Cesium carbonate-catalyzed synthesis of phosphorothioates via S-phosphination of thioketones

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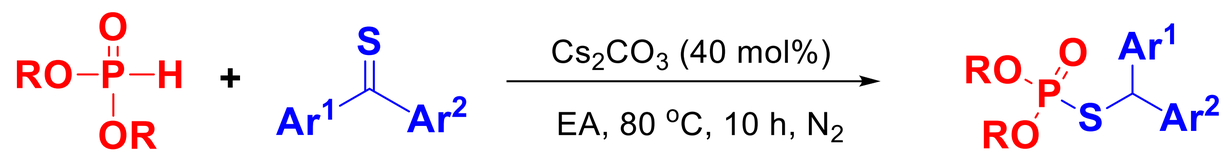
Introduction

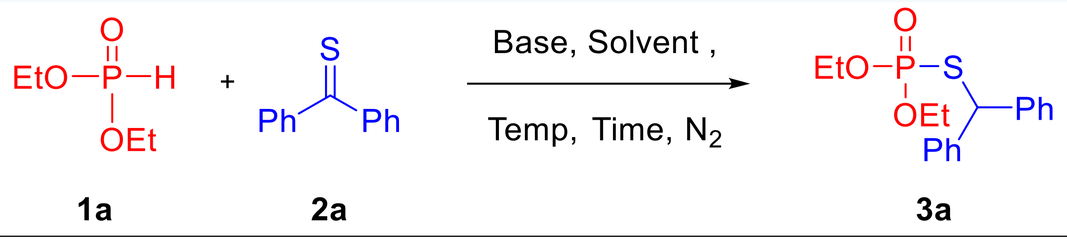
A highly efficient and environmentally-friendly base-mediated transition metal-free direct thiophilic catalytic approach is reported for the synthesis of S-benzhydryl-phosphorothioates by reacting phosphite nucleophiles with diarylmethanethione. A wide variety of thioketones were coupled with different phosphite derivatives to provide the corresponding phosphorothioates in good to excellent yields. The control experiments and density functional theory (DFT) calculations rely on the regio-selective thiophilic addition of a phosphite nucleophile via umpolung protocols



