ChemInform Abstract: Metal-Free Ring Expansion of Indoles with Nitroalkenes: A Simple, Modular Approach to 3-Substituted 2-Quinolones.

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Metal-free ring expansion of indoles with nitroalkenes: a simple, modular approach to 3-substituted 2-quinolones†

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3-Substituted 2-quinolones are obtained *via* a novel metal-free transannulation reaction of 2-nitroolefins with 2-substituted indoles in polyphosphoric acid. This acid-mediated cascade transformation operates *via* the ANRORC (Addition of Nucleophile, Ring Opening, and Ring Closure) mechanism and can be used in combination with the Fisher indole synthesis to offer a practical three-component hetero-annulation approach to 2-quinolones from arylhydrazines, 2-nitroalkenes, and acetophenone. An alternative entry to this chemistry employing the alkylation of electron-rich arenes and hetarenes with 1-(2-indolyl)-2-nitroalkene has also been demonstrated.

Introduction

3-Substituted 2-quinolones are attractive targets for medicinal chemistry[1–3] and important tools for material science.[4–6] (Fig. 1) shows a brief analysis of general approaches to 2-quinolones that include Vilsmeier–Haack (a),[3d,7] Knorr (b),[8] and Friedlander reactions (c).[9] Along with transition metal-catalyzed versions of the above methods,[10] and the recently emerged carbonylative cross-coupling reactions (d and f)[11] and RCM (e),[12] the cumulative prior art provides access to a wide variety of C3- and/or C4-substituted 2-quinolones. The two classical methods, Vilsmeier–Haack and Knorr, offer the advantage of employing readily available mono-substituted aromatic starting materials, whereas other described methods rely on availability of the more advanced *ortho*-disubstituted aromatic synthons.

In contrast, approaches to 4-unsubstituted analogs are much less developed. Thus, general routes (a–c) provide poor results in reactions involving aldehydes or formamide derivatives ($R^3 = H$). Du and Zhao disclosed an elegant metal-free approach to 3-aryl-2-quinolones (g) involving an iodine(III)-mediated cyclization with a 1,2-aryl shift, to produce 4-unsubstituted products.[13] Recently, we communicated a new approach to a range of 3-aryl- and 3-alkylsubstituted 2-quinolones *via* a metal-free condensation reaction of readily available 2-substituted indoles with β-nitroalkenes proceeding *via* an ANRORC (Addition of Nucleophile, Ring Opening, and Ring Closure) pathway in polyphosphoric acid (PPA).[14] We have also probed a one-pot preparation of 2-quinolones from arylhydrazines by merging this new methodology with Fisher indole synthesis. Herein we disclose a full account on this unusual transformation.

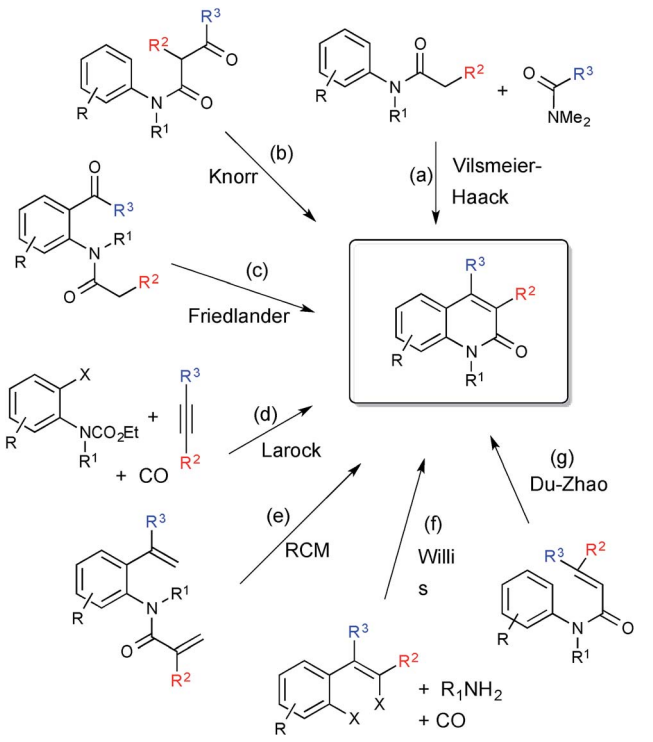

Fig. 1 General approaches to 2-quinolone scaffolds.

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† Electronic supplementary information (ESI) available: ^{1}H, ^{13}C NMR and HRMS spectral charts for all new compounds. See DOI: 10.1039/c4ra14406f

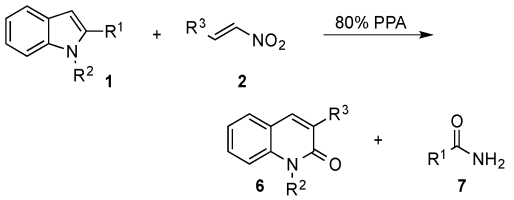
Results and discussion

Reaction of indoles with nitroalkenes

Our studies of the reactivity of nitro compounds with arenes in polyphosphoric acid[15] have brought us to the serendipitous discovery of an unusual transannulation reaction of hydroxamic acid **3**, formed upon electrophilic alkylation of indoles **1** with nitroolefins **2** (Scheme 1).[14] Instead of the anticipated acid-assisted ring-opening of indole leading to 2(1*H*)-3,4-dihydroquinolinone **5**, the test reaction between 2-phenylindole (**1b**) and β-nitrostyrene (**2a**) produced 3-phenyl-2-quinolone (**6aa**) lacking an acyl substituent at C4. Evidently, after a facile 5 → 6 ring expansion, the reaction took an unexpected turn: the R^1 substituent of the indole together with the adjacent carbon atom (C2) was sacrificed to produce benzamide **7b** as a byproduct, together with quinolone **6aa** isolated in high yield (Table 1, entry 2).

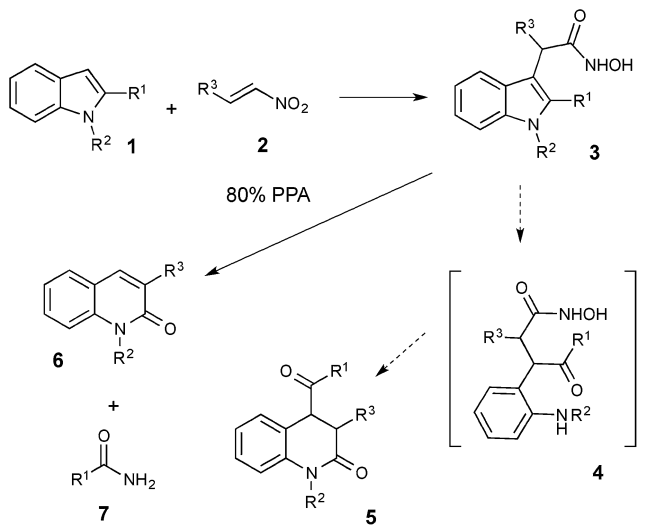
Subsequent optimization of the reaction conditions revealed that best results are produced upon heating a mixture of the 2-substituted indole (**1**) and the nitroalkene (**2**) in 80% PPA (a composition corresponding to diphosphoric acid, $H_4P_2O_7$) at 80–85 °C for 30 min and then at 95–100 °C for additional 2.5–3 h. iso-Skatole (**1a**) has been identified as a more practical model substrate because it provides comparable yields of 2-quinolones (Table 1, compare entries 1–2, 3–4, 14–15, 16–17, 18–19, 20–21), but gives acetamide **7a** as a byproduct, which is easily removable by routine aqueous workup. Systematic screening of various nitroolefins (Table 1) showed that electron-donating (entries 3–8) or weak electron-withdrawing groups (entries 9–13) on nitrostyrenes improve product yield. The reaction appeared to be very sensitive to sterics at the *ortho*-position of the nitrostyrenes: both 2-methyl- (**1a**) and 2-phenylindoles (**1b**) afforded low yield (entries 14–17) or no product at all (entries 18 and 19) with nitroalkenes bearing an *ortho*-substituent (**2l–o**). Aliphatic nitroolefin **2p** reacted uneventfully with both model indoles (entries 20 and 21). Employment of nitroethene (**2q**) gave poor yields of products **6aq** and **6cq** lacking substituents at C3 (entries 22–24). This can be attributed to the reduced stability of **2q** at elevated temperatures. Very different results were obtained in reactions of nitrostyrenes **2a** and **i** with *N*-substituted indoles **1c–e**, which upon exposure to standard reaction conditions exclusively produced the corresponding hydroxamic acids **3** (entries 26–28; yields are shown in parentheses). Attempts to force transannulation by increasing the reaction temperature to 130 °C resulted in good yields of products **6ca** and **6ci** starting from 1,2-dimethylindole (**1c**) (entries 25 and 26). However, high temperature reactions of indoles **1d** and **1e**, bearing a bulky substituent at nitrogen atom or at C2, resulted in substantial decomposition and poor yields of quinolones **6ca** and **6ea** (entries 27 and 28).

