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Darzens Reaction Rate Enhancement Using Aqueous Media Leading to a High Level of Kinetically Controlled Diastereoselective Synthesis of Steroidal Epoxyketones

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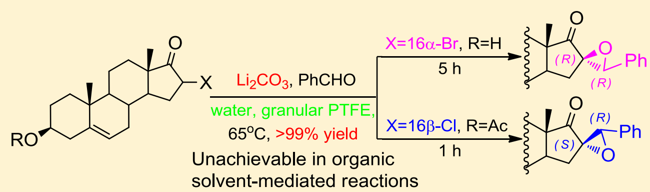
Supporting Information

ABSTRACT: Darzens reactions between halocarbonyls and aldehydes have been carried out in water in the presence of a Li^+-containing base, a phase-transfer catalyst, and granular polytetrafluoroethylene under mechanical stirring. Reactions using both aromatic and aliphatic aldehydes produced epoxides stereoselectively in good to excellent yields. This is the first time that aliphatic aldehydes with α-H have been used in aqueous Darzens reactions. The Darzens reactions were much faster in water than in organic solvents. This aqueous rate enhancement occurred for Darzens reactions between enantiopure steroidal haloketones and aldehydes, yielding enantiopure spiroepoxides with a high level of kinetically controlled diastereoselectivity. Chromatography was avoided in the purifications of the steroidal spiroepoxides. This is an example of preparing enantiopure epoxyketones via aqueous Darzens reaction using chiral α-haloketone substrates.



INTRODUCTION

The Darzens reaction is a nonoxidative method in the construction of epoxycarbonyls and related compounds.[1] Classically, this reaction is performed in the presence of a halocarbonyl, an aldehyde, and a base in organic solvents. To achieve high yield, stereoselectivity, and enantioselectivity and to ensure the survival of the substrates bearing base-liable groups, the reaction needs to be performed under mild conditions at the cost of reaction rates.[2] It is quite often that the reactions take 1 or 2 days or even 10 days.[2] In some cases, a two-step procedure (an aldol-type reaction and an intramolecular cyclization) was used to achieve better results.[3] The asymmetric version of the Darzens reaction has been realized by using chiral catalysts or auxiliaries.[2a] For example, enantiopure camphor-based α-bromoketones were used in the asymmetric Darzens reaction.[4] However, the ketones with the camphor-based auxiliary and the chiral epoxy acids were produced instead of chiral epoxyketones without auxiliary. To the best of our knowledge, there have been no reports of asymmetric Darzens reaction using chiral α-haloketone leading to α,β-epoxyketones.

The advantages of water-mediated reactions over organic solvent mediated ones include better yields, better stereoselectivities, and faster speeds.[5] In particular, we have noted the neighboring heteroatom effect unique to aqueous aldol reactions.[5g] In this work, our goal was to investigate whether this effect could be extended to aqueous Darzens reactions to yield the products diastereoselectively.

RESULTS AND DISCUSSION

Initially, comparisons of Darzens reactions promoted by LiOH or Li_2CO_3 were carried out in water and in organic solvents (Table 1). In accordance with our previous work,[5e−g] the aqueous reactions involving water-insoluble high melting point organic substrates were accelerated by addition of granular polytetrafluoroethylene (granular PTFE, or PTFE sand; see the Supporting Information) and agitation with a modified stirring rod. Mechanically stirring a mixture of chloroketone **1a** (500 mg), Li_2CO_3 (1.2 equiv), benzaldehyde **2a** (1.05 equiv), Aliquat 336 (50 mg), water (4 mL), and granular PTFE (5 g) at 60 °C produced epoxyketone **3a** in 86% yield in a short time (0.3 h). However, no reactions took place for either the homogeneous (Table 1, entries 2−4) or heterogeneous (Table 1, entries 5−7) organic solvent systems even after a longer period (1 h). The reactions for chloroamides **1b** and **1c** with **2a** were achieved in the aqueous system and failed in methanol (Table 1, entries 8−11). The reaction between **1a** and aliphatic aldehyde **2b** had a faster reaction rate and a higher yield than those in the control experiment in methanol (Table 1, entries 12 and 13).

These improved performances in aqueous media encouraged us to investigate a series of aqueous Darzens reactions between chlorocarbonyls and aromatic and aliphatic aldehydes with α-H. The results are summarized in Scheme 1. For the reactions with aromatic aldehydes and formaldehyde, Aliquat 336 was used as the phase-transfer catalyst (PTC) to produce epoxides **3e−k** (Scheme 1) in excellent yields. For the aliphatic aldehydes,

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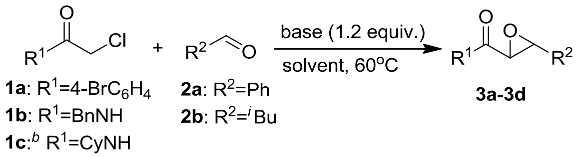
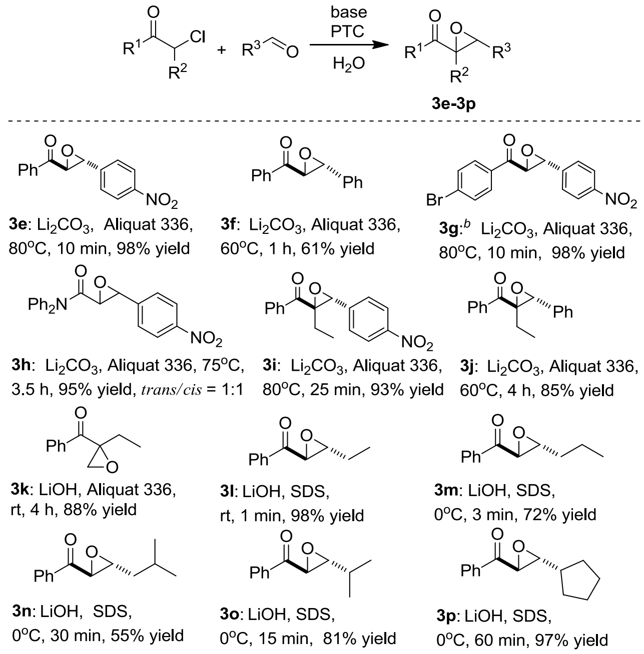
Table 1. Comparison of Aqueous and Organic Solvent Mediated Darzens Reactions[a,b]



entry	carbonyl	aldehyde	solvent	base	time (h)	yield[c,d] (%)
1	**1a**	**2a**	H_2O	Li_2CO_3	0.3	86, **3a**
2	**1a**	**2a**	EtOH	Li_2CO_3	1	NR[e]
3	**1a**	**2a**	DMF	Li_2CO_3	1	NR[e]
4	**1a**	**2a**	CH_3CN	Li_2CO_3	1	NR[e]
5	**1a**	**2a**	THF−H_2O (3:1)	Li_2CO_3	1	trace
6	**1a**	**2a**	PhMe−H_2O (3:1)	Li_2CO_3	1	NR[e]
7	**1a**	**2a**	*t*-BuOH−H_2O (3:1)	Li_2CO_3	1	NR[e]
8	**1b**	**2a**	H_2O	LiOH	5.5	52, **3b**
9	**1b**	**2a**	MeOH	LiOH	5	trace
10	**1c**	**2a**	H_2O	LiOH	3	44, **3c**
11	**1c**	**2a**	MeOH	LiOH	5	trace
12	**1a**	**2b**	H_2O	Li_2CO_3	1	53, **3d**
13	**1a**	**2b**	MeOH	Li_2CO_3	12	32, **3d**

[a]Reaction conditions in water: **1a−c** (500 mg, 1.0 equiv), base (1.2 equiv), aldehyde (1.05 equiv for **2a**, 1.2 equiv for **2b**), Aliquat 336 (50 mg), water (4 mL) and granular PTFE (5 g), mechanical stirring (400 rmp) at 60 °C. Reaction conditions in organic solvents: **1a-1c** (500 mg, 1.0 equiv), base (1.2 equiv), aldehyde (1.05 equiv for **2a**, 1.2 equiv for **2b**) and organic solvent (4 mL), magnetic stirring at 60 °C. [b]Cy = cyclohexyl. [c]Isolated yield. [d]**3a** and **3d** were *trans*-isomers, **3b** and **3c** were a mixture of *cis*- and *trans*-isomers (1:1). [e]NR, no reaction.

