); exact mass (ESI) *m*/*z* calcd for $C_{19}H_{15}BrNO$ $(M - H)^-$ 352.0343, found 352.0340.

3-[(2-Methylphenyl)amino]cyclohex-2-en-1-one (22).[54] 2-Methylaniline (0.40 mL, 3.75 mmol) was added to AcOH (6 mL) followed by cyclohexane-1,3-dione (0.420 g, 3.75 mmol), and the mixture was stirred at 97 °C (N_2 atmosphere) for 4 h (TLC monitoring). The solvent was then evaporated at 40 °C, and the residue was dissolved in the minimum of $CHCl_3$ and applied to the top of a chromatography column made up with silica gel (2.5 × 20 cm) and hexane. Flash chromatography, using first 1:1 EtOAc-hexane (ca. 250 mL), then 1:1 hexane-EtOAc, and finally pure EtOAc, gave **22** (0.580 g, 77%) as a cream colored solid: mp 162−166 °C; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.26−7.16 (m, 4 H), 5.90 (br s, 1 H), 5.10 (s, 1 H), 2.53 (t, *J* = 6.20 Hz, 2 H), 2.37 (t, *J* = 6.53 Hz, 2 H), 2.24 (s, 3 H), 2.11−2.04 (m, 2 H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz) δ 197.8 (s), 162.9 (s), 136.0 (s), 134.1 (s), 131.1 (s), 127.2 (d), 126.92 (d), 126.87 (d), 99.7 (d), 36.4 (t), 29.4 (t), 22.0 (t), 17.7 (q).

3-[Benzyl(2-methylphenyl)amino]cyclohex-2-en-1-one (23). NaH (60% w/w in mineral oil, 60 mg, 1.5 mmol) was tipped into a stirred solution of **22** (200 mg, 0.994 mmol) in dry DMF (6 mL) (N_2 atmosphere), and stirring was continued for 2 h. There was gas evolution initially, and the mixture gradually became dark. BnCl (0.145 mL, 1.15 mmol) was injected at a fast dropwise rate, and stirring was continued overnight, by which time reaction was complete (TLC, silica, 1:1 EtOAc-hexane). The mixture was diluted with EtOAc, water was added, and the aqueous phase was extracted with EtOAc. The combined organic extracts were dried ($MgSO_4$) and

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evaporated. Flash chromatography of the residue over silica gel (2 × 25 cm), using 1:1 hexane-EtOAc (300 mL) and then EtOAc, gave **23** (225 mg, 78%) as a thick, bright yellow liquid: FTIR (CH_2Cl_2 cast film) 3060, 2946, 2868, 1622, 1554, 1185, 1081, 726 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.33−7.21 (m, 7 H), 7.16 (br t, J = 7.42 Hz, 1 H), 7.02 (d, J = 7.78 Hz, 1 H), 5.59 (br s, 1 H), 4.96 (br d, J = 13.55 Hz, 1 H), 4.48 (br d, J = 15.84 Hz, 1 H), 2.32 (t, J = 6.41 Hz, 2 H), 2.13 (s, 3 H), 1.94 (br s, 3 H); ^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz) δ 197.5 (s), 165.0 (s), 142.7 (s), 131.5 (d), 128.6 (d), 128.2 (d), 127.6 (d), 127.1 (d), 55.6 (t), 36.1 (t), 22.4 (t), 17.6 (q); exact mass (ESI) m/z calcd for $C_{20}H_{21}NNaO$ (M + Na)$^+$ 314.1515, found 314.1515.

3-[Benzyl(2-methylphenyl)amino]-2-chlorocyclohex-2-en-1-one (23b). $NaHCO_3$ (155 mg, 1.85 mmol) and $BnNMe_3{\cdot}ICl_2$ (138 mg, 0.397 mmol) were tipped into a flask containing **23** (77.3 mg, 0.265 mmol) and a magnetic stir bar. The flask was closed with a septum, flushed with N_2, and kept under a static pressure of N_2. A 2:1 mixture of CH_2Cl_2 and MeOH (3 mL in total) was injected, and the mixture was stirred at room temperature for 3 h. At this stage, TLC (silica, 24:1 CH_2Cl_2-MeOH) showed no **23**. The mixture was filtered through a sintered disc and evaporated. Flash chromatography of the residue over silica gel (2 × 15 cm), using 99.5:0.5 CH_2Cl_2-MeOH, gave **23b** (83.9 mg, 97%) as a thick, yellow oil: FTIR (neat film) 3061, 2951, 2868, 1649, 1536, 1276, 721 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.36−7.27 (m, 5 H), 7.21−7.11 (m, 4 H), 5.13 (br s, 2 H), 2.52−2.48 (m, 4 H), 2.17 (s, 3 H), 1.85 (quint, J = 6.34 Hz, 2 H); ^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz) δ 190.9 (s), 159.4 (s), 145.1 (s), 137.4 (s), 134.8 (s), 131.1 (d), 128.7 (d), 127.6 (d), 127.1 (d), 127.0 (d), 126.9 (d), 109.5 (s), 58.0 (t), 37.4 (t), 31.9 (t), 20.5 (t), 18.1 (q); exact mass (ESI) m/z calcd for $C_{20}H_{20}ClNNaO$ (M + H)$^+$ 348.1126, found 348.1128.

3-[Benzyl(2-methylphenyl)amino]phenol (23c). DBU (21 μL, 0.14 mmol) was injected at a fast dropwise rate into a stirred solution of **23b** (22.7 mg, 0.070 mmol) in dry MeCN (2 mL) (N_2 atmosphere), and stirring was continued for 40 h at which point some **23b** remained (TLC, silica, CH_2Cl_2). Stirring was continued for a further 30 h at which point TLC showed that only a trace of **23b** was left. Evaporation of the solvent and flash chromatography of the residue over silica gel (2 × 20 cm), using CH_2Cl_2, gave **23c** (14.6 mg, 72%) as a pale mauve solid: mp 94−95 °C; FTIR (solid) 3507, 3056, 2923, 2852, 1618, 1575, 1164, 727 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.40 (d, J = 7.32 Hz, 2 H), 7.36−7.32 (m, 3 H), 7.29−7.25 (m, 4 H), 7.01 (t, J = 8.15 Hz, 1 H), 6.19 (br dd, J = 11.35, 1.83 Hz, 2 H), 6.01 (t, J = 2.29 Hz, 1 H), 4.84 (s, 2 H), 4.58 (s, 1 H), 2.19 (s, 3 H); ^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz) δ 156.4 (s), 150.2 (s), 145.6 (s), 138.9 (s), 137.0 (s), 131.7 (d), 130.0 (d), 129.3 (d), 128.5 (d), 127.5 (d), 127.0 (d), 126.8 (d), 106.2 (d), 104.2 (d), 100.4 (d), 56.2 (t), 18.3 (q); exact mass (ESI) m/z calcd for $C_{20}H_{18}NO$ (M − H)$^-$ 288.1394, found 288.1391.

