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REACTION OF 1-BENZOPYRYLIUM SALTS WITH TRIALKYL PHOSPHITE: FORMATION OF 2,4-DISUBSTITUTED 1-BENZOPYRAN DERIVATIVES

Hideharu Iwasaki and Kin-ya Akiba*

Department of Chemistry, Faculty of Science, Hiroshima University
Higashisenda-machi, Hiroshima City 730, Japan

Abstract- Reaction of 1-benzopyrylium perchlorate (1) with triethyl phosphite gave 2H-benzopyran-2-phosphonate (2) in good yield. Deprotonation of 2 with sec-BuLi at -78 °C followed by addition of aromatic aldehydes gave exomethylene compound (4). Reaction of ketene silyl acetal (7) with 2-substituted 1-benzopyrylium salt (6), generated in situ from 4 by addition of CF_3SO_3H, afforded the corresponding 2,4-disubstituted 1-benzopyran (8).

We have reported the reaction of readily available heteroaromatic cations, such as pyridinium, isoquinolinium and quinolinium with trialkyl phosphite to afford the corresponding dihydroazaaromatic phosphonates in high yield. By the proton abstraction with base, the phosphonates were used to react with electrophiles which provided unique methods for regioselective introduction of substituents into azaaromatics.[1-3] Here we extend the scope of the reaction to oxygen heterocycles by use of 1-benzopyrylium salt.[4] When 1-benzopyrylium perchlorates (1a, 1b) were allowed to react with $P(OEt)_3$ and NaI in MeCN under nitrogen atmosphere at room temperature, 2H-benzopyran-2-phosphonates were obtained in excellent yield (2a, 98% ;2b, 86%).[5] In order to elucidate the optimum conditions for the generation of the phosphonate carbanion (A), we tried to react three kinds of bases with 2a under listed conditions (Table 1). Although the carbanion was unexpectedly difficult to be formed and unstable, the reagent of choice was sec-BuLi and the resulting carbanion was trapped quantitatively with D_2O within 10 min at -78 °C (entry 7, 8).

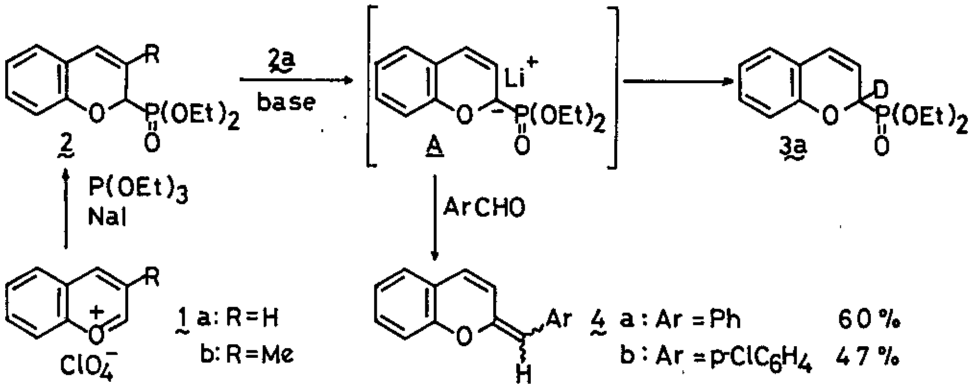


Table 1 Deprotonation of 2 with Base

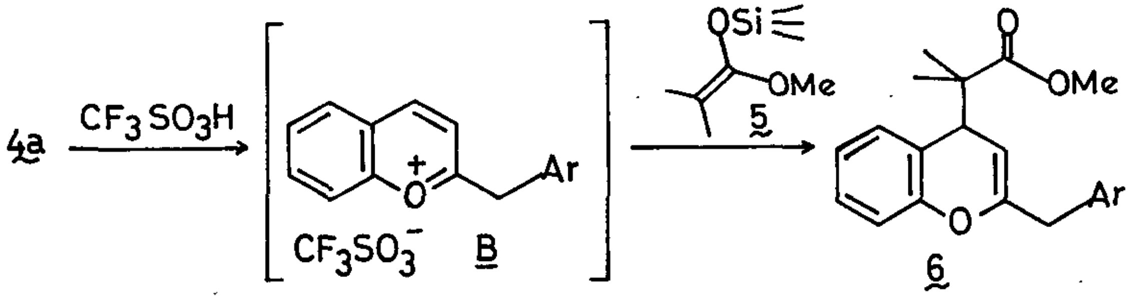
entry	base	Time(min.)	temp.(°C)	Yield (%)		
				2a	3a	decomp.
1	n-BuLi	5	-100	100	-	-
2		5	-78	-	50	50
3		10	-78	-	-	100
4	LDA	10	-78	100	-	-
5		30	-78	100	-	-
6		30	-28	100	-	-
7	sec-BuLi	5	-78	-	100	-
8		10	-78	-	100	-
9		20	-78	-	50	50

