Basic Alumina-Supported Synthesis of Aryl-Heteroarylmethanes *via* Palladium Catalyzed Cross-Coupling under Microwave Irradiation

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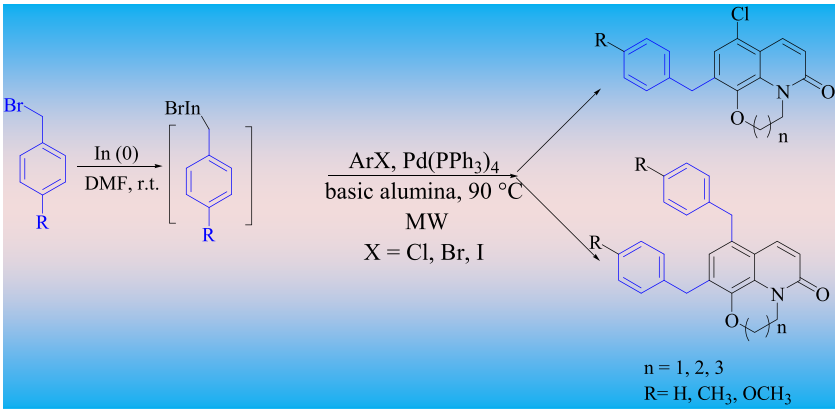

A basic alumina-supported microwave assisted simple methodology has been developed for the synthesis of aryl-heteroaryl methanes (benzylated quinolones) *via* transition metal catalyzed cross-coupling reaction of halo substituted polynuclear oxa-aza quinolones with benzyl indium, an organometallic reagent easily derived from commercially available benzyl bromide.

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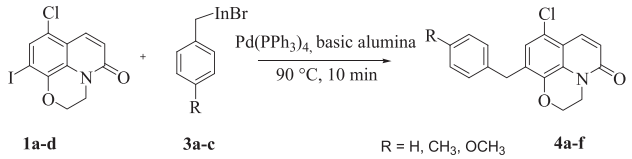
INTRODUCTION

Diaryl methyl moiety (ArAr′CH-) is a common subunit present in a variety of physiologically active compounds, like (*R*)-neobenodine [1], CDP-840 [2], tolterodine [3] (DetrolLA), and also in precursors to new ligand scaffolds [4], e.g., tetraarylethanes. Moreover, diaryl and triaryl methane derivatives are important constituents of dyes and have shown a wide range of biological activities [5]. In recent years, reports have appeared in the literature dealing with the synthesis of di-arylmethane moieties following the Suzuki-Miyaura cross-coupling reaction of benzyl halide with aryl boronic acids/phosphonates or carbonates [6–8]. Although these methods are efficient and show excellent functional-group tolerance under mild reaction conditions, the main drawbacks of these methods are the restricted availability as well as the high cost of the desired boronic acids. In an attempt to overcome these limitations, Chupak et al. [9] reported a simple methodology using a benzyl indium reagent to couple with aryl halides and efficiently synthesized a number of simple diaryl methanes having a variety of functional groups in both the coupling partners. Inspired by this result, we tried to apply this synthetic protocol to the more complex heterocyclic systems like fused quinolones [10,11], that constitute the core structures of a variety of biologically active compounds. But surprisingly it was found that this protocol is ineffective on complex system of halo-substituted fused polynuclear oxa-aza quinolones and in most of the cases dehalogenation of the substrates took place instead of benzylation. So the search for an alternative synthetic protocol with particular emphasis on a cleaner and more environmentally benign way to make target molecules appealed to us.

Organic reactions on solid supports [12] and those assisted by microwaves [13] especially under solvent-free conditions [14] have attracted much attention in recent years because of their enhanced selectivity, milder reaction conditions, and associated ease of manipulation. As a part of our drug discovery program, we reported the synthesis of tri-indolylmethanes (TRIMs) [15] from indoles, and of fused tri-, tetra-, penta-, and hexacyclic quinolones and quinolinium salts from quinolin-8-ols, using phase transfer

Scheme 1. Cross-coupling reaction of quinolones **1a–d** with benzylindium complex **3a–c**.



catalytic (PTC) conditions [16–20] and green approaches [21,22]. We also prepared mono- and di-arylated quinolone derivatives employing the most versatile and widely used Suzuki-Miyaura cross-coupling reaction [23,24] for the selective construction of carbon–carbon bonds through sp^2–sp^2 coupling of aryl halides with aryl boronic acids. We contemplated to synthesize novel diaryl methane scaffolds where one component will be aromatic while the other would be heteroaromatic. The contemplated synthesis, more specifically, involved the introduction of a benzyl moiety as substituent into heteroaromatics like the differently substituted fused quinolones [16–22] and that too without using aryl boronic acids (Scheme 1).

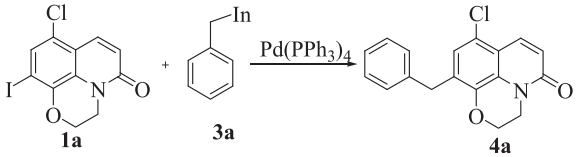
In this communication, we wish to report an efficient procedure for the generation of novel unsymmetrical aryl-heteroaryl methane-based polynuclear heteroaromatics (mono/di-benzylated quinolones) *via* basic alumina supported palladium catalyzed cross-coupling (sp^2–sp^3 coupling) reaction of quinolones with freshly prepared benzyl indium organometallic reagent.

RESULTS AND DISCUSSION

At the outset, we prepared the benzyl indium organometallic reagent from benzyl halides with commercially available indium powder using minimum amount of DMF as solvent

Table 1

Optimization of catalyst [$Pd(PPh_3)_4$] loading on different solid supports.[a]

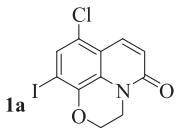
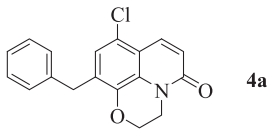
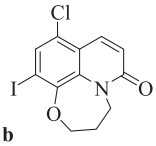
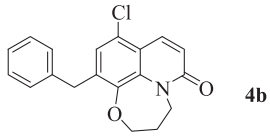
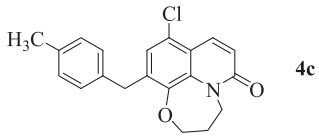
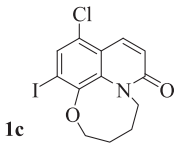
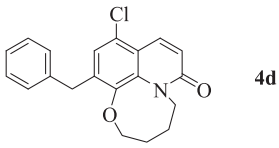
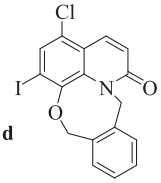
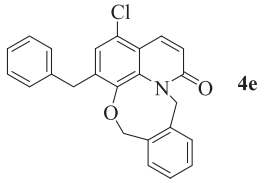
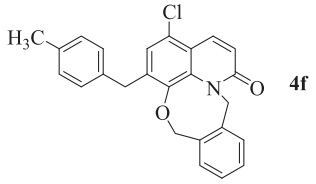