4-[(3-Oxocyclohex-1-en-1-yl)amino]benzonitrile (24).[13] 4-Aminobenzonitrile (500 mg, 4.23 mmol) was added to AcOH (7 mL) followed by cyclohexane-1,3-dione (474 mg, 4.23 mmol), and the mixture was stirred at 97 °C (N_2 atmosphere) overnight. The solvent was then evaporated at 40 °C, and the residue was dissolved in the minimum of EtOAc and applied to the top of a chromatography column made up with silica gel (2 × 20 cm) and hexane. Flash chromatography, using first hexane (ca. 100 mL) and then pure EtOAc, gave **24** (0.517 g, 57%) as a yellow solid: mp 216−218 °C; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.66−7.62 (m, 2 H), 7.29−7.25 (m, 2 H), 5.81 (s, 1 H), 6.23 (br s, 1 H), 2.55 (t, J = 6.18 Hz, 2 H), 2.43 (t, J = 7.14 Hz, 2 H), 2.13−2.07 (m, 2 H); ^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz) δ 198.3 (s), 158.7 (s), 142.7 (s), 133.5 (d), 122.0 (d), 118.4 (s), 107.5 (s), 103.0 (d), 36.5 (t), 30.0 (t), 21.6 (t).

The preparation of **24** was repeated without acetic acid: 4-Aminobenzonitrile (508 mg, 4.30 mmol) was added to PhH (7 mL) followed by cyclohexane-1,3-dione (0.482 g, 4.299 mmol), and the mixture was refluxed (N_2 atmosphere) overnight. The solvent was then evaporated at 40 °C, and the residue was dissolved in the minimum of EtOAc and applied to the top of a chromatography column made up with silica gel (2 × 21 cm) and hexane. Flash chromatography, using first hexane (ca 100 mL) and then pure EtOAc, gave **24** (535 mg, 59%) as a yellow solid.

4-[Benzyl(3-oxocyclohex-1-en-1-yl)amino]benzonitrile (25). NaH (60% w/w in mineral oil, 112 mg, 2.80 mmol) was tipped into a stirred solution of **24** (400 mg, 1.88 mmol) in dry DMF (8 mL) (N_2 atmosphere), and stirring was continued for 2 h. There was gas evolution initially, and the mixture gradually became dark. BnCl (0.247 mL, 2.15 mmol) was injected at a fast dropwise rate, and stirring was continued overnight. The mixture was diluted with EtOAc, water was added, and the aqueous phase was extracted with EtOAc. The combined organic extracts were dried ($MgSO_4$) and evaporated. Flash chromatography of the residue over silica gel (2 × 20 cm), using 97.5:2.5 CH_2Cl_2-MeOH, gave **25** (295 mg, 52%) as a thick, yellow oil, which slowly solidified: mp 94−96 °C; FTIR (CH_2Cl_2 cast film) 3059, 2946, 2872, 2227, 1628, 1559, 1186, 733 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.64 (d, J = 8.61 Hz, 2 H), 7.32−7.26 (m, 5 H), 7.18 (d, J = 7.14 Hz, 2 H), 5.43 (s, 1 H), 4.87 (s, 2 H), 2.38 (t. J = 5.04 Hz, 2 H), 2.32 (t, J = 6.96 Hz, 2 H), 1.9 (quint, J = 6.32 Hz, 2 H); ^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz) δ 197.7 (s), 163.4 (s), 148.5 (s), 135.8 (s), 133.5 (d), 128.9 (d), 128.0 (d), 127.8 (d), 126.6 (d), 118.0 (s), 110.5 (s), 104.4 (d), 56.3 (t), 36.2 (t), 28.7 (t), 22.6 (t); exact mass (ESI) m/z calcd for $C_{20}H_{18}N_2NaO$ (M + Na)$^+$ 325.1311, found 325.1312.

4-[Benzyl(2-chloro-3-oxocyclohex-1-en-1-yl)amino]-benzonitrile (25b). $NaHCO_3$ (84.0 mg, 1.00 mmol) and $BnNMe_3{\cdot}ICl_2$ (73.7 mg, 0.212 mmol) were tipped into a flask containing **25** (42.7 mg, 0.141 mmol) and a magnetic stir bar. The flask was closed with a septum, flushed with N_2, and kept under a static pressure of N_2. A 2:1 mixture of CH_2Cl_2 and MeOH (3 mL in total) was injected, and the mixture was stirred at room temperature for 3 h. At this stage, TLC (silica, 24:1 CH_2Cl_2-MeOH) showed the presence of only a trace of **25**. Even so, the mixture was filtered through a sintered disc and evaporated. Flash chromatography of the residue over silica gel (2 × 18 cm), using 99.5:0.5 CH_2Cl_2-MeOH, gave **25b** (38.8 mg, 82%) as a light brown solid: mp 48−50 °C; FTIR (liquid film) 3063, 2953, 2872, 2220, 1675, 1584, 1293, 1045, 734 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.54−7.52 (m, 2 H), 7.40−7.37 (m, 2 H), 7.34−7.27 (m, 3 H), 6.91−6.89 (m, 2 H), 5.02 (s, 2 H), 2.73 (t, J = 6.00 Hz, 2 H), 2.62 (t, J = 6.23 Hz, 2 H), 2.04 (quint, J = 6.41 Hz, 2 H); ^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz) δ 191.2 (s), 157.7 (s), 148.9 (s), 136.5 (s), 133.4 (d), 129.1 (d), 127.8 (d), 126.2 (d), 123.0 (s), 119.1 (s), 118.9 (d), 104.5 (s), 54.8 (t), 37.7 (t), 31.0 (t), 20.8 (t); exact mass (ESI) m/z calcd for $C_{20}H_{17}ClN_2NaO$ (M + H)$^+$ 359.0922, found 359.0919.

