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Efficient microwave-assisted synthesis of 1-(1*H*-indol-1-yl)-2-phenyl-3-(1*H*-1,2,4-triazol-1-yl)-propan-2-ols as antifungal agents

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Abstract—New conazole antifungals, in the series of triazole alcohols **23a**–**d** and **24a**–**e** incorporating an indole moiety substituted at 5-position by halogens, a cyano or 4-methoxyphenyl group, have been synthesized by ring opening of corresponding oxiranes **15** and **16**. These dihalogeno intermediates and their congeneers could be prepared in high yields by Corey–Chaykovsky reaction under microwave irradiation.

1. Introduction

In recent years, the increase of opportunistic fungal infections and the emergence of azole resistance strains have intensified the work of pharmacochemists to develop new antifungal drugs.[1] Microwave-assisted organic synthesis has also received great attention due to reduction in reaction times, minimization of by-products and increased yields.[2] So the application of microwaves is a particularly attractive tool for the preparation of key intermediates and new bioactive molecules. Loupy et al.[3,4] have proved that antifungal intermediates such as 1-(2′,4′-dichlorophenacyl)azoles can be synthesized by a selective microwave solvent free N-alkylation of azoles with 2,2′,4′-trichloroacetophenone.

Oxiranes of 2-(1*H*-1,2,4-triazol-1-yl)acetophenones are precursors widely used in the synthesis of conazoles.[5] These intermediates are most often prepared by a Corey–Chaykovsky epoxidation, performed in DMSO, THF or ionic liquids, in the presence of (i) a base such as NaH, KOH, or *n*-BuLi, and (ii) trimethylsulfoxonium iodide or trimethylsulfonium iodide.[6–8] To the best of our knowledge, no report of microwave-assisted Corey–Chaykovsky epoxidation has been published up to now. We have experimented the interest of this method starting with phenacyltriazoles **8** and **9** and confirmed the generality of the process using five other phenacyltriazoles **10**–**14**.

In our ongoing interest in the preparation of new antifungal compounds with indole moiety,[9] we describe in the present work application of microwave irradiation in the synthesis of various 1-(1*H*-indol-1-yl)-2-phenyl-3-(1*H*-1,2,4-triazol-1-yl)propan-2-ols.

The general route for the preparation of indole derivatives **23a**–**d** and **24a**–**e** is reported in Scheme 1. The first step consisted in the N1-alkylation of 1*H*-1,2,4-triazole by 2,2′,4′-trihalogenoacetophenones **1** and **2** and their congeneers **3**–**7**. Following the microwave solvent-free and base-free procedure recently published,[4] our preliminary experiments gave nonreproducible results due to the problem of homogenization of the reagents on large scale in our focused microwave oven (open oven, monomode system). Among the various experimental conditions tested to synthesize 2-(1*H*-1,2,4-triazol-1-yl)acetophenones **8**–**14**, the N1-alkylation was easily performed in good yield, using K_2CO_3 as a base in

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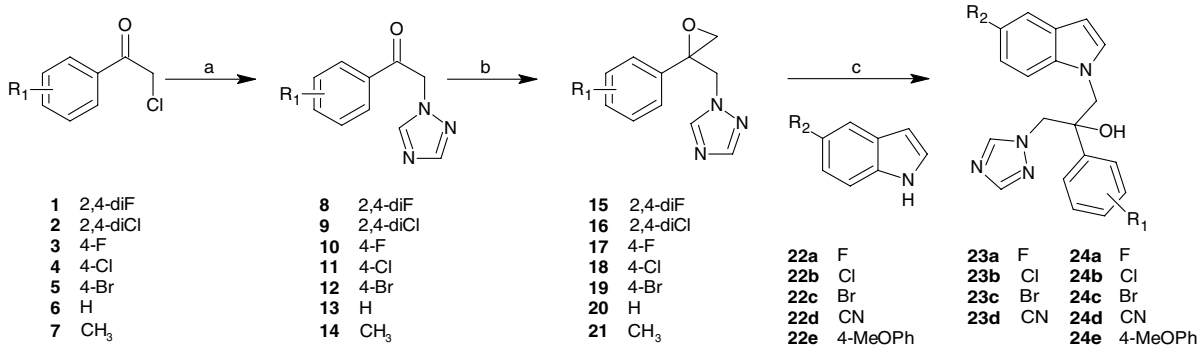

Scheme 1. Reagents and conditions: (a) K_2CO_3, 1*H*-1,2,4-triazole, CH_3CN, MW 85 °C (P 50 W), 50 min; (b) $NaOH_{aq}$, TMSOI, toluene, MW 80 °C (P 50 W), 50 min; (c) NaH, indole derivative, DMSO, rt, 12 h.

acetonitrile for 50 min under microwave irradiation programmed at 50 W, heating at a fixed temperature of 85 °C.

