



Tetrahedron Letters 44 (2003) 4909-4912

TETRAHEDRON LETTERS

A novel method of synthesis of 1,2-diketones from 1,2-diols using N-bromosuccinimide

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Abstract—A simple and convenient procedure is reported for the synthesis of benzils and aliphatic 1,2-diketones of cyclic and open chain compounds from corresponding hydrobenzoins and 1,2-diols by refluxing with *N*-bromosuccinimide in carbon tetrachloride in presence or absence of pyridine. © 2003 Published by Elsevier Science Ltd.

Benzils have received a great deal of attention because of their applications as photosensitive agents in photocurable coatings,¹ as starting materials in organic and pharmaceutical synthesis,² and also as biologically important compounds.³ Conventionally benzils are prepared by the oxidation of corresponding benzoins with oxidizing agents such as CuSO₄/Py, Bi₂O₃/H⁺, HNO₃ in aq. solution,⁴ RuO₄,⁵ oxidation of acyloins,⁵ oxidative hydrolysis of silver salts of α -keto dithianes,⁶ coupling of acid chlorides using SmI_2 ,⁷ and SeO_2 oxidation of mono ketones.⁸ Oxidation of acetylenes with $NaIO_4/RuO_2$,⁹ $Tl(NO_3)_3^{10}$ and $KMnO_4^{11}$ has been reported to afford α -diketones in low yields. The oxidation of 1,2diols to 1,2-diketones, on the other hand, is reported by aq. NaOCl, 4-MeO-TEMPO,^{12a} (4-AcNH-TEMPO)-OTs-TsOH,^{12b} 4-PhCO₂-TEMPO-electrolysis,^{12c} n- $Bu_4N[MoO(O_2)_2(C_5H_4N(\tilde{O})CO_2)]^{13}$ H₂O₂-[C₅H₅N- $(CH_2)_{15}CH_3]_3$ {PO₄[W(O)(O₂)₂]₄},^{14a} and O₂-Co(acac)₃-N-hydroxyphthalimide^{14b} and has its drawbacks in terms of expensive reagents, difficult reaction conditions and low yields. In some cases, even the starting materials require a series of steps for their preparation. In view of the importance of the said transformation, we decided to investigate a simple and inexpensive procedure.

We report herein a simple and convenient procedure for the synthesis of a variety of benzils from the corresponding hydrobenzoins and aliphatic 1,2-diketones of cyclic and open-chain compounds by the oxidation of corresponding 1,2-diols with N-bromosuccinimide (NBS) in refluxing carbon tetrachloride (80-85°C) in the presence or absence of pyridine. Benzils and 1,2diketones were obtained in nearly quantitative yields by a simple work up procedure. A number of reactions were carried out with hydrobenzoin as model substrate and NBS by changing the molar ratio of hydrobenzoin to NBS, the solvent and the reaction temperature in order to optimize the reaction conditions for quantitative conversion. We observed that hydrobenzoin, 4,4'dichlorohydrobenzoin, 4,4'-dibromohydrobenzoin, 3,3'-dibromohydrobenzoin, α, α' -dihydronaphthoin and β , β '-dihydronaphthoin (runs 2–12) underwent complete oxidation using a molar ratio of 1:2.5 or 1:3 of substrate:NBS (see Table 1) in refluxing carbon tetrachloride to give the corresponding benzils, but 4,4'-dimethylhydrobenzoin underwent oxidation with concomitant benzylic bromination under these conditions and 4.4'-dimethoxyhydrobenzoin also gave a mixture. In order to prevent bromination of the side-chains in hydrobenzoins, reaction was carried out with NBS in the presence of proton acceptors viz. CaCO₃, triethylamine and pyridine. The reactions of 4,4'-dimethylhydrobenzoin, carried out in presence of CaCO₃ and triethylamine, were not complete and yielded a mixture of products. However, the reaction of 4,4'-dimethylhydrobenzoin carried out in the presence of pyridine using a 1:3:10 molar ratio (substrate:NBS:pyridine) was complete after 4 h and yielded a mixture of 4,4'-dimethylbenzoin and 4,4'-dimethylbenzil (run 13). A reaction repeated with a lower molar ratio of pyridine (1:3:1) vielded 4,4'-dimethylbenzil exclusively after 1 h 45 min (run 14). This suggests that pyridine not only prevents the benzylic bromination but also retards the rate of oxidation if used in higher molar amounts. Subse-