4-[Benzyl(3-hydroxyphenyl)amino]benzonitrile (25c). DBU (31.6 μL, 0.212 mmol) was injected at a fast dropwise rate into a stirred solution of **25b** (35.6 mg, 0.106 mmol) in dry MeCN (3 mL) (N_2 atmosphere), and stirring was continued for 24 h. Evaporation of the solvent and flash chromatography of the residue over silica gel (2 × 20 cm), using 99.5:0.5 CH_2Cl_2-MeOH, gave **25c** (19.8 mg, 62%) as a solid: mp 114−116 °C; FTIR (solid) 3336, 3032, 2880, 2221, 1592, 1510, 1376, 1201, 699 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.40−7.33 (m, 4 H), 7.31−7.26 (m, 4 H), 6.87 (dd, J = 7.97, 1.19 Hz, 1 H), 6.82−6.80 (m, 3 H), 6.75 (d, J = 8.08 Hz, 1 H), 5.35 (br s, 1 H), 5.00 (s, 2 H); ^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz) δ 157.1 (s), 151.2 (s), 147.4 (s), 137.4 (s), 133.3 (d), 130.9 (d), 128.8 (d), 127.3 (d), 126.3 (d), 120.1 (s), 118.3 (d), 115.0 (d), 113.29 (d), 113.25 (d), 99.8 (s), 56.3 (t); exact mass (ESI) m/z calcd for $C_{20}H_{16}N_2NaO$ (M + Na)$^+$ 323.1155, found 323.1159.

3-[(4-Bromophenyl)amino]cyclohex-2-en-1-one (26).[13] PhMe (20 mL) followed by AcOH (ca. 1 mL) was added to a flask containing cyclohexane-1,3-dione (1.04 g, 9.45 mmol) and 4-bromoaniline (1.62 g, 9.35 mmol), and the mixture was refluxed overnight under a Dean-Stark trap. The solution was cooled and evaporated, and flash chromatography of the residue over silica gel (3 × 15 cm), using 9:1 CH_2Cl_2-MeOH, gave **26** (2.19 g, 88%) as a yellow solid: mp 174−176 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.50−7.46 (m, 2 H), 7.09−7.05 (m, 2 H), 5.98 (br s, 1 H), 5.57 (s, 1 H), 2.51 (t, J = 6.20 Hz, 2 H), 2.39 (t, J = 6.82 Hz, 2 H), 2.07 (quint, J = 6.6 Hz, 2 H); ^{13}C{^{1}H} NMR ($CDCl_3$, 175 MHz) δ 198.1 (s), 161.1

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(s), 137.1 (s), 132.4 (d), 125.3 (d), 118.4 (s), 100.5 (d), 36.4 (t), 29.7 (t), 21.7 (t).

3-[(4-Bromophenyl)(methyl)amino]cyclohex-2-en-1-one (27).[35] Dry DMF (20 mL) was injected into a flask containing the enaminone **26** (0.90 g, 3.39 mmol) (N_2 atmosphere), and the stirred mixture was cooled in an ice bath. NaH (60% w/w dispersion in oil, 0.27 g, 6.75 mmol) was tipped into the resulting solution under a stream on N_2, the ice bath was removed, and stirring was continued for 2 h. MeI (0.53 mL, 8.51 mmol) was then injected dropwise over about 2 min, and stirring was continued overnight. The mixture was poured into water (250 mL) and extracted with EtOAc (4 × 50 mL). The combined organic extracts were washed with brine (2 × 25 mL), dried (Na_2SO_4), and evaporated. Flash chromatography of the residue over silica gel (2 × 15 cm), using 49:1 CH_2Cl_2-MeOH, gave **27** (0.52 g, 55%) as a beige solid.

4-Bromo-*N*-methylaniline.[55] Oven-dried K_2CO_3 (2.433 g, 17.61 mmol) was added to a solution of 4-$BrC_6H_4NH_2$ (2.00 g, 11.70 mmol) in dry THF (18 mL), then MeI (1.46 mL, 23.4 mmol) was injected, and the mixture was stirred overnight at room temperature. Examination of the mixture by TLC (silica, 5:95 EtOAc-hexane) showed 4-$BrC_6H_4NH_2$ and two new spots. The mixture was diluted with EtOAc and water, and the aqueous phase was extracted with EtOAc. The combined organic extracts were dried ($MgSO_4$) and evaporated. Flash chromatography of the residue over gel (2 × 22 cm), using 19:1 hexane-EtOAc, gave 4-bromo-*N*-methylaniline (419.9 mg, 19.4%) as a pale yellow liquid: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.30 (d, J = 8.15 Hz, 2 H), 6.51 (d, J = 8.97 Hz, 2 H), 3.71 (br s, 1 H), 2.83 (s, 3 H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz) δ 148.3 (d), 131.8 (d), 113.9 (d), 108.7 (s), 30.7 (q).

3-[(4-Bromophenyl)(methyl)amino]cyclohex-2-en-1-one (27).[35] 4-Bromo-*N*-methyl-aniline (419.9 mg, 2.269 mmol) was added to AcOH (7 mL) followed by cyclohexane-1,3-dione (254.4 mg, 2.269 mmol), and the mixture was stirred at 95 °C (N_2 atmosphere) for 6 h. The solvent was then evaporated at 40 °C, and the residue was dissolved in the minimum of CH_2Cl_2 and applied to the top of a chromatography column made up with silica gel (2 × 25 cm) and CH_2Cl_2. Flash chromatography, using 24:1 CH_2Cl_2-MeOH, gave **27** (546.9 mg, 86%) as a pinkish white solid: mp 162−164 °C; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.51−7.49 (m, 2 H), 7.03−6.98 (m, 2 H), 5.27 (s, 1 H), 3.18 (s, 3 H), 2.27 (t, J = 6.23 Hz, 2 H), 2.19 (t, J = 6.18 Hz, 2 H), 1.88 (quint, J = 6.41 Hz, 2 H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz) δ 197.5 (s), 164.4 (s), 144.3 (s), 132.8 (d), 128.8 (d), 120.9 (s), 101.2 (d), 40.6 (q), 36.0 (t), 28.4 (t), 22.4 (t).

