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Polycyclic Aromatic Hydrocarbons via Iron(III)-Catalyzed Carbonyl−Olefin Metathesis

Christopher C. McAtee, Paul S. Riehl, and Corinna S. Schindler*

Willard Henry Dow Laboratory, Department of Chemistry, University of Michigan, 930 North University Avenue, Ann Arbor, Michigan 48109, United States

Supporting Information

ABSTRACT: Polycyclic aromatic hydrocarbons are important structural motifs in organic chemistry, pharmaceutical chemistry, and materials science. The development of a new synthetic strategy toward these compounds is described based on the design principle of iron(III)-catalyzed carbonyl−olefin metathesis reactions. This approach is characterized by its operational simplicity, high functional group compatibility, and regioselectivity while relying on $FeCl_3$ as an environmentally benign, earth-abundant metal catalyst. Experimental evidence for oxetanes as reactive intermediates in the catalytic carbonyl−olefin ring-closing metathesis has been obtained.

Polycyclic aromatic compounds (PACs),[1] including phenanthrenes, pyrenes, and chrysenes, are important structural motifs that exhibit desirable optical,[2] electronic,[3] and chelating[4] properties. Consequently, diverse fields of research such as materials science,[4,5] natural product synthesis,[6] asymmetric catalysis,[7] and molecular recognition[8] rely on efficient strategies to access condensed polyaromatic compounds. Established procedures toward these motifs include McMurry coupling reactions[9,10] that are mediated by low-valent titanium reagents (Figure 1A II) or oxidative photocyclization strategies[11] of stilbene derivatives. These classical approaches[12] have been hampered by the need for stoichiometric reagents, harsh reaction conditions, or competing substrate dimerization. Complementary approaches have been developed to overcome these challenges that are based on Diels−Alder cycloaddition reactions,[13] radical cyclizations,[14] and metal-mediated cycloisomerizations.[15] Additionally, rhodium- and ruthenium-catalyzed procedures have been reported that rely on bis(*N*-tosylhydrazone)[16] **2** as substrate (Figure 1A I) and olefin-metathesis reactions of bis(alkenes)[17] **4** (Figure 1A III). We have recently reported the development of an efficient iron(III)-catalyzed carbonyl−olefin metathesis reaction[18] that proceeds under mild reaction conditions and ambient temperature. Our synthetic strategy for ring-closing metathesis enables the direct coupling of carbonyl and olefin functional groups upon activation by a Lewis acid catalyst to forge the desired alkene bonds. On the basis of this design principle, we report the development of a new strategy for the synthesis of electronically and sterically diverse PACs. This strategy is compatible with both ketones and aldehydes, proceeding via intermediate oxetanes **6** to provide the corresponding metathesis products in good to excellent yields (Figure 1B). Although several Lewis acids were previously found capable of promoting carbonyl−olefin metathesis reactions,[18,19] a fine-tuned combination of Lewis acidity[20] and oxophilicity[21] proved essential to give high yields of product. Indeed, when biaryl ketone **8** was reacted with numerous Lewis acids (e.g., $TiCl_4$, $SnCl_4$, $FeCl_2$, $Cu(OTf)_2$) no formation or only trace amounts of the metathesis product **9** was observed (entries 1−4, Table 1). Stronger Lewis acids, $GaCl_3$ and $AlCl_3$,[18] were able to promote the desired transformation in 88% and 93% yield, respectively, with complete conversion of starting material **8** (entries 7 and 8, Table 1). Notably, substoichiometric $BF_3{\cdot}Et_2O$ led to the formation of **9** in only modest yield and conversion (entry 6, Table 1).[22] Ultimately, 5 mol % $FeCl_3$ in either dichloroethane or toluene was identified as an optimal set of reaction conditions, resulting in quantitative formation of the product **9** in 97% and 99% yield, respectively (entries 9 and 11, Table 1). More dilute reaction conditions led to slightly lower yields of **9** (entry 10, Table 1). When the reaction was conducted in ethereal solvents (1,4-dioxane), or polar aprotic solvents (DMF), no formation of phenanthrene **9** was observed, presumably due to competing Lewis basicity of these solvents (entries 12 and 13, Table 1). Moreover, the Brønsted acids, anhydrous HCl[23] and *p*TsOH in dichloroethane, did not form phenanthrene **9** and resulted in quantitative reisolation of starting material (entries 14 and 15, Table 1).