Keywords: *N*-bromosuccinimide; oxidation; benzils; 1,2-diketones; 1,2-diols.

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quently, oxidation of 2,2'-dimethylhydrobenzoin and 4,4'-dimethoxyhydrobenzoin was carried out with NBS in presence of pyridine which yielded 2,2'-dimethylbenzil and 4,4'-dimethoxybenzil, respectively (runs 17–18). All the starting hydrobenzoins investigated for oxidation were mixtures of *meso-* and *dl*-isomers (Eq. (1)).

$$\begin{array}{c|c} Ar - CH - CH - Ar & NBS, CCI_4 & Ar - C - C - Ar \\ | & | & | \\ OH & OH & (Pyr) \Delta, 80-85 \ ^{\circ}C & 0 \\ \hline & 1a-j & 2a-j \\ \hline & a: Ar = C_6H_5; \ b: Ar = 4-CIC_6H_4; \ c: Ar = 2-CIC_6H_4; \\ d: Ar = 4-BrC_6H_4; \ e: Ar = 3-BrC_6H_4; \ f: Ar = 1-naphthyl; \\ g: Ar = 2-Naphthyl; \ h: Ar = 4-CH_3C_6H_4; \ i: Ar = 2-CH_3C_6H_4; \\ j: Ar = 4-OCH_3C_6H_4 \end{array}$$

In order to determine if steric factors have any role on the rate of oxidation of 1,2-diols, reactions of pure *meso-* and *dl*-hydrobenzoins, *meso-* and *dl-4,4'*dichlorohydrobenzoins and *meso-* and *dl-4,4'-*dimethyl hydrobenzoins were carried out with NBS under identical reaction conditions (runs 9–12, 15–16). It was observed that *meso-*hydrobenzoins underwent oxidation faster than the corresponding *dl*-isomers to give benzils.

The scope of the reagent was then extended to the oxidation of cyclic and open-chain aliphatic 1,2-diols. Aliphatic 1,2-diols on oxidation with N-bromosuccinimide in carbon tetrachloride gave a mixture of products in the presence or absence of pyridine. After various attempts, it was observed that aliphatic 1,2diols could also be oxidized with N-bromosuccinimide in carbon tetrachloride at lower temperatures, i.e. 60-70°C in the presence of pyridine to give 1,2-diketones in high yields. The oxidation of aliphatic 1,2-diols gave a mixture of products in absence of pyridine and the oxidations were incomplete at temperatures below 60°C (Eq. (2)). Thus, different cyclic, open-chain and fatty 1,2-diols 3a-j could be oxidized to the corresponding 1,2-diketones in high yields **4a**–**i** by a simple quenching procedure (runs 19–30). Further, N-bromosuccinimide has also been observed to bring about oxidation of acyloins 5a-c to the corresponding 1,2-diketones 6a-c in high yields in carbon tetrachloride at 60–70°C in the presence of pyridine (Eq. (3)) (runs 31–33).