The oxirane intermediates were then obtained by the Corey–Chaykovsky epoxidation, in the presence of trimethylsulfoxonium iodide and an aqueous solution of NaOH, under microwave irradiation for 50 min (P 10 W). In the first assays (Table 1, entries 1–6), we determined the influence of solvent on the yield of epoxidation of **9** at a temperature of 40 °C. The presence of a biphasic system (aqueous solution of NaOH and organic solvent) was necessary to avoid the intermediates and epoxide degradation. A solvent like dichloromethane, chloroform, cyclohexane or toluene, at 40 °C for 50 min, afforded epoxide **16** in very poor yields (entries 1, 2, 3, and 6) and no result was obtained with water or DMSO (entries 4 and 5). The influence of reaction temperature rise was studied in toluene which afforded the purest compound (entries 6–9); a clear-cut increase in yield from 5% to 52% and 97% was observed when temperature moved from 40 to 60 °C and 80 °C; but heating at 100 °C led to complete degradation of the epoxide. This mild procedure (entry 8) afforded the desired epoxides **15** and **16** in high yields without further purification. The present protocol allowed to obtain the corresponding oxiranes **17**–**21** (Table 2). Under similar experimental conditions (80 °C for 50 min), but using an oil bath, the same quantity of starting material furnished **16** in only a 31% yield (entry 10).[8] Moreover, in comparison with the use of ionic liquids, the microwave application avoids the rearrangement of acetophenones to 2-phenylpropanaldehydes due to the absence of Lewis acidity.

Table 1. Influence of solvent, temperature, and activation mode on the yield of microwave-assisted epoxidation of phenacyltriazole **9**

Entry	Solvent	Temperature (°C)	Activation	% Yield
1	CH_2Cl_2	40	MW 10 W	26
2	$CHCl_3$	40	MW 10 W	7
3	Cyclohexane	40	MW 10 W	6
4	Water	40	MW 10 W	0
5	DMSO	40	MW 10 W	0
6	Toluene	40	MW 10 W	5
7	Toluene	60	MW 10 W	52
8	Toluene	80	MW 10 W	97
9	Toluene	100	MW 10 W	0
10	Toluene	80	Oil bath	31

Table 2. Synthesis of oxiranes **17**–**21** by Corey–Chaykovsky reaction under microwave irradiation (conditions of entry 8, Table 1)

Compd	R_1	% Conversion[a]
17	4-F	88
18	4-Cl	97
19	4-Br	76
20	H	90
21	4-CH_3	100

[a] Determined by ^1H NMR.

Finally, the ring opening of oxiranes **15** and **16** was achieved with various indoles to produce target compounds **23a**–**d** and **24a**–**e**. The reaction was carried out by addition of oxirane on the sodium salt of the corresponding indole and stirring for 12 h; yields were generally satisfactory (45–90%) except for compounds **23a**, **23b** and **24e** which were more difficult to purify. The intermediate indoles **22a**–**d** are commercially available; 5-(4-methoxyphenyl)indole **22e** was prepared by Suzuki Pd-mediated cross coupling reaction between 4-methoxyphenyl boronic acid and 5-bromoindole **22c**. Among the numerous experimental conditions found in the lit.,[10] we chose to carry out the Suzuki reaction by using palladium acetate as catalyst and $Ba(OH)_2{\cdot}8H_2O$ as base in ethanol/H_2O (1/1) for 10 min under microwave irradiation (40 W, 80 °C). The desired 5-(4-methoxyphenyl)indole **22e** was obtained in a 66% yield. In similar experimental conditions (80 °C, 10 min), operating with the same quantity of starting materials, the conventional heating gave a very poor yield of **22e** (10%).