Table 1 Reactions of 2-substituted indoles with 2-nitroalkenes in PPA



	1	R^1	R^2	2	R^3	6	Yield[a], %
1	**1a**	Me	H	**2a**	Ph	**6aa**	90
2	**1b**	Ph	H	**2a**	Ph	**6aa**	92
3	**1a**	Me	H	**2b**	4-$MeOC_6H_4$	**6ab**	70
4	**1b**	Ph	H	**2b**	4-$MeOC_6H_4$	**6ab**	74
5	**1a**	Me	H	**2c**	4-i-PrC_6H_4	**6ac**	89
6	**1a**	Me	H	**2d**	3,4-$Me_2C_6H_3$	**6ad**	88
7	**1a**	Me	H	**2e**	3,4-$(MeO)_2C_6H_3$	**6ae**	78
8	**1a**	Me	H	**2f**	4-$EtOC_6H_4$	**6af**	79
9	**1a**	Me	H	**2g**	2-FC_6H_4	**6ag**	68
10	**1a**	Me	H	**2h**	3-FC_6H_4	**6ah**	66
11	**1a**	Me	H	**2i**	4-FC_6H_4	**6ai**	72
12	**1a**	Me	H	**2j**	3,4-$Cl_2C_6H_3$	**6aj**	88
13	**1a**	Me	H	**2k**	3-BrC_6H_4	**6ak**	67
14	**1a**	Me	H	**2l**	2-C_5H_4N	**6al**	49
15	**1b**	Ph	H	**2l**	2-C_5H_4N	**6al**	46
16	**1a**	Me	H	**2m**	2-$NO_2C_6H_4$	**6am**	36
17	**1b**	Ph	H	**2m**	2-$NO_2C_6H_4$	**6am**	35
18	**1a**	Me	H	**2n**	2-BrC_6H_4	**6an**	NR
19	**1a**	Me	H	**2o**	2,3-$(MeO)_2C_6H_3$	**6ao**	NR
20	**1a**	Me	H	**2p**	*n*-Pr	**6ap**	63
21	**1b**	Ph	H	**2p**	*n*-Pr	**6ap**	62
22	**1a**	Me	H	**2q**	H	**6aq**	29
23	**1c**	Me	Me	**2q**	H	**6cq**	27
24	**1d**	Ph	Me	**2q**	H	**6cq**	11
25	**1c**	Me	Me	**2a**	Ph	**6ca**	84[b]
26	**1c**	Me	Me	**2i**	4-FC_6H_4	**6ci**	74 (92)[b]
27	**1e**	Me	*n*-Bu	**2a**	Ph	**6ea**	24 (89)[b]
28	**1d**	Ph	Me	**2a**	Ph	**6ca**	3 (94)[b]

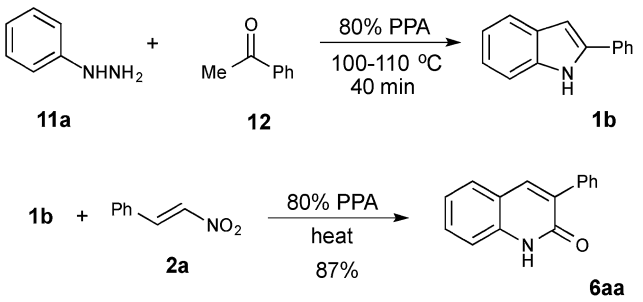
[a] Isolated yields of purified 2-quinolones. [b] Hydroxamic acids were obtained as sole products under standard conditions. Their isolated yields are provided in parentheses. Indicated yields of 2-quinolones were obtained under forcing reaction conditions at 130 °C.



Scheme 1

Three-component coupling involving Fisher indole synthesis

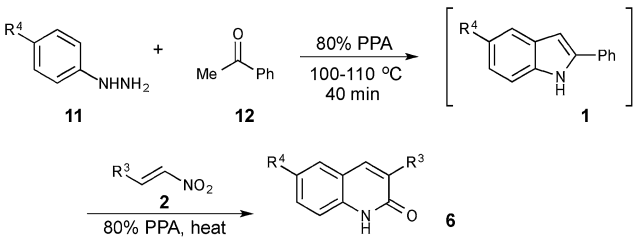
We envisioned a practical extension of this methodology in directly accessing the quinolines from easily available



Scheme 2

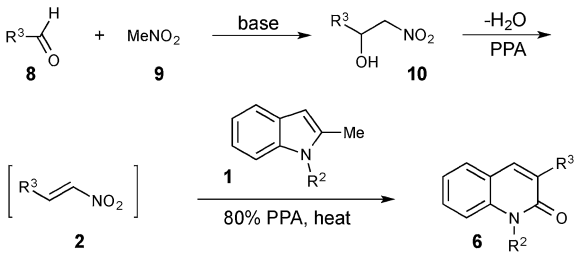
hydrazines by merging the Fisher indole synthesis[16] with the above-described methodology in a one-pot transformation.[17] The Fisher indole synthesis is known to proceed efficiently at elevated temperatures in orthophosphoric acid, so we anticipated 80% PPA (diphosphoric acid) to serve as a suitable medium for this reaction. Indeed, in our test experiment, a mixture of phenylhydrazine (**11a**) and acetophenone (**12**) heated in PPA at 100–110 °C quickly and cleanly produced desired indole **1b**. In this case acetophenone was chosen for its high boiling point to alleviate material loss due to evaporation. Upon completion of the first step, nitroalkene **2a** was added and subsequent heating of the reaction mixture afforded product **6aa** in high yield (Scheme 2, Table 2, entry 1). Other nitroalkanes (Table 2, entries 2–13) as well as *para*-substituted

Table 2 Three-component one-pot synthesis of 2-quinolones



	11	R^4	2	R^3	6	Yield[a], %
1	**11a**	H	**2a**	H	**6aa**	87
2	**11a**	H	**2b**	4-$MeOC_6H_4$	**6ab**	68
3	**11a**	H	**2c**	4-i-PrC_6H_4	**6ac**	85
4	**11a**	H	**2d**	3,4-$Me_2C_6H_3$	**6ad**	86
5	**11a**	H	**2e**	3,4-$(MeO)_2C_6H_3$	**6ae**	71
6	**11a**	H	**2f**	4-$EtOC_6H_4$	**6af**	71
7	**11a**	H	**2g**	2-FC_6H_4	**6ag**	62
8	**11a**	H	**2h**	3-FC_6H_4	**6ah**	58
9	**11a**	H	**2i**	4-FC_6H_4	**6ai**	66
10	**11a**	H	**2j**	3,4-$Cl_2C_6H_3$	**6aj**	82
11	**11a**	H	**2k**	3-BrC_6H_4	**6ak**	60
12	**11a**	H	**2l**	2-C_5H_4N	**6al**	42
13	**11a**	H	**2m**	2-$NO_2C_6H_4$	**6am**	29
14	**11e**	Me	**2a**	Ph	**6ha**	82
15	**11f**	MeO	**2a**	Ph	**6fa**	79
16	**11g**	Cl	**2a**	Ph	**6ga**	84

[a] Isolated yields of purified products.



1a: R^2 = H; **1c**: R^2 = Me
2a, 8a, 10a: R^3 = Ph
2c, 8c, 10c: R^3 = 4-*i*-PrC_6H_4
2d, 8d, 10d: R^3 = 3,4-$Me_2C_6H_3$
2q, 8q, 10q: R^3 = H

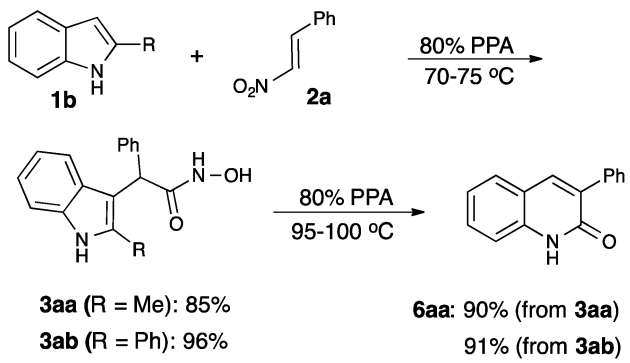
6aa: R^2 = H, R^3 = Ph; 81%
6ac: R^2 = H, R^3 = 4-*i*-PrC_6H_4; 88%
6ad: R^2 = H, R^3 = 3,4-$Me_2C_6H_3$; 91%
6aq: R^2 = H, R^3 = H; 37%
6cq: R^2 = Me, R^3 = H; 47%

Scheme 3

hydrazines **11e–g** (Table 2, entries 14–16) subjected to the one-pot transformation demonstrated efficiencies comparable to those obtained with pre-isolated indoles (Table 1).