Scheme 1. Aqueous Darzens Reactions Using Aromatic and Aliphatic Aldehydes.[a]



[a]Reaction conditions for **3e−k**: haloketone (500 mg), base (1.2 equiv, Li_2CO_3 for **3e−j** or LiOH for **3k**), aldehyde (5.0 equiv for **3k** and 1.05 equiv for the others), Aliquat 336 (50 mg), granular PTFE (5 g), and water (4 mL), mechanical stirring (400 rmp) for **3e−i** or magnetic stirring (400 rmp) for **3j** and **3k**. Reaction conditions for **3l−p**: haloketone (500 mg), LiOH (2.0 equiv), 20% (w/w) aqueous SDS (500 mg), aldehyde (2.0 equiv), magnetic stirring (400 rmp) [b]Without the granular PTFE, the conversion was only 37% in 1 h.

sodium dodecyl sulfate (SDS) was used as the PTC because it gave higher yields (Scheme 1, **3l−p**) than Aliquat 336 did. Some of the aqueous reactions occurred instantly (Scheme 1, **3l** and **3m**), and most of the reaction times were less than 1 h. With the exception of **3h** and **3k**, *anti*-epoxides were stereoselectively obtained for all reactions.

Aqueous Darzens reactions have been reported by Tanaka et al. and Shi et al.[6] The differences between literature works and this work are as follows. First, weak bases Li_2CO_3 and LiOH were used in this work, which ensures the survival of ester and amide groups (Table 1, entries 8 and 10; Scheme 1, **3h**; Table 3, entry 16; and Table 4, entry 9). Strong base NaOH was used in the literature examples. Second, lipophilic Aliquat 336 used in this work functions as both a PTC and a reaction medium for water-insoluble high melting point organic substrates. Third, granular PTFE used in this work was especially useful in the promotion of aqueous reactions for water-insoluble high melting point organic substrates. In the presence of the granular PTFE, the reaction took 10 min to produce **3g** in 98% yield (Scheme 1). In the control experiment for preparing **3g** in the absence of granular PTFE, the reaction ended in only 37% conversion in 1 h. Finally, haloamides, both aliphatic and aromatic haloketones, and aldehydes were used in this work. In the literature work, only *ω*-chloroacetophenones and aromatic aldehydes were used.

Previously, Darzens reactions using aliphatic aldehydes have only been performed in organic solvents. The literature results of Darzens reactions using aliphatic aldehydes in organic solvents are compared with the aqueous reaction results from this work in Table 2. All the reactions performed in organic solvents were sluggish[7−9] with reaction times from 5 to 134 h

Table 2. Darzens Reaction Performances Using Aliphatic Aldehydes in Organic Solvents versus Water

entry	product	solvent	temp (°C)	time	yield (%)
1[a]	**3l**	*n*-Bu_2O	4	117 h	32
2[b]	**3l**	$CHCl_3$	rt	5 h	49
3[c]	**3l**	H_2O	rt	1 min	98
4[a]	**3m**	*n*-Bu_2O	4	60 h	82
5[d]	**3m**	CH_2Cl_2	−20	72 h	93
6[c]	**3m**	H_2O	0	3 min	72
7[a]	**3n**	*n*-Bu_2O	4	134 h	73
8[c]	**3n**	H_2O	0	30 min	55
9[a]	**3o**	*n*-Bu_2O	4	60 h	80
10[c]	**3o**	H_2O	0	15 min	81

[a]See ref 7. [b]See ref 8. [c]This work. [d]See ref 9.

(Table 2, entries 1, 2, 4, 5, 7, and 9). However, in our aqueous system, the reactions were much faster (1 min to 0.5 h, Table 2, entries 3, 6, 8, and 10). In addition, most of the yields were excellent (Scheme 1). Obviously, Darzens reactions can be dramatically accelerated by using an aqueous medium, which is probably because of the high concentrations of the substrates in the PTC phase, the neighboring heteroatom effect[5g] of the halocarbonyls in the aqueous system, and the acceleration effect of granular PTFE for the aqueous reaction for water-insoluble high melting point organic substrates. The ratio of substrate to

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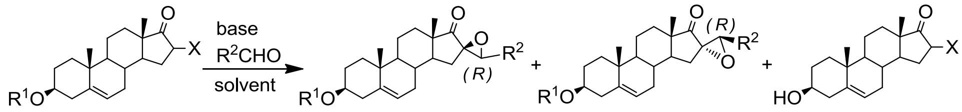
Table 3. Comparison of the Diastereoselectivity in Aqueous and Organic Solvent-Mediated Darzens Reactions[a]



						yield[c] (%)		
entry[b]	ketone	solvent	base	time (h)	conv[c] (%)	epoxide (dr[c])	7	8
1	**4a**	H_2O	LiOH	1	100	95[d] (**5a** only)	0	0
2	**4a**	MeOH	LiOH	10	100	91[d] (**5a**:**6a**= 11.3:1)	0	0
3	**4a**	EtOH	LiOH	10	94	63 (**5a**:**6a** = 8.1:1)	7	24
4	**4a**	DMF	LiOH	10	88	69 (**5a**:**6a** = 8.1:1)	4	15
5	**4a**	*i*-PrOH	LiOH	10	82	65 (**5a**:**6a** = 3.3:1)	5	13
6	**4a**	CH_3CN	LiOH	10	75	19 (**5a**:**6a** = 1.5:1)	10	46
7	**4a**	PhMe−H_2O (3:1)	LiOH	10	28	12 (**5a**:**6a** = 0.5:1)	5	11
8	**4a**	H_2O	Li_2CO_3	5	100	>99[d] (**5b** only)	0	0
9[e]	**4a**	H_2O	Li_2CO_3	5.5	100	>99[d] (**5b** only)	0	0
10[e]	**4a**	H_2O	Li_2CO_3	5	100	>99[d] (**5b** only)	0	0
11[f]	**4a**	H_2O	Li_2CO_3	5	100	>99[d] (**5b** only)	0	0
12[f]	**4a**	H_2O	Li_2CO_3	6	100	>99[d] (**5b** only)	0	0
13	**4a**	H_2O	Na_2CO_3	8	100	>99[d] (**5b** only)	0	0
14	**4a**	H_2O	K_2CO_3	5	trace	trace	0	0
15	**4a**	H_2O	Cs_2CO_3	5	trace	trace	0	0
16	**4a**	MeOH	Li_2CO_3	24	73	38 (**5b**:**6b** = 0.3:1)	35	0
17	**4a**	MeOH	Na_2CO_3	5	100	91[d] (**5b**:**6b** = 0.5:1)	0	0
18	**4a**	MeOH	K_2CO_3	1	100	93[d] (**5b**:**6b** = 0.8:1)	0	0
19	**4a**	MeOH	Cs_2CO_3	0.5	100	93[d] (**5b**:**6b** = 1.3:1)	0	0
20	**4b**	H_2O	Li_2CO_3	1	100	>99[d] (**6c**:**5c**= 20:1)	0	0
21	**4b**	H_2O	Na_2CO_3	1.5	100	>99[d] (**6c**:**5c**= 17:1)	0	0
22	**4b**	H_2O	K_2CO_3	5	100	>99[d] (**6c**:**5c** = 15:1)	0	0
23	**4b**	H_2O	Cs_2CO_3	10	100	>99[d] (**6c**:**5c** = 18:1)	0	0