In conclusion, we have successfully demonstrated that the Corey–Chaykovsky epoxidation can be achieved under microwave irradiation. This mild and original procedure facilitates the access of oxirane precursors, which can lead to various 1-(1*H*-indol-1-yl)-2-phenyl-3-(1*H*-1,2,4-triazol-1-yl)propan-2-ols with antifungal potency. This work constitutes a new illustration of the utility of microwave application in the synthesis of new bioactive compounds.

Table 3. Experimental data of synthesized compounds **8**–**21** and **22e**

Compd	R_1	R_2	Yield[a] (%)	Mp (°C)	Molecular formula and weight	^{1}H NMR (DMSO d_6)
8	2,4-DiF	—	99	98–99 (CH_2Cl_2) lit.[11] 103–105	$C_{10}H_7F_2N_3O$ (223.18)	5.89 (s, 2H), 7.35 (ddd, 1H, $J = J = 8.9$ Hz, $J = 2.4$ Hz), 7.58 (ddd, 1H, $J = 11.6$ Hz, $J = 9.5$ Hz, $J = 2.4$ Hz), 8.04 (d, 1H, $J = 8.9$ Hz), 8.06 (s, 1H), 8.53 (s, 1H)
9	2,4-DiCl	—	98	106–107 (CH_2Cl_2) lit.[12] 113–115	$C_{10}H_7Cl_2N_3O$ (256.09)	5.90 (s, 2H), 7.67 (dd, 1H, $J = 8.4$ Hz, $J = 1.7$ Hz), 7.85 (d, 1H, $J = 1.7$ Hz), 8.00 (d, 1H, $J = 8.4$ Hz), 8.01 (s, 1H), 8.58 (s, 1H)
10	4-F	—	91	78–79 (CH_2Cl_2) lit.[11] 73–75	$C_{10}H_8FN_3O$ (205.19)	6.03 (s, 2H), 7.48 (dd, 2H, $J = J = 8.6$ Hz), 8.07 (s, 1H), 8.18 (dd, 2H, $J = 8.6$ Hz, $J = 5.5$ Hz), 8.55 (s, 1H)
11	4-Cl	—	90	121–122 (CH_2Cl_2) lit.[11] 110–111	$C_{10}H_8ClN_3O$ (221.64)	6.03 (s, 2H), 7.77 (d, 2H, $J = 8.9$ Hz), 8.07 (s, 1H), 8.10 (d, 2H, $J = 8.9$ Hz, $J = 5.5$ Hz), 8.55 (s, 1H)
12	4-Br	—	86	167–168 (CH_2Cl_2) lit.[13] 178–180	$C_{10}H_8BrN_3O$ (266.09)	6.03 (s, 2H), 7.87 (d, 2H, $J = 8.6$ Hz), 8.02 (d, 2H, $J = 8.6$ Hz, $J = 5.5$ Hz), 8.06 (s, 1H), 8.54 (s, 1H)
13	H	—	78	108 (CH_2Cl_2/MeOH:95/5) lit.[12] 117–118	$C_{10}H_9N_3O$ (187.20)	6.03 (s, 2H), 7.64 (dd, 2H, $J = 8.0$ Hz, $J = 7.5$ Hz), 7.76 (d, 1H, $J = 7.5$ Hz), 8.06 (s, 1H), 8.09 (d, 2H, $J = 8.0$ Hz), 8.55 (s, 1H)
14	4-CH_3	—	70	109–111 (CH_2Cl_2/MeOH:95/5)	$C_{11}H_{11}N_3O$ (201.23)	2.45 (s, 3H), 5.99 (s, 2H), 7.44 (d, 2H, $J = 8.0$ Hz), 7.99 (d, 2H, $J = 8.0$ Hz), 8.05 (s, 1H), 8.54 (s, 1H)