Reaction of indoles with 2-nitroethanols

The following modification of the standard protocol described above addresses some limitations of the Henry reaction,[18] which was employed in this study to prepare starting nitroalkenes. The Henry reaction involves a base-assisted condensation of nitromethane **9** with corresponding aldehydes **8**, and requires elimination of water in the last step, which proceeds smoothly for derivatives of aromatic aldehydes (R^3 = Ar). Condensation of aliphatic aldehydes (R^3 = Alk), unless carried out under much harsher conditions, often stops at the stage of alcohol **10** (Scheme 3). Having faced this problem, we reasoned that nitroalcohol **10** could potentially be employed in the described transformation as a surrogate of nitroolefin **2**. Indeed, at elevated temperatures, PPA should force elimination of water producing *in situ* the required nitroalkene **2**, which would subsequently react with indoles **1** (Scheme 3). Implementation of this idea afforded the corresponding 2-quinolones **6** in yields matching or exceeding those obtained *via* the original protocol (Scheme 3). This modification is particularly useful for the preparation of quinolones unsubstituted or alkyl-



Scheme 4

substituted at C3, for which the required 2-nitroethanols are much more readily available than the corresponding 2-nitroalkenes.

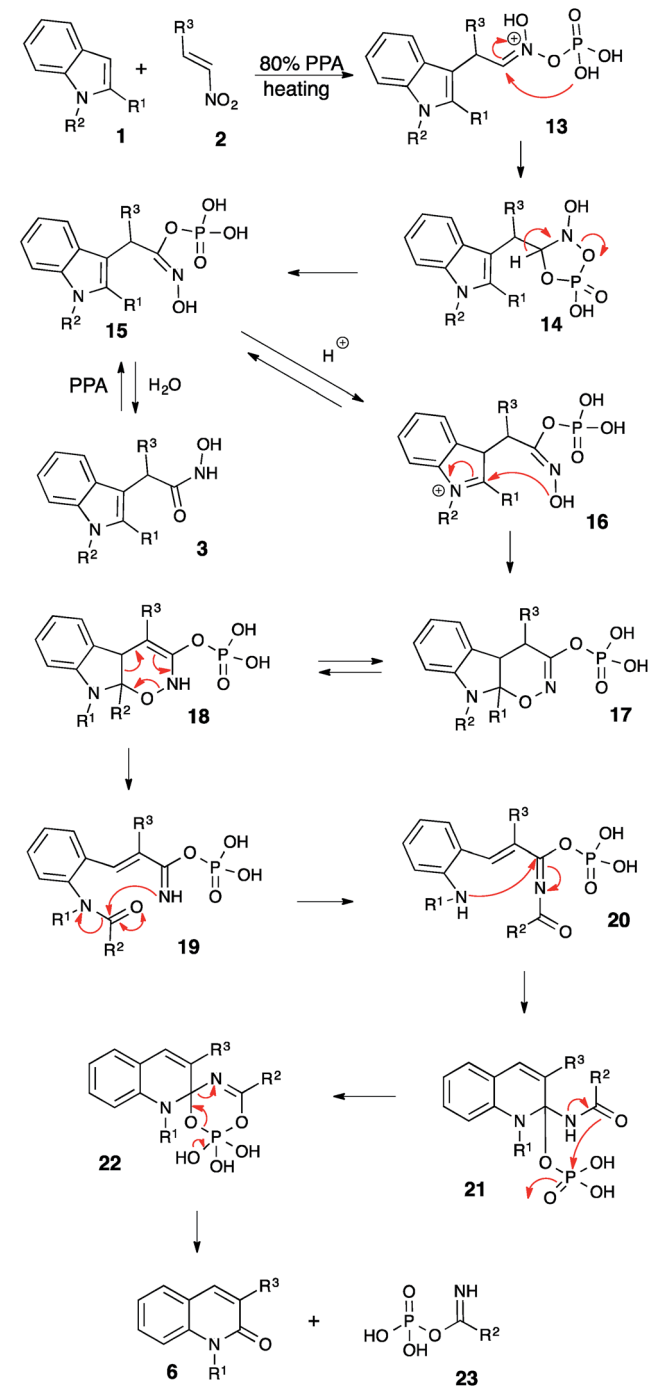
Mechanistic rationale

While detailed mechanistic study is underway in our laboratories, the ANRORC mechanism described below (Scheme 5) represents, in our opinion, the most plausible scenario out of several mechanistic hypotheses that could potentially account for the acquired body of empirical results, and is backed by literature precedence for the related elementary mechanistic steps.

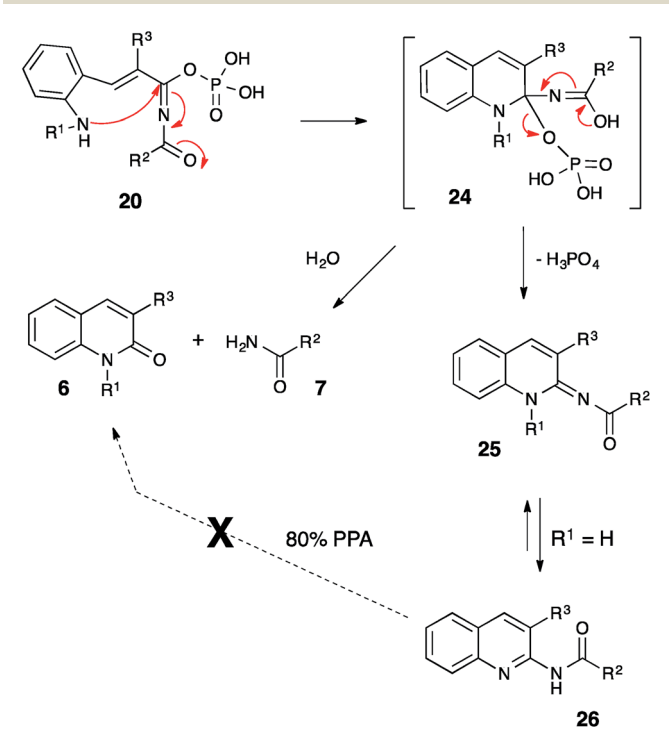
The reaction commences with the initial electrophilic attack by the nitroalkene at C3 of indole to produce alkylideneazinic acid **13**. In the presence of PPA this aci-species undergoes rearrangement to hydroxamic acid anhydride **16**, which upon hydrolysis provides hydroxamic acid **3**.[19] Indeed, acids **3aa** (R^1 = Me, R^3 = Ph, R^2 = H) and **3ab** (R^1 = R^3 = Ph, R^2 = H) were isolated as sole products after aqueous treatment of the mixtures when the reactions were carried out below 80 °C. When re-subjected to the standard reaction conditions, both **3aa** and **3ab** provided 2-quinolone **6aa** in high yield (Scheme 4).

Subsequent steps involve intramolecular nucleophilic attack by the oxime moiety at the iminium functionality in **16** to afford tricyclic imine **17** (nucleophilic addition step of an ANRORC sequence), which in the presence of acid tautomerizes into enamine **18**. The latter undergoes a retro-Diels–Alder reaction to produce anilide **19** (ring-opening step of an ANRORC sequence). Next, migration of the acyl group from aniline to the more nucleophilic imine nitrogen followed by the nucleophilic attack by the aniline at the acyliminium moiety in **20** (ring closure step of an ANRORC sequence)[20] affords aminoquinoline species **21**, which may cyclize into spiro-dioxaphosphazine **22**. Finally, 2-quinolone **6** is produced after the extrusion of imide anhydride **23**, which upon hydrolytic cleavage gives rise to the amide byproduct **7** (Scheme 5).