Table 1. Reaction of hydrobenzoins, aliphatic and cyclic 1,2-diols with NBS in carbon tetrachloride^a

	Substrate(s)	Molar ratio S:NBS:pyridine	Time (h)	% isolated yield (2, 4, 6)
1	Hydrobenzoin (1a)	1:2:0	4	_b
2	Hydrobenzoin (1a)	1:2.5:0	2.5	94
3	4,4'-Dichlorohydrobenzoin (1b)	1:3:0	2.75	96
4	2,2'-Dichlorohydrobenzoin (1c)	1:3:0	2	82
5	4,4'-Dibromohydrobenzoin (1d)	1:3:0	3	87
6	3,3'-Dibromohydrobenzoin (1e)	1:3:0	1.75	37
7	α, α' -Dihydronaphthoin (1f)	1:3:0	3	82
8	β , β' -Dihydronaphthoin (1g)	1:3:0	2.75	90
9	meso-Hydrobenzoin (1a)	1:2.5:0	1.25	81
10	dl-Hydrobenzoin (1a)	1:2.5:0	2.50	93
11	meso-4,4'-Dichlorohydrobenzoin (1b)	1:3:0	1.5	90
12	dl-4,4'-Dichlorohydrobenzoin (1b)	1:3:0	3	87
13	4,4'-Dimethylhydrobenzoin (1h)	1:3:10	4	_c
14	4,4'-Dimethylhydrobenzoin (1h)	1:3:1	1.75	83
15	meso-4,4'-Dimethylhydrobenzoin (1h)	1:3:1	1.25	77
16	dl-4,4'-Dimethylhydrobenzoin (1h)	1:3:1	1.75	71
17	2,2'-Dimethylhydrobenzoin (1i)	1:3:5	2.50	72
18	4,4'-Dimethoxyhydrobenzoin (1j)	1:3:2	1.50	83
19	Octan-4,5-diol (3a)	1:3:1	1.75	75
20	Hexan-3,4-diol (3b)	1:3:1	2	79
21	trans-Cyclohexan-1,2-diol (3c)	1:3:1	1.50	74
22	meso-Tartaric acid (3d)	1:3:0	1	84
23	(+)-Tartaric acid (3d)	1:3:0	1.50	82
24	(+)-Dimethyl tartarate (3e)	1:3:0	1.25	82
25	meso-Dimethyl tartarate (3e)	1:3:0	1	80
26	9,10-Dihydroxystearic acid (3f)	1:3:2	2	50
27	Methyl 9,10-dihydroxystearate (3g)	1:3:2	1.75	75
28	2,3-Dihydroxy-3-phenyl propanoic acid (3h)	1:3:1	3	88
29	Methyl 2,3-dihydroxy 3-phenyl propionate (3i)	1:1.5:1	2.50	84
30	Hexatriacontane-18,19-diol (3j)	1:3:2	2	84
31	Butyroin (5a)	1:1.5:1	1.25	96
32	Propyroin (5b)	1:1.5:1	1.50	82
33	Stearoin (5c)	1:1.5:1	2	76

^a 50 mL of dry solvent was used/g of the substrate.

^b Reaction was complete. TLC showed both benzil and benzoin as the products.

^c A mixture of 4,4'-dimethylbenzoin and 4,4'-dimethyl benzil was obtained.

$$\begin{array}{c|c} R-CH-CH-R' & \underline{NBS, CCl_4} & R-C-C-R' \\ | & | & \\ OH & OH & \\ \end{array} \xrightarrow{(Pyr) \Delta, 60-70 \ ^{\circ}C} & 0 & O \\ \hline 3a-j & & 4a-j \end{array}$$

$$(2)$$

 $\begin{array}{l} a:R, R'=n-C_{3}H_{7}; \ b:R, R'=C_{2}H_{5}; \ c:R, R'=-(CH_{2})_{4}\\ d:R, R'=COOH; \ e:R, R'=COOCH_{3}; \ f:R=C_{8}H_{17}, R'=C_{7}H_{14}COOH\\ g:R=C_{8}H_{17}, R'=C_{7}H_{14}COOCH_{3}; \ h:R=C_{6}H_{5}, R'=COOH\\ i:R=C_{6}H_{5}, R'=COOCH_{3}; \ j:R=n-C_{17}H_{35}, R'=n-C_{17}H_{35}\\ \end{array}$