15	2,4-DiF	—	97	Colorless oil	$C_{11}H_9F_2N_3O$ (237.21)	2.99 (d, 1H, $J = 4.9$ Hz), 3.13 (d, 1H, $J = 4.9$ Hz), 4.62 (d, 1H, $J = 14.7$ Hz), 4.81 (d, 1H, $J = 14.7$ Hz), 7.05 (ddd, 1H, $J = 8.5$ Hz, $J = 2.4$ Hz, $J = 0.9$ Hz), 7.24 (ddd, 1H, $J = 10.3$ Hz, $J = 8.5$ Hz, $J = 2.1$ Hz), 7.31 (ddd, 1H, $J = 10.7$ Hz, $J = 9.2$ Hz, $J = 2.1$ Hz), 7.94 (s, 1H), 8.43 (s, 1H)
16	2,4-DiCl	—	97	Red oil	$C_{11}H_9Cl_2N_3O$ (270.11)	2.97 (d, 1H, $J = 4.5$ Hz), 3.17 (d, 1H, $J = 4.5$ Hz), 4.58 (d, 1H, $J = 14.9$ Hz), 4.91 (d, 1H, $J = 14.9$ Hz), 7.15 (d, 1H, $J = 8.2$ Hz), 7.39 (dd, 1H, $J = 8.2$ Hz, $J = 2.1$ Hz), 7.70 (d, 1H, $J = 2.1$ Hz), 7.95 (s, 1H), 8.44 (s, 1H)
17	4-F	—	88[b]	Red oil	$C_{11}H_{10}FN_3O$ (219.22)	2.90 (d, 1H, $J = 4.9$ Hz), 3.05 (d, 1H, $J = 4.9$ Hz), 4.69 (d, 1H, $J = 15.0$ Hz), 5.06 (d, 1H, $J = 15.0$ Hz), 7.20 (dd, 2H, $J = J = 9.2$ Hz), 7.45 (dd, 2H, $J = 9.2$ Hz, $J = 6.7$ Hz), 7.95 (s, 1H), 8.42 (s, 1H)
18	4-Cl	—	95	Red oil	$C_{11}H_{10}ClN_3O$ (235.67)	2.90 (d, 1H, $J = 4.9$ Hz), 3.08 (d, 1H, $J = 4.9$ Hz), 4.67 (d, 1H, $J = 15.0$ Hz), 5.10 (d, 1H, $J = 15.0$ Hz), 7.43 (s, 4H), 7.95 (s, 1H), 8.43 (s, 1H)
19	4-Br	—	76[b]	Red oil	$C_{11}H_{10}BrN_3O$ (280.12)	2.89 (d, 1H, $J = 4.9$ Hz), 3.08 (d, 1H, $J = 4.9$ Hz), 4.66 (d, 1H, $J = 15.0$ Hz), 5.11 (d, 1H, $J = 15.0$ Hz), 7.36 (d, 2H, $J = 8.6$ Hz), 7.57 (d, 2H, $J = 8.6$ Hz), 7.95 (s, 1H), 8.43 (s, 1H)
20	H	—	90[b]	Yellow oil	$C_{11}H_{11}N_3O$ (201.23)	2.89 (d, 1H, $J = 5.0$ Hz), 3.03 (d, 1H, $J = 5.0$ Hz), 4.71 (d, 1H, $J = 15.0$ Hz), 5.06 (d, 1H, $J = 15.0$ Hz), 7.25–7.49 (m, 5H), 7.93 (s, 1H), 8.41 (s, 1H)
21	4-CH_3	—	98	Yellow oil	$C_{12}H_{13}N_3O$ (215.25)	2.30 (s, 3H), 2.86 (d, 1H, $J = 5.2$ Hz), 3.00 (d, 1H, $J = 5.2$ Hz), 4.68 (d, 1H, $J = 15.0$ Hz), 5.03 (d, 1H, $J = 15.0$ Hz), 7.17 (d, 2H, $J = 7.9$ Hz), 7.29 (d, 2H, $J = 7.9$ Hz), 7.94 (s, 1H), 8.40 (s, 1H)
22e	—	4-OMePh	66	98–99 (Cyclohexane)	$C_{15}H_{13}NO$ (223.27)	3.81 (s, 3H), 6.50 (d, 1H, $J = 2.8$ Hz), 7.03 (d, 2H, $J = 8.8$ Hz), 7.37 (dd, 1H, $J = 8.4$ Hz, $J = 2.0$ Hz), 7.40 (d, 1H, $J = 2.8$ Hz), 7.48 (d, 1H, $J = 8.4$ Hz), 7.61 (d, 2H, $J = 8.8$ Hz), 7.78 (d, 1H, $J = 2.0$ Hz), 11.14 (s, 1H)

[a] Isolated yield.
[b] Conversion determined by ^{1}H NMR.