3-[(4-Bromophenyl)(methyl)amino]-2-chlorocyclohex-2-en-1-one (27b). $BnNMe_3\cdot ICl_2$ (365.1 mg, 1.05 mmol) was tipped into a stirred solution of **27** (195.0 mg, 0.696 mmol) in a mixture of dry CH_2Cl_2 (8 mL) and dry MeOH (4 mL) followed immediately by $NaHCO_3$ (418.9 mg, 4.99 mmol), which was also added in one portion (N_2 atmosphere). Stirring was continued for 45 min, and the mixture was then filtered through a sintered disc. Evaporation of the filtrate and flash chromatography of the residue over silica gel (2 × 15 cm), using 1:1 hexane-EtOAc, gave **27b** (195.7 mg, 89%) as a yellow solid: FTIR ($CDCl_3$, cast film) 2956, 2924, 1651, 1542, 1488, 1322, 1266, 1187, 1007, 824 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.51−7.43 (m, 2 H), 6.96−6.88 (m, 2 H), 3.47 (s, 3 H), 2.59 (q, J = 6.6, 6.2 Hz, 4 H), 2.09−1.93 (m, 2 H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 176 MHz) δ 191.1 (s), 160.0 (s), 145.3 (s), 132.4 (d), 124.7 (d), 117.6 (s), 114.3 (s), 41.8 (q), 37.6 (t), 31.3 (t), 20.8 (t); exact mass (ESI) m/z calcd for $C_{13}H_{13}BrClNO$ $(M + Na)^+$ 335.9761, found 335.9761.

3-[(4-Bromophenyl)(methyl)amino]phenol (27c). DBU (62.5 μL, 0.419 mmol) was injected at a fast dropwise rate into a stirred solution of **27b** (65.5 mg, 0.209 mmol) in dry MeCN (3 mL) (N_2 atmosphere), and stirring was continued for 20 h. At this point, TLC (silica, 99:1 CH_2Cl_2-MeOH) showed two spots but no **27b**. Evaporation of the solvent and flash chromatography of the residue over silica gel (2 × 19.5 cm), using 99:1 CH_2Cl_2-MeOH, gave **27c** as two successive fractions with identical TLC R_f values and NMR spectra (42.7 mg, 74% in total) as viscous liquids: FTIR (CH_2Cl_2, cast film) 3371, 2882, 2814, 1583, 1489, 1348, 1127, 1008, 943, 814 cm^{-1}; ^{1}H NMR ($CDCl_3$, 700 MHz) δ 7.38−7.33 (m, 2 H), 7.11 (t, J = 8.1 Hz, 1 H), 6.93−6.88 (m, 2 H), 6.56 (ddd, J = 8.2, 2.2, 0.9 Hz, 1 H), 6.46 (t, J = 2.3 Hz, 1 H), 6.43 (ddd, J = 8.1, 2.4, 0.9 Hz, 1 H), 4.62 (s, 1 H), 3.25 (s, 3 H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 176 MHz) δ 156.4 (s), 150.1 (s), 147.8 (s), 132.1 (d), 130.2 (d), 122.6 (d), 114.1 (s), 112.7 (d), 108.5 (d), 107.1 (d), 40.2 (q); exact mass (ESI) m/z calcd for $C_{13}H_{12}BrNO$ $(M - H)^-$ 276.0030, found 276.0029.

4-Bromo-*N*-[(4-methoxyphenyl)methyl]aniline.[56] 4-$MeOC_6H_4CHO$ (0.71 mL, 5.84 mmol) was added dropwise to a stirred solution of 4-bromoaniline (1.198 g, 7.00 mmol) in anhydrous EtOH (30 mL). A pale greenish precipitate formed. $CeCl_3\cdot 7H_2O$ (44 mg, 0.12 mmol) was added, the reaction flask was stoppered, and stirring was continued for an arbitrary period of 3 h. At that stage, $NaBH_4$ (442 mg, 11.7 mmol) was added in one portion. Immediate bubbling was observed, the precipitate dissolved, and the mixture became light brown. Stirring was continued overnight with the flask open to the atmosphere. Evaporation of EtOH gave a residue, which was partitioned between EtOAc and water. The aqueous phase was washed twice with EtOAc, and the combined organic extracts were dried (Na_2SO_4) and evaporated. Flash chromatography of the residue over silica gel (2 × 15 cm), using first hexane (ca. 200 mL) and then 1:4 hexane-EtOAc, gave 4-bromo-*N*-[(4-methoxyphenyl)methyl]-aniline (1.59 g, 77%) as a white solid: mp 79−81 °C; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.32−7.25 (m, 2 H), 6.93−6.89 (m, 2 H), 6.54−6.51 (m, 2 H), 4.25 (s, 2 H), 4.03 (br s, 1 H), 3.83 (s, 3 H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 175 MHz) δ 159.0 (s), 146.8 (s), 131.9 (d), 130.6 (s), 128.7 (d), 114.5 (d), 114.0 (d), 109.2 (s), 55.2 (q), 47.8 (t).

3-[(4-Bromophenyl)[(4-methoxyphenyl)methyl]amino]-cyclohex-2-ene-1-one (28). *N*-[4-Methoxybenzyl]-4-bromoaniline (150 mg, 0.513 mmol) was added to AcOH (6 mL) followed by cyclohexane-1,3-dione (57.5 mg, 0.513 mmol), and the mixture was stirred at 95 °C (N_2 atmosphere) for 4 h (TLC monitoring, silica, EtOAc). The solvent was then evaporated at 40 °C, and the residue was dissolved in the minimum of EtOAc and applied to the top of a chromatography column made up with silica gel (2 × 15 cm) and hexane. Flash chromatography, using first hexane (ca 200 mL) and then 1:9 hexane-EtOAc, gave **28** (0.130 g, 65%) as a bright yellow solid: mp 89−91 °C; FTIR (CH_2Cl_2 cast film) 2946, 2834, 1623, 1556, 1186, 819 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.48 (d, J = 8.00 Hz, 2 H), 7.09 (d, J = 8.66 Hz, 2 H), 7.01−6.96 (m, 2 H), 6.84 (d, J = 7.97 Hz, 2 H), 5.43 (s, 1 H), 4.74 (s, 2 H), 3.80 (s, 3 H), 2.35−2.28 (m, 4 H), 1.98−1.91 (m, 2 H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz) δ 197.7 (s), 164.5 (s), 159.1 (s), 143.2 (s), 132.8 (d), 129.6 (d), 128.5 (d), 127.9 (s), 121.2 (s), 114.2 (d), 101.9 (d), 55.9 (t), 55.3 (q), 36.0 (t), 28.6 (t), 22.4 (t); exact mass (ESI) m/z calcd for $C_{20}H_{21}BrNNaO_2$ $(M + Na)^+$408.0570, found 408.0571.0749.

