Rh(II) Catalyzed Three-Component Reactions of Diazoacetates with Benzenemethanol and Indane-1, 2, 3-Triones

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Abstract: A facile synthesis of 2-substituted-2-hydroxyindane-1,3-diones is reported *via* the reaction of diazoacetates with benzenemethanol and indane-1,2,3-triones catalyzed by dirhodium acetate.

Keywords: Multi-component reaction, diazo compounds, carbenoids, oxonium ylide, dirhodium acetate, indane-1, 3-diones.

INTRODUCTION

It is well known that metal carbenoids react with heteroatoms to form onium ylides [1]. The chemistry of onium ylides is an area of continuing interest [2]. Phosphorus, sulfur, ammonium, carbonyl and oxonium vlides have been widely utilized in organic synthesis [3]. Previously, we reported novel three component reactions, in which, an alcoholic/ ammonium ylide in situ generated from a diazo compound and an alcohol/amine in the presence of rhodium acetate can be trapped by carbonyls [4], imines [4b, 5] and azodicarboxylates [6]. As for the alcoholic ylide trapping process, the reactions were successful when electron-deficient aldehydes and isatins were used due to a competing process from an intramolecular proton transfer of the alcoholic ylide leading to an O-H insertion side product [4]. To extend the scope of this method, we envision that indane-1, 2, 3-triones would serve as good trapping reagents for the reaction, because the strong electrophilicity of the 2carbonyl functionality of the 1, 2, 3-triones made them widely used in aldol type reactions [7]. Trapping of the alcoholic ylide with indane-1, 2, 3-triones would provide an easy entry to polyfunctional 2-hydroxyindane-1, 3-diones with a C-C and C-O bond formation in one step (Scheme 1).

molar ratio, and the results are summarized in Table 1. The best yield of 69% was obtained when 1.5 equivalent of both 1a and benzenemethanol (2) were used (Table 1, entry 3). However, significant amount of the O-H insertion side product 5 occurred due to large excess of both the diazo compound and the alcohol. In order to decrease the formation of 5, we reduced the amount of the diazo compound **1a** to a substrate ratio of 1a:2:3a = 1.1:1.5:1. The desired three-component product 4a was isolated with similar good yield (65%) and the O-H insertion side product 5 was suppressed to less than 10 % (Table 1, entry 6). The structure of product 4a was determined based on its spectroscopic and analytical data and confirmed by single crystal X-ray analysis. The X-ray structure confirmed that the nucleophilic attacking to the indane-1, 2, 3-trione specifically occurred at the 2-position (Fig. 1).

Having established the preferred reaction conditions, we applied the synthetic strategy to a variety of aryl diazoacetates and indane-1,

2, 3-triones (Table 2) [8]. Reactions of aryl diazoacetates bearing either an electron-donating group or an electron-withdrawing group on the aromatic ring at the *para*-position gave the products with similar yield (Table 2, entries 2, 3).



Scheme 1. The three-component reaction for 2-substituted-2-hydroxyindane-1, 3-diones formation.

RESULTS AND DISCUSSION

Methyl phenyldiazoacetate (1a) was used as a standard substrate to demonstrate the strategy. The reaction was first carried out in refluxing CH_2Cl_2 with different substrate

The aryl diazoacetates with the *ortho*-substituents gave lower yields than those with the *meta*- and *para*-substituents (Table **2**, entries 2-5). The low yield is probably due to steric effects of the *ortho*-substituents which slow down the desired nucleophilic addition process. Decreased yields were also obtained with the use of indane-1, 2, 3-triones bearing substituents on the *ortho*-position of the aromatic ring (Table **2**, entries 6-9).