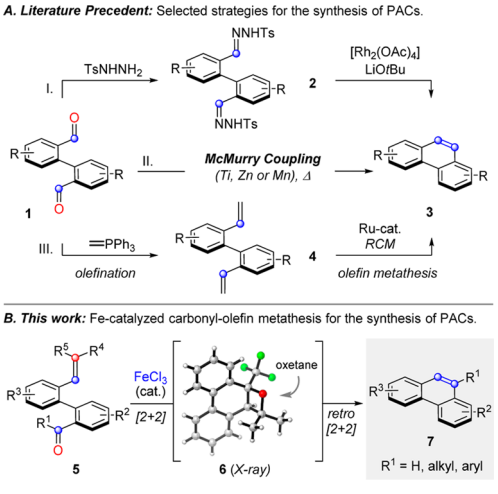

Figure 1. (A) Select strategies to access PACs. (B) Carbonyl−olefin metathesis approach reported.

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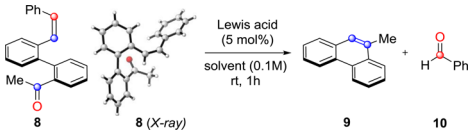
Table 1. Reaction Optimization for Synthesis of 9*



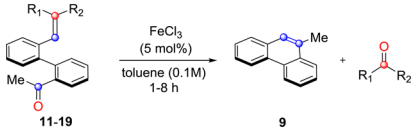
8 8 (*X-ray*) 9 10

entry	Lewis acid	solvent	yield **9** (%)	conversion (%)
1	$TiCl_4$	DCE	3	7
2	$SnCl_4$	DCE	0	6
3	$FeCl_2$	DCE	0	2
4	$Cu(OTf)_2$	DCE	0	0
5	$ZnCl_2$	DCE	22	26
6	$BF_3{\cdot}Et_20$	DCE	31	35
7	$AlCl_3$	DCE	93	100
8	$GaCl_3$	DCE	88	100
9	$FeCl_3$	DCE	97	100
10	$FeCl_3$	DCE (0.01 M)	95	100
11	$FeCl_3$	toluene	99	100
12	$FeCl_3$	DMF	0	0
13	$FeCl_3$	1,4-dioxane	0	6
14	HCl	DCE	0	0
15	*p*TsOH	DCE	0	0

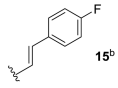
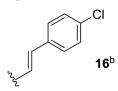
*Conditions: biaryl **8** (0.13 mmol), Lewis or Brønsted acid (5 mol %) in solvent listed (0.1−0.01M), rt, 1 h; yield determined by ^{1}H NMR analysis with 1,3,5-trimethoxy-benzene as internal standard.

We next sought to investigate the ability of biaryl substrates with various olefin subunits (**11**−**19**) to undergo the metathesis reaction (Table 2). Although both electron-rich and electron-

Table 2. Alkene Evaluation for Formation of 9*



11-19 9

entry	alkene		yield (%)	entry	alkene		yield (%)
1		**11**[a]	90	5		**15**[b]	80
2		**12**[b]	82	6		**16**[b]	84
3		**13**[b]	89	7		**17**	79
4		**14**[b]	86	8		**18**[b]: R= Me	18
				9		**19**[b]: R= H	n.r.

*Conditions: biaryl (0.13 mmol), $FeCl_3$ (5 mol %) in toluene (0.1 M); [a]mixture of *E*/*Z* (2:1) isomers; [b]reaction heated to 50 °C.

poor styrenes (entries 1−6, Table 2) proved to be efficient substrates resulting in high yields of **9**, all but styrene **11** and prenylated **17** required elevated temperatures of 50 °C to proceed to full conversion. Notably, no difference in reactivity between *E*- and *Z*-isomers was observed; both *para*-methylstyrenes **12** and **13** formed metathesis product **9** in yields up to 89%, which indicates an indiscriminate reaction pathway of the carbonyl−olefin metathesis reaction. Although the formation of the respective benzaldehydes was observed as the corresponding metathesis byproducts in the course of the reaction, they did not impede reaction progress. Moreover, substrates **11**−**16** bearing styrenyl moieties proved superior to their prenylated analog **17**, which resulted in the formation of **9** in only 79% yield (entries 1−7, Table 2). In comparison, no reaction was observed when terminal alkene **19** was subjected to the optimized reaction conditions (entry 9, Table 2). Conversion of biaryl **18** bearing a crotyl moiety under the reaction conditions resulted in low yields (18%) of the desired product. The hampered yields of the nonstyrenyl substrates **17** and **18** were found to be caused by a competing carbonyl−ene reaction pathway that led to the formation of **20** and **21** in 21% and 47% yield, respectively, when subjected to the optimized reaction conditions (Figure 2). These

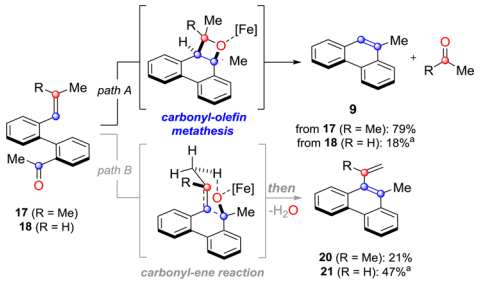
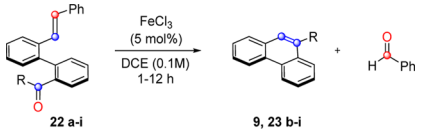