3-[(4-Bromophenyl)[(4-methoxyphenyl)methyl]amino]-2-chlorocyclohex-2-en-1-one (28b). $BnNMe_3\cdot ICl_2$ (216.2 mg, 0.621 mmol) was tipped into a stirred solution of **28** (197.1 mg, 0.510 mmol) in a mixture of dry CH_2Cl_2 (8 mL) and dry MeOH (2 mL) followed immediately by $NaHCO_3$ (306.2 mg, 3.64 mmol), which was also added in one portion (N_2 atmosphere). Stirring was continued for 1 h, and the mixture was then filtered through a sintered disc. Evaporation of the filtrate and flash chromatography of the residue over silica gel (2 × 15 cm), using 1:1 hexane-EtOAc, gave **28b** (157.0 mg, 73%) as a solid: mp 134−136 °C; FTIR (CH_2Cl_2, cast film) 2954, 2835, 2244, 1655, 1574, 1487, 1248, 1184, 1006, 731 cm^{-1}; ^{1}H NMR ($CDCl_3$, 700 MHz) δ 7.34 (d, J = 8.4 Hz, 2 H), 7.15 (d, J = 8.2 Hz, 2 H), 6.84 (t, J = 7.6 Hz, 4 H), 4.97 (s, 2 H), 3.77 (s, 3 H), 2.62 (t, J = 6.0 Hz, 2 H), 2.50 (t, J = 6.5 Hz, 2 H), 1.89 (quint, J = 6.2 Hz, 2 H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 176 MHz) δ 191.1 (s), 159.0 (s), 158.9 (s), 145.3 (s), 132.1 (d), 129.1 (s), 127.6 (d), 124.3 (d), 117.0 (s), 115.9 (s), 114.3 (d), 55.9 (t), 55.3 (q), 37.5 (t), 31.3 (t), 20.7 (t); exact mass (ESI) m/z calcd for $C_{20}H_{19}BrClNO_2$ $(M + Na)^+$ 442.0180, found 442.0181.

3-[(4-Bromophenyl)[(4-methoxyphenyl)methyl]amino]-phenol (28c). DBU (93 μL, 0.62 mmol) was injected at a fast dropwise rate into a stirred solution of **28b** (131.1 mg, 0.311 mmol) and LiCl (27 mg, 0.64 mmol) in dry MeCN (3 mL) (N_2 atmosphere), and stirring was continued for 48 h. Evaporation of

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the solvent and flash chromatography of the residue over silica gel (1 × 10 cm), using 1:1 hexane-EtOAc, gave **28c** (101.7 mg, 84%) as a purplish oil: FTIR (CH_2Cl_2, cast film) 3399, 2999, 2953, 2933, 2835, 1610, 1584, 1489, 1245, 819 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 7.34−7.28 (m, 2 H), 7.23−7.17 (m, 2 H), 7.09 (t, J = 8.1 Hz, 1 H), 6.97−6.90 (m, 2 H), 6.87−6.81 (m, 2 H), 6.63 (dd, J = 8.2, 2.2 Hz, 1 H), 6.52 (t, J = 2.3 Hz, 1 H), 6.43 (dd, J = 8.0, 2.4 Hz, 1 H), 4.92 (s, 1 H), 4.87 (s, 2 H), 3.78 (s, 3 H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 176 MHz) δ 158.6 (s), 156.5 (s), 149.3 (s), 146.8 (s), 132.1 (d), 130.4 (s), 130.3 (d), 127.6 (d), 122.6 (d), 114.1 (d), 113.9 (s), 113.2 (d), 108.8 (d), 107.7 (d), 55.6 (t), 55.3 (q); exact mass (ESI) m/z calcd for $C_{20}H_{18}BrNO_2$ (M − H)$^-$ 382.0448, found 382.045.

3-(Diphenylamino)cyclohex-2-en-1-one (29).[13] Diphenylamine (0.507 g, 3.00 mmol) was added to AcOH (6 mL) followed by cyclohexane-1,3-dione (0.336 g, 3.00 mmol), and the mixture was stirred at 96 °C (N_2 atmosphere) for 52 h (TLC monitoring, silica, EtOAc). Although the reaction was still not complete (TLC), the solvent was evaporated at 40 °C and the residue was dissolved in the minimum of EtOAc and applied to the top of a chromatography column made up with silica gel (2 × 15 cm) and hexane. Flash chromatography, using first hexane (ca. 200 mL), then 1:1 hexane-EtOAc, and finally pure EtOAc, gave **29** (0.573 g, 72%) as a cream-colored solid: mp 156−158 °C; ^1H NMR ($CDCl_3$, 500 MHz) δ 7.40−7.35 (m, 4 H), 7.29−7.24 (m, 2 H), 7.22−7.19 (m, 4 H), 5.32 (s, 1 H), 2.42 (t, J = 6.13 Hz, 2 H), 2.37 (t, J = 6.5 Hz, 2 H), 2.01 (quint, J = 6.34 Hz, 2 H);$^{13}C\{^1H\}$ NMR ($CDCl_3$, 175 MHz) δ 198.0 (s), 165.2 (s), 144.0 (s), 129.6 (d), 127.8 (d), 126.9 (d), 105.7 (d), 36.4 (t), 29.1 (t), 22.8 (t).

2-Chloro-3-(diphenylamino)cyclohex-2-en-1-one (29b). $NaHCO_3$ (210 mg, 2.50 mmol) and $BnNMe_3{\cdot}ICl_2$ (188 mg, 0.541 mmol) were tipped into a flask containing **29** (95 mg, 0.36 mmol) and a magnetic stir bar. The flask was closed with a septum, flushed with N_2, and kept under a static pressure of N_2. A 2:1 mixture of CH_2Cl_2 and MeOH (4.5 mL in total) was injected, and the mixture was stirred at room temperature for an arbitrary period of 15 h. At this stage, TLC (silica, 24:1 CH_2Cl_2-MeOH) showed no **29**. The mixture was filtered through a sintered disc and evaporated. Flash chromatography of the residue over silica gel (2 × 24 cm), using first 17:3 hexane-EtOAc (ca. 200 mL), then 3:1 hexane-EtOAc (ca 200 mL), and finally 1:1 hexane-EtOAc, gave **29b** (51.8 mg, 48%) as a pale green solid, the corresponding iodide (**29b′**) (18 mg, 12%) as a pale brown solid and the corresponding 4-iodo enaminone (**29b″**) (33 mg, 31%) as a brown solid. Compound **29b**: mp 139−141 °C; FTIR (CH_2Cl_2 cast film) 3062, 2951, 2867, 1663, 1557, 1263, 1009, 756 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 7.31−7.36 (m, 4 H), 7.18 (t, J = 8.70 Hz, 2 H), 7.05−7.01 (m, 4 H), 2.66−2.61 (m, 4 H), 2.01 (quint, J = 6.96 Hz, 2 H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz) δ 191.5 (s), 158.2 (s), 145.2 (s), 129.3 (d), 125.3 (d), 125.2 (d), 118.5 (s), 38.1 (t), 32.4 (t), 21.2 (t); exact mass (ESI) m/z calcd for $C_{18}H_{16}ClNNaO$ (M + Na)$^+$ 320.0813, found 320.0812.