Entry	Solid support and bases	$Pd(PPh_3)_4$ (mol %)	Temp. (°C)	Time (min)	Yield[b] (%)
1	Silica gel-CH_3COONa	1.0	90	30	15
2	Silica gel-CH_3COONa	2.0	90	30	15
3	Silica gel-KF	1.0	90	30	15
4	Silica gel-KF	1.0	90	20	15
5	Silica gel-KF	2.0	90	20	25
6	Silica gel-K_2CO_3	1.0	90	20	28
7	Silica gel-K_2CO_3	2.0	90	20	28
8	Silica gel-Cs_2CO_3	1.0	100	20	33
9	Silica gel-Cs_2CO_3	2.0	100	20	33
10	Neutral alumina-KF	1.0	100	20	39
11	Neutral alumina-KF	2.0	100	20	39
12	Neutral alumina-Cs_2CO_3	1.0	100	20	45
13	Neutral alumina-Cs_2CO_3	2.0	100	20	45
14	Neutral alumina-K_2CO_3	1.0	100	20	55
15	Neutral alumina-K_2CO_3	2.0	100	20	55
16	Basic alumina-K_2CO_3	1.0	100	20	90
17	Basic alumina-K_2CO_3	2.0	100	20	90
18	Basic alumina-K_2CO_3	1.0	100	10	90
19	Basic alumina-K_2CO_3	1.0	90	10	90
Without base					
20	Basic alumina	1.0	90	10	90
21	Basic alumina	2.0	90	10	90
22	Basic alumina	0.75	90	10	90
23	Basic alumina	0.5	90	10	90
24	Basic alumina	0.1	90	10	72
25	Basic alumina	0.5	80	10	70
26	Basic alumina	–	90	10	NR[c]

[a]Under microwave irradiation condition.
[b]Isolated yield.
[c]No result.

Table 2

Cross–coupling reaction of quinolone **1a–d** with freshly prepeard benzyl indium complex (**3**).[a]

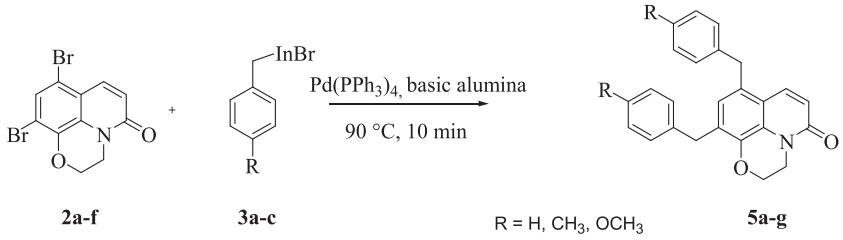
Entry no.	Quinolone[b]	Benzyl indium	Product	Yield (%)[c]
1	 **1a**	**3a**	 **4a**	90
2	 **1b**	**3a**	 **4b**	92
3	**1b**	**3b**	 **4c**	87
4	 **1c**	**3a**	 **4d**	88
5	 **1d**	**3a**	 **4e**	89
6	**1d**	**3b**	 **4f**	88

[a]Carried out in basic alumina using $Pd(PPh_3)_4$ at 90°C.
[b]Quinolones were prepared according to the literature [17,18].
[c]Isolated yield.

at room temperature. The formation of the organometallic reagent, monitored by thin-layer chromatography, was found to be complete within an hour. No precautions were necessary to exclude air or moisture during the preparation.

For the optimization of the sp^2–sp^3 coupling reaction, quinolone **1a** and the freshly prepared benzyl indium complex **3a** were chosen as two model coupling partners. It was revealed from the studies that the reactions catalyzed by $PdCl_2/PPh_3$ in toluene–H_2O using bases like KF, Cs_2CO_3, CH_3COONa, and K_3PO_4 were ineffective. Similar reactions performed in solvents like dioxane, DCM, or THF under otherwise identical conditions were also found to give low yield. Next, we attempted the reaction in DMF with $Pd(PPh_3)_4$ as catalyst and Na_2CO_3 as base; this yielded the desired biaryl product though with moderate yield (40–50%). Interestingly, reaction using K_2CO_3, DMF-H_2O, and $Pd(PPh_3)_4$ produced somewhat better yield (55–60%). We then explored our optimization protocol with $Pd(PPh_3)_4$ in using different solid supports like silica gel, neutral alumina, or basic alumina because organic groups can robustly anchor to their surface [25–31]. The reactions were performed in presence of different inorganic

Scheme 2. Cross-coupling reaction of quinolones **2a-f** with benzylindium complex **3a-c**.



bases as shown in Table 1. Indeed, using 1 mol % of Pd $(PPh_3)_4$, the silica gel-supported reaction in the presence of K_2CO_3 yielded 28%, neutral alumina with K_2CO_3 yielded 55% (Table 1, entries 6, 14), while basic alumina alone afforded the most effective conversion (90%) to the biaryl product (Table 1, entry 18). It is notable that only 0.5 mol % of Pd $(PPh_3)_4$ with basic alumina could afford 90% yield just in 10 min (Table 1, entry 23). Increase of the reaction time did not alter the yield of the product. No addition of base from outside is required to promote the catalytic reaction in basic alumina, which itself acts as the base during the course of the reaction, whereas neutral alumina or silica gels are totally ineffective in absence of base.

Evidence for the benzylation of quinolone was obtained from ^{1}H-, ^{13}C-NMR data and mass spectral analysis of the product. In order to check the efficacy of microwave irradiation over traditional heating, we performed the reaction using an oil bath at 120°C and only 35% yield of product was achieved even after overnight heating.

Following the reaction protocol thus achieved, we extended the study of C-C bond forming reaction with other chloro-, iodo-substituted oxazino, oxazepino, and oxazocino quinolones having tri-, tetra-, penta- and hexa-membered (**1a–d**) ring systems (Scheme 1) and a series of benzylated quinolone products were obtained in good yields (Table 2).

Next we applied this reaction protocol on dibromo-substituted quinolones (**2a–f**) possessing similar structural features as stated earlier (Scheme 2) and a series of dibenzylated quinolones (**5a–g**) were obtained (Table 3).

We performed few more reactions using the derivatives of **3a** viz 4-methyl- (**3b**) and 4-methoxy- (**3c**) benzyl bromides in a similar fashion. In these cases also the method proved to be effective and produced very well to excellent yield of the products. Finally, the applicability of this simple methodology was checked by performing reaction on simple aromatic system like the coupling between iodobenzene and benzyl bromide; the method proved as effective as in the complex systems.

It is worthy of mention that no product formation was observed when the reaction was performed in absence of the palladium catalyst. Benzylation took place with quinolones having bromo- or iodo-substitution, i.e., monobenzylated quinolones (**4a–f**) were obtained from chloro-, iodo-substituted quinolones (**1a–d**) but dibenzylated quinolones (**5a–g**) were obtained from dibromoquinolones (**2a–f**). It is also to be noted that in no case dehalogenation of the substrates was observed.

The plausible pathway of the reaction is depicted in Scheme 3. It is presumed that the reaction is initiated with the basic alumina (**III**) transforming the oxidative reaction product **II** to produce intermediate **V**, while the benzyl indium (**3**) gets converted to intermediate **VI**. The migration of $ArCH_2$- from **VI** to **V** produces intermediate **VIII**, which is simultaneously converted to [Pd(II) to Pd(0)] intermediate **I** and desired benzylquinolone *via* reductive elimination reaction.