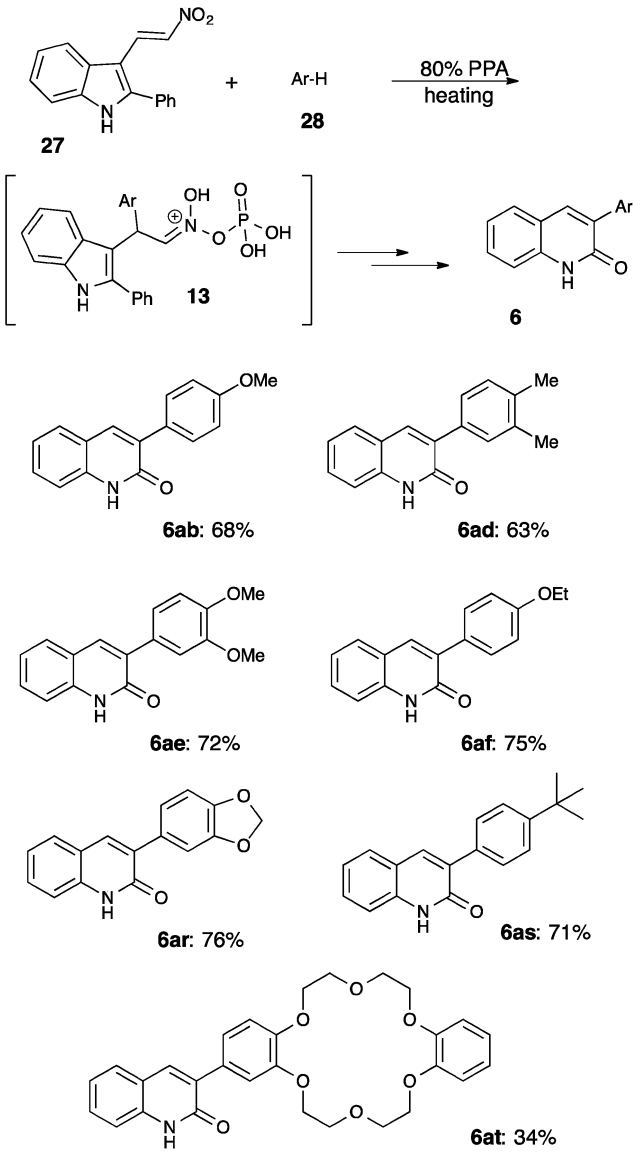
One of the possible alternative end-games involving formation of *N*-acylaminoquinoline **26** as an intermediate and its subsequent acid-assisted solvolysis into the final product has been ruled out. Indeed, if this mechanism were operating,



Scheme 5



Scheme 6



Scheme 7

compound **20** possessing R^1 = H would quickly undergo aromatization into the thermodynamically more stable acylaminoquinoline **26** (Scheme 6). We demonstrated, however, that these compounds prepared by alternative methods do not show the expected reactivity under the featured reaction conditions.

3-Aryl-2-quinolones *via* arylation of nitroolefins

We have also envisioned an alternative route to 3-aryl-substituted 2-quinolones **6** *via* the electrophilic alkylation of arenes **28** with easily available[21] 3-indolyl nitroalkene **27**. This mode would proceed *via* the key intermediate **13** (Scheme 5) and allow for easy diversification of an aromatic substituent R^3 at the very last step of the synthesis. It would be particularly advantageous for the rapid assembly of 3-arylquinolone libraries[22] as well as for efficient coupling of 2-quinolones with structurally advanced electron-rich aromatic fragments. To test this approach, nitroolefin **27** was treated with PPA in the presence of anisole under standard reaction conditions. We were pleased to find that this transformation proceeded smoothly to give the expected product **6ab** (Scheme 7). Alkylation of other electron-rich arenes (*o*-xylene, veratrol, [1,3]-benzodioxole, phenetole, and *tert*-butylbenzene) afforded 3-arylsubstituted 2-quinolones **6ad**, **6ae**, **6ar**, **6af**, and **6as** respectively, in good yields (Scheme 7). Application of this methodology for a single-step installation of a useful quinolone chromophore into a complex aromatic structure was also probed. Exposure of indole **27** and dibenzo-18-crown-6 ether to PPA under standard reaction conditions provided desired product **6at** in 34% yield (Scheme 7), along with small amounts of two diastereomeric products resulted from alkylation of both benzene rings.

Conclusion

We have developed a new, convenient and general approach to 3-substituted 2-quinolones *via* a metal-free cascade transformation starting from 2-substituted indoles and 2-nitroalkenes in polyphosphoric acid. The unique features of PPA that serves as a mild proton donor, a source for a good leaving group, a water scavenger, and a high-boiling solvent, make it an ideal medium for the described transformation. This uncatalyzed C–C bond forming reaction operates *via* an unusual ANRORC transannulation mechanism involving the extrusion of one carbon atom of an indole and incorporation of two new carbon atoms from a nitroolefin. This reaction was successfully combined with the Fisher indole synthesis, which led to the development of an efficient, sequential, three-component heteroannulation methodology for the construction of the 3-aryl-2-quinolone scaffold. This one-pot method offers a practical synthetic advantage over many known methods, which rely on 1,2-disubstituted aromatic precursors. Indeed, the featured methodology allows for the direct conversion of arylhydrazines into substituted 2-quinolones, which makes it very attractive for diversity oriented synthesis. An alternative entry to this transformation was explored, involving alkylation of electron-rich arenes with 2-indolyl nitroalkenes. This direct, non-catalytic C–H functionalization offers the possibility for an easy variability of the aromatic group at C3 of 2-quinolone.

Experimental section

All reagents, solvents and catalysts were purchased from commercial sources and used without purification. All reactions were performed in oven-dried flasks open to the atmosphere and monitored by thin layer chromatography. Flash column chromatography was performed on silica gel (32–63 μm, 60 Å pore size). Nitroalkenes **2a**,**b**,**e**,**g**,**h**,**j**,**k**, **m**,**n**,**o** were obtained from commercial sources, compounds **2c**,**d**,**f**,**i**,**l** (ref. 23) and **2p**,**q** (ref. 24) were synthesized employing published procedures. Commercial 2-nitroethanol (**10q**) was used. 1-Aryl-2-nitroethanoles **10a**,**c**,**d** were synthesized using standard literature procedure.[25]

Reactions of 2-substituted indoles with 2-nitroalkenes in PPA

Method A: general procedure for the synthesis 6a–r. A mixture of indole **1** (1 mmol), nitrostyrol **2** (1.2 mmol) and 80% PPA (2–3 g) was heated at 80–85 °C for 30 min. Consumption of starting indole was monitored by TLC. After indole reacted completely the temperature was increased to 95–100 °C and the reaction mixture was heated for 1 h, then cooled to room temperature, poured into water (50 mL), and neutralized with aqueous ammonia. Aqueous phase was extracted with chloroform (2 × 15 mL) and filtered through a short pad of silica gel. The solvent was removed by evaporation, and the residual crude material was purified by recrystallization.

Method B: reaction of indoles with 2-nitroethanoles. A mixture of indole **1** (1 mmol), nitroalcohol **10** (1.2 mmol) and 80% PPA (2–3 g) was heated at 80–85 °C for 30 min. Subsequently, the reaction was carried out and worked up in the manner described for Method A (*vide supra*).

Method C: three-component coupling involving Fisher indole synthesis. A mixture of arylhydrazone **11** (1.0 mmol), acetophenone **12** (1.0 mmol), and 80% PPA (2–3 g) was stirred at 100–110 °C for 40 min. When consumption of starting arylhydrazine 11 was confirmed by TLC, the temperature was decreased to 80–85 °C and nitrostyrol **2** (1.2 mmol) was added in one portion. The mixture was heated for additional 30 min, while consumption of intermediate indole was monitored by TLC. After the indole reacted completely, the temperature was increased to 95–100 °C and the reaction mixture was heated for 1 h. The post-reaction work up and isolation of the products is the same as in Method A (*vide supra*).

Reaction of 3-nitrovinylindoles with arenes

A mixture of 3-nitrovinylindole **27** (1 mmol), selected arene (1.2 mmol) and PPA (2–3 g) was heated at 80–85 °C for 30 min. The consumption of starting materials was monitored by TLC. After indole reacted completely, the temperature was increased to 95–100 °C and the reaction mixture was heated for 1 h, then cooled to room temperature, poured into water (50 mL) and neutralized with aqueous ammonia. The organic portion was extracted twice with chloroform and filtered through silica gel. Concentration of the filtrate in vacuum followed recrystallization of the residue afforded the corresponding 2-quinolones.