Figure 2. Competing metathesis and carbonyl−ene reactions. Conditions: biaryl (0.13 mmol), $FeCl_3$ (5 mol %) in dichloroethane (0.1 M), rt, 1h; [a]reaction heated to 50 °C for 6 h.

findings contrast distinctly with previous results obtained in our lab[18] in the iron(III)-catalyzed carbonyl−olefin metathesis reaction of aliphatic aryl ketones, in which prenylated substrates proved superior to the analogous styrenes.

The conditions developed for the iron(III)-catalyzed carbonyl−olefin metathesis reaction proved efficient for a range of sterically and electronically differentiated ketones and aldehydes (entries 1−9, Table 3). Although aldehydes have previously been

Table 3. Evaluation of Carbonyl Substituents*



22 a-i 9, 23 b-i

entry	substrate		yield (%)	entry	substrate		yield (%)
1		**22a**	99	6		**22f**	53
2		**22b**	75				
3		**22c**	79	7		**22g**[a]	50
4		**22d**	55[a]	8		**22h**	72
5		**22e**	67	9		**22i**[a]	52

*Conditions: biaryl (0.13 mmol), $FeCl_3$ (5 mol %) in dichloraethane (0.1M), rt, 1−12 h; [a]reaction heated to 50 °C.

found unreactive in catalytic carbonyl−olefin ring-closing metathesis reactions,[18] **22b** was found to yield the desired metathesis product **23b** in 75% under the optimized conditions.

In addition to methyl ketone **22a** and aldehyde **22b**, substrates bearing sterically demanding isopropyl (**22c**) and *tert*-butyl (**22d**) moieties formed the alkylated phenanthrenes in 79% and

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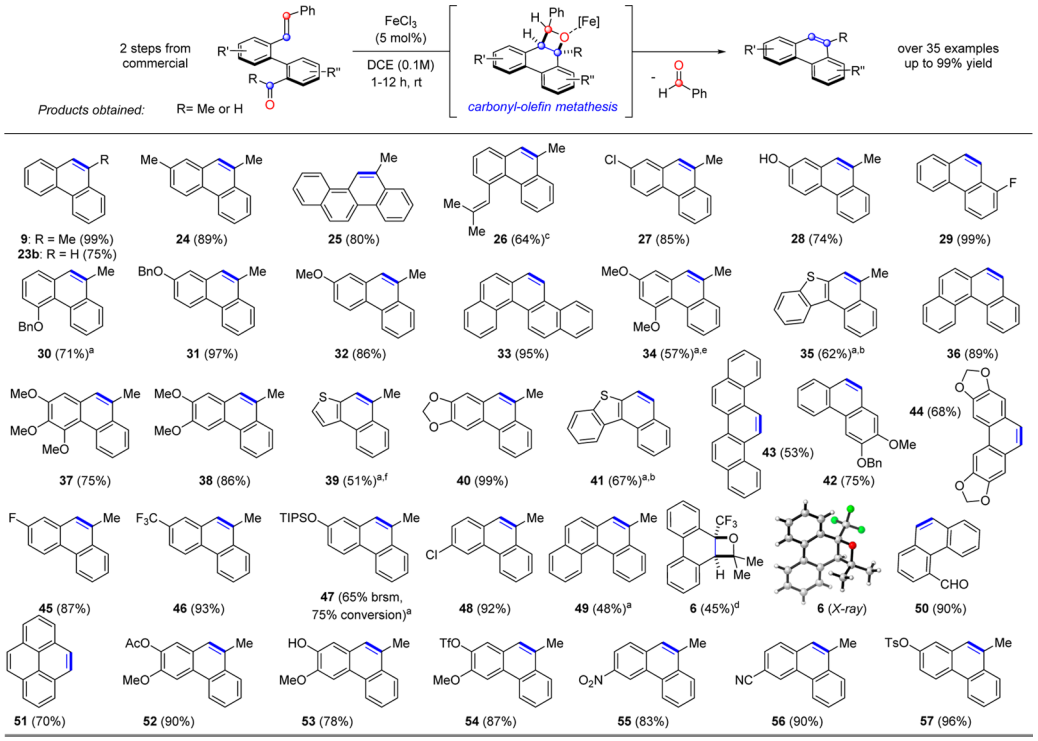
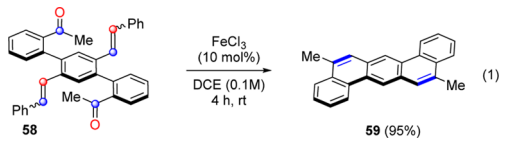
Table 4. Scope of the Iron(III)-Catalyzed Carbonyl−Olefin Metathesis Reaction for the Synthesis of PACs*