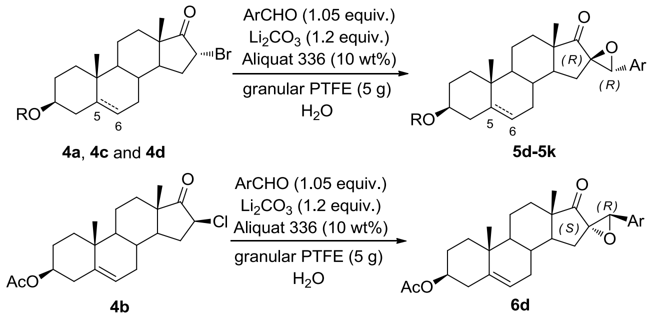
[a]Aqueous reaction conditions: haloketone (**4a** or **4b**, 500 mg), aldehyde (5.0 equiv for entries 1−7, 1.05 equiv for entries 8−23), base (1.2 equiv), water (4 mL), Aliquat 336 (50 mg), and granular PTFE (5 g), mechanical stirring (400 rmp). Organic solvent-mediated reaction conditions: ketone (**4a** or **4b**, 500 mg), aldehyde (5.0 equiv for entries 2−7, 1.05 equiv for entries 16−19), base (1.2 equiv), organic solvent (4 mL), mechanical stirring (400 rmp). [b]Reaction temperatures: 25 °C for entries 1−7, 65 °C for entries 8−23. [c]Determined by ^1H NMR. [d]Isolated yield. [e]The amounts of water were 2 mL for entry 9 and 8 mL for entry 10. [f]The stirring rates were 800 rmp for entry 11 and 200 rmp for entry 12.

granular PTFE is 10:1 (w/w). The latter functions as hundreds of costirrers to smash the former.

With this fast reaction rate procedure in hand, we proceeded to test if the high reaction rates can lead to a kinetically controlled diastereoselective synthesis of epoxyketones. Enantiopure bromoketone **4a** (16*α*-Br) and chloroketone **4b** (16*β*-Cl) were chosen to react with formaldehyde or benzaldehyde and the results are summarized in Table 3. Mechanically stirring a mixture of haloketone **4a** (500 mg), formaldehyde (5.0 equiv), LiOH (1.2 equiv), water (4 mL), Aliquat 336 (50 mg), and granular PTFE (5 g) at room temperature for 1 h gave (16*R*)-spiroepoxide **5a** as the only product in 95% yield (Table 3, entry 1). In contrast, the stereoselectivities were poor in organic solvent mediated reactions, and the ratios of the diastereoisomers (**5a**:**6a**) ranged from 11.3:1 to 0.5:1 with much longer reaction times (Table 3, entries 2−7). The aqueous condensation of **4a** and benzaldehyde at 65 °C promoted by Li_2CO_3 or Na_2CO_3 led to the stereospecific and quantitative production of (16*R*)-spiroepoxide **5b** (Table 3, entries 8 and 13). However, in the presence of K_2CO_3 or Cs_2CO_3, no reaction took place at 65 °C (Table 3, entries 14 and 15). This indicates that hard ions Li^+ and Na^+ can chelate with the bidentate haloenolate and soft ions K^+ and Cs^+ cannot. Another explanation for the better performance of Li_2CO_3 compared to other carbonates is the appropriate size of Li^+ allowing its incorporation in a chelated five-membered ring without strain. In the control experiments in methanol, the diastereoselectivity was poor (Table 3, entries 16−19). In terms of reaction rate, yield, and diastereoselectivity, the Cs_2CO_3-promoted reaction (Table 3, entry 19) was the best among the four carbonate-promoted reactions mediated by methanol. This is because Cs_2CO_3 is the strongest base among the four carbonates and the chelations between M^+ and the haloenolates are not important in methanol.

Three sets of control experiments were carried out to test the effects of the amount of water, the stirring speed, and the nature of PTC on the reactions of **4a**. Only a slight change in the reaction times was observed when the amount of water was decreased from 4 mL (Table 3, entry 8, 5 h) to 2 mL (Table 3, entry 9, 5.5 h). The reaction time (5 h) was almost the same after doubling the amount of water from 4 mL (Table 3, entry 8) to 8 mL (Table 3, entry 10). A possible reason is that Li_2CO_3 is slightly soluble in water (solubility at 60 °C: 10 mg/mL). If the amount of water is too low, a smaller amount of Li_2CO_3 gets dissolved to take part in the reaction. Raising the stirring speed from 400 rmp (Table 3, entry 8) to 800 rmp

Table 4. Aqueous Diastereoselective Darzens Reactions for Spiroepoxyketones[a]



entry	substrate	R	C_{5-6} or $C_{5\text{-}H}$	T (°C)	time (h)	product	Ar	yield[d] (%)
1	**4a**	H	d[b]	65	3	**5d**	4-$NO_2C_6H_4$	67
2	**4a**	H	d[b]	80	5	**5e**	4-$MeOC_6H_4$	77
3	**4a**	H	d[b]	70	10.5	**5f**	4-ClC_6H_4	63
4	**4a**	H	d[b]	70	10	**5g**	4-BrC_6H_4	65
5	**4c**	H	s[c], α	65	5	**5h**	Ph	60
6	**4c**	H	s[c], α	80	2.5	**5i**	4-$MeOC_6H_4$	65
7	**4d**	Bn	d[b]	65	8	**5j**	Ph	76
8	**4d**	Bn	d[b]	80	5.5	**5k**	4-$MeOC_6H_4$	67
9	**4b**			65	1	**6d**	4-$NO_2C_6H_4$	53

[a]Reaction conditions: haloketone (**4a**-**4d**, 500 mg), aldehyde (1.05 equiv), Li_2CO_3 (1.2 equiv), water (4 mL), Aliquat 336 (50 mg), and granular PTFE (5 g), mechanical stirring. [b]Double bond. [c]Single bond. [d]Isolated yield after crystallization.

(Table 3, entry 11) did not change the reaction time. The reaction time was 1 h longer when the stirring speed was decreased to 200 rmp (Table 3, entry 12). A stirring rate of 400 rmp was appropriate. Without lipophilic Aliquat 336 or replacing it with water-soluble tetrabutylammonium bromide or SDS, the aqueous reactions for steroidal haloketones **4a** did not occur.