The reaction was repeated in the dark, but again all three products were formed (TLC monitoring).

3-(Diphenylamino)-2-iodocyclohex-2-en-1-one (29b′).[37] 3-(Diphenylamino)-2-iodocyclohex-2-en-1-one (**29b′**): mp 113−115 °C; FTIR (CH_2Cl_2 cast film) 3061, 2948, 2865, 1658, 1586, 1544, 1252, 754, 693 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 7.37−7.32 (m, 4 H), 7.17 (t, J = 7.45 Hz, 2 H), 7.06−7.02 (m, 4 H), 2.73 (t, J = 7.14 Hz, 2 H), 2.61 (t, J = 6.00 Hz, 2 H), 2.03−1.97 (m, 2 H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz) δ 193.3 (s), 166.9 (s), 145.0 (s), 129.4 (d), 125.4 (d), 124.9 (d), 95.5 (s), 37.0 (t), 34.0 (t), 21.7 (t); exact mass (ESI) m/z calcd for $C_{18}H_{16}INNaO$ (M + Na)$^+$ 412.0169, found 412.0169.

3-(Diphenylamino)-4-iodocyclohex-2-en-1-one (29b″). 3-(Diphenylamino)-4-iodocyclohex-2-en-1-one (**29b″**): mp 120−122 °C; FTIR (CH_2Cl_2 cast film) 3021, 2919, 2897, 1616, 1584, 1561, 1274, 758 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 7.42−7.35 (m, 4 H), 7.30−7.25 (m, 2 H), 7.19 (br d, J = 7.51 Hz, 4 H), 5.52 (s, 1 H), 5.22 (t, J = 3.20 Hz, 1 H), 2.62−2.44 (m, 2 H), 2.28 (ddt, J = 14.89, 4.98, 2.52 Hz, 1 H), 1.97 (ddt, J = 14.82, 12.81, 4.18 Hz, 1 H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz) δ 196.6 (s), 164.1 (s), 144.0 (s), 129.7 (d), 126.8 (d), 126.6 (d), 109.9 (d), 35.5 (t), 31.9 (t), 25.0 (d); low-resolution mass (ESI) m/z calcd for $C_{18}H_{16}INaO$ (M + Na)$^+$ 412.0169, found 412.0. The location of the iodine at C(4) was established by a 1D ROESY experiment, which showed that the *ortho* aromatic hydrogens are close to the C(4) hydrogen.

3-(Diphenylamino)phenol (29c).[37] DBU (16.6 μL, 0.111 mmol) was injected at a fast dropwise rate into a stirred solution of **29b** (16.5 mg, 0.055 mmol) in dry MeCN (3 mL) (N_2 atmosphere), and stirring was continued for 24 h. Evaporation of the solvent and flash chromatography of the residue over silica gel (2 × 24 cm), using 99:1 CH_2Cl_2-MeOH, gave **29c** (11.4 mg, 79%) as a white solid: mp 110−112 °C; FTIR (CH_2Cl_2 cast film) 3523, 3035, 2923, 2849, 1589, 1492, 1275, 1148, 754, 697 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 7.31−7.26 (m, 4 H), 7.14−7.09 (m, 5 H), 7.05 (t, J = 7.23 Hz, 2 H), 6.66 (ddd, J = 8.13, 2.04, 0.73 Hz, 1 H), 6.55 (t, J = 2.24 Hz, 1 H), 6.49 (ddd, J = 8.03, 2.45, 0.78 Hz, 1 H), 4.63 (br s, 1 H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 155.8 (s), 148.9 (s), 147.2 (s), 129.6 (d), 128.8 (d), 124.2 (d), 122.6 (d), 115.6 (d), 109.9 (d), 108.9 (d); exact mass (EI) m/z calcd for $C_{18}H_{14}NO$ (M − H)$^-$ 260.1081, found 260.1079.

The corresponding 2-iodo enaminone (**29b′**), when subjected to the same conditions, afforded **29c** in 42% yield, and the 4-iodo enaminone (**29b″**) gave **29c** in 54% yield.

3-[Benzyl(methyl)amino]cyclohex-2-en-1-one (30). *N*-Methylbenzylamine (3.1 mL, 4.32 g, 35.7 mmol) was added to a solution of cyclohexane-1,3-dione (4.03 g, 35.9 mmol) in PhMe (100 mL), and the mixture was refluxed for 5 h under a Dean-Stark trap. The resulting dark red solution was cooled and evaporated, and flash chromatography of the residue over silica gel (5 × 15 cm), using first 1:1 CH_2Cl_2-EtOAc and then pure MeOH, gave **30** (from the MeOH fractions) (6.61 g, 96%) as a dark orange oil that solidified at room temperature: mp 65−67 °C; FTIR ($CDCl_3$, cast film) 3028, 2942, 1620, 1585, 1555, 1452, 1263, 1190, 938, 736 cm^{-1}; ^1H NMR ($CDCl_3$, 700 MHz) δ 7.35 (t, J = 7.6 Hz, 2 H), 7.28 (t, J = 7.4 Hz, 1 H), 7.10 (d, J = 7.6 Hz, 2 H), 5.27 (s, 1 H), 4.51 (s, 2 H), 2.96 (s, 3 H), 2.49 (t, J = 6.2 Hz, 2 H), 2.30 (dd, J = 7.2, 5.9 Hz, 2 H), 1.98 (quint, J = 6.4 Hz, 2 H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 176 MHz) δ 197.0 (s), 165.4 (s), 129.0 (d), 127.6 (d), 99.4 (d), 55.1 (t), 38.4 (q), 35.6 (t), 26.8 (t), 22.3 (t); exact mass (ESI) m/z calcd for $C_{14}H_{17}NO$ (M + H)$^+$ 216.1383, 216.1381.

