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Ph_3BiCO_3: a mild reagent for in situ oxidation of urazoles to triazolinediones

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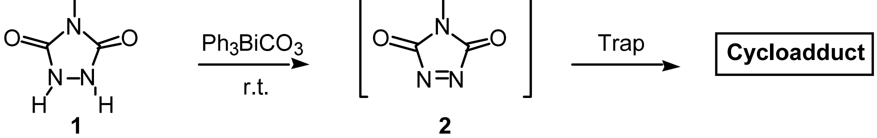
Abstract—A novel method for the selective oxidation of urazoles is reported. The resulting triazolinediones are trapped in situ by cycloaddition with anthracene derivatives. The process described herein involves as mild oxidant, the pentavalent bismuth species Ph_3BiCO_3.

4-Substituted-1,2,4-triazoline-3,5-diones **2** (TAD's)[1] are compounds of high reactivity toward cycloadditions[2] and ene reactions.[3] However, they have only been parsimoniously employed in synthesis. Recently, Corey and co-workers reported that triazolinediones could act as protecting group of indolic 2,3-π bond systems.[4] This strategy was applied with success to the total synthesis of okaramine N.[5] The classical method for the preparation of TAD's implies oxidation of the corresponding urazole with a strong oxidizing agent such as iodobenzene diacetate,[6] N_2O_4,[7] periodic acid,[8] *tert*-butyl hypochlorite[9] or potassium dichromate.[10] Even though the aforementioned methods afforded a satisfactory yield of product, the harsh conditions that are involved precluded in situ oxidation of urazoles in the presence of other sensitive groups. We found that, upon treatment with triphenylbismuth carbonate (Ph_3BiCO_3)[11] in CH_2Cl_2, urazoles **1** could readily be converted to triazolinediones **2**. Since TAD's **2** are highly reactive, their purification is arduous to achieve. However, under our reaction conditions, the oxidized species can be trapped in situ by Diels–Alder cycloaddition with dienes (Scheme 1).

The mildness of the Ph_3BiCO_3-mediated oxidation[12] thus allows smooth conversion of urazoles in the presence of dienes bearing various functional groups. The resulting TAD's are then capable of further reacting with the internal trapping agent. Results are summarized in Table 1.

The overall yields of the two-step process are in every case studied, excellent. The oxidation reaction has been extended to diversely substituted urazoles, e.g. phenyl- (entries 1–4), methyl- (entries 5, 6) and *p*-NHBoc-phenylurazole (entry 7). The resulting triazolinediones are then capable to undergo cycloaddition with miscellaneous dienes. The intense red color, which is usually characteristic of triazolinediones, did not appear in the course of the reaction. This observation suggests that rapid addition takes place as soon as urazoles are oxidized to TAD's. The Bi^V oxidation conditions are



Scheme 1.

Keywords: bismuth; oxidation; triazolinediones; urazoles.