We also investigated the reusability of the solid support, which is important for industrial purpose as well as essential for environmental pollution. Basic alumina can be reused after calcinations at 150°C for 5 h (after washing with water and acetone) could be recycled at least 3–4 times with minimum loss on its activity.

CONCLUSION

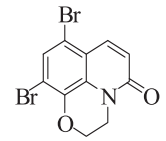
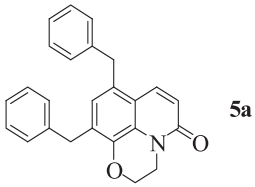
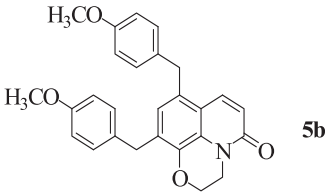
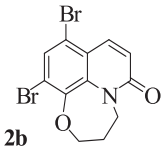
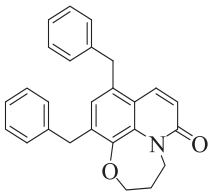
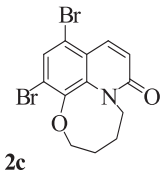
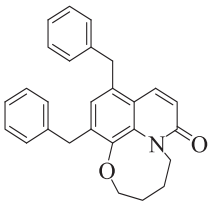
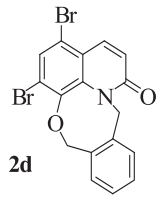
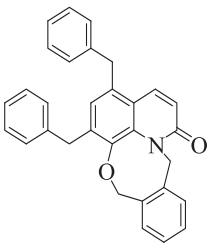
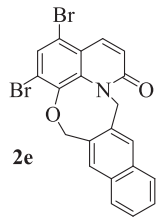
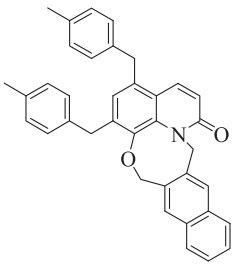
In summary, we have demonstrated a new catalytic system for the Suzuki-Miyaura type cross-coupling (sp^2–sp^3 coupling) reaction for the synthesis of quinolone-based diaryl methane derivatives by the reaction of halogenated quinolones with benzyl indium organometallic reagent. The procedure offers broad synthetic route for the construction of new polynuclear heteroaromatic systems having potential biological activity. The method is easy, simple, and avoids the use of highly reactive organometallic reagents.

EXPERIMENTAL

General experimental. Melting points were determined with capillary melting point apparatus and are uncorrected. The NMR spectra were taken on a BRUKER 600/300 DPX spectrometer operating at 600/300 MHz for ^{1}H and at 150/75 MHz for ^{13}C, respectively, with tetramethylsilane (TMS) as an internal standard and the chemical shifts are reported in δ units. High resolution mass spectrometry (HRMS) (positive mode) were obtained using electro spray ionisation quadrapole time of flight mass spectrometer combined with liquid chromatography (LC-ESI-Q-TOF) micro mass spectrometer. All chromatographic purifications were performed on silica gel (60–120 mesh) that was obtained from E. Merck India Ltd.,

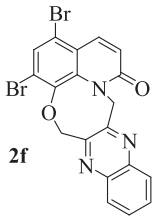
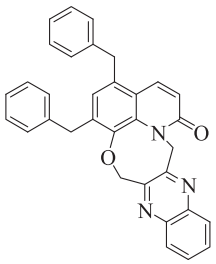
Table 3

Cross-coupling reactions of quinolones **2a–f** with benzyl indium complex **3**.[a]

Entry no.	Quinolone[b]	Benzyl indium	Product	Yield (%)[c]
1	 **2a**	**3a**	 **5a**	88
2	**2a**	**3c**	 **5b**	85
3	 **2b**	**3a**	 **5c**	82
4	 **2c**	**3a**	 **5d**	85
5	 **2d**	**3a**	 **5e**	81
6	 **2e**	**3b**	 **5f**	81

(*Continued*)

Table 3
(*Continued*)

Entry no.	Quinolone[b]	Benzyl indium	Product	Yield (%)[c]
7	 **2f**	**3a**	 **5g**	83

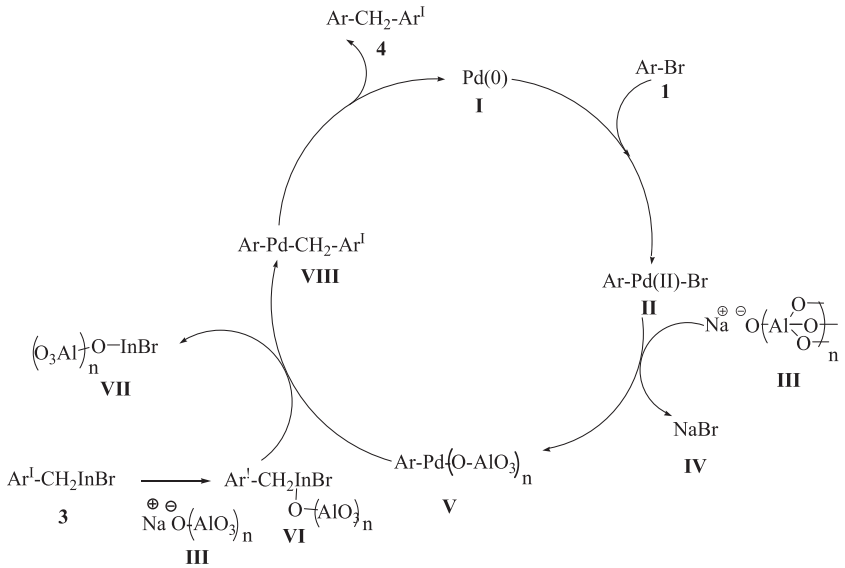
[a]Reactions were carried out in basic alumia using $Pd(PPh_3)_4$ at 90 °C.
[b]Quinolones were prepared according to the literature [17,18].
[c]Isolated yield.

Mumbai. Thin layer chromatography (TLC) was performed on pre-coated silica gel 60 F_{254} aluminum sheets (E. Merck, Germany) using different solvent systems and the spots were visualized either under UV torch or on heating after spraying Liebermann–Burchard solution. Organic solvents used for the chemical synthesis and also for chromatography were of analytical grade and were acquired from E. Merck (India). 8-Hydroxyquinoline derivatives, dibromo-alkanes or xylenes and benzyl bromides were purchased from Aldrich Chemical Ltd. (USA).

General reaction procedure. To a solution of benzyl bromide (342 mg, 2 mmol) in dimethyl formamide (DMF) (2 mL), indium dust (344 mg, 3 mmol) was added. The reaction mixture was stirred at room temperature until the benzyl bromide disappeared from the reaction mixture (assessed by TLC). The mixture of quinolone component (1 mmol in case of **1a–d**, and 0.5 mmol in case of **2a–f**), basic alumina (600 mg) and 11.6 mg (0.01 mmol) of $Pd(PPh_3)_4$ was taken in a microwave vessel and the benzyl indium solution was then transferred to it. The resulting mixture was placed in the microwave reactor (CEM, Discover, USA) and irradiated at (150 W) for 10 min. The reaction mixture transformed to brown-black and the bulk temperature was found to be 90°C. After cooling, resulting mixture was stirred with EtOAc (50 mL) for 10 min and filtered through a sintered funnel. The filtrate was washed with water (3× 30 mL) followed by brine (1× 30 mL). The organic part was separated, dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The residue was subjected to column chromatography over neutral alumina followed by crystallization to yield the products. In the recycling experiment, the residue (solid support) obtained was washed with acetone and water (3–5 times) and subjected to calcinations at 150°C for further use in the reaction.