3-[Benzyl(methyl)amino]-2-chlorocyclohex-2-en-1-one (30b). $NaHCO_3$ (606.8 mg, 7.224 mmol) and $BnNMe_3{\cdot}ICl_2$ (538.7 mg, 1.548 mmol) were tipped into a flask containing **30** (222.2 mg, 1.032 mmol) and a magnetic stir bar. The flask was closed with a septum, flushed with N_2, and kept under a static pressure of N_2. A 2:1 mixture of CH_2Cl_2 and MeOH (6 mL in total) was injected, and the mixture was stirred at room temperature for 75 min. At this stage, TLC (silica, 24:1 CH_2Cl_2-MeOH) showed no **30**. The mixture was filtered through a sintered disc and evaporated. Flash chromatography of the residue over silica gel (2 × 25 cm), using 99:1 CH_2Cl_2-MeOH, gave **30b** (239.2 mg, 94%) as a thick, dark brown oil: FTIR ($CDCl_3$, cast film) 3060, 2943, 1640, 1541, 1495, 1354, 1323, 1289, 1068, 734 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 7.46−7.37 (m, 2 H), 7.36−7.30 (m, 1 H), 7.28−7.22 (m, 2 H), 4.71 (s, 2 H), 3.17 (s, 3 H), 2.67 (t, J = 6.1 Hz, 2 H), 2.55−2.49 (m, 2 H), 1.99−1.90 (m, 2 H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 126 MHz) δ 190.4 (s), 162.3 (s), 136.8 (s), 128.9 (d), 127.7 (d), 126.7 (d), 106.1 (s), 57.4 (t), 41.6 (q), 37.1 (t), 31.0 (t), 20.4 (t); exact mass (ESI) m/z calcd for $C_{14}H_{16}ClNO$ (M + Na)$^+$ 272.0813, found 272.0812.

3-[Benzyl(methyl)amino]phenol (30c).[57] The following experiment was run at a higher concentration than normally used; under the standard conditions, the yield was lower (36%) after a reaction time of 42 h. DBU (0.2247 mL, 1.503 mmol) was injected at a fast dropwise rate into a stirred solution of **30b** (187.3 mg, 0.7519 mmol) in dry MeCN (3 mL) (N_2 atmosphere), and stirring was continued for 42 h, at which point only a trace of **30b** remained (TLC, silica, CH_2Cl_2). Evaporation of the solvent and flash chromatography of the residue over silica gel (2 × 23 cm), using 99.5:0.5 CH_2Cl_2-MeOH, gave **30c** (106.3 mg, 66%) as a pale yellow liquid containing some impurities (^1H NMR). Rechromatography over silica gel (1 × 20 cm),

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using 19:1 hexane-EtOAc, gave **30c** (94.7 mg, 59%) as a yellow oil: FTIR (CH_2Cl_2 cast film) 3374, 3061, 2924, 1618, 1578, 1239, 1169 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.36−7.32 (m, 2 H), 7.30−7.22 (m, 3 H), 7.10 (t, J = 8.15 Hz, 1 H), 6.38 (dd, J = 8.33, 1.92 Hz, 1 H), 6.26 (t, J = 2.33 Hz, 1 H), 6.22 (ddd, J = 7.92, 2.33, 0.64 Hz, 1 H), 4.80 (br s, 1 H), 4.55 (s, 2 H), 3.03 (s, 3 H); ^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz) δ 156.6 (s), 151.4 (s), 138.8 (s), 130.1 (d), 128.61 (d), 126.9 (d), 126.7 (d), 105.3 (d), 103.5 (d), 99.4 (d), 56.5 (t), 38.6 (q); exact mass (ESI) m/z calcd for $C_{14}H_{14}NO$ (M − H)$^-$ 212.1081, found 212.1081.

3-(Dibenzylamino)cyclohex-2-en-1-one (31). Bn_2NH (0.529 mL, 2.76 mmol) was added to AcOH (8 mL) followed by cyclohexane-1,3-dione (309 mg, 2.75 mmol), and the mixture was stirred overnight at 92 °C (N_2 atmosphere) (TLC monitoring, silica, EtOAc after 6 h had shown the presence of both reactants). The solvent was evaporated at 40 °C, and the residue was dissolved in the minimum of $CHCl_3$ and applied to the top of a chromatography column made up with silica gel (2 × 21 cm) and hexane. Flash chromatography, using first hexane (ca. 200 mL), then 1:1 hexane-EtOAc (ca 200 mL), and finally 9:1 hexane-EtOAc, gave **31** (515 mg, 64%) as a yellowish-red viscous liquid: FTIR (CH_2Cl_2 cast film) 3061, 2945, 2878, 1622, 1556, 1187, 734 cm exact mass (ESI) m/z calcd for $C_{20}H_{21}NNaO$ (M + Na)$^+$ 314.1515, found 314.1515.

2-Chloro-3-(dibenzylamino)cyclohex-2-en-1-one (31b). $NaHCO_3$ (103 mg, 1.23 mmol) and $BnNMe_3{\cdot}ICl_2$ (73.7 mg, 0.212 mmol) were tipped into a flask containing **31** (51.5 mg, 0.177 mmol) and a magnetic stir bar. The flask was closed with a septum, flushed with N_2, and kept under a static pressure of N_2. A 2:1 mixture of CH_2Cl_2 and MeOH (4.5 mL in total) was injected, and the mixture was stirred at room temperature for 3 h. At this stage, TLC (silica, 49:1 CH_2Cl_2-MeOH) showed the presence of **31** and so more $BnNMe_3{\cdot}ICl_2$ (37 mg, 0.11 mmol) was tipped into the reaction flask. After an additional stirring period of 20 min, all **31** had been consumed. The mixture was filtered through a sintered disc and evaporated. Flash chromatography of the residue over silica gel (2 × 22 cm), using first CH_2Cl_2 to elute a red fraction, and then 49:1 CH_2Cl_2-MeOH, gave **31b** (51.4 mg, 90%) as a yellow oil: FTIR (CH_2Cl_2 cast film) 3028, 2949, 1647, 1539, 1277, 1190, 960, 698 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.40−7.35 (m, 2 H), 7.34−7.29 (m, 2 H), 7.23 (d, J = 7.26 Hz, 4 H), 4.68 (s, 4 H), 2.67 (t, J = 6.13 Hz, 2 H), 2.53 (t, J = 6.87 Hz, 2 H), 1.88 (quint, J = 6.5 Hz, 2 H); ^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz) δ 190.7 (s), 162.7 (s), 137.1 (s), 128.9 (d), 127.6 (d), 127.0 (d), 108.7 (s), 55.1 (t), 37.2 (t), 31.2 (t), 20.5 (t); exact mass (ESI) m/z calcd for $C_{20}H_{20}ClNNaO$ (M + Na)$^+$ 348.1126, found 348.1122.