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Table 1. Reaction of Methyl Phenyldiazoacetate with BnOH and Indane-1, 2, 3-Trione with Different Substrate Molar Ratio^a



Entry	1a : 2 : 3a	Yield of 4a (%) ^b
1	1:1:1	27
2	1.2:1.2:1	41
3	1.5:1.5:1	69
4	2:2:1	67
5	1.1:1.2:1	38
б	1.1:1.5:1	65
7	1.1:2:1	64

^aThe reaction of methyl phenyldiazoacetate with BnOH and indane-1,2,3-trone was carried out in refluxing CH₂Cl₂ for 1 h. ^bIsolated yield after column chromatography purification.



Fig. (1). Crystal structure of compound 4a.

We were gratified to find that the reaction gave 56% yield when EDA (ethyl diazoacetate) was used instead of aryl diazoacetates (Scheme 2). In contrast, in the reactions of ammonium or alcoholic ylide with aldehydes, much lower yields were obtained when EDA was employed [4a, 4c].

A reaction mechanism shown in Scheme 3 is similar to that we proposed previously [4d]. The reaction initially forms a free oxonium ylide 6 or a metal associated ylide 7 from aryldiazoacetate 1a and benzenemethanol catalyzed by $Rh_2(OAc)_4$. Nucleophilic addition of the ylide 5 or 6 to the indane-1, 2, 3-triones would produce intermediate adduct 8 or 9. Product 4a would be subsequently formed by a "delayed proton transfer" process.

In summary, we report here dirhodium acetate catalyzed three-component reactions of diazo compounds with benzenemethanol and indane-1, 2, 3-triones to give polyfunctional 2-hydroxyindane-1, 3-diones in a single step.

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Table 2. Reaction of Different Aryl Diazoacetates with BnOH and Substituted Indane-1, 2, 3-Triones^a



Entry	1	3	Product	Yield(%) ^b
1	1a, Ar=Ph	3a, R=H	4a	65
2	1b, Ar=p-MeOC ₆ H ₄	3 a	4b	54

Entry	1	3	Product	Yield(%) ^b
3	1c , Ar=p-BrC ₆ H ₄	3a	4c	53
4	1d , Ar=m-BrC ₆ H ₄	3a	4d	55
5	1e , Ar=o-ClC ₆ H ₄	3a	4e	26
6	1a	3b, R= F	4f	24
7	1 a	3c, R=Cl	4g	30
8	1 a	3d, R=Br	4h	29
9	1a	3e, R=Me	4 i	21

^aThe reaction was conducted in refluxing CH₂Cl₂ for 1h with substrate molar ratio of 1:2:3=1.1:1.5:1. ^bIsolated yield after column chromatography purification.



Scheme 2. The reaction of EDA with BnOH and indane-1, 2, 3-trione.



Scheme 3. The proposed mechanism for the three-component reaction.

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Typical Procedure of the Three-component Reaction

To a refluxing CH₂Cl₂ (20 mL) solution of Rh₂(OAc)₄ (2.4 mg, 1 mol%), BnOH (75 μ L, 0.75mmol) and indane-

1,2,3-trione (89.1 mg, 0.5 mmol) was added methyl phenyldiazoacetate **1a** (96.8 mg, 0.55 mmol) in 5 mL of CH_2Cl_2 over 1 h *via* a syringe pump. The reaction mixture was cooled to r.t., and the solvent was removed. The crude product was purified by flash chromatography on silica gel by using 10% EtOAc–light PE as eluents to give a white solid **4a** (135.4 mg, 0.33 mmol) with 65% yield. Analytical

data of **4a**: ¹H NMR (500 MHz, CDCl₃): $\delta = 8.00-7.75$ (m, 4 H), 7.50-7.00 (m, 8 H), 6.87-6.75 (m, 2 H), 4.82 (d, J = 12.2Hz, 1 H), 4.44 (d, J = 12.2 Hz, 1 H), 3.88 (s, 3 H); ¹³C NMR (125 MHz, CDCl₃): $\delta = 197.72$, 195.38, 170.67, 142.53, 141.91, 137.84, 135.80, 135.68, 131.17, 129.23, 128.49, 128.06, 128.04, 127.11, 126.10, 123.30, 123.21, 87.31, 80.13, 68.58, 52.91.

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