2. Experimental procedures

2.1. Alkylation of 2-chloroacetophenone 2

To a solution of 2,2′,4′-trichloroacetophenone **2** (2.50 g, 11.19 mmol) in 40 mL of acetonitrile was added 1*H*-1,2,4-triazole (1.55 g, 22.37 mmol) and K_2CO_3 (3.09 g, 22.37 mmol). The reaction mixture was irradiated for 50 min in a microwave oven (Discover, CEM), programmed to obtain reflux with a maximum power output of 50 W. After cooling, the mixture was filtered and evaporated under reduced pressure. The residue

Table 4. Experimental data of synthesized compounds **23a–d** and **24a–e**

Compd	R_1	R_2	Yield (%)	Mp (°C)	Molecular formula and weight	^{1}H NMR (DMSO-d_6)
23a	2,4-DiF	F	25	125–126 (Hexane)	$C_{19}H_{15}F_3N_4O$ (372.34)	4.54 (d, 1H, $J = 14.8$ Hz), 4.58 (d, 1H, $J = 14.2$ Hz), 4.69 (d, 1H, $J = 14.8$ Hz), 4.88 (d, 1H, $J = 14.2$ Hz), 6.30 (s, 1H), 6.37 (d, 1H, $J = 3.1$ Hz), 6.85 (ddd, 1H, $J = 8.6$ Hz, $J = J = 2.4$ Hz), 6.92 (ddd, 1H, $J = J = 9.2$ Hz, $J = 2.5$ Hz), 7.19 (d, 1H, $J = 3.1$ Hz), 7.27 (dd, 1H, $J = 7.0$ Hz, $J = 2.5$ Hz), 7.16–7.27 (m, 2H), 7.36 (dd, 1H, $J = 9.2$ Hz, $J = 4.3$ Hz), 7.82 (s, 1H), 8.34 (s, 1H)
23b	2,4-DiF	Cl	18	96–97 (Hexane)	$C_{19}H_{15}ClF_2N_4O$ (388.80)	4.53 (d, 1H, $J = 15.0$ Hz), 4.59 (d, 1H, $J = 14.4$ Hz), 4.70 (d, 1H, $J = 15.0$ Hz), 4.88 (d, 1H, $J = 14.4$ Hz), 6.30 (s, 1H), 6.38 (d, 1H, $J = 3.1$ Hz), 6.85 (ddd, 1H, $J = 8.9$ Hz, $J = J = 2.4$ Hz), 7.14–7.25 (m, 2H), 7.08 (dd, 1H, $J = 8.5$ Hz, $J = 1.8$ Hz), 7.28 (d, 1H, $J = 3.1$ Hz), 7.39 (d, 1H, $J = 8.5$ Hz), 7.52 (d, 1H, $J = 1.8$ Hz), 7.83 (s, 1H), 8.34 (s, 1H)
23c	2,4-DiF	Br	90	132–133 (Hexane)	$C_{19}H_{15}BrF_2N_4O$ (433.25)	4.54 (d, 1H, $J = 14.8$ Hz), 4.59 (d, 1H, $J = 14.2$ Hz), 4.70 (d, 1H, $J = 14.8$ Hz), 4.88 (d, 1H, $J = 14.2$ Hz), 6.31 (s, 1H), 6.38 (d, 1H, $J = 3.1$ Hz), 6.85 (ddd, 1H, $J = 8.2$ Hz, $J = J = 2.4$ Hz), 7.15–7.27 (m, 2H), 7.18 (dd, 1H, $J = 8.9$ Hz, $J = 1.5$ Hz), 7.27 (d, 1H, $J = 3.1$ Hz), 7.36 (d, 1H, $J = 8.9$ Hz), 7.67 (d, 1H, $J = 1.5$ Hz), 7.83 (s, 1H), 8.34 (s, 1H)
23d	2,4-DiF	CN	80	115–116 (Hexane)	$C_{20}H_{15}F_2N_5O$ (379.36)	4.60 (d, 1H, $J = 15.0$ Hz), 4.63 (d, 1H, $J = 14.5$ Hz), 4.79 (d, 1H, $J = 15.0$ Hz), 4.90 (d, 1H, $J = 14.5$ Hz), 6.33 (s, 1H), 6.54 (d, 1H, $J = 3.4$ Hz), 6.84 (ddd, 1H, $J = 8.2$ Hz, $J = J = 2.5$ Hz), 7.12–7.26 (m, 2H), 7.38 (d, 1H, $J = 3.4$ Hz), 7.45 (dd, 1H, $J = 8.6$ Hz, $J = 1.2$ Hz), 7.54 (d, 1H, $J = 8.6$ Hz), 7.85 (s, 1H), 8.03 (d, 1H, $J = 1.2$ Hz), 8.35 (s, 1H)