In the aqueous reactions of **4b** and benzaldehyde at 65 °C (Table 3, entries 20−23), Li_2CO_3 was the base that produced the epoxides (**6c**:**5c** = 20:1) in the highest rate among the four carbonates because Li^+ is harder than Na^+, K^+, and Cs^+. This is in agreement with the neighboring heteroatom effect unique to aqueous reactions.[5g] The ester group of **4b** survived the basic conditions. If the water is replaced by organic solvents, the ester group becomes hydrolyzed.[10] Other advantages of the aqueous reaction over the organic solvent mediated ones are that the isomerization[11] of **4a** (16α-Br) to **7** (16β-Br) (Table 3, entries 3−7 and 16), the hydrolysis[11] of **4a** to side product **8** (Table 3, entries 3−7), and the lower conversions and reaction rates (Table 3, entries 3−7 and 12) occurring in organic solvent mediated reactions were not observed in the aqueous reactions. All these results indicate that faster reaction rates result in better diastereoselectivities in both the aqueous (Table 3, entries 1, 8−15, and 20−23) and organic solvent mediated (Table 3, entries 2−7 and 16−19) reactions.

The reaction conditions were further applied to the preparations of nine enantiopure epoxyketones (Table 4 entries 1−9, **5d**−**k** and **6d**) from four haloketones (**4a**−**d**) and five aldehydes with good isolated yields (53−77%) in water at 65−80 °C. At the end of the reactions, the granular PTFE precipitated on the bottom of the flask. The purifications of the products were performed only by filtration and crystallization, and the granular PTFE was collected and reused. The organic solvent extractions in the workup and chromatography were avoided. The configurations at C-16 for **5** (**5a**,**b**,**d**−**k**) and **6** (**6c**,**d**) are 16*R* and 16*S*, respectively, which originate from (16α-Br)-steroidal ketones **4a**, **4c**, and **4d** for **5** and (16β-Cl)-steroidal ketone **4b** for **6** and are complementary to each other stereochemically.

In summary, the reaction rates of Darzens reactions were greatly enhanced by using aqueous media because of the neighboring heteroatom effect of the halocarbonyls and the acceleration effects of granular PTFE for water-insoluble high melting point organic substrates. The yields and stereoselectivities were good to excellent for both aromatic and aliphatic aldehydes in the aqueous reactions. This is the first time that aliphatic aldehydes have been used in aqueous Darzens reactions. As weak bases were used, esters and amides could survive the reactions. Altogether, 12 enantiopure (16*R*)- and (16*S*)-steroidal spiroepoxyketones were produced in good to excellent yields in a high level of kinetically controlled diastereoselectivity.

■ EXPERIMENTAL SECTION

General Information. Steroidal haloketones **4a**−**c**[11b] and **4d**[12] were prepared according to the literature. Other halocarbonyls were obtained from commercial sources or prepared according to standard methods.[13] ^1H NMR, NOESY (400 or 600 MHz), and $^{13}C\{^1H\}$ NMR (100 or 151 MHz) spectra were recorded with a 400 or 600 MHz spectrometer using TMS as an internal standard. Chemical shifts (δ) are reported relative to TMS (^1H) or $CDCl_3$ (^{13}C), and multiplicities are reported as follows: singlet (s), doublet (d), triplet (t), quartet (q), and multiplet (m). Infrared analyses (KBr pellet) were performed on a FT-IR spectrometer. Elemental analyses for C, H, and N were performed on an elemental analyzer. High-resolution mass spectra (HRMS) were recorded on a QTOF mass analyzer with electrospray ionization (ESI). Melting points were recorded with a micro melting point apparatus. The aqueous reactions for insoluble high melting point organic substrates were conducted in 100 mL flasks and agitated by the modified stirring rod.[5g] The polytetrafluoroethylene (PTFE) plate (Supporting Information) was cut into granular PTFE (70 pieces/g, Supporting Information).

General Procedures for the Aqueous Darzens Reactions Using Aliquat 336 as Phase-Transfer Catalyst. Procedure A: a mixture of halocarbonyl (500 mg, 1.0 equiv), Aliquat 336 (50 mg), aldehyde (1.2 equiv for aliphatic aldehyde, 1.05 equiv for aromatic aldehyde, 5.0 equiv for formaldehyde), granular PTFE (5 g), base (Li_2CO_3 or LiOH, 1.2 equiv), and water (4 mL) were mechanically stirred (400 rmp). After TLC indicated completion of the reaction, the crude product suspended in water was filtrated, leaving the granular PTFE precipitating on the bottom to be recovered. For products **3a**,**d**,**f**, **5d**−**i**, and **6d**, the crude product was crystallized in methanol (2 mL) to give the desired product. For products **5j** and **5k**, the crude product was crystallized in ethyl acetate (2 mL). For products **3b**,**c**,**i**, chromatography was used. For products **3e**,**g**,**h**, **5a**,**b**, and **6c**, the desired product were obtained after the crude product was washed with 1.5 mL of cold aqueous acetone (75% v/v). For **3j** and **3k**, the reaction was magnetically stirred. After extraction (ethyl acetate, 5 mL × 3), drying (Na_2SO_4), and concentration under reduced pressure, the crude product was purified via bulb-to-bulb distillation under reduced pressure.

General Procedures for the Darzens Reactions Using Aqueous Sodium Dodecyl Sulfate as the Reaction Medium. Procedure B: After a mixture of halocarbonyl (500 mg, 1.0 equiv), aliphatic aldehyde (2.0 equiv), and 20% (w/w) aqueous SDS (500 mg) was magnetically stirred (400 rmp) for 15 min, LiOH (2.0 equiv) was added. The reaction mixture was stirred for an additional period of time. After TLC indicated completion of the reaction, 1.0 equiv of acetic acid was added. The water and excess aldehyde were removed under reduced pressure. Crude product **3l** was purified via bulb-to-bulb distillation under reduced pressure. For products **3m**−**p**, chromatography was used.

*trans-1-(4-Bromophenyl)-2,3-epoxy-3-phenyl-1-propanone (**3a**).* Procedure A: 469 mg, 86% yield; white solid; mp 134−135 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (d, J = 7.5 Hz, 2H), 7.64 (d, J = 7.6 Hz, 2H), 7.42−7.36 (m, 5H), 4.22 (s, 1H), 4.08 (s, 1H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 192.3, 135.3, 134.1, 132.3, 129.9, 129.4, 129.2, 128.8, 125.8, 61.1, 59.4. Product **3a** is a known compound.[14]

*N-Benzyl-3-phenyl-2,3-epoxy-1-propanamide (**3b**).* Procedure A: 359 mg, 52% yield; white solid; ^{1}H NMR (600 MHz, $CDCl_3$) 7.35−7.16 (m, 9H), 6.70 (d, J = 7.2 Hz, 1H), 6.64 (s, 0.5H), 6.19 (s, 0.5H), 4.45−4.41 (m, 1H), 4.31 (d, J = 4.6 Hz, 0.5H, *trans*-isomer), 4.28 (dd, J = 14.9, 6.9 Hz, 0.5H), 4.04 (dd, J = 15.0, 5.0 Hz, 0.5H), 3.88 (d, J = 1.3 Hz, 0.5H, *cis*-isomer), 3.81 (d, J = 4.7 Hz, 0.5H, *trans*-isomer), 3.55 (d, J = 1.5 Hz, 0.5H, *cis*-isomer); ^{13}C NMR (151 MHz, $CDCl_3$) δ 166.2, 137.0, 133.1, 128.6, 128.5, 127.5, 127.3, 126.6, 58.3, 56.4, 42.7, 29.7. Product **3b** is a known compound.[15]