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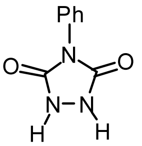
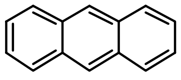
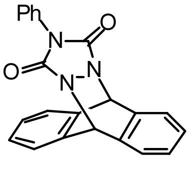
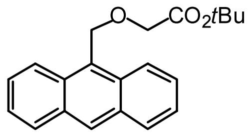
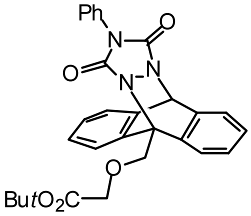
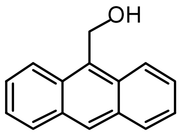
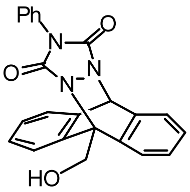
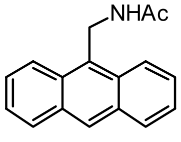
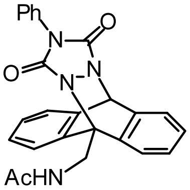
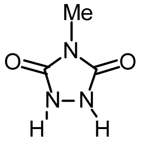
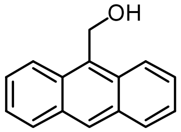
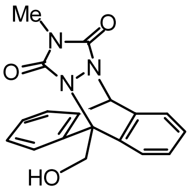
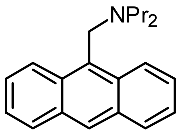
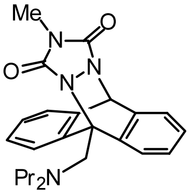
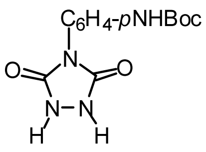
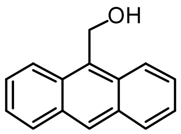
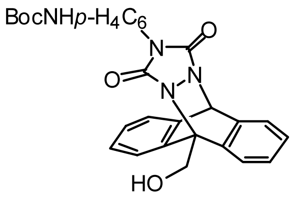
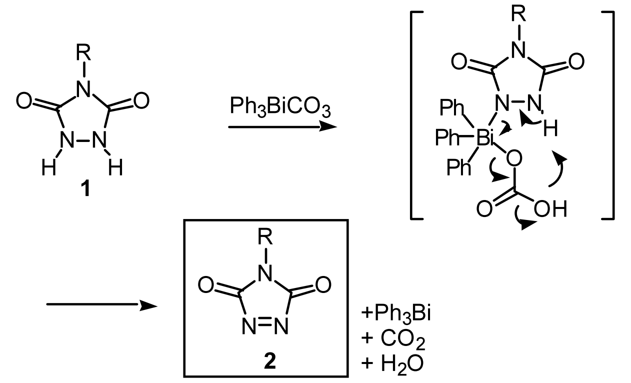
compatible with some functional groups, including acid sensitive Boc (entry 7) and *t*-butyl ester (entry 2), oxidizible alcohols (entries 3, 5 and 7) and nitrogen-containing compounds (entries 4 and 6). Attempts to run the reaction in the presence of anthracene-9-yl-methylamine were unsuccessful. This result can be ascribed, in part, to the ability of pentavalent bismuth species to arylate primary amines[13] and other organic substrates.[14] This leads to consumption of the bismuth reagent prior to oxidation. Moreover, TAD itself seems

Table 1. Examples of oxidation/trapping of urazoles

entry	urazole	trap	cycloadduct	yield (%)[a]
1				84
2	″			92
3	″			91
4	″			95
5				96
6	″			91[b]
7				84

[a] Isolated yields.

[b] NMR yield. The cycloadduct readily underwent retro Diels–Alder upon chromatography (64% isolated yield).



Scheme 2.

to be substrate sensitive. Indeed, authentic phenyltriazolinedione (PTAD) failed also to react cleanly with anthracene-9-yl-methylamine and yielded many by-products.

A postulated mechanism for the oxidation process is illustrated in Scheme 2. The first step involves the formation of a N–Bi bonded intermediate by nucleophilic attack of the nitrogen atom on Ph_3BiCO_3. The existence of an analogous intermediate has been well demonstrated by Barton and co-workers in the case of phenols.[15] Subsequent rearrangement, via collapse of the transient species, leads to oxidized triazolinedione with concomitant release of triphenylbismuth, carbon dioxide and water.

In conclusion, we showed that urazoles oxidation can be performed, under mild conditions, using triphenylbismuth carbonate. The procedure described herein permits not only the synthesis of triazolinediones in high yield but also the in situ trapping of the latter by functionalized dienes. As a reminder, bismuth is the least toxic of the heavy metals.

General procedure for the cycloaddition of anthracene derivatives with triazolinediones starting from urazoles

To a solution of 9-anthracenemethanol (0.071 g, 0.9 equiv.) in 4 mL of anhydrous CH_2Cl_2 are added in one portion, 4-methylurazole (0.043 g, 3.8 mmol, 1 equiv.) and triphenylbismuth carbonate (0.206 g, 1.1 equiv.). The milky solution is stirred at room temperature for 2 h. The solvent is then evaporated under reduced pressure and the crude is purified by chromatography on silica (EtOAc/cyclohexane, 2/8). The cycloadduct is obtained as a yellow solid (0.104 g, 96%). ^{1}H NMR ($CDCl_3$) δ 2.89 (s, 3H), 4.46 (t, $J=7.7$ Hz, 1H), 5.18 (d, $J=7.7$ Hz, 2H), 6.23 (s, 1H), 7.24–7.30 (m, 4H), 7.43 (m, 2H), 7.54 (m, 2H). ^{13}C NMR ($CDCl_3$) δ 25.5, 58.5, 59.2, 67.2, 122.5, 123.7, 128.0, 137.8, 137.9, 153.9, 154.4. IR (KBr): 757, 1007, 1188, 1395, 1459, 1709, 1759, 2950, 3549. MS (ESI/TOF): 344 (M+23).

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