24a	2,4-DiCl	F	73	145–147 (Hexane)	$C_{19}H_{15}Cl_2FN_4O$ (405.25)	4.60 (d, 1H, $J = 14.4$ Hz), 4.74 (d, 1H, $J = 15.0$ Hz), 4.91 (d, 1H, $J = 15.0$ Hz), 5.29 (d, 1H, $J = 14.4$ Hz), 6.38 (s, 1H), 6.38 (d, 1H, $J = 3.7$ Hz), 6.97 (ddd, 1H, $J = J = 9.2$ Hz, $J = 2.4$ Hz), 7.20 (d, 1H, $J = 3.7$ Hz), 7.22 (dd, 1H, $J = 8.9$ Hz, $J = 2.1$ Hz), 7.27 (dd, 1H, $J = 4.6$ Hz, $J = 2.4$ Hz), 7.36 (d, 1H, $J = 8.9$ Hz), 7.49 (dd, 1H, $J = 9.2$ Hz, $J = 4.3$ Hz), 7.62 (d, 1H, $J = 2.1$ Hz), 7.80 (s, 1H), 8.33 (s, 1H)
24b	2,4-DiCl	Cl	47	157–158 (Hexane)	$C_{19}H_{15}Cl_3N_4O$ (421.71)	4.61 (d, 1H, $J = 14.7$ Hz), 4.75 (d, 1H, $J = 15.0$ Hz), 4.92 (d, 1H, $J = 15.0$ Hz), 5.29 (d, 1H, $J = 14.7$ Hz), 6.38 (s, 1H), 6.39 (d, 1H, $J = 3.7$ Hz), 7.12 (dd, 1H, $J = 8.9$ Hz, $J = 2.0$ Hz), 7.22 (dd, 1H, $J = 8.5$ Hz, $J = 2.1$ Hz), 7.23 (d, 1H, $J = 3.7$ Hz), 7.33 (d, 1H, $J = 8.5$ Hz), 7.52 (d, 1H, $J = 8.9$ Hz), 7.54 (d, 1H, $J = 2.0$ Hz), 7.62 (d, 1H, $J = 2.1$ Hz), 7.81 (s, 1H), 8.33 (s, 1H)
24c	2,4-DiCl	Br	45	167–168 (Hexane)	$C_{19}H_{15}BrCl_2N_4O$ (466.16)	4.62 (d, 1H, $J = 14.3$ Hz), 4.74 (d, 1H, $J = 15.0$ Hz), 4.92 (d, 1H, $J = 15.0$ Hz), 5.28 (d, 1H, $J = 14.3$ Hz), 6.38 (s, 1H), 6.38 (d, 1H, $J = 3.4$ Hz), 7.21 (dd, 1H, $J = 8.9$ Hz, $J = 2.1$ Hz), 7.23 (d, 1H, $J = 3.4$ Hz), 7.24 (dd, 1H, $J = 8.9$ Hz, $J = 1.8$ Hz), 7.35 (d, 1H, $J = 8.9$ Hz), 7.48 (d, 1H, $J = 8.9$ Hz), 7.62 (d, 1H, $J = 1.8$ Hz), 7.68 (d, 1H, $J = 2.1$ Hz), 7.80 (s, 1H), 8.32 (s, 1H)
24d	2,4-DiCl	CN	46	165–167 (Hexane)	$C_{20}H_{15}BrCl_2N_5O$ (412.27)	4.67 (d, 1H, $J = 14.7$ Hz), 4.78 (d, 1H, $J = 15.3$ Hz), 5.01 (d, 1H, $J = 15.3$ Hz), 5.29 (d, 1H, $J = 14.7$ Hz), 6.42 (s, 1H), 6.55 (d, 1H, $J = 2.8$ Hz), 7.20 (dd, 1H, $J = 7.3$ Hz, $J = 2.1$ Hz), 7.31 (d, 1H, $J = 7.3$ Hz), 7.33 (d, 1H, $J = 2.8$ Hz), 7.48 (dd, 1H, $J = 7.6$ Hz, $J = 1.2$ Hz), 7.63 (d, 1H, $J = 2.1$ Hz), 7.65 (d, 1H, $J = 7.6$ Hz), 7.84 (s, 1H), 8.05 (d, 1H, $J = 1.2$ Hz), 8.35 (s, 1H)
24e	2,4-DiCl	4-OMePh	10	128–130 (Hexane)	$C_{26}H_{22}Cl_2N_4O_2$ (493.38)	3.82 (s, 3H), 4.59 (d, 1H, $J = 14.7$ Hz), 4.80 (d, 1H, $J = 15.0$ Hz), 4.90 (d, 1H, $J = 15.0$ Hz), 5.32 (d, 1H, $J = 14.7$ Hz), 6.40 (s, 1H), 6.44 (d, 1H, $J = 3.1$ Hz), 7.03 (d, 2H, $J = 8.6$ Hz), 7.24 (dd, 1H, $J = 8.9$ Hz, $J = 3.4$ Hz), 7.40 (d, 1H, $J = 8.9$ Hz), 7.42 (d, 1H, $J = 3.1$ Hz), 7.44–7.53 (m, 1H), 7.57 (d, 1H, $J = 8.2$ Hz), 7.61 (d, 2H, $J = 8.6$ Hz), 7.64 (d, 1H, $J = 3.4$ Hz), 7.71 (s, 1H), 7.80 (s, 1H), 8.34 (s, 1H)