*N-Cyclohexyl-3-phenyl-2,3-epoxy-1-propanamide (**3c**).* Procedure A: 307 mg, 44% yield; white solid; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.36−7.26 (m, 5H), 6.14 (d, J = 6.3 Hz, 0.5H), 5.71 (d, J = 6.0 Hz, 0.5H), 4.31 (d, J = 4.7 Hz, 0.5H, *trans*-isomer), 3.85 (s, 0.5H, *cis*-isomer), 3.82−3.77 (m, 1H), 3.76 (d, J = 4.8 Hz, 0.5H, *trans*-isomer), 3.51 (s, 0.5H, *cis*-isomer), 1.96−1.89 (m, 1H), 1.76−1.72 (m, 1.5H), 1.64−1.60 (m, 1H), 1.49−1.47 (m, 0.5 H), 1.41−1.33 (m, 1.5 H), 1.28−0.99 (m, 4H), 0.49−0.43 (m, 0.5 H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 165.0, 133.3, 128.4, 128.3, 126.6, 58.1, 56.2, 47.2, 32.7, 32.2, 29.7, 25.3, 24.6, 24.4. Product **3c** is a known compound.[16]

*trans-1-(4-Bromophenyl)-2,3-epoxy-5-methyl-1-hexanone (**3d**).* Procedure A: 316 mg, 53% yield; white solid; mp 44−45 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.90 (d, J = 8.5 Hz, 2H), 7.64 (d, J = 8.5 Hz, 2H), 3.94 (d, J = 1.7 Hz, 1H), 3.16 (ddd, J = 6.7, 4.9, 1.9 Hz, 1H), 1.95−1.85 (m, 1H), 1.66 (ddd, J = 12.1, 7.3, 4.8 Hz, 1H), 1.61−1.55 (m, 1H), 1.01 (d, J = 6.5 Hz, 3H), 1.00 (d, J = 6.4 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 193.7, 134.1, 132.0, 129.8, 128.9, 59.1, 57.2, 40.8, 26.4, 22.7, 22.4; IR (KBr) ν 3069, 2960, 2870, 1683, 1583, 1435, 1393, 1233, 1068, 1003, 909, 832, 736, 512 cm^{-1}, Anal. Calcd for $C_{13}H_{15}BrO_2$: C, 55.14; H, 5.34. Found: C, 55.01; H, 5.30.

*trans-2,3-Epoxy-3-(nitrophenyl)-1-phenyl-1-propanone (**3e**).* Procedure A: 852 mg, 98% yield; white solid; mp 149−151 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.27 (d, J = 8.7 Hz, 2H), 8.01 (d, J = 7.4 Hz, 2H), 7.65 (t, J = 7.4 Hz, 1H), 7.56 (d, J = 8.7 Hz, 2H), 7.52 (t, J = 7.8 Hz, 2H), 4.28 (d, J = 1.7 Hz, 1H), 4.21 (d, J = 1.4 Hz, 1H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 192.1, 148.3, 142.8, 135.2, 134.3, 129.0, 128.4, 126.7, 124.0, 60.8, 58.0. Product **3e** is a known compound.[17]

*trans-2,3-Epoxy-1,3-diphenyl-1-propanone (**3f**).* Procedure A: 442 mg, 61% yield; white solid; mp 89−90 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03 (d, J = 7.3 Hz, 2H), 7.64 (t, J = 7.4 Hz, 1H), 7.51 (t, J = 7.7 Hz, 2H), 7.45−7.38 (m, 5H), 4.33 (d, J = 1.7 Hz, 1H), 4.10 (d, J = 1.4 Hz, 1H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 193.1, 135.6, 134.0, 129.1, 128.9, 128.8, 128.4, 125.9, 61.0, 59.4. Product **3f** is a known compound.[18]

*trans-1-(4-Bromophenyl)-2,3-epoxy-3-(4-nitrophenyl)-1-propanone (**3g**).* Procedure A: 731 mg, 98% yield; white solid; mp 164−165 °C; ^{1}H NMR (600 MHz, DMSO-d_6) δ 8.24 (d, J = 7.7 Hz, 2H), 7.90 (d, J = 7.5 Hz, 2H), 7.66−7.59 (m, 4H), 4.41 (d, J = 2.4 Hz, 1H), 4.23 (d, J = 2.4 Hz, 1H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 191.3, 148.4, 142.5, 133.9, 132.4, 129.9, 126.7, 124.1, 60.9, 58.0. Product **3g** is a known compound.[19]

*N,N-Diphenyl-2,3-epoxy-3-(4-nitrophenyl)-1-propanamide (**3h**).* Procedure A: 697 mg, 95% yield; white solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.27 (d, J = 7.6 Hz, 1H), 8.17 (d, J = 7.7 Hz, 1H), 7.64 (d, J = 7.8 Hz, 1H), 7.64−6.99 (m, 11H), 4.33 (s, 0.5H, *cis*-isomer), 4.05 (d, J = 4.3 Hz, 0.5H, *trans*-isomer), 3.84 (d, J = 4.3 Hz, *trans*-isomer), 3.30 (s, 0.5H, *cis*-isomer); ^{13}C NMR (151 MHz, $CDCl_3$) δ 165.5, 163.9, 148.1, 142.7, 140.9, 130.0, 129.0, 128.4, 128.1, 126.7, 126.5, 125.9, 125.3, 123.8, 123.4, 58.7, 58.2, 57.9, 57.4. Product **3h** is a known compound.[20]

*trans-2-Ethyl-2,3-epoxy-3-(4-nitrophenyl)-1-phenyl-1-propanone (**3i**).* Procedure A: 300 mg of 2-chloro-1-phenyl-1-butanone and 1 mL of water were used; 454 mg of **3i** was obtained, 93% yield; yellow solid; mp 85−87 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18 (d, J = 8.7 Hz, 2H), 7.98 (d, J = 8.7 Hz, 2H), 7.54 (t, J = 7.4 Hz, 1H), 7.50 (d, J = 8.7 Hz, 2H), 7.42 (t, J = 7.7 Hz, 2H), 4.15 (s, 1H), 1.88 (dq, J = 15.0, 7.6 Hz, 1H), 1.38 (dq, J = 14.8, 7.5 Hz, 1H), 0.87 (t, J = 7.5 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 197.2, 147.9, 141.5, 134.4, 133.8, 129.3, 128.7, 127.5, 123.6, 70.8, 60.8, 21.7, 9.2; IR (KBr) ν 3110, 3085, 3065, 2971, 2934, 1685, 1599, 1582, 1517, 1448, 1340, 1267, 1238, 1177, 841, 798, 717, 688 cm^{-1}; HRMS calcd for $C_{17}H_{15}NO_4Na$ [M + Na^+] 320.0899, found 320.0905.