3-Phenylquinolin-2(1*H*)-one (6aa).[26] White solid, mp 234–235 °C (CH_2Cl_2/EtOH). ^{1}H NMR ($CDCl_3$) δ, ppm: 10.79 (bs, 1H), 7.92 (s, 1H), 7.79 (m, 2H), 7.61 (dd, J = 6.6, 1.2 Hz, 1H), 7.52–7.47 (m, 3H), 7.43–7.39 (m, 1H), 7.30–7.22 (m, 2H); ^{13}C NMR (DMSO-d_6) δ, ppm: 161.7, 139.1, 138.3, 137.0.132.2, 130.8, 129.4, 128.8, 128.6, 128.5, 122.5, 120.2, 115.4; the NMR spectral data are consistent with published results.[10a] IR (KBr): 3456, 1647 cm^{-1}; HRMS calcd for $C_{15}H_{11}NONa$ $(M + Na)^+$ 244.0738, found 244.0736.

3-(4-Methoxyphenyl)quinolin-2(1*H*)-one (6ab). White solid, mp 259–261 °C (CH_2Cl_2/EtOH). ^{1}H NMR ($CDCl_3$) δ, ppm: 11.57 (bs, 1H), 7.86 (s, 1H), 7.76 (d, J = 8.6 Hz, 2H), 7.60 (d, J = 7.8 Hz, 1H), 7.47 (t, J = 7.8 Hz, 1H), 7.27 (m, 1H), 7.22 (t, J = 7.6 Hz, 1H), 7.01 (d, J = 8.3 Hz, 2H), 3.88 (s, 3H); ^{13}C NMR (DMSO-d_6) δ, ppm: 161.2, 159.0, 138.1, 136.3, 131.0, 129.9, 129.8, 128.5, 127.8, 121.8, 119.7, 114.6, 113.3, 55.1; the NMR spectral data are consistent with published results.[10a] IR: 3480, 1661 cm^{-1}; HRMS calcd for $C_{16}H_{13}NO_2Na$ $(M + Na)^+$ 274.0844, found 274.0838.

3-(4-i-Propylphenyl)quinolin-2(1*H*)-one (6ac). White solid, mp 220–221 °C (CH_2Cl_2/EtOH). ^{1}H NMR ($CDCl_3$) δ, ppm: 11.46 (bs, 1H), 7.92 (s, 1H), 7.77 (d, J = 8.2 Hz, 2H), 7.62 (d, J = 7.7 Hz, 1H), 7.50 (ddd, J = 7.8, 7.7, 1.1 Hz, 1H), 7.37 (d, J = 8.7 Hz, 1H), 7.36 (d, J = 8.2 Hz, 1H), 7.21 (dd, J = 8.7, 7.7 Hz, 1H), 3.02–2.94 (m, 1H), 1.31 (d, J = 6.9 Hz, 6H); ^{13}C NMR ($CDCl_3$) δ, ppm: 162.5, 148.5, 137.4, 137.3, 133.0, 131.9, 129.6, 128.3, 127.2, 125.9, 122.1, 119.9, 114.9, 33.5, 23.4 (2C); IR: 3445, 1652 cm^{-1}. EA: calcd for $C_{18}H_{17}NO$: C, 82.10; H, 6.51; N, 5.32. Found: C, 82.21; H, 6.46; N, 5.27. HRMS calcd for $C_{18}H_{17}NONa$ $(M + Na)^+$ 286.1208, found 286.1201.

3-(3,4-Dimethyl)quinolin-2(1*H*)-one (6ad). White solid, mp 252–253 °C (CH_2Cl_2/EtOH). ^{1}H NMR ($CDCl_3$) δ, ppm: 11.71 (bs, 1H), 7.87 (s, 1H), 7.59–7.58 (m, 2H), 7.55 (d, J = 7.8 Hz, 1H), 7.46 (dd, J = 7.8, 7.7 Hz, 1H), 7.36 (d, J = 8.2 Hz 1H), 7.24 (d, J = 7.8 Hz, 1H), 7.20 (dd, J = 8.2, 7.7 Hz, 1H), 2.35 (s, 3H), 2.33 (s, 3H); ^{13}C NMR ($CDCl_3$) δ, ppm: 163.3, 138.0, 137.9, 136.9, 136.5, 133.9, 132.8, 130.2, 130.1, 129.7, 127.8, 126.5, 122.6, 120.8, 115.6, 20.6, 19.8; IR: 3442, 1656 cm^{-1}; EA: calcd for $C_{17}H_{15}NO$: C, 81.90; H, 6.06; N, 5.62. Found: C, 82.04; H, 6.01; N, 5.56; HRMS calcd for $C_{17}H_{15}NONa$ $(M + Na)^+$: 272.1051, found 272.1048.

3-(3,4-Dimethoxy)quinolin-2(1*H*)-one (6ae).[10a] White solid, mp 209–210 °C (CH_2Cl_2/EtOH). ^{1}H NMR (DMSO-d_6) δ, ppm: 11.87 (bs, 1H), 8.09 (s, 1H), 7.71 (d, J = 7.5 Hz, 1H), 7.48 (ddd, J = 9.7, 7.7, 0.9 Hz, 1H), 7.42 (d, J = 1.8 Hz, 1H), 7.38 (dd, J = 8.4, 1.9 Hz, 1H), 7.34 (d, J = 8.2 Hz, 1H), 7.19 (t, J = 7.4 Hz, 1H), 7.01 (d, J = 8.4 Hz, 1H), 3.81 (s, 3H), 3.80 (s, 3H); ^{13}C NMR (DMSO-d_6) δ, ppm: 161.1, 148.8, 148.1, 138.1, 136.5, 131.1, 129.8, 128.9, 127.9, 121.8, 121.3, 119.7, 114.6, 112.6, 111.3, 55.6, 55.5; IR: 3462, 1651 cm^{-1}; HRMS calcd for $C_{17}H_{15}NO_3Na$ $(M + Na)^+$: 304.0950, found 304.0946.

3-(4-Ethoxyphenyl) quinolin-2(1*H*)-one (6af). White solid, mp 215–217 °C (CH_2Cl_2/EtOH). ^{1}H NMR ($CDCl_3$) δ, ppm: 11.37 (bs, 1H), 7.87 (s, 1H), 7.77 (d, J = 8.6 Hz, 2H), 7.59 (d, J = 7.8 Hz, 1H) 7.47 (dd, J = 7.8, 7.7 Hz, 1H), 7.33 (d, J = 8.2 Hz, 1H), 7.21 (dd, J = 8.2, 7.8 Hz, 1H), 7.00 (d, J = 8.6 Hz, 2H), 4.11 (q, J = 7.0 Hz, 2H), 1.46 (t, J = 7.0 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ, ppm: 163.2, 159.3, 137.8, 137.3, 132.2, 130.2, 130.0, 128.5, 127.8, 122.7, 120.7, 115.4, 114.5, 63.6, 15.0; IR: 3455, 1648 cm^{-1}; EA: calcd for $C_{17}H_{15}NO_2$: C, 76.96; H, 5.70; N, 5.28. Found: C, 77.19; H, 5.61; N, 5.23; HRMS calcd for $C_{17}H_{15}NO_2Na$ $(M + Na)^+$: 288.1000, found 288.0991.

3-(2-Fluorophenyl)quinolin-2(1*H*)-one (6ag). White solid, mp 233–235 °C (CH_2Cl_2/EtOH). ^{1}H NMR ($CDCl_3$) δ, ppm: 11.50 (bs, 1H), 7.92 (s, 1H),7.63 (ddd, J = 9.3, 7.5, 1.7 Hz, 1H), 7.59 (dd, J = 7.8, 1.1 Hz, 1H), 7.50 (ddd, J = 7.8, 7.7, 1.3 Hz, 1H), 7.42–7.37 (m, 1H), 7.35 (d, J = 8.2 Hz, 1H), 7.28–7.18 (m, 3H); ^{13}C NMR ($CDCl_3$) δ, ppm: 162.5, 161.5, 159.5, 140.9, 138.4, 131.9, 130.8, 130.1, 128.1, 127.8, 124.0, 122.9, 120.0, 116.1, 115.8. IR: 3502, 1650 cm^{-1}; EA: calcd for $C_{15}H_{10}NFO$: C, 75.30; H, 4.21; N, 5.85. Found: C, 75.48; H, 4.16; N, 5.78; HRMS calcd for $C_{15}H_{10}NFONa$ $(M + Na)^+$: 262.0644, found 262.0639.