was diluted with H_2O and extracted with ethyl acetate; then the organic layer was washed with brine, dried over anhydrous sodium sulfate, and concentrated in vacuo. The residue was purified by silica gel column chromatography using dichloromethane as eluent to obtain **9** as white crystals in a 98% yield.

2.2. Corey epoxidation of phenacyltriazole 9

To a solution of 2-(1*H*-1,2,4-triazol-1-yl)-2′,4′-dichloroacetophenone **9** (0.15 g, 0.59 mmol) in 5 mL of toluene was added trimethylsufoxonium iodide (0.26 g, 1.17 mmol) and sodium hydroxide (0.23 g, 5.86 mmol, 20% in aqueous solution). The reaction mixture was irradiated for 50 min in a microwave oven programmed to maintain a constant temperature (80 °C) with a maximum power output of 10 W. After cooling, the mixture was extracted with ethyl acetate; the organic layer was washed with brine, dried over anhydrous sodium sulfate, and concentrated in vacuo to give **16** (97%) as a red oil.

2.3. Suzuki coupling with 5-bromoindole 22c

Under argon atmosphere, to a solution of 5-bromoindole **22c** (0.80 g, 4.08 mmol) in 10 mL of ethanol/H_2O (1/1) was added 4-methoxyphenylboronic acid (0.76 g, 4.90 mmol), $Ba(OH)_2{\cdot}8H_2O$, (3.84 g, 12.24 mmol), and palladium acetate (0.08 g, 0.41 mmol). The reaction mixture was irradiated for 10 min in a microwave oven programmed to maintain a constant temperature (80 °C) with a maximum power output of 40 W. After cooling, the mixture was filtered and concentrated in vacuo. The residue was diluted with H_2O and extracted with chloroform. The organic layer was washed with brine, dried over anhydrous sodium sulfate, and concentrated in vacuo. The residue was purified by recrystallization in cyclohexane and **22e** was obtained as white crystals in a 66% yield.

2.4. Ring opening of oxirane 16

Sodium hydride (0.08 g, 3.47 mmol) was dissolved in DMSO (20 mL) and 5-fluoroindole **22a** (0.47 g, 3.47 mmol) was added portionwise. After 1 h, 2-(2,4-dichlorophenyl)-3-(1*H*-1,2,4-triazol-1-yl)-1,2-epoxypropane **16** (0.72 g, 2.67 mmol) in 5 mL of DMSO was added, and the mixture was further stirred for 12 h under argon. The mixture was diluted with H_2O and extracted with ethyl acetate. The organic layer was washed with brine, dried over anhydrous sodium sulfate, and concentrated in vacuo. The residue was purified by silica gel column chromatography (ethyl acetate/hexane: 1/1) and **24a** was obtained as a yellow powder in a 73% yield.

Experimental data of all synthesized compounds are gathered in Tables 3 and 4.

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