*Conditions: biaryl (0.13 mmol), $FeCl_3$ (5 mol %), in DCE (0.1M), rt, 1−12 h; [a]reaction heated to 50 °C; [b]reaction was run with 20 mol % catalyst loading; [c]starting material is bis-prenylated biaryl ketone (see Supporting Information for details); [d]substrate is the prenylated analog of **22i**; reaction was run in toluene as solvent; [e]starting material is reisolated; [f]substrate decomposition was observed at the elevated reaction temperatures; [g]low solubility in organic solvents.

55%, respectively, although the latter required elevated temperatures for efficient conversion (entries 3 and 4, Table 3). Phenyl and naphthyl substituted carbonyl substrates (**22e** and **22f**) were able to undergo metathesis in efficient yields (entries 5 and 6, Table 3). Importantly, biaryl enone **22g** led to the corresponding polycycle **23g** incorporating an exocyclic alkene as a functional handle in 50% yield, albeit at elevated temperatures (entry 7, Table 3). Additionally, *β*-ketoester **22h** resulted in the formation of metathesis product **23h** in satisfactory yield (72%), whereas electron-deficient trifluoromethyl ketone **22i** also proved viable as a substrate, converting to 9-trifluoromethyl phenanthrene **23i** in 52% (entries 8 and 9, Table 3). Various PAC frameworks were accessible utilizing the optimal reaction conditions (Table 4). Upon subjection to metathesis conditions, the desired PACs were obtained with benzaldehyde as the corresponding byproduct. Electron-deficient phenanthrenes bearing halogen, trifluoromethyl, nitro, or nitrile substitution were formed in yields greater than 85% (**27**, **29**, **45**, **46**, **55**, and **56**, Table 4). Similarly, electron-rich substrates incorporating methoxy or benzyl ether functionalities underwent the desired transformation in excellent yields (**30**, **31**, **32**, **38**, and **42**, Table 4). However, diminished yields of 75% and 57% were observed for substrates bearing *ortho*-methoxy substitution (**34** and **37**, Table 4). Dioxoles **40** and **44** were formed in 99% and 68% yield, respectively, under the optimized reaction conditions. Moreover, sulfur-containing heterocycles proved viable substrates for metathesis and resulted in the formation of thiophene **39** and benzothiophenes **35** and **41** in good yields. Alternative strategies to these structural motifs are currently hampered by harsh reaction conditions and competing reaction pathways resulting in low overall yields.[24] Unprotected phenols as well as aldehydes readily underwent metathesis resulting in the formation of phenanthrene **28** or aldehyde **50** in 74% and 90% yield, respectively. Furthermore, extended PACs are accessible employing this metathesis strategy. Specifically, methylchrysene **25** is generated in 80% yield, whereas benzo(*c*)phenanthrene **36** is accessible in 89% yield from the respective biaryl aldehyde (Table 4). Notably, dibenz[*a*,*h*]anthracene **59** is afforded in excellent yield via biscarbonyl−olefin metathesis (eq 1).



Interestingly, when the prenylated analog of **22i** was converted under the optimized reaction conditions, no formation of the desired carbonyl−olefin metathesis product **23i** was observed. Oxetane **6** was identified as the major product (45% yield, Table 4). This result supports our hypothesis that iron(III)-catalyzed carbonyl−olefin metathesis reactions do proceed via oxetanes as reactive intermediates.[18]

The development of a new approach toward the synthesis of polyaromatic hydrocarbons is reported relying on the design principle of an iron(III)-catalyzed carbonyl−olefin metathesis reaction. This strategy is characterized by its operational simplicity, mild reaction conditions, as well as chemo- and regioselectivity. Analysis of the two reaction partners (olefin and carbonyl) revealed that the respective olefin moieties can readily couple to a variety of differentiated aryl-ketones or aryl aldehydes to garner the corresponding functionalized PACs as metathesis products. Isolation of aryl oxetane **6** supports the

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notion that this new strategy for the synthesis of polyaromatic hydrocarbons does indeed proceed via oxetanes as reactive intermediates.[18]

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/jacs.7b01114.

Experimental data (PDF)
Data for $C_{22}H_{18}O$ (CIF)
Data for $C_{18}H_{15}F_3O$ (CIF)
Data for $C_{38}H_{30}O_2$ (CIF)
Data for $C_{24}H_{18}$ (CIF)

■ AUTHOR INFORMATION

Corresponding Author

*corinnas@umich.edu

ORCID

Corinna S. Schindler: 0000-0003-4968-8013

Notes

The authors declare no competing financial interest.

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