3-(3-Fluorophenyl)quinolin-2(1*H*)-one (6ah). White solid, mp 220–221 °C (CH_2Cl_2/EtOH). ^{1}H NMR ($CDCl_3$) δ, ppm: 12.22 (bs, 1H), 7.95 (s, 1H), 7.65–7.57 (m, 3H), 7.52 (dt, J = 7.7, 0.8 Hz, 1H), 7.48–7.39 (m, 2H), 7.24 (t, J = 7.5, 1H), 7.12 (ddd, J = 8.4, 8.3, 2.3 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ, ppm: 163.8, 163.1, 161.9, 139.1, 138.3, 131.1, 130.9, 129.8, 128.1, 124.6, 123.0, 120.3, 116.3, 115.8, 115.1; IR: 3495, 1648 cm^{-1}; EA: calcd for $C_{15}H_{10}NFO$: C, 75.30; H, 4.21; N, 5.85. Found: C, 75.46; H, 4.17; N, 5.74; HRMS calcd for $C_{15}H_{10}NFONa$ (M + Na)$^+$: 262.0644, found 262.0637.

3-(4-Fluorophenyl)quinolin-2(1*H*)-one (6ai). White solid, mp 246–248 °C (CH_2Cl_2/EtOH). ^{1}H NMR (DMSO-d_6) δ, ppm: 11.97 (bs, 1H), 8.11 (s, 1H), 7.85–7.81 (m, 2H), 7.72 (d, J = 7.7 Hz, 1H), 7.50 (dd, J = 7.7, 7.6 Hz, 1H), 7.33 (d, J = 8.2 Hz, 1H), 7.17–7.28 (m, 3H); ^{13}C NMR (DMSO-d_6) δ, ppm: 163.1, 161.0, 160.6, 138.4, 137.6, 132.6, 130.8, 130.3, 128.1, 122.0, 119.5, 114.9, 114.7; IR: 3588, 1651 cm^{-1}; EA: calcd for $C_{15}H_{10}NFO$: C, 75.30; H, 4.21; N, 5.85. Found: C, 75.42; H, 4.17; N, 5.73; HRMS calcd for $C_{15}H_{10}NFONa$ (M + Na)$^+$: 262.0644, found 262.0640.

3-(3,4-Dichlorophenyl)quinolin-2(1*H*)-one (6aj). White solid, mp 298–299 °C (CH_2Cl_2/EtOH). ^{1}H NMR (DMSO-d_6) δ, ppm: 12.06 (bs, 1H), 8.27 (s, 1H), 8.11 (d, J = 2.0 Hz, 1H), 7.80 (dd, J = 8.4, 2.0 Hz, 1H), 7.74 (d, J = 7.6 Hz, 1H), 7.70 (d, J = 8.4 Hz, 1H), 7.53 (dd, J = 7.7, 7.6, 1H), 7.34 (d, J = 8.2 Hz, 1H), 7.21 (dd, J = 8.2, 7.7 Hz, 1H); ^{13}C NMR (DMSO-d_6) δ, ppm: 160.7, 138.7, 138.6, 136.8, 130.8, 130.6, 130.4, 130.3, 130.1, 128.8, 128.5, 128.4, 122.1, 119.3, 114.8; IR: 3495, 1648 cm^{-1}; EA: calcd for $C_{15}H_9Cl_2NO$: C, 62.09; H, 3.13; N, 4.83. Found: C, 62.28; H, 3.07; N, 4.72; HRMS calcd for $C_{15}H_9Cl_2NONa$ (M + Na)$^+$: 311.9959, found 311.9954.

3-(3-Bromophenyl)quinolin-2(1*H*)-one (6ak). White solid, mp 211–212 °C (CH_2Cl_2/EtOH). 1H NMR ($CDCl_3$) δ, ppm: 11.35 (bs, 1H), 7.96 (bs, 1H), 7.92 (s, 1H), 7.75 (d, J = 7.7 Hz, 1H), 7.62 (d, J = 7.8 Hz, 1H), 7.55–7.51 (m, 2H), 7.36–7.33 (m, 2H), 7.24 (t, J = 7.7 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ, ppm: 162.6, 139.0, 138.3, 138.2, 131.9, 131.3, 131.1, 130.9, 129.9, 128.2, 127.7, 123.0, 122.5, 120.3, 115.6; IR: 3485, 1648 cm^{-1}; EA: calcd for $C_{15}H_{10}BrNO$: C, 60.02; H, 3.36; N, 4.67. Found: C, 60.16; H, 3.29; N, 4.59; HRMS calcd for $C_{15}H_{10}BrNONa$ (M + Na)$^+$: 321.9843, found 321.9843.

3-Pyridin-2-ylquinolin-2(1*H*)-one (6al).[27] Cream-colored solid, mp 232–233 °C (1,4-dioxane); ^{1}H NMR (DMSO-d_6) δ, ppm: 12.07 (s, 1H), 8.78 (s, 1H), 8.69 (d, J = 4.6 Hz, 1H), 8.52 (d, J = 8.1 Hz, 1H), 7.86 (m, 2H), 7.55 (t, J = 8.3 Hz, 1H), 7.38 (m, 2H), 7.23 (t, J = 7.6 Hz, 1H); ^{13}C NMR (DMSO-d_6) δ, ppm: 161.1, 152.6, 149.2, 139.3, 138.8, 136.2, 131.0, 128.8, 123.8, 123.0, 122.0, 119.2, 114.7; IR: 3475, 1645 cm^{-1}; HRMS calcd for $C_{14}H_{10}N_2ONa$ (M + Na)$^+$: 245.0691, found 245.0686.

3-(2-Nitro-phenyl)quinolin-2(1*H*)-one (6am).[28] Pale yellow solid, mp 317–318 °C (THF/diethyl ether); ^{1}H NMR (DMSO-d_6) δ, ppm: 12.00 (s, 1H), 8.17 (s, 1H), 8.06 (d, J = 7.8 Hz, 1H), 7.83 (t, J = 7.8 Hz, 1H), 7.78 (d, J = 7.8 Hz, 1H), 7.67 (t, J = 7.8 Hz, 1H), 7.65 (d, J = 7.8 Hz, 1H), 7.56 (t, J = 8.1 Hz, 1H), 7.36 (d, J = 8.1 Hz, 1H), 7.25 (t, J = 7.8 Hz, 1H); ^{13}C NMR (DMSO-d_6) δ, ppm: 133.6, 132.2, 131.0, 130.9, 130.6, 129.4, 128.2, 123.9, 122.1, 119.3, 115.0; the NMR spectral data are consistent with published results.[28] IR: 2281 s, 1532 s, 1330 s cm^{-1}; HRMS calcd for $C_{15}H_{10}N_2O_3Na$ (M + Na)$^+$: 289.0589, found 289.0585.

3-*n*-Propylquinolin-2(1*H*)-one (6ap).[29] White solid, mp 142–143 °C (hexane/ethyl acetate); ^{1}H NMR ($CDCl_3$) δ, ppm: 12.77 (bs, 1H), 7.57 (s, 1H), 7.49–7.39 (m, 3H), 7.15 (ddd, J = 2 and 8.6 Hz, 1H), 2.67 (t, J = 7 Hz, 2H), 1.75 (sextet, J = 7 Hz, 2H), 1.04 (t, J = 7 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ, ppm: 164.5, 137.4, 136.4, 133.7, 129.0, 126.7, 122.1, 120.1, 115.7, 32.3, 21.6, 14.0. The NMR spectral data are consistent with published results.[27] IR: 3455, 1655 cm^{-1}; HRMS calcd for $C_{12}H_{13}NONa$ (M + Na)$^+$: 210.0885, found 210.0891.

Quinolin-2(1*H*)-one (6aq).[30] White solid, mp 197–199 °C (CH_2Cl_2/EtOH). ^{1}H NMR ($CDCl_3$) δ, ppm: 7.85 (d, J = 9.2 Hz, 1H), 7.58 (d, J = 8.0 Hz, 1H), 7.54 (d, J = 8.4 Hz, 1H), 7.52–7.46 (m, 1H), 7.26–7.22 (m, 1H), 6.75 (d, J = 9.2 Hz, 1H), 2.14 (br. s, 1H). The NMR spectral data are consistent with published results.[30] HRMS calcd for C_9H_7NONa (M + Na)$^+$: 168.0425, found 168.0420.