Characterization data of compounds. 4a: White solid. M.p. 145–147°C; R_f (10% $CHCl_3$–pet. ether) 0.75; ^{1}H-NMR (600 MHz, $CDCl_3$) δ 4.03 (2H, s), 4.26–4.27 (2H, m), 4.36–4.39 (2H, m), 6.72 (1H, d J = 9.6 Hz), 7.02 (1H, s), 7.20–7.23 (3H,

Scheme 3. Plausible mechanistic pathway for basic alumina supported synthesis of aryl-heteroaryl methane.



m), 7.28–7.30 (2H, m), 8.05 (1H, d J = 9.6 Hz); ^{13}C-NMR (150 MHz, $CDCl_3$) δ 35.4 (CH_2), 40.1 (CH_2), 63.6 (CH_2), 117.0 (C), 121.4 (CH), 124.0 (C), 124.4 (CH), 126.4 (CH), 127.8 (C), 128.6 (2× CH), 128.8 (2× CH), 130.8 (C), 135.6 (CH), 139.3 (C), 139.5 (C), 160.0 (C). HRMS [ESI], *m/z* calculated for $C_{18}H_{14}ClNO_2Na$: $[M+Na]^+$ 334.0611; found: 334.0622. Analysis calculated for $C_{18}H_{14}ClNO_2$ (311.76): C, 69.35; H, 4.53; N, 4.49. Found: C, 69.65; H, 4.43; N, 4.79.

4b: White solid. M.p. 142–144°C; R_f (10% $CHCl_3$–pet-ether) 0.77; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 2.27–2.31 (2H, m), 4.02 (2H, s), 4.13–4.17 (2H, m), 4.59–4.61 (2H, m), 6.69 (1H, d J = 9.9 Hz), 7.05 (1H, s), 7.12–7.20 (3H, m), 7.26–7.29 (2H, m), 7.99 (1H, d J = 9.6 Hz); ^{13}C-NMR (75 MHz, $CDCl_3$) δ 27.3 (CH_2), 36.0 (CH_2), 41.7 (CH_2), 70.5 (CH_2), 118.5 (C), 121.6 (CH), 124.7 (CH), 125.7 (C), 126.0 (CH), 128.2 (2× CH), 128.3 (2× CH), 134.5 (C), 135.0 (CH), 135.2 (C), 139.4 (C), 145.4 (C), 161.8 (C). HRMS [ESI], *m/z* calculated for $C_{19}H_{16}ClNO_2Na$: $[M+Na]^+$ 348.0767; found: 348.0795. Analysis calculated for $C_{19}H_{16}ClNO_2$ (325.79): C, 70.05; H, 4.95; N, 4.30. Found: C, 70.35; H, 5.05; N, 4.50.

4c: White solid. M.p. 141–143°C; R_f (10% $CHCl_3$–pet-ether) 0.77; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 2.30–2.39 (5H, m), 4.35 (2H, t J = 6.9 Hz), 4.48 (2H, s), 4.61 (2H, t J = 5.7 Hz), 6.76 (1H, d J = 9.4 Hz), 7.14 (2H, d J = 7.8 Hz), 7.28 (2H, d J = 7.8 Hz), 7.65 (1H, s), 8.00 (1H, d J = 9.9 Hz); ^{13}C-NMR (75 MHz, $CDCl_3$) δ 21.2 (CH_3), 27.3 (CH_2), 33.7 (CH_2), 42.3 (CH_2), 71.2 (CH_2), 120.3 (C), 123.0 (CH), 127.0 (C), 128.9 (2× CH), 129.4 (2× CH), 132.2 (CH), 134.0 (C), 134.7 (2× C), 135.2 (CH), 138.3 (C), 147.0 (C), 161.7 (C). HRMS [ESI], *m/z* calculated for $C_{20}H_{18}ClNO_2Na$: $[M+Na]^+$ 362.0924; found: 362.0915. Analysis calculated for $C_{20}H_{18}ClNO_2$ (339.82): C, 70.69; H, 5.34; N, 4.12. Found: C, 70.55; H, 5.25; N, 4.30.

4d: White solid. M.p. 140–142°C; R_f (10% $CHCl_3$–pet-ether) 0.78; ^{1}H-NMR (600 MHz, $CDCl_3$) δ 2.02–2.05 (2H, m), 2.25 (2H, bs), 3.84–3.96 (2H, m), 4.16–4.38 (2H, m), 4.82–4.89 (2H, m), 6.74 (1H, d J = 9.6 Hz), 7.06 (1H, s), 7.20–7.22 (2H, m), 7.23–7.24 (1H, m), 7.29–7.32 (2H, m), 8.08–8.10 (1H, m); ^{13}C-NMR (150 MHz, $CDCl_3$) δ 22.5 (CH_2), 26.5 (CH_2), 36.0 (CH_2), 44.5 (CH_2), 76.1 (CH_2), 118.3 (C), 122.0 (CH), 125.2 (CH), 126.5 (CH), 128.1 (C), 128.7 (CH), 128.9 (CH), 129.96 (CH), 129.0 (CH), 135.4 (CH), 138.0 (C), 138.8 (C), 139.6 (C), 141.7 (C), 162.6 (C). HRMS [ESI], *m/z* calculated for $C_{20}H_{18}ClNO_2Na$: $[M+Na]^+$ 362.0924; found: 362.0915. Analysis calculated for $C_{20}H_{18}ClNO_2$ (339.82): C, 70.69; H, 5.34; N, 4.12. Found: C, 70.35; H, 5.25; N, 4.38.

4e: White solid. M.p. 138–140°C; R_f (10% $CHCl_3$–pet-ether) 0.78; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 4.13–4.26 (2H, m), 4.86 (1H, d J = 15.0 Hz), 5.53 (1H, d J = 15.0 Hz), 5.86 (1H, d J = 13.5 Hz), 6.01 (1H, d J = 13.5 Hz), 6.72 (1H, d J = 9.6 Hz), 6.87 (1H, d J = 6.9 Hz), 7.06 (1H, s), 7.22–7.33 (7H, m), 7.61 (1H, d J = 6.9 Hz), 8.00 (1H, d J = 9.6 Hz); ^{13}C-NMR (75 MHz, $CDCl_3$) δ 36.1 (CH_2), 46.9 (CH_2), 78.0 (CH_2), 119.0 (C), 122.3 (CH), 125.3 (CH), 125.6 (CH), 126.6 (CH), 128.19 (CH), 128.25 (CH), 128.7 (2× CH), 128.8 (2× CH), 132.4 (CH), 134.6 (C), 135.1 (CH), 135.5 (2× C), 135.6 (C), 137.8 (C), 139.5 (C), 144.3 (C), 162.6 (C). HRMS [ESI], *m/z* calculated for $C_{24}H_{18}ClNO_2Na$: $[M+Na]^+$ 410.0924; found: 410.0970. Analysis calculated for $C_{24}H_{18}ClNO_2$ (387.86): C, 74.32; H, 4.68; N, 3.61. Found: C, 74.65; H, 4.53; N, 3.79.