★ Transition metal-free ★ Environment-friendly

★ Oxidant-free ★ Gram scales

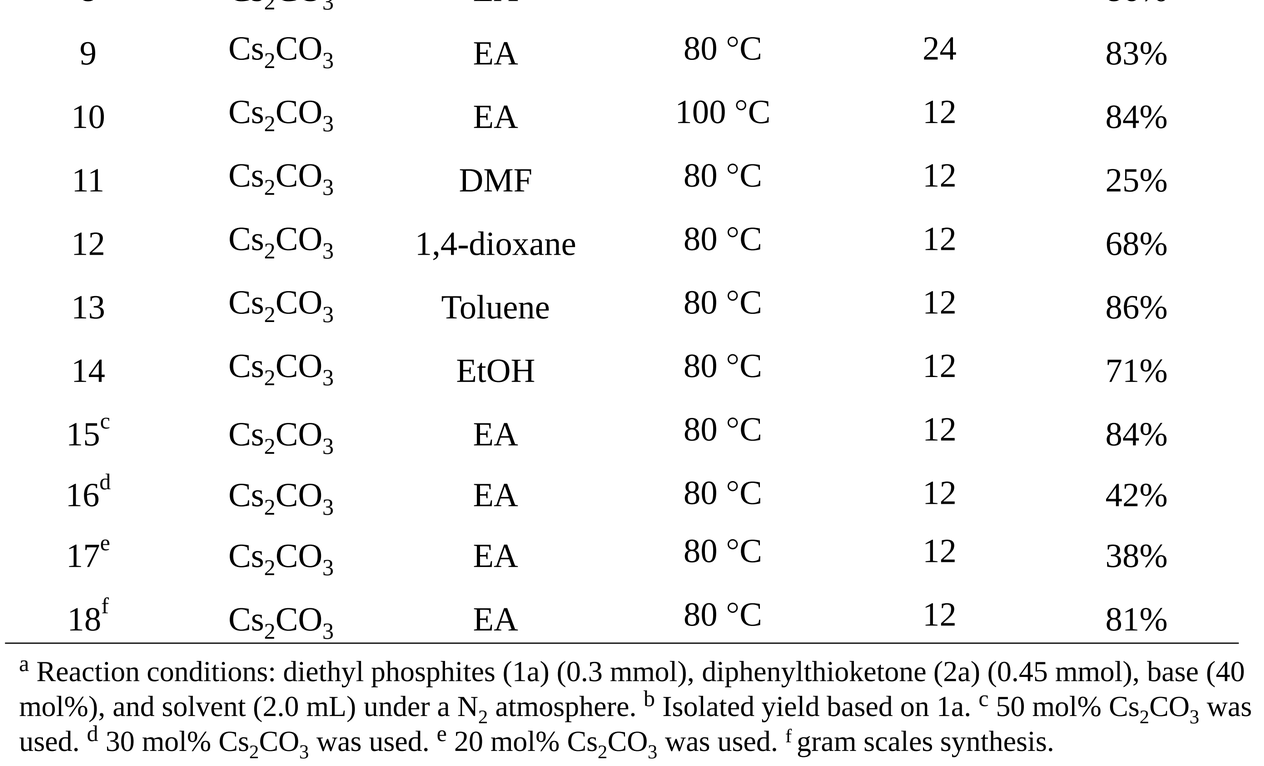
Results and Discussion



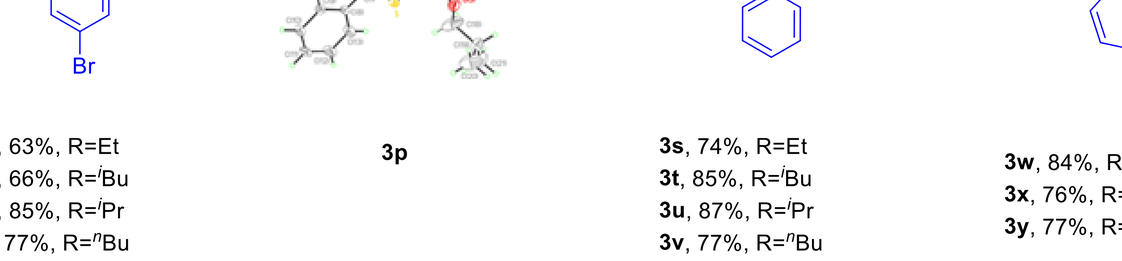
Entry	Base	Solvent	Temp (°C)	Time (h)	Yield [b](%)
1	Et_3N	EA	80 °C	12	64%
2	DABCO	EA	80 °C	12	N.R.
3	-	EA	80 °C	12	N.R.
4	CsF	EA	80 °C	12	39%
5	K_2CO_3	EA	80 °C	12	48%
6	Na_2CO_3	EA	80 °C	12	43%
7	Cs_2CO_3	EA	80 °C	6	45%
8	Cs_2CO_3	EA	80 °C	12	86%
9	Cs_2CO_3	EA	80 °C	24	83%
10	Cs_2CO_3	EA	100 °C	12	84%
11	Cs_2CO_3	DMF	80 °C	12	25%
12	Cs_2CO_3	1,4-dioxane	80 °C	12	68%
13	Cs_2CO_3	Toluene	80 °C	12	86%
14	Cs_2CO_3	EtOH	80 °C	12	71%
15[c]	Cs_2CO_3	EA	80 °C	12	84%
16[d]	Cs_2CO_3	EA	80 °C	12	42%
17[e]	Cs_2CO_3	EA	80 °C	12	38%
18[f]	Cs_2CO_3	EA	80 °C	12	81%