3-(Benzo[*d*][1,3]dioxol-5-yl)quinolin-2(1*H*)-one (6ar). White solid, mp 215–218 °C (EtOH). ^{1}H NMR (DMSO-d_6) δ, ppm: 11.88 (bs, 1H), 8.13 (s, 1H), 7.71 (d, J = 7.49 Hz, 1H), 7.49 (ddd, J = 9.7, 7.7, 0.9 Hz, 1H), 7.43 (d, J = 1.8 Hz, 1H), 7.40 (dd, J = 8.4, 1.9 Hz, 1H), 7.37 (d, J = 8.2 Hz, 1H), 7.19 (t, J = 7.4 Hz, 1H), 7.10 (d, J = 8.4 Hz, 1H), 5.95 (s, 2H); ^{13}C NMR (DMSO-d_6) δ, ppm: 161.4, 146.3, 145.9, 138.0, 136.5, 131.2, 129.8, 128.3, 127.9, 121.8, 121.5, 119.7, 114.6, 109.7, 107.4; HRMS calcd for $C_{16}H_{11}NO_3Na$ (M + Na)$^+$: 288.0637, found 288.0635.

3-(4-*tert*-Butylphenyl)quinolin-2(1*H*)-one (6as). White solid, mp 247–249 °C (EtOH). ^{1}H NMR ($CDCl_3$) δ, ppm: 11.84 (bs, 1H), 7.93 (s, 1H), 7.77 (d, J = 8.3 Hz, 2H), 7.61 (dd, J = 7.6, 0.6 Hz, 1H), 7.51 (d, J = 8.4 Hz, 2H), 7.40 (d, J = 8.2 Hz, 1H), 7.23 (ddd, J = 7.6, 6.5, 0.7 Hz, 1H), 1.39 (s, 9H); ^{13}C NMR ($CDCl_3$) δ, ppm: 163.2, 151.4, 138.5, 137.8, 133.2, 132.3, 130.4, 128.7 (2C), 127.9, 125.5 (2C), 123.0, 120.7, 115.8, 34.8, 31.5; HRMS calcd for $C_{19}H_{19}NONa$ (M + Na)$^+$: 300.1364, found 300.1357.

1-Methylquinolin-2(1*H*)-one (6cq).[29] White solid, mp 75–76 °C (hexane/EtOAc); ^{1}H NMR ($CDCl_3$) δ, ppm: 7.66 (d, J = 9.0 Hz, 1H), 7.56 (t, J = 8.0 Hz, 1H), 7.55 (d, J = 8.1 Hz, 1H), 7.36 (d, J = 8.0 Hz, 1H), 7.23 (t, J = 8.1 Hz, 1H), 6.71 (d, J = 9.0 Hz, 1H), 3.72 (s, 3H); ^{13}C NMR ($CDCl_3$) δ, ppm: 162.2, 139.9, 138.8, 130.5, 128.6, 122.0, 121.6, 120.6, 114.0, 29.4. IR: 1650 cm^{-1}. HRMS calcd for $C_{10}H_9NONa$ (M + Na)$^+$: 182.0582, found 182.0577.

1-Methyl-3-phenylquinolin-2(1*H*)-one (6ca).[29] White solid, mp 140–142 °C (ligroin); ^{1}H NMR ($CDCl_3$) δ, ppm: 7.58 (s, 1H), 7.70 (d, J = 8.1 Hz, 2H), 7.59 (d, J = 8.2 Hz, 1H), 7.55 (t, J = 8.1 Hz, 1H), 7.43 (t, J = 8.2 Hz, 2H), 7.39–7.34 (m, 2H), 7.24 (t, J = 8.0 Hz, 1H), 3.79 (s, 3H); ^{13}C NMR ($CDCl_3$) δ, ppm: 161.4, 139.5, 136.7, 132.4, 130.2, 128.9, 128.7, 128.0, 127.9, 122.1, 120.6, 113.9, 30.0, one carbon signal is missing due to overlap; IR: 1645 cm^{-1}. The NMR and IR spectral data are consistent with published results.[29,31,32] HRMS calcd for $C_{16}H_{13}NONa$ (M + Na)$^+$: 258.0895, found 258.0888.

1-Methyl-3-(4-fluorophenyl)quinolin-2(1*H*)-one (6ci). White solid, mp 172–173 °C (ligroin); ^{1}H NMR ($CDCl_3$) δ, ppm: 7.78 (s, 1H), 7.72–7.68 (m, 2H), 7.63–7.57 (m, 2H), 7.39 (d, J = 1.6 Hz, 1H), 7.28–7.25 (m, 2H), 7.12 (t, J = 8.6 Hz, 2H), 3.8 (s, 3H); ^{13}C NMR ($CDCl_3$) δ, ppm: 164.0, 161.6 (2C), 139.7, 136.8, 132.9 (2C), 131.6, 130.9, 130.8, 130.5, 129.0, 122.4, 120.8, 115.3, 115.1,

114.2, 30.2; HRMS calcd for $C_{16}H_{12}NFONa$ (M + Na)$^+$: 276.0801, found 276.0797.

1-Butyl-3-phenylquinolin-2(1*H*)-one (6ea). White solid, mp 154–153 °C (ligroin); ^{1}H NMR ($CDCl_3$) δ, ppm: 7.81 (s, 1H), 7.73 (d, J = 7.2 Hz, 1H), 7.62 (d, J = 7.7 Hz, 1H), 7.56 (ddd, J = 7.9, 7.8, 1.2 Hz, 1H), 7.45–7.42 (m, 2H), 7.39–7.37 (m, 2H), 7.24–7.22 (m, 1H), 4.36 (t, J = 7.8 Hz, 2H), 1.83–1.75 (m, 2H), 1.55–1.50 (m, 2H), 1.02 (t, J = 7.3 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ, ppm: 161.4, 139.0, 136.9 (2C), 132.6, 130.3, 129.2 (3C), 128.3 (2C), 128.2, 122.1, 121.2, 114.2, 43.0, 29.7, 20.6, 14.0; HRMS calcd for $C_{19}H_{19}NO_2Na$ (M + Na)$^+$: 300.1364, found 300.1358.

6-Methyl-3-phenylquinolin-2(1*H*)-one (6ha).[33] White solid, mp 218–219 °C (EtOH); 11.87 (s, 1H), 8.02 (s, 1H), 7.75–7.73 (m, 2H), 7.51 (s, 1H), 7.44–7.41 (m, 2H), 7.37 (d, J = 7.22 Hz, 1H), 7.34 (d, J = 8.3 Hz, 1H), 7.24 (d, J = 8.37 Hz, 1H), 2.35 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ, ppm: 160.9, 137.4, 136.4, 131.5 (2C), 130.8, 128.7 (2C), 127.9 (2C), 125.7, 127.5, 119.5, 114.6, 99.5, 20.4. The NMR spectral data are consistent with published results.[32] IR: 3450, 1660 cm^{-1}; HRMS calcd for $C_{16}H_{13}NONa$ (M + Na)$^+$: 258.0895, found 258.0887.

6-Methoxy-3-phenyl(1*H*)quinolin-2(1*H*)-one (6fa).[10b] Pale yellow solid, mp 248–249 °C ($CHCl_3$/EtOAc); ^{1}H NMR ($CDCl_3$) δ, ppm: 10.89 (br. s, 1H), 7.86 (s, 1H), 7.8 (s, 1H), 7.79 (s, 1H), 7.48 (m, 2H), 7.42 (m, 1H), 7.23 (d, J = 9.0 Hz, 1H), 7.14 (dd, J = 6.1, 2.7 Hz, 1H), 7.04 (d, J = 2.7 Hz, 1H), 3.88 (s, 3H); ^{13}C NMR (DMSO-d_6) δ, ppm: 160.7, 154.3, 137.4, 136.6, 133.1, 132.0, 128.8, 128.0, 127.9, 120.3, 119.6, 116.1, 109.6, 55.6. The NMR spectral data are consistent with published results.[10b] IR: 3445, 1642 cm^{-1}; HRMS calcd for $C_{16}H_{13}NO_2Na$ (M + Na)$^+$: 274.0844, found 274.0838.

6-Chloro-3-phenylquinolin-2(1*H*)-one (6ga).[29] White solid, mp 249–250 °C (hexane/EtOAc); ^{1}H NMR (DMSO-d_6) δ, ppm: 12.06 (br. s, 1H), 8.11 (s, 1H), 7.86 (d, J = 2.0 Hz, 1H), 7.77 (d, J = 7.1 Hz, 2H), 7.56 (dd, J = 9.3, 2.0 Hz, 1H), 7.50–7.42 (m, 3H), 7.38 (d, J = 9.3 Hz, 1H); ^{13}C NMR (DMSO-d_6) δ, ppm: 160.7, 136.9, 136.4, 135.8, 132.7, 129.9, 128.6, 128.0, 127.9, 126.9, 125.6, 120.6, 116.5. The NMR spectral data are consistent with published results.[29] IR: 3455, 1650 cm^{-1}; HRMS calcd for $C_{15}H_{10}NClONa$ (M + Na)$^+$: 278.0349, found 278.0345.