4f: White solid. M.p. 139–141°C; R_f (10% $CHCl_3$–pet-ether) 0.78; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 2.46 (3H, s), 4.27–4.35 (2H, m), 4.50 (1H, d J = 15.0 Hz), 5.29 (1H, d J = 15.0 Hz), 5.93 (1H, d J = 15.3 Hz), 6.29 (1H, d J = 13.3 Hz), 6.76–6.82 (2H, m), 7.13–7.33 (5H, m), 7.50–7.52 (3H, m), 8.01(1H, d J = 9.6 Hz); ^{13}C-NMR (75 MHz, $CDCl_3$) δ 21.3 (CH_3), 36.0 (CH_2), 46.0 (CH_2), 75.9 (CH_2), 119.3 (C), 122.4 (CH), 125.4 (CH), 125.7 (CH), 128.18 (CH), 128.21 (CH), 128.3 (C), 129.0 (2× CH), 129.3 (2× CH), 132.3 (CH), 133.6 (C), 134.6 (C), 134.8 (CH), 135.4 (C), 136.0 (C), 138.1 (C), 138.4 (C), 142.4 (C), 162.5 (C). HRMS [ESI], *m/z* calculated for $C_{25}H_{20}ClNO_2Na$: $[M+Na]^+$ 424.1080; found: 410.1065. Analysis calculated for $C_{25}H_{20}ClNO_2$ (401.88): C, 74.71; H, 5.02; N, 3.49. Found: C, 74.45; H, 4.93; N, 3.59.

5a: White solid. M.p. 137–140°C; R_f (10% $CHCl_3$–pet-ether) 0.85; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 4.05 (2H, s), 4.11–4.15 (4H, m), 4.60–4.61 (2H, m), 6.55 (1H, d J = 9.9 Hz), 6.89 (1H, s), 7.07–7.09 (2H, m), 7.18–7.20 (4H, m), 7.24–7.29 (4H, m), 7.71 (1H, d J = 9.9 Hz); ^{13}C-NMR (75 MHz, $CDCl_3$) δ 36.6 (CH_2), 38.3 (CH_2), 42.0 (CH_2), 70.6 (CH_2), 119.9 (C), 120.8 (CH), 126.0 (CH), 126.3 (CH), 127.1 (CH), 128.3 (2× CH), 128.4 (2× CH), 128.6 (4× CH), 131.8 (C), 134.4 (2× C), 135.7 (CH), 140.1 (C), 140.6 (C), 146.0 (C), 162.3 (C). HRMS [ESI], *m/z* calculated for $C_{25}H_{21}NO_2Na$: $[M+Na]^+$ 390.1470; found: 390.1450. Analysis calculated for $C_{25}H_{21}NO_2$ (367.44): C, 81.72; H, 5.76; N, 3.81. Found: C, 81.55; H, 5.45; N, 3.78.

5b: White solid. M.p. 139–141°C; R_f (10% $CHCl_3$–pet-ether) 0.75; ^{1}H-NMR (600 MHz, $CDCl_3$) δ 3.42–3.44 (4H, m), 3.86–3.88 (6H, m), 4.34–4.41 (4H, m), 6.63 (1H, d J = 10.2 Hz), 6. 98–7.02 (4H, m), 7.17 (1H, s), 7.31–7.33 (2H,m), 7.56–7.57 (2H, m), 7.82 (1H, d J = 9.6 Hz); ^{13}C-NMR (150 MHz, $CDCl_3$) δ 32.0 (CH_2), 37.6 (CH_2), 40.3 (CH_2), 54.3 (CH_3), 54.4 (CH_3), 63.7 (CH_2), 113.7 (2× CH), 113.9 (2× CH), 118.0 (C), 120.4 (CH), 125.6 (CH), 127.6 (C), 129.3 (C), 129.8 (C), 130.8 (2× CH), 131.0 (2× CH), 131.2 (C), 132.0 (C), 133.7 (C), 137.6 (C), 137.6 (CH), 139.0 (C), 159.2 (C), 159.3 (C), 162.3 (C). HRMS [ESI], *m/z* calculated for $C_{27}H_{25}NO_4Na$: $[M+Na]^+$ 450.1681; found: 450.1650. Analysis calculated for $C_{27}H_{25}NO_4$ (427.49): C, 75.86; H, 5.89; N, 3.28. Found: C, 75.73; H, 5.54; N, 3.18.

5c: White solid. M.p. 139–141°C; R_f (10% $CHCl_3$–pet-ether) 0.80; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 2.23–2.32 (2H, m), 4.04 (2H, s), 4.13–4.19 (4H, m), 4.59–4.63 (2H, m), 6.55 (1H, d J = 9.6 Hz), 6.89 (1H, s), 7.06–7.09 (2H, m) 7.11–7.28 (8H, m), 7.71 (1H, d J = 9.6 Hz); ^{13}C-NMR (75 MHz, $CDCl_3$) δ 27.7 (CH_2), 36.4 (CH_2), 38.1 (CH_2), 41.9 (CH_2), 70.4 (CH_2), 119.8 (C), 120.6 (CH), 125.9 (CH), 126.1 (CH), 126.9 (CH), 128.1 (2× CH), 128.2 (2× CH), 128.4 (2× CH), 128.5 (2× CH), 131.6 (C), 134.3 (2× C), 135.5 (CH), 139.9 (C), 140.5 (C), 145.8 (C), 162.2 (C). HRMS [ESI], *m/z* calculated for $C_{26}H_{23}NO_2Na$: $[M+Na]^+$ 404.1626; found: 404.1647. Analysis calculated for $C_{26}H_{23}NO_2$ (381.47): C, 81.86; H, 6.08; N, 3.67. Found: C, 82.03; H, 6.34; N, 3.81.

5d: White solid. M.p. 141–143°C; R_f (10% $CHCl_3$–pet-ether) 0.80; ^{1}H-NMR (600 MHz, $CDCl_3$) δ 1.78 (2H, m), 2.25–2.29 (2H, m), 4.04 (2H, s), 4.12–4.19 (4H, m), 4.61 (2H, m), 6.54 (1H, d J = 9.6 Hz), 6.88 (1H, s), 7.07–7.10 (2H, m), 7.17–7.22 (4H, m) 7.24–7.28 (4H, m), 7.70–7.20 (1H, m); ^{13}C-NMR (150 MHz, $CDCl_3$) δ 20.7 (CH_2), 27.8 (CH_2), 36.5 (CH_2), 38.2 (CH_2), 42.0 (CH_2), 70.5 (CH_2), 119.9 (C), 120.8 (CH), 126.0 (CH), 126.3 (CH), 127.0 (CH), 128.2 (2× CH), 128.3 (2× CH), 128.56 (2× CH), 128.57 (2× CH), 131.7 (C), 134.39 (C), 134.41 (C), 135.7 (CH), 140.0 (C), 140.6 (C), 146.0 (C), 162.3 (C). HRMS [ESI], *m/z* calculated for $C_{27}H_{25}NO_2Na$: $[M+Na]^+$

418.1783; found: 418.1747. Analysis calculated for $C_{27}H_{25}NO_2$ (395.49): C, 82.00; H, 6.37; N, 3.54. Found: C, 81.83; H, 6.34; N, 3.51.