*trans-2,3-Epoxy-2-ethyl-1,3-diphenyl-1-propanone (**3j**).* Procedure A: 587 mg, 85% yield; colorless oil; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.11 (d, J = 7.6 Hz, 2H), 8.01 (d, J = 7.7 Hz, 2H), 7.59 (t, J = 7.3 Hz, 1H), 7.58 (t, J = 7.3 Hz, 1H), 7.49 (t, J = 7.7 Hz, 2H), 7.45 (t, J = 7.7 Hz, 2H), 6.06 (dd, J = 8.0, 4.4 Hz, 1H), 2.14−1.99 (m, 2H), 1.12 (t, J = 7.4 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 198.3, 134.9, 134.1, 133.5, 129.3, 128.6, 128.4, 128.2, 126.6, 70.5, 61.8, 21.6, 9.2. Product **3j** is a known compound.[21]

*2,3-Epoxy-2-ethyl-1-phenyl-1-propanone (**3k**).* Procedure A: 424 mg, 88% yield; colorless oil; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.03 (d, J = 7.8 Hz, 2H), 7.57 (t, J = 7.4 Hz, 1H), 7.46 (t, J = 7.7 Hz, 2H), 2.96 (d, J = 5.0 Hz, 1H), 2.89 (d, J = 5.0 Hz, 1H), 2.28 (dq, J = 15.0, 7.5 Hz, 1H), 1.83 (dq, J = 14.8, 7.5 Hz, 1H), 1.02 (t, J = 7.5 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 198.3, 134.8, 133.3, 129.2, 128.4, 64.0, 50.5, 25.9, 8.8. Product **3k** is a known compound.[21]

*trans-2,3-Epoxy-3-ethyl-1-phenyl-1-propanone (**3l**).* Procedure B: 559 mg, 98% yield; colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (d, J = 7.8 Hz, 2H), 7.61 (t, J = 7.5 Hz, 1H), 7.50 (t, J = 7.5 Hz, 2H), 4.02 (s, 1H), 3.14 (t, J = 5.2 Hz, 1H), 1.88−1.71 (m, 2H), 1.09 (t, J = 7.5 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 194.7, 135.6, 133.8, 128.8, 128.3, 60.9, 57.2, 25.0, 9.6. Product **3l** is a known compound.[7]

*trans-2,3-Epoxy-3-propanyl-1-phenyl-1-propanone (**3m**).* Procedure B: 443 mg, 72% yield; colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 (d, J = 7.8 Hz, 2H), 7.61 (t, J = 7.4 Hz, 1H), 7.49 (t, J = 7.4 Hz, 2H), 4.01 (s, 1H), 3.15 (t, J = 5.4 Hz, 1H), 1.81−1.50 (m, 4H), 1.01 (t, J = 7.3 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 194.7, 135.6, 133.8, 128.8, 128.3, 59.8, 57.4, 34.0, 19.2, 13.8. Product **3m** is a known compound.[7]

*trans-2,3-Epoxy-3-(2-methylpropanyl)-1-phenyl-1-propanone (**3n**).* Procedure B: 364 mg, 55% yield; colorless oil; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.02 (d, J = 7.9 Hz, 2H), 7.62 (t, J = 7.4 Hz, 1H), 7.50 (t, J = 7.6 Hz, 2H), 3.99 (d, J = 1.4 Hz, 1H), 3.17 (t, J = 4.7 Hz, 1H), 1.99−1.82 (m, 1H), 1.67 (ddd, J = 12.1, 7.0, 4.9 Hz, 1H), 1.63−1.56 (m, 1H), 1.01 (t, J = 6.1 Hz, 6H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 194.7, 135.6, 133.8, 128.8, 128.3, 59.0, 57.4, 41.1, 26.5, 22.8, 22.5. Product **3n** is a known compound.[7]

trans-2,3-Epoxy-3-(2-propanyl)-1-phenyl-1-propanone (**3o**). Procedure B: 498 mg, 81% yield; colorless oil; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.02 (d, *J* = 7.9 Hz, 2H), 7.62 (t, *J* = 7.4 Hz, 1H), 7.50 (t, *J* = 7.6 Hz, 2H), 3.99 (d, *J* = 1.4 Hz, 1H), 3.18−3.15 (m, 1H), 1.96−1.85 (m, 1H), 1.71−1.64 (m, 1H), 1.64−1.55 (m, 2H), 1.01 (t, *J* = 6.1 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 194.8, 135.6, 133.7, 128.8, 128.2, 65.0, 56.6, 30.6, 18.9, 18.2. Product **3o** is a known compound.[7]

trans-3-cyclopentanyl-2,3-epoxy-1-phenyl-1-propanone (**3p**). Procedure B: 678 mg, 97% yield; colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 (d, *J* = 7.5 Hz, 2H), 7.62 (t, *J* = 7.3 Hz, 1H), 7.50 (t, *J* = 7.5 Hz, 2H), 4.04 (s, 1H), 3.08 (d, *J* = 6.4 Hz, 1H), 2.10−2.00 (m, 1H), 1.91−1.82 (m, 2H), 1.69−1.45 (d, 6H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 194.7, 135.6, 133.8, 128.8, 128.2, 63.2, 57.0, 41.4, 29.1, 28.8, 25.4. Product **3p** is a known compound.[22]

(16R)-3β-Hydroxy-5-androstene-16-spiro-2′-oxiran-17-one (**5a**). Procedure A: 409 mg, 95% yield; white solid; mp 200−201 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.39 (d, *J* = 4.7 Hz, 1H), 3.59−3.52 (m, 1H), 3.12 (d, *J* = 6.3 Hz, 1H), 2.97 (d, *J* = 6.3 Hz, 1H), 2.35 (dd, *J* = 12.8, 3.6 Hz, 1H), 2.26 (t, *J* = 12.2 Hz, 1H), 1.94−1.87 (m, 4H), 1.77−1.41 (m, 9H), 1.07 (s, 3H), 1.05 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 215.8, 141.1, 120.6, 71.5, 59.5, 51.6, 50.0, 49.3, 48.1, 42.1, 37.0, 36.6, 31.5, 31.3, 31.2, 30.6, 28.4, 20.1, 19.5, 13.9; IR (KBr): ν 3474, 2925, 2899, 1744, 1463, 1435, 1378, 1066, 1002, 934, 729 cm^{-1}. Anal. Calcd for $C_{20}H_{28}O_3$: C, 75.91; H, 8.92. Found: C, 75.83; H, 9.01.

(3′R,16R)-3β-Hydroxy-3′-phenyl-5-androstene-16-spiro-2′-oxiran-17-one (**5b**). Procedure A: 539 mg, quantitative yield; white solid; mp 253−254 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47 (d, *J* = 7.2 Hz, 2H), 7.37−7.29 (m, 3H), 5.41 (d, *J* = 5.0 Hz, 1H), 4.24 (s, 1H), 3.60−3.52 (m, 1H), 2.39−2.23 (m, 3H), 2.09 (dd, *J* = 14.1, 6.8 Hz, 2H), 1.87 (d, *J* = 10.3 Hz, 2H), 1.06 (s, 3H), 0.93 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 211.6, 141.2, 133.3, 128.2, 127.8, 126.5, 120.6, 71.5, 66.3, 65.4, 50.0, 48.6, 48.0, 42.2, 37.0, 36.6, 31.5, 31.4, 31.0, 30.5, 29.6, 20.0, 19.4, 13.0; IR (KBr) ν 3387, 2936, 2903, 2861, 1746, 1454, 1376, 1058, 998, 751, 698, 616 cm^{-1}. Anal. Calcd for $C_{26}H_{32}O_3$: C, 79.56; H, 8.22. Found: C, 79.48; H, 8.29.