(i) LDA could not deprotonate 2.

(ii) Compound 3a was determinated by ms and also by the absence of 2H (δ 5.25) in ^{1}H-nmr.

(iii) Two equivalents of sec-BuLi were necessary to generate A quantitatively. When one eq. of sec-BuLi was used, almost 50% of A was generated and 50% of 2 remained intact for some unknown reason.

The resulting carbanion (A) *reacted with aromatic aldehydes to give the* exomethylene compound (4).[4] In a typical run, sec-BuLi (2 eq) was added to 1a (0.75 g, 2.8 mmol) in THF (5 ml) at -78 °C under nitrogen. After the mixture was stirred for 5 min, benzaldehyde (5.60 mmol, 2 eq) was added. Then the mixture was allowed to warm to room temperature and was stirred for ca. 15h.[7] After the mixture was quenched with 10% aqueous sodium carbonate (10 ml), the product 4a was extracted with ether (20 ml X 3), and the solvent was evaporated in vacuo after being dried over anhydrous magnesium sulfate. The crude 4a was purified by TLC (SiO_2) with hexane:ethyl acetate=9:1 as eluent to afford 0.30g of pure 4a (60% yield). When aliphatic aldehydes were used in the reaction, we could detect the vinyl protons in ^1H- nmr in the crude product, but could not obtain the pure product, probably because of the decomposition on TLC. When 4a was protonated by CF_3SO_3H (1 eq), it resulted in 2-substituted 1-benzopyrylium salt (B). The formation of B was confirmed by ^1H-nmr (CD_3CN) according to the observation of extremely low field proton (δ 9.47, 1H, 3H). In fact B reacted with ketene silyl acetal 5 to give 6 in 62% yield. Thus the reaction sequence provides a new unique route to 2,4-disubstituted 1-benzopyrans.



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5 **2a**: Yellow liquid. ^{1}H-nmr ($CDCl_3$): δ 1.10-1.42 (m, 6H), 3.82-4.36 (m, 4H), 5.25 (ddd, 1H, J=13.2, 4.5, 2.4 Hz), 5.82 (ddd, 1H, J=10, 6.9, 4.5 Hz), 6.45 (ddd, 1H, J=10, 6, 4.5 Hz), 6.62-7.20 (m, 4H). *Anal*. calcd for $C_{16}H_{12}O$: C, 58.43; H, 6.03. Found: C, 58.33; H, 6.00.

6 **4a**: mp 142-144 °C. ^{1}H-nmr ($CDCl_3$): δ 5.33 (s, 1H), 6.10-8.66 (m, 11H). *Anal*. calcd for $C_{16}H_{12}O$: C, 87.24; H, 5.49. Found: C, 86.99; H, 5.64. **4b**: mp 124-126 °C. ^{1}H-nmr ($CDCl_3$): δ 5.47 (s, 1H), 6.00-8.06(m, 10H). *Anal*. calcd for $C_{16}H_{11}OCl$: C, 75.44; H, 4.35. Found: C, 75.24; H, 4.29.

7 Rather long stirring (10-15h) was necessary to obtain **4** in good yield (60-70%)

8 **6**: Yellow liquid. ^{1}H-nmr ($CDCl_3$): δ 1.00 (s, 3H), 1.03 (s, 3H), 3.58 (s, 3H) 3.62 (s, 2H), 3.75 (d, 1H, J=6.5Hz), 4.66(d, 1H, J=6.5Hz), 6.90-7.52 (m, 9H). *Anal*. calcd for $C_{21}H_{22}O_3$: C, 78.23; H, 6.87. Found: C, 78.05; H, 6.62.

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