5e: White solid. M.p. 140–142°C; R_f (10% $CHCl_3$–pet-ether) 0.80; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 4.15 (2H, s), 4.21 (2H, s), 4.85 (1H, d J = 15.0 Hz), 5.48 (1H, d J = 15.0 Hz), 5.86–5.99 (2H, m), 6.56 (1H, d J = 9.9 Hz), 6.85–6.89 (2H, m), 7.05 (2H, d J = 6.9 Hz), 7.22–7.33 (10H, m), 7.63 (1H, d J = 6.9 Hz), 7.70 (1H, d J = 9.6 Hz); ^{13}C-NMR (75 MHz, $CDCl_3$) δ 36.3 (CH_2), 38.5 (CH_2), 47.1 (CH_2), 78.0 (CH_2), 120.0 (C), 121.1 (CH), 125.4 (CH), 126.29 (CH), 126.32 (CH), 127.3 (CH), 127.9 (2× CH), 128.2 (2× CH), 128.5 (2× CH), 128.6 (2× CH), 128.7 (2× CH), 132.4 (CH), 133.7 (C), 134.8 (C), 135.0 (C), 135.3 (CH), 135.8 (C), 136.6 (C), 139.8 (C), 140.4 (C), 144.7 (C), 162.7 (C). HRMS [ESI], *m/z* calculated for $C_{31}H_{25}NO_2Na$: $[M+Na]^+$ 466.1783; found: 466.1811. Analysis calculated for $C_{31}H_{25}NO_2$ (443.54): C, 83.95; H, 5.68; N, 3.16. Found: C, 83.53; H, 5.34; N, 3.51.

5f: White solid. M.p. 185–187°C; R_f (10% $CHCl_3$–pet-ether) 0.65; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 2.36 (6H, s), 4.50 (4H, s), 5.62 (1H, d J = 14.7 Hz), 5.83–5.98 (2H, m), 6.51 (1H, d J = 13.5 Hz), 6.77 (1H, d J = 9.6 Hz), 7.13–7.15 (4H, m), 7.25–7.29 (4H, m), 7.42–7.50 (2H, m), 7.56 (1H, s), 7.63 (1H, s), 7.70–7.73 (1H, m), 7.78–7.81 (1H, m), 7.90 (1H, d J = 9.9 Hz), 8.02 (1H, s); ^{13}C-NMR (75 MHz, $CDCl_3$) δ 21.2 (2× CH_3), 33.7 (2× CH_2), 46.2 (CH_2), 76.0 (CH_2), 118.9 (CH), 121.1 (C), 123.2 (CH), 125.3 (CH), 126.4 (CH), 126.8 (CH), 127.2 (CH), 127.9 (CH), 128.9 (3× CH), 129.4 (4× CH), 130.1 (CH), 131.4 (CH), 132.5 (C), 132.6 (2×C), 133.2 (C), 134.7 (3× C), 136.1 (C), 137.4 (CH), 138.3 (3×C), 142.7 (C), 162.0 (C). HRMS [ESI], *m/z* calculated for $C_{37}H_{31}NO_2Na$: $[M+Na]^+$ 544.2252; found: 544.2211. Analysis calculated for $C_{37}H_{31}NO_2$ (521.65): C, 85.19; H, 5.99; N, 2.69. Found: C, 84.73; H, 5.54; N, 2.51.

5g: White solid. M.p. 185–187°C; R_f (10% $CHCl_3$–pet-ether) 0.65; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 4.17–4.27 (4H, m), 4.92 (1H, d J = 15.9 Hz), 5.47 (1H, d J = 15.9 Hz), 5.91 (1H, d J = 14.1 Hz), 6.06 (1H, d J = 14.1 Hz), 6.59 (1H, d J = 9.9 Hz), 7.10–7.11 (2H, d J = 7.2 Hz), 7.20–7.35 (9H, m), 7.73–7.79, (3H, m), 7.94–7.97 (1H, m), 8.21–8.24 (1H, m); ^{13}C-NMR (75 MHz, $CDCl_3$) δ 36.5 (CH_2), 38.4 (CH_2), 52.2 (CH_2), 78.5 (CH_2), 120.3 (C), 121.5 (CH), 126.4 (2× CH), 127.3 (CH), 128.18 (CH), 128.24 (2× CH), 128.59 (3× CH), 128.62 (3× CH), 129.6 (CH), 129.8 (CH), 130.3 (CH), 133.8 (C), 135.1 (C), 135.8 (CH), 136.3 (C), 139.6 (C), 140.0 (C), 140.9 (C), 141.5 (C), 145.9 (C), 150.0 (C), 151.3 (C), 163.4 (C). HRMS [ESI], *m/z* calculated for $C_{33}H_{25}NO_2Na$: $[M+Na]^+$ 518.1844; found: 518.1840. Analysis calculated for $C_{33}H_{25}NO_2$ (467.56): C, 79.98; H, 5.08; N, 8.48. Found: C, 79.73; H, 5.04; N, 8.71.

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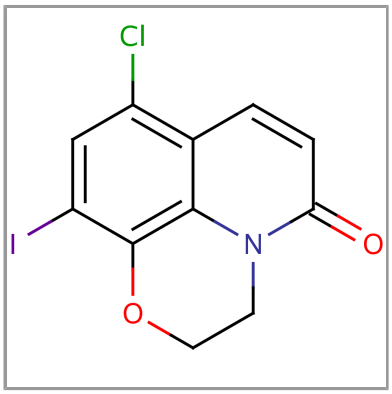
1a



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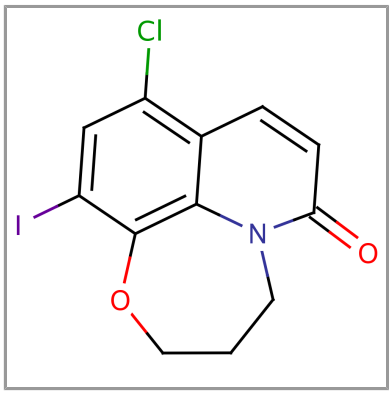

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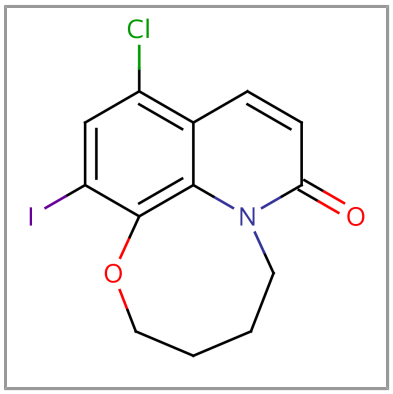

