Generation of a Ketocarbenoid from α,α-Dibromodeoxybenzoin by Samarium(II) Di-iodide and Its Trapping by Alkene Cycloaddition

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α,α-Dibromodeoxybenzoin reacts with samarium(II) di-iodide and alkenes to give dihydrofuran derivatives, regio- and stereo-selectively.

Since the pioneering work of Kagan[1] in 1980, samarium(II) di-iodide (SmI_2) has been recognized as a useful reagent for carbon–carbon bond formation.[2]† We have already shown that it is effective for the synthesis of γ-lactones from α,β-unsaturated esters and carbonyl compounds.[3] We now report the regio- and stereo-selective synthesis of dihydrofurans by treatment of α,α-dibromodeoxybenzoin (**1**) with SmI_2 in the presence of alkenes.[4]

Treatment of a mixture of (**1**) and a five-fold excess of styrene with SmI_2 (2 mol. equiv.) in refluxing tetrahydrofuran (THF)–hexamethylphosphoramide (HMPA) (10 : 1) for 2 h afforded the dihydrofuran (**2**; R^1 = Ph, R^2 = H), uncontaminated by the regioisomer.† Isolation of the dihydrofuran was effected by preparative t.l.c. [elution with hexane–diethyl ether (10 : 1)] and the structure of this 1 : 1 adduct was determined by ^{1}H n.m.r. spectroscopy. Analogous reactions with *p*-methylstyrene or 1,1-diphenylethylene produced the corresponding heterocycles (**3**) and (**4**) (Table 1).

These dihydrofurans may represent the product of formal 1,3-dipolar addition of the ketocarbenoid to alkenes. On the other hand, the zinc powder method has been reported as generating ketocarbenoid by α-elimination of (**1**).[4a] Yields of the products are very poor, although the method requires great excess of alkene and severe reaction conditions: *e.g.* heating under reflux in benzene for 2 days.

It is noteworthy that the reaction with α-methylstyrene gave the C–H insertion product (**6**) in addition to the expected dihydrofuran (**5**). Isomerization of (**5**) to (**6**) or (**6**) to (**5**) is not involved, because the ratio of (**5**) to (**6**) was unchanged with longer reaction time. Since C–H insertion is one of the typical reactions of a carbene or a carbenoid,[5,6] the ketocarbenoid is a reasonable intermediate in this reaction.

High regio- and stereo-selectivities were observed in the reaction with *trans*-β-methylstyrene. The oxygen atom of (**1**) added selectively to the phenyl-substituted carbon of the alkene, and the stereochemistry was *trans* with respect to phenyl and methyl groups;‡ compound (**7**) was the sole product of the reaction. With indene, the dihydrofuran (**8**) was the sole product, as a result of regio- and stereo-selective addition. In this case the stereochemistry was *cis*; however, assignment of the *cis*-stereochemistry rests on n.m.r. coupling constant arguments and should be considered tentative.§

Conjugated dienes such as isoprene and penta-1,3-diene reacted in a selective 1,2-fashion to give the corresponding single regioisomers (**9**) and (**10**), respectively.

The results are summarized in Table 1. Unfortunately, with aliphatic alkenes such as hex-1-ene and cyclohexene, we have not yet succeeded in isolating any dihydrofurans. However, by virtue of the high regio- and stereo-selectivities, mild reaction

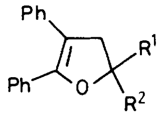
Table 1. The reaction of (**1**) with alkenes and SmI_2.[a]

Alkene	Product and isolated yield (%)
Styrene	(**2**) (66)
p-Methylstyrene	(**3**) (77)
1,1-Diphenylethylene	(**4**) (80)
α-Methylstyrene	(**5**) (30), (**6**) (40)
trans-β-Methylstyrene	(**7**) (17)
Indene	(**8**) (27)
Isoprene	(**9**) (76)
Penta-1,3-diene[b]	(**10**) (33)

[a] (**1**) (2 mmol), alkene (10 mmol), SmI_2 (4 mmol), THF–HMPA (10–1 ml): reflux, 2 h. [b] *cis–trans*-mixture.

PhCOCBr$_2$Ph

(**1**)

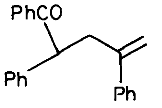


(**2**) R^1 = Ph, R^2 = H

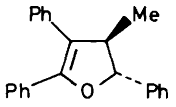
(**3**) R^1 = p-MeC_6H_4, R^2 = H

(**4**) R^1 = R^2 = Ph

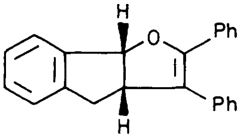
(**5**) R^1 = Ph, R^2 = Me



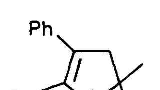
(**6**)



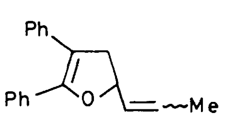
(**7**)



(**8**)



(**9**)



(**10**)

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† In a typical procedure, to the refluxing deep green solution of SmI_2 (0.5 M, 4 mmol) in THF–HMPA (7–1 ml), was added styrene (10 mmol) then a THF (3 ml) solution of (**1**) (2 mmol). The solution immediately turned reddish brown and was allowed to react at reflux for 2 h. The solution was then quenched by aqueous $Na_2S_2O_3$, and was then extracted with diethyl ether; the extract was dried over $MgSO_4$. Evaporation of the solvent left a yellow oil, which was subjected to preparative t.l.c. [elution with hexane–diethyl ether (10 : 1) (R_f 0.70)], to afford (**2**) (1.32 mmol, 66%).

‡ The *trans*-stereochemistry was assigned on the basis of comparison of the coupling constant of the benzylic proton in (**7**) (*J* 7.0 Hz) with *trans*- (*J* 7.0 Hz) or *cis*- (*J* 9.5 Hz) 3-methoxycarbonyl-5-(4′-methoxyphenyl)-2,4-dimethyl-4,5-dihydrofuran.[7]

§ δ_H (60 MHz) in (**8**); 3.0—3.4 (m, 2H, benzylic CH_2), 4.2—4.6 (m, 1H, allylic CH), 6.04 (d, 1H, *J* 8.0 Hz, *H*C–O–C), 7.0—7.5 (m, 14H). The coupling constant of this last proton on agrees well with the corresponding coupling constant in the structurally similar heterocycles *cis*-ethyl 3a,8b-dihydrofuro[3,2-*b*]benzofuran-2-carboxylate and the corresponding 2-methyl-3-carboxylate.[7,8]

conditions, simple procedure, and usually good yields, we believe that SmI_2 should be an effective reagent for dihydrofuran synthesis by the ketocarbene route.

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