(3′R,16S)-3β-Acetoxy-3′-phenyl-5-androstene-16-spiro-2′-oxiran-17-one (**6c**). Procedure A: 601 mg (with 5% amount of **5c**), quantitative yield; white solid; mp 176−178 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.38 (t, *J* = 7.3 Hz, 2H), 7.34 (t, *J* = 7.3 Hz, 1H), 7.26 (d, *J* = 7.1 Hz, 2H), 5.35 (d, *J* = 5.2 Hz, 1H), 4.63−4.57 (m, 1H), 4.15 (s, 1H), 2.38−2.25 (m, 1H), 2.03 (s, 3H), 1.01 (s, 3H), 0.96 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 214.5, 170.5, 139.9, 134.6, 128.5, 128.4, 126.2, 121.6, 66.7, 62.8, 49.9, 48.5, 47.5, 38.0, 36.8, 36.7, 31.2, 30.9, 30.6, 27.7, 25.7, 21.4, 20.0, 19.3, 13.8; IR (KBr): ν 3350, 2930, 2885, 2859, 1748, 1457, 1377, 1352, 1056, 1010, 978, 921, 853, 766, 746, 699 cm^{-1}. Anal. Calcd for $C_{28}H_{34}O_4$: C, 77.39; H, 7.89. Found: C, 77.48; H, 7.84.

(3′R,16R)-3β-Hydroxy-3′-(4-nitrophenyl)-5-androstene-16-spiro-2′-oxiran-17-one (**5d**). Procedure A: 399 mg, 67% yield; white solid; mp 218−221 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.20 (d, *J* = 8.6 Hz, 2H), 7.64 (d, *J* = 8.6 Hz, 2H), 5.39 (d, *J* = 4.8 Hz, 1H), 4.29 (s, 1H), 3.58−3.50 (m, 1H), 2.37−2.22 (m, 3H), 2.14−2.05 (m, 2H), 1.85 (d, *J* = 10.4 Hz, 2H), 1.04 (s, 3H), 0.90 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 211.4, 147.8, 141.2, 140.5, 127.6, 123.1, 120.5, 71.5, 66.4, 64.0, 49.9, 48.5, 48.1, 42.1, 37.0, 36.6, 31.5, 31.4, 30.9, 30.5, 29.5, 19.9, 19.5, 13.0; IR (KBr) ν 3406, 2934, 2861, 1749, 1604, 1517, 1436, 1350, 1057, 1046, 865, 733 cm^{-1}. Anal. Calcd for $C_{26}H_{31}NO_5$: C, 71.37; H, 7.14; N, 3.20. Found: C, 71.23; H, 7.19; N, 3.15.

(3′R,16R)-3β-Hydroxy-3′-(4-methoxyphenyl)-5-androstene-16-spiro-2′-oxiran-17-one (**5e**). Procedure A: 443 mg, 63% yield; white solid; mp 210−212 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.39 (d, *J* = 8.5 Hz, 2H), 6.86 (d, *J* = 8.6 Hz, 2H), 5.39 (d, *J* = 4.6 Hz, 1H), 4.18 (s, 1H), 3.79 (s, 3H), 3.62−3.48 (m, 1H), 2.33 (dd, *J* = 12.9, 3.3 Hz, 1H), 2.30−2.21 (m, 2H), 2.11−2.02 (m, 2H), 1.85 (d, *J* = 10.7 Hz, 2H), 1.76−1.61 (m, 6H), 1.55−1.33 (m, 3H), 1.11−1.05 (m, 2H), 1.03 (s, 3H), 0.91 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 212.1, 159.5, 141.1, 127.8, 125.3, 120.7, 113.3, 71.5, 66.4, 65.5, 55.2, 49.9, 48.5, 48.0, 42.1, 37.0, 36.6, 31.5, 31.4, 31.0, 30.5, 29.5, 20.0, 19.5, 13.0; IR (KBr) ν 3230, 2933, 2861, 1743, 1613, 1515, 1250, 1173, 1035, 921, 733 cm^{-1}. Anal. Calcd for $C_{27}H_{34}O_4$: C, 76.74; H, 8.11. Found: C, 76.63; H, 8.20.

(3′R,16R)-3β-Hydroxy-3′-(4-chlorophenyl)-5-androstene-16-spiro-2′-oxiran-17-one (**5f**). Procedure A: 366 mg, 52% yield; white solid; mp 264−267 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.40 (d, *J* = 8.4 Hz, 2H), 7.30 (d, *J* = 8.5 Hz, 2H), 5.39 (d, *J* = 5.2 Hz, 1H), 4.18 (s, 1H), 3.57−3.51 (m, 1H), 2.33 (ddd, *J* = 13.1, 4.8, 1.8 Hz, 1H), 2.07 (dt, *J* = 14.1, 5.9 Hz, 1H), 1.85 (d, *J* = 9.8 Hz, 1H), 1.03 (s, 3H), 0.90 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 211.6, 141.1, 134.1, 131.8, 128.1, 128.0, 120.6, 71.5, 66.3, 64.7, 49.9, 48.5, 48.0, 42.2, 37.0, 36.6, 31.5, 31.4, 31.0, 30.5, 29.5, 20.0, 19.5, 13.0; IR (KBr) ν 2945, 2900, 2861, 2835, 1745, 1492, 1449, 1379, 1093, 1062, 1013, 1000, 921, 866, 789 cm^{-1}. Anal. Calcd for $C_{26}H_{31}ClO_3$: C, 73.14; H, 7.32. Found: C, 73.23; H, 7.25.

(3′R,16R)-3β-Hydroxy-3′-(4-bromophenyl)-5-androstene-16-spiro-2′-oxiran-17-one (**5g**). Procedure A: 417 mg, 65% yield; white solid; mp 253−256 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.46 (d, *J* = 8.4 Hz, 1H), 7.34 (d, *J* = 8.4 Hz, 1H), 5.39 (d, *J* = 5.1 Hz, 1H), 4.18 (s, 1H), 3.59−3.50 (m, 1H), 2.33 (dd, *J* = 13.0, 3.2 Hz, 1H), 2.30−2.21 (m, 1H), 2.07 (dd, *J* = 14.2, 7.0 Hz, 1H), 1.85 (d, *J* = 10.1 Hz, 1H), 1.03 (s, 3H), 0.90 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 211.8, 141.1, 132.2, 131.0, 128.3, 122.4, 120.6, 71.5, 66.2, 64.8, 49.8, 48.5, 48.0, 42.1, 37.0, 36.6, 31.5, 31.4, 30.9, 30.5, 29.4, 20.0, 19.5, 13.0; IR (KBr) ν 3470, 2943, 2898, 2859, 1745, 1489, 1449, 1422, 1140, 1062, 1009, 921, 865, 786, 619, 525 cm^{-1}. Anal. Calcd for $C_{26}H_{31}BrO_3$: C, 66.24; H, 6.63. Found: C, 66.12; H, 6.65.