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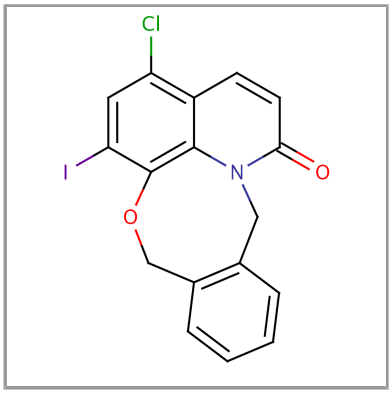
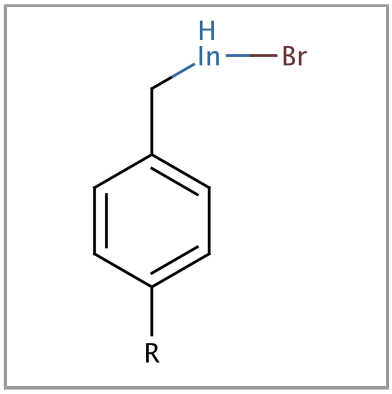


Compound Details Structure Search

3



Compound Details Structure Search

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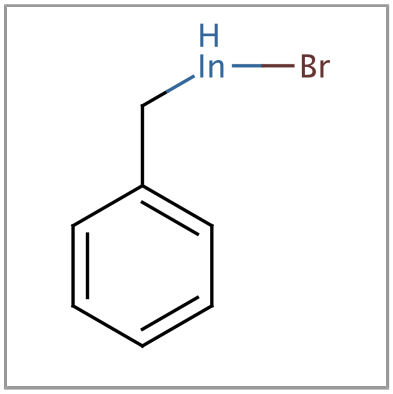

Compound Details Structure Search

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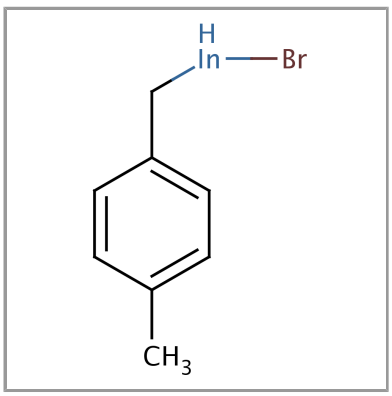

Compound Details Structure Search

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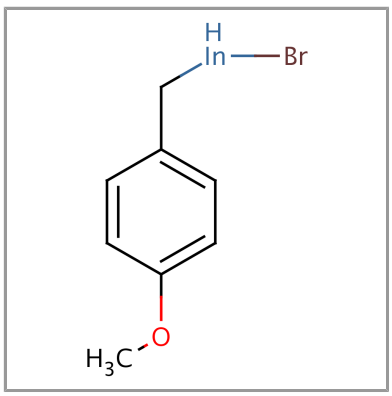

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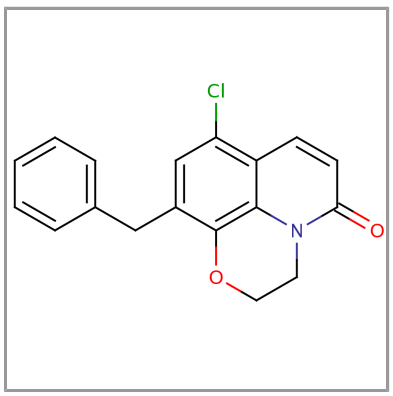

Compound Details Structure Search

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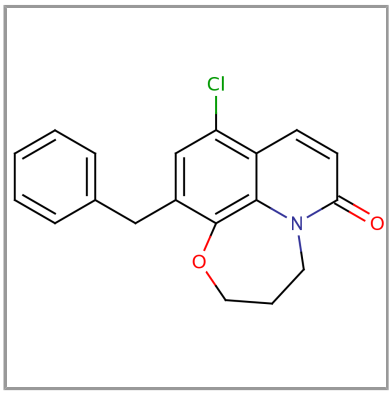

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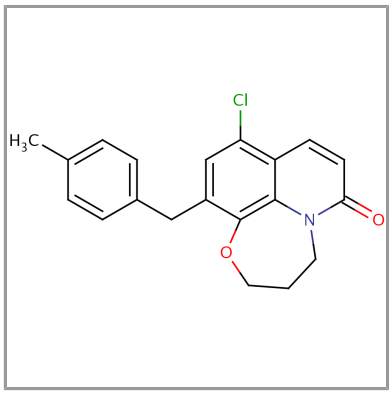

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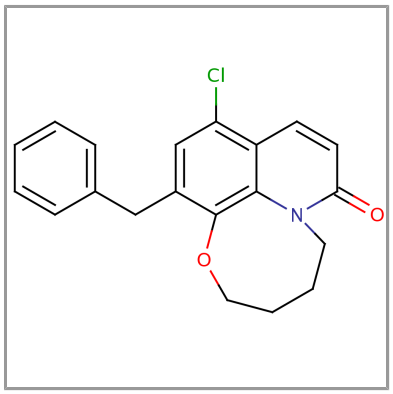

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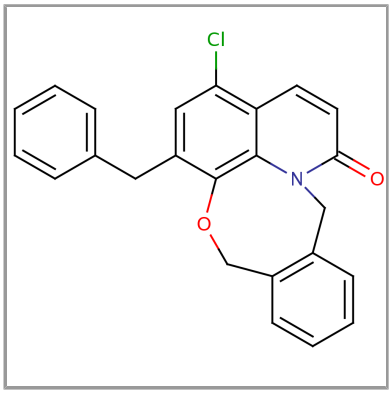

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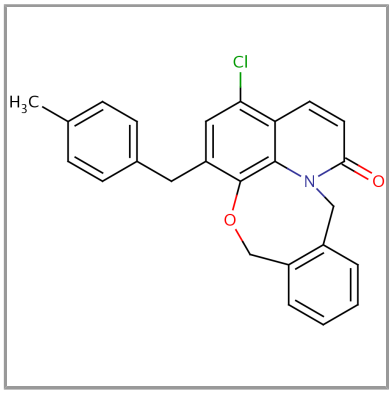

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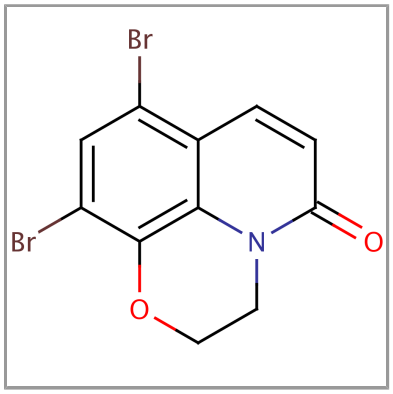

Compound Details Structure Search

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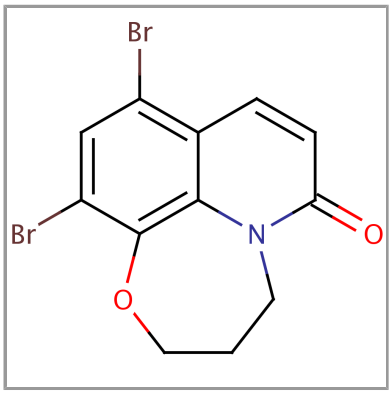