$$\begin{array}{cccc}
 & O & OH \\
 & \parallel & \mid \\
 R-CH-CH-R & \hline (Pyr) \Delta, 60-70 \ ^{\circ}C \end{array} \xrightarrow[]{} \begin{array}{c}
 & O & O \\
 & \parallel & \parallel \\
 & R-C-C-R \\
 & \mathbf{5a-c} & \mathbf{6a-c} \quad (3)
\end{array}$$

a : R = n-C₃H₇; b : R = C₂H₅; c : R = n-C₁₇H₃₅

The mechanism of oxidation of alcohols with NBS has not been clearly established although two interpretations have been advanced and it is generally accepted that a positive halogen is the attacking species.¹⁵ We believe that the hydrobenzoins react with NBS to form a hypobromite which readily loses hydrogen bromide to form the carbonyl product (Eq. (4)). 4,4'-Dichlorohydrobenzoin dimethyl ether and 4,4'-dimethylhydrobenzoin dimethyl ether did not undergo any oxidation with NBS even after prolonged reaction times under otherwise identical reaction conditions and the starting materials were recovered unchanged due to the nonavailability of hydroxyl hydrogens as (required by the mechanism proposed) above. The oxidations are undoubtedly proceeding via the corresponding acyloins as has been confirmed by the presence of acyloins when the progress of various reactions was monitored. It appears from the available data that the initial oxidation of 1,2-diols is faster than the oxidation of corresponding acyloins. Benzopinacole did not undergo any oxidation with NBS under these conditions as expected.

The reactions of hydrobenzoins were also attempted with *N*-chlorosuccinimide under different reaction conditions. Although the reaction of hydrobenzoin was complete after 5 h and benzil was isolated, reactions of substituted hydrobenzoins were incomplete and also yielded mixtures of benzoins and benzils. In the case of aliphatic 1,2-diols, namely, hexane-3,4-diol and 9,10dihydroxystearic acid, no oxidation took place and starting materials were recovered unchanged. Therefore, we conclude that *N*-bromosuccinimide is a simple and efficient reagent for the oxidation of hydrobenzoins to benzils and 1,2-diols to 1,2-diketones in high yields under mild conditions.

General procedure: In a typical procedure, a 100 mL round-bottomed flask was mounted over a magnetic stirrer, fitted with a reflux condenser and a mercury trap. A mixture of hydrobenzoin¹⁶ **1a** (1.0 g, 4.67 mmol) and NBS (2.5 g, 14.01 mmol) in dry CCl₄ (50 mL) was refluxed in an oil bath maintained at 80–85°C.

The progress of the reaction was monitored by TLC using benzene/ethyl acetate (90:10 v/v) as eluent. The starting material disappeared after 1 h and two new spots were observed on TLC analysis corresponding to benzoin and benzil. The reaction was allowed to continue until only one product was observed on TLC (2.5 h). The reaction was quenched with water (100 mL) and the carbon tetrachloride layer was separated. The aqueous layer was extracted with CCl_4 (2×10 mL). The combined organic layers were dried over anhyd. MgSO₄, filtered and concentrated on a rotary evaporator to afford a yellow solid which was recrystallized from ethanol and was identified as benzil (0.92 g 94%) by mp, mixed mp, IR and NMR spectra.

The reaction of substrates 1h-j (1 g, n mmol) were carried out with NBS in the presence of dry pyridine (according to the molar ratios shown in Table 1) as above. In the reactions of aliphatic 1,2-diols (1 g, n mmol) with NBS in the presence of dry pyridine, the temperature of the oil bath was maintained at 60–70°C. All the reactions were worked up as detailed above. The reaction of tartaric acid was not quenched with water owing to the high solubility of the product in water. The carbon tetrachloride was evaporated and the product was extracted by triturating with ether.

Acknowledgements

B.M.K. thanks CSIR, New Delhi, India for a Junior Research Fellowship.

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