3-(6,7,9,10,17,18,20,21-Octahydro-5,8,11,16,19,22-hexaoxadibenzo[*a*,*j*]cyclooctadecen-2-yl)-1*H*-quinolin-2-one (6at). A mixture of 3-nitrovinylindole (1.0 mmol), dibenzo-18-crown-6 ether (1 mmol), and PPA (2–3 g) was heated at 80–85 °C for 30 min. Reaction progress was monitored by TLC. When all indole was consumed, the reaction temperature was increased to 95–100 °C and the mixture was heated for 1 h, then cooled to room temperature, poured into water (50 mL), and neutralized by aqueous ammonia. The aqueous phase was extracted twice with chloroform, concentrated, and isolated by flash chromatography (eluent EtOAc/petroleum ether). The compound was finally purified by recrystallization from EtOAc. White solid, mp 208–209 °C (EtOAc); ^{1}H NMR (DMSO-d_6) δ, ppm: 11.86 (br. s, 1H), 8.10 (s, 1H), 7.70 (d, J = 7.7 Hz, 1H), 7.47 (t, J = 8.3 Hz, 1H), 7.40–7.37 (m, 2H), 7.32 (d, J = 8.2 Hz, 1H), 7.18 (t, J = 7.6 Hz, 1H), 7.00 (d, J = 8.3 Hz, 1H), 6.99–6.95 (m, 2H), 6.89–6.86 (m, 2H), 4.18–4.10 (m, 4H), 4.10–4.04 (m, 4H), 3.92–3.81 (m, 8H); ^{13}C NMR (DMSO-d_6) δ, ppm: 161.1, 148.0, 147.9 (2C), 147.3, 138.0, 136.5, 131.0, 129.8, 128.7, 127.8, 121.8, 121.3, 120.7 (2C), 119.6, 114.5, 113.1, 112.5 (2C), 111.9, 68.9 (4C), 67.9, 67.8, 67.6 (2C); HRMS calcd for $C_{29}H_{29}NO_7Na$ (M + Na)$^+$: 526.1842, found 526.1834.

Experiments on isolation of intermediate hydroxamic acid and its further conversion into 2-quinolone

A mixture of indole **1a,d,c,e** (1.0 mmol), β-nitrostyrene **2a,i** (1.2 mmol) and PPA (4 g) was stirred at 70–75 °C for 30 min. The reaction mixture was cooled down to room temperature, poured into water (50 mL), and neutralized by aqueous ammonia to pH ~8. The formed precipitate was filtered off and recrystallized.

Hydroxamic acids **3aa,ab,db,ci,ea** obtained as described above (1 mmol) were stirred in PPA at 95–100 °C for 3 h. The mixtures were cooled down, poured into water (50 mL), and neutralized with aqueous ammonia to pH ~8. The aqueous portions were extracted with chloroform (2 × 50 mL) and combined organic phases were filtered through a short pad of silica gel (32–63 μm, 60 Å pore size). The filtrates were concentrated in vacuum to afford samples of quinolones **6aa,cq,ci,ea** identical to the material described above.

***N*-Hydroxy-2-(2-methyl-1*H*-indol-3-yl)-2-phenylacetamide (3aa).** White solid, mp 110–112 °C (toluene); ^{1}H NMR (400 MHz, DMSO-d_6) δ, ppm: 10.86 (br. s, 1H), 10.79 (br. s, 1H), 8.86 (br. s, 1H), 7.52 (d, J = 7.9 Hz, 1H), 7.37 (s, 1H), 7.26–7.20 (m, 5H), 6.94 (ddd, J = 7.45, 7.37 and 0.64 Hz, 1H), 6.83 (t, J = 7.2 Hz, 1H), 4.93 (s, 1H), 2.30 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ, ppm: 168.7, 140.5, 135.1, 133.2, 128.1 (2C), 127.9 (2C), 127.7, 126.1, 119.9, 119.8, 118.0, 110.2, 108.5, 45.3, 11.9; HRMS calcd for $C_{17}H_{16}N_2O_2Na$ (M + Na)$^+$: 303.1109, found 303.1105. Yield 238 mg (0.85 mmol, 85%).

***N*-Hydroxy-2-(2-phenyl-1*H*-indol-3-yl)-2-phenylacetamide (3ab).** White solid, mp 220–221 °C (toluene). The NMR spectral data are consistent with published results.[14] HRMS calcd for $C_{22}H_{18}N_2O_2Na$ (M + Na)$^+$: 365.1266, found 365.1260. Yield 329 mg (0.96 mmol, 96%).

***N*-Hydroxy-2-(1-methyl-2-phenyl-1*H*-indol-3-yl)-2-phenylacetamide (3db).** White solid, mp 152–155 °C (toluene). ^{1}H NMR (DMSO-d_6) δ, ppm: 10.64 (br. s, 1H), 8.08 (br. s, 1H), 7.70 (d, J = 8.0 Hz, 1H), 7.54–7.47 (m, 3H), 7.45–7.37 (m, 3H), 7.23–7.19 (m, 2H), 7.15–7.12 (m, 4H), 6.94 (t, J = 7.5 Hz, 1H), 4.76 (s, 1H), 3.53 (s, 3H); ^{13}C NMR (DMSO-d_6) δ, ppm: 168.5, 140.6, 138.9, 136.9, 130.9, 130.6 (2C), 128.5 (2C), 128.4, 127.9 (2C), 127.8 (2C), 126.4, 126.1, 122.2, 121.2, 118.8, 110.3, 109.6, 46.3, 30.7. HRMS calcd for $C_{23}H_{20}N_2O_2Na$ (M + Na)$^+$: 379.1422, found 379.1415. Yield 335 mg (0.94 mmol, 94%).

2-(4-Fluoro-phenyl)-*N*-hydroxy-2-(1-methyl-2-phenyl-1*H*-indol-3-yl)-acetamide (3ci). White solid, mp 174–175 °C (toluene). ^{1}H NMR (DMSO-d_6) δ, ppm: 10.65 (br. s, 1H), 8.82 (br. s, 1H), 7.69 (d, J = 8.0 Hz, 1H), 7.53–7.49 (m, 3H), 7.45 (d, J = 8.3 Hz, 1H),7.39–7.37 (m, 2H), 7.17–7.10 (m, 3H), 7.05–7.01 (m, 2H), 6.96 (t, J = 7.5 Hz, 1H), 4.74 (s, 1H), 3.53 (s, 3H); ^{13}C NMR (DMSO-d_6) δ, ppm: 168.4, 161.8, 159.4, 139.0, 136.9, 136.7 (2C), 130.8, 130.6 (2C), 129.7 (2C), 128.5 (2C), 128.4, 126.3, 121.8, 121.3, 119.0, 114.7, 114.5, 110.2, 109.7, 45.6, 30.7; HRMS calcd for $C_{23}H_{19}N_2FO_2Na$ (M + Na)$^+$: 397.1328, found 397.1323. Yield 344 mg (0.92 mmol, 92%).

2-(1-Butyl-2-phenyl-1*H*-indol-3-yl)-*N*-hydroxy-2-phenylacetamide (3ea). White solid, mp 132–134 °C (CH_2Cl_2/EtOH). ^{1}H NMR (DMSO-d_6) δ, ppm: 10.64 (br. s, 1H), 8.82 (br. s, 1H), 7.71 (d, J = 8.0 Hz, 1H), 7.51–7.38 (m, 6H), 7.22–7.19 (m, 2H), 7.15–7.12 (m, 4H), 6.92 (t, J = 7.5 Hz, 1H), 4.70 (s, 1H), 4.02–3.96 (m, 2H), 1.49–1.45 (m, 2H), 1.07–1.02 (m, 2H), 0.67 (t, J = 7.24 Hz, 3H); ^{13}C NMR (DMSO-d_6) δ, ppm: 168.6, 140.6, 138.7, 136.1, 136.2, 130.7, 128.5 (2C), 128.4 (2C), 127.9 (2C), 127.8 (2C), 126.6, 126.1, 122.4, 121.2, 118.7, 110.6, 109.8, 46.2, 42.8, 31.4, 19.2, 13.3; HRMS calcd for $C_{26}H_{26}N_2O_2Na$ $(M + Na)^+$: 421.1892, found 421.1887. Yield 355 mg (0.89 mmol, 89%).

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