3-(Dibenzylamino)phenol (31c).[58] DBU (47.2 μL, 0.316 mmol) was injected at a fast dropwise rate into a stirred solution of **31b** (51.4 mg, 0.158 mmol) in dry MeCN (3 mL) (N_2 atmosphere), and stirring was continued for 24 h. Evaporation of the solvent and flash chromatography of the residue over silica gel (2 × 23 cm), using 99:1 CH_2Cl_2-MeOH, gave **31c** (32.8 mg, 72%) as a clear, viscous liquid: FTIR (liquid film) 3520, 3403, 3027, 2906, 2866, 1617, 1580, 1504, 1169, 735 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.40−7.33 (m, 4 H), 7.32−7.28 (m, 5 H), 7.06 (t, J = 8.10 Hz, 1 H), 6.39 (dd, J = 8.29, 1.97 Hz, 1 H), 6.24 (t, J = 2.29 Hz, 1 H), 6.22 (dd, J = 7.92, 1.69 Hz, 1 H), 4.67 (s, 4 H), 4.61 (s, 1 H); ^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz) δ 156.6 (s), 150.8 (s), 138.4 (s), 130.2 (d), 128.7 (d), 126.9 (d), 126.6 (d), 105.4 (d), 103.8 (d), 99.5 (d), 54.1 (t); exact mass (EI) m/z calcd for $C_{20}H_{18}NO$ (M − H)$^-$ 288.1394, found 288.1393.

3-(Piperidin-1-yl)cyclohex-2-en-1-one (32).[17] Piperidine (1.548 mL, 15.68 mmol) was added to a solution of cyclohexane-1,3-dione (1.00 g, 8.92 mmol) in PhMe (12 mL), and the mixture was refluxed for 24 h under a Dean-Stark trap. The resulting dark red solution was cooled and evaporated. Flash chromatography of the residue over silica gel (2.5 × 22 cm), using first CH_2Cl_2 and then 49:1 CH_2Cl_2-MeOH, gave **32** (1.269 g, 80%) as a red oil: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 5.22 (s, 1 H), 3.49−3.22 (m, 4 H), 2.35 (t, J = 6.23 Hz, 2 H), 2.21 (dd, J = 7.10, 6.00 Hz, 2 H), 1.92 (quint, J = 0.37 Hz, 2 H), 1.63−1.59 (m, 2 H), 1.55−1.50 (m, 4 H); ^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz) δ 197.0 (s), 164.5 (s), 99.2 (d), 47.5 (t), 35.5 (t), 26.9 (t), 25.4 (t), 24.2 (t), 22.2 (t).

2-Chloro-3-(piperidin-1-yl)cyclohex-2-en-1-one (32b). $NaHCO_3$ (840 mg, 10.0 mmol) and $BnNMe_3{\cdot}ICl_2$ (643 mg, 1.85 mmol) were tipped into a flask containing **32** (276 mg, 1.54 mmol) and a magnetic stir bar. The flask was closed with a septum, flushed with N_2, and kept under a static pressure of N_2. A 2:1 mixture of CH_2Cl_2 and MeOH (4.5 mL in total) was injected, and the mixture was stirred at room temperature for 3 h. The mixture was filtered through a sintered disc and evaporated. Flash chromatography of the residue over silica gel (2 × 26 cm), using first CH_2Cl_2 to elute a red fraction, and then 49:1 CH_2Cl_2-MeOH, gave **32b** (263 mg, 80%) as an oil that slowly changed to a dark brown semi-solid: FTIR (CH_2Cl_2 cast film) 2936, 2857, 1640, 1542, 1289, 1187, 970, 778 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 3.51 (br s, 4 H), 2.60 (t, J = 6.20 Hz, 2 H), 2.48 (t, J = 6.60 Hz, 2 H), 1.94 (quint, J = 6.68 Hz, 2 H), 1.68 (br s, 6 H); ^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz) δ 189.7 (s), 162.6 (s), 105.9 (s), 50.7 (t), 36.8 (t), 30.3 (t), 26.5 (t), 24.1 (t), 20.4 (t); exact mass (ESI) m/z calcd for $C_{11}H_{16}ClNNaO$ (M + Na)$^+$ 236.0813, found 236.0813.

3-(Piperidine-1-yl)phenol (32c).[49] DBU (0.30 mL, 1.10 mmol) was injected at a fast dropwise rate into a stirred solution of **32b** (117.6 mg, 0.550 mmol) in dry MeCN (3 mL) (N_2 atmosphere), and stirring was continued for 24 h. Evaporation of the solvent and flash chromatography of the residue over silica gel (2 × 21 cm), using 4:1 hexane-EtOAc, gave **32c** (56.1 mg, 58%) as a beige solid: mp 122−124 °C; FTIR (CH_2Cl_2 cast film) 3064, 2938, 2857, 1596, 1446, 1242, 1134, 765 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.11 (t, J = 8.10 Hz, 1 H), 6.55 (dd, J = 8.24, 1.92 Hz, 1 H), 6.40 (d, J = 2.01 Hz, 1 H), 6.31 (ddd, J = 7.97, 2.29, 0.82 Hz, 1 H), 5.32 (br s, 1 H), 3.16−3.13 (m, 4 H), 1.74−1.69 (m, 4 H), 1.62−1.57 (m, 2 H); ^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz) δ 156.5 (s), 153.5 (s), 129.9 (d), 109.1 (d), 106.4 (d), 103.7 (d), 50.5 (t), 25.6 (t), 24.3 (t); exact mass (ESI) m/z calcd for $C_{11}H_{14}NO$ (M − H)$^-$ 176.1081, found 176.1080.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.joc.0c02284.

NMR spectra for compounds in this study (PDF)
X-ray data for compound (**i**) (PDF)
X-ray data for compound **34** (PDF)

Accession Codes

CCDC 2043613−2043614 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

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Notes

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