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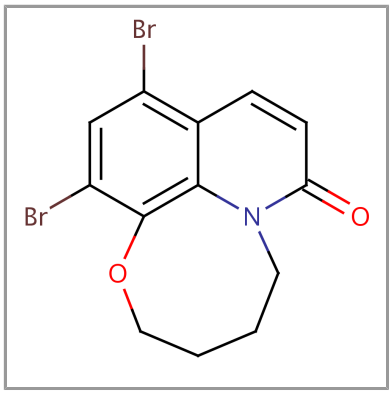

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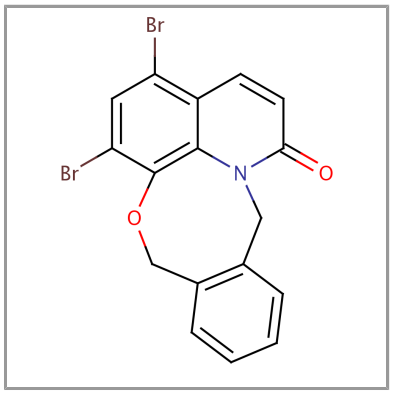

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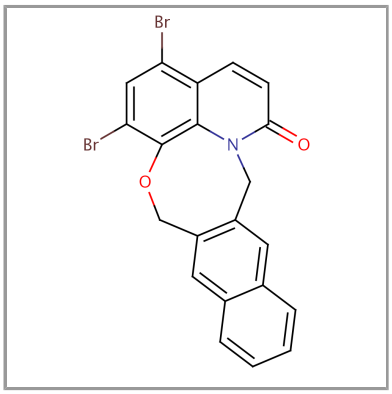

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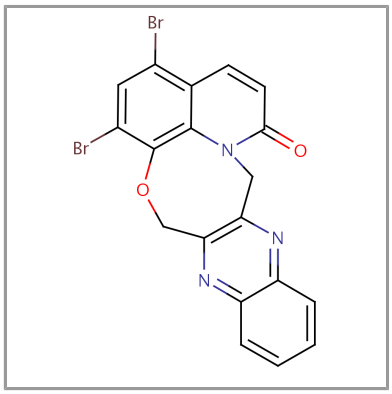

Compound Details Structure Search

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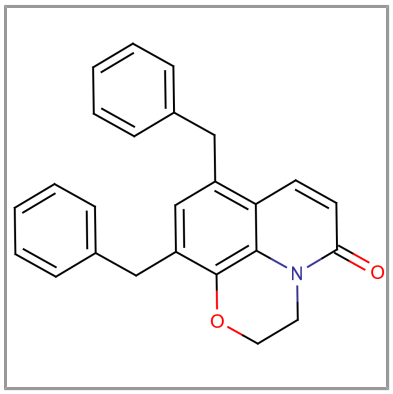

Compound Details Structure Search

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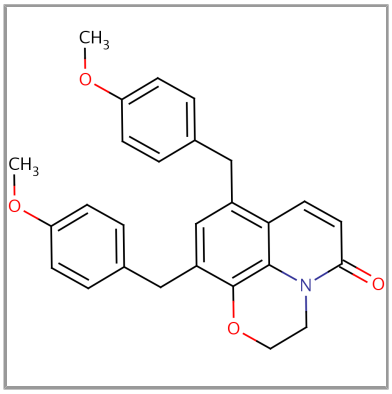

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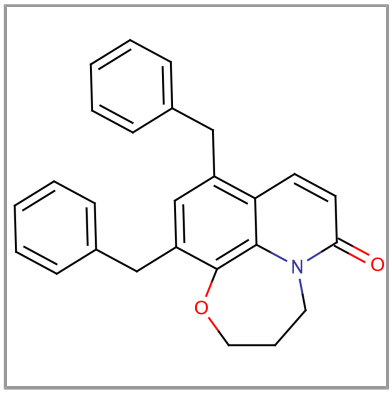

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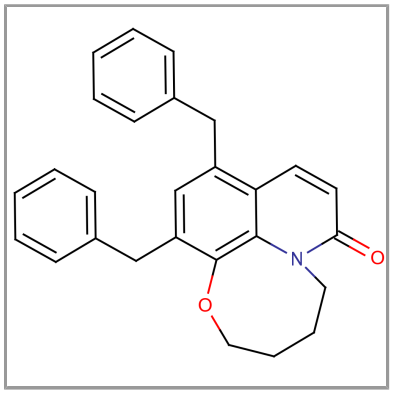

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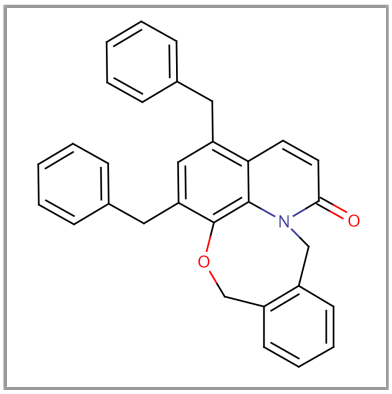

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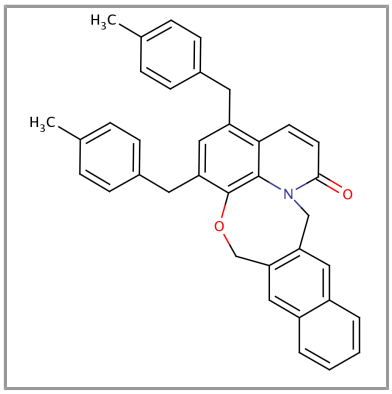

Compound Details Structure Search

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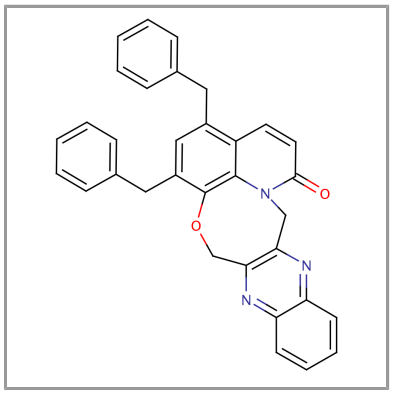

Compound Details Structure Search

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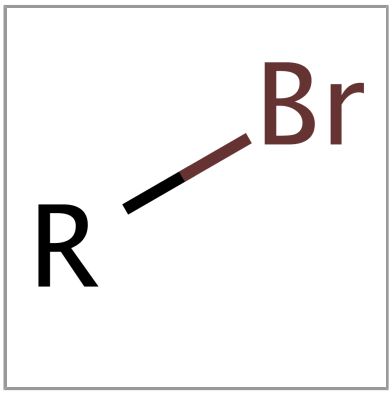

Compound Details Structure Search

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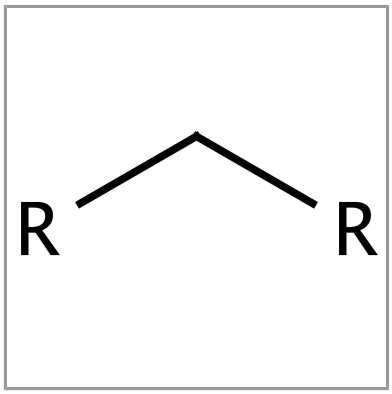

Compound Details Structure Search