(3′R,16R)-3β-Hydroxy-3′-phenyl-16-spiro-2′-oxiran-17-androstanone (**5h**). Procedure A: 321 mg, 60% yield; white solid; mp 237−240 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.44 (d, *J* = 7.3 Hz, 2H), 7.33 (t, *J* = 7.2 Hz, 2H), 7.29 (d, *J* = 7.2 Hz, 1H), 4.21 (s, 1H), 3.63−3.58 (m, 1H), 2.25 (t, *J* = 13.3 Hz, 1H), 2.04 (dd, *J* = 14.2, 6.8 Hz, 1H), 1.81 (d, *J* = 11.7 Hz, 1H), 0.88 (s, 3H), 0.83 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 212.0, 133.2, 128.3, 127.8, 126.5, 71.1, 66.3, 65.4, 54.1, 48.2, 48.2, 44.7, 38.0, 36.7, 35.7, 35.0, 31.4, 31.1, 30.6, 29.5, 28.3, 20.1, 13.2, 12.3; IR (KBr) ν 3680, 3388, 2929, 2857, 1748, 1628, 1450, 1374, 1338, 1155, 1042, 990, 915, 868, 750, 699 cm^{-1}. Anal. Calcd for $C_{26}H_{34}O_3$: C, 79.15; H, 8.69. Found: C, 79.08; H, 8.65.

(3′R,16R)-3β-Hydroxy-3′-(4-methoxyphenyl)-16-spiro-2′-oxiran-17-androstanone (**5i**). Procedure A: 374 mg, 65% yield; white solid; mp 194−196 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.38 (d, *J* = 8.7 Hz, 2H), 6.85 (d, *J* = 8.7 Hz, 2H), 4.15 (s, 1H), 3.79 (s, 3H), 3.64−3.55 (m, 1H), 3.48 (s, 1H), 2.27−2.19 (m, 1H), 2.02 (dd, *J* = 14.2, 7.1 Hz, 1H), 1.81 (d, *J* = 12.5 Hz, 1H), 0.88 (s, 3H), 0.83 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 212.1, 159.5, 127.8, 125.4, 113.3, 71.1, 66.5, 65.5, 55.2, 54.1, 48.3, 48.2, 44.7, 38.0, 36.8, 35.7, 34.9, 31.4, 31.1, 30.6, 29.5, 28.3, 20.1, 13.2, 12.3; IR (KBr) ν 3473, 3293, 2932, 2858, 1744, 1615, 1515, 1451, 1252, 1173, 1037, 992, 871, 834, 816, 790 cm^{-1}. Anal. Calcd for $C_{27}H_{36}O_4$: C, 76.38; H, 8.55. Found: C, 76.30; H, 8.57.

(3′R,16R)-3β-(Benzyloxy)-3′-phenyl-5-androstene-16-spiro-2′-oxiran-17-one (**5j**). Procedure A: 401 mg, 76% yield; white solid; mp 260−262 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.45 (d, *J* = 7.4 Hz, 2H), 7.37−7.27 (m, 8H), 5.38 (d, *J* = 5.0 Hz, 1H), 4.57 (s, 2H), 4.23 (s, 1H), 3.33−3.26 (m, 1H), 2.46 (dd, *J* = 13.2, 2.3 Hz, 1H), 2.29 (t, *J* = 13.5 Hz, 2H), 2.07 (dd, *J* = 14.3, 7.1 Hz, 2H), 1.98 (d, *J* = 12.6 Hz, 1H), 1.04 (s, 3H), 0.91 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 211.7, 141.3, 139.0, 133.3, 128.4, 128.2, 127.8, 127.6, 127.5, 126.5, 120.5, 78.3, 70.0, 66.3, 65.4, 50.0, 48.6, 48.0, 39.2, 37.0, 37.0, 31.4, 31.0, 30.5, 29.6, 28.3, 20.0, 19.5, 13.0; IR (KBr) ν 3033, 2970, 2930, 2906, 2892, 2866, 1744, 1495, 1455, 1370, 1249, 1208, 1108, 1023, 1001, 918, 863, 744, 698 cm^{-1}. Anal. Calcd for $C_{33}H_{38}O_3$: C, 82.12; H, 7.94. Found: C, 82.17; H, 7.89.

(3′R,16R)-3β-(Benzyloxy)-3′-(methoxyphenyl)-5-androstene-16-spiro-2′-oxiran-17-one (**5k**). Procedure A: 376 mg, 67% yield; white solid; mp 221−223 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.39 (d, *J* = 8.6 Hz, 2H), 7.37−7.27 (m, 5H), 6.86 (d, *J* = 8.7 Hz, 2H), 5.38 (d, *J* = 5.1 Hz, 1H), 4.57 (s, 2H), 4.18 (s, 1H), 3.79 (s, 3H), 3.33−3.26 (m, 1H), 2.46 (ddd, *J* = 13.2, 4.3, 2.1 Hz, 1H), 2.33−2.23 (m, 2H), 1.04 (s, 3H), 0.91 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 211.8, 159.6, 141.3, 139.0, 128.4, 127.9, 127.6, 127.5, 125.3, 120.6, 113.3, 78.3, 70.0, 66.4, 65.5, 55.2, 50.0, 48.6, 48.0, 39.2, 37.0, 37.0, 31.4, 31.0, 30.5, 29.5, 28.3, 20.0, 19.5, 13.0; IR (KBr) ν 3030, 2933, 2903, 2843, 1744, 1613,

1517, 1458, 1252, 1179, 1032, 1003, 919, 868, 840, 783 cm^{-1}. Anal. Calcd for $C_{34}H_{40}O_4$: C, 79.65; H, 7.86. Found: C, 79.53; H, 7.91.

*(3′R,16S)-3β-Acetoxy-3′-(4-nitrophenyl)-5-androstene-16-spiro-2′-oxiran-17-one (**6d**).* Procedure A: 349 mg, 53% yield; white solid; mp 268−270 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.25 (d, J = 8.7 Hz, 2H), 7.46 (d, J = 8.7 Hz, 2H), 5.36 (d, J = 5.0 Hz, 1H), 4.64−4.55 (m, 1H), 4.26 (s, 1H), 2.36−2.26 (m, 2H), 2.03 (s, 3H), 1.02 (s, 3H), 0.97 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 213.3, 170.5, 148.0, 142.0, 140.0, 127.0, 123.9, 121.4, 73.6, 66.9, 61.5, 49.8, 48.5, 47.6, 38.0, 36.7, 36.7, 31.2, 30.8, 30.5, 27.6, 25.6, 21.4, 19.9, 19.3, 13.8; IR (KBr) ν 3064, 3037, 2943, 2908, 2869, 1738, 1495, 1374, 1251, 1034, 997, 922, 904, 748, 697, 615 cm^{-1}. Anal. Calcd for $C_{28}H_{33}NO_6$: C, 70.13; H, 6.94; N, 2.92. Found: C, 70.01; H, 6.88; N, 2.99.

*Stereochemistry for **3i**, **5a**, **5b** ,and **6c**.* The configurations of the epoxide groups for **3i**, **5a**, **5b**, and **6c** were indicated by the NOESY spectra.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Pictures of the granular PTFE. Copies of ^{1}H NMR spectra for known compounds. Copies of ^{1}H NMR, ^{13}C NMR, and NOESY spectra for new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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