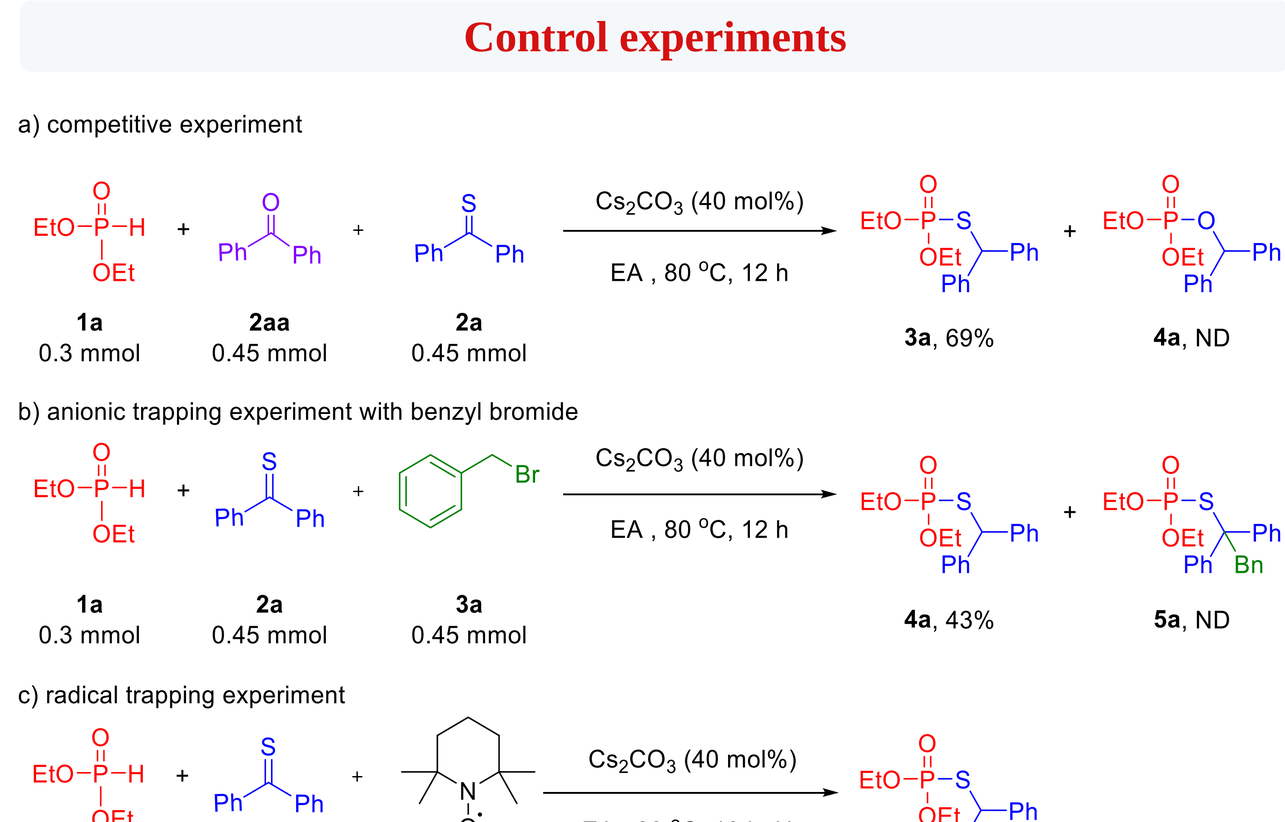
[a] Reaction conditions: diethyl phosphites (1a) (0.3 mmol), diphenylthioketone (2a) (0.45 mmol), base (40 mol%), and solvent (2.0 mL) under a N_2 atmosphere. [b] Isolated yield based on 1a. [c] 50 mol% Cs_2CO_3 was used. [d] 30 mol% Cs_2CO_3 was used. [e] 20 mol% Cs_2CO_3 was used. [f] gram scales synthesis.

Plausible reaction mechanism



Substrate scope of phosphonates and thioketones





3a, 86%, R=Et
3b, 88%, R=^{i}Bu
3c, 76%, R=^{i}Pr
3d, 75%, R=^{n}Bu

3e, 67%, R=Et
3f, 74%, R=^{i}Bu
3g, 82%, R=^{i}Pr
3h, 81%, R=^{n}Bu

3i, 91%, R=Et
3j, 85%, R=^{i}Bu
3k, 76%, R=^{i}Pr
3l, 68%, R=^{n}Bu

3m, 52%, R=Et
3n, 64%, R=^{i}Bu

3o, 63%, R=Et
3p, 66%, R=^{i}Bu
3q, 85%, R=^{i}Pr
3r, 77%, R=^{n}Bu

3p

3s, 74%, R=Et
3t, 85%, R=^{i}Bu
3u, 87%, R=^{i}Pr
3v, 77%, R=^{n}Bu

3w, 84%, R=Et
3x, 76%, R=^{i}Bu
3y, 77%, R=^{i}Pr

Control experiments

a) competitive experiment

b) anionic trapping experiment with benzyl bromide

c) radical trapping experiment

Acknowledgement

We are grateful to the National Chung Hsing University and the Ministry of Science and Technology, Taiwan (MOST) for supporting this work