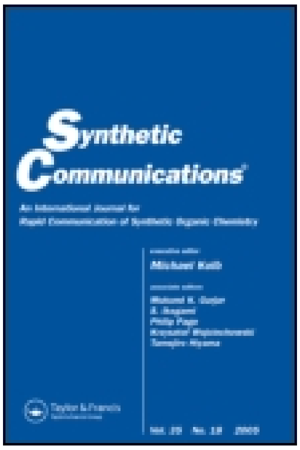

Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry
Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/lsyc20

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To cite this article: Renata de S. Rianelli , Maria Cecília B. V. de Souza & Vitor F. Ferreira (2004): Mild Diazo Transfer Reaction Catalyzed by Modified Clays, Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry, 34:5, 951-959

To link to this article: http://dx.doi.org/10.1081/SCC-120028368

SYNTHETIC COMMUNICATIONS®
Vol. 34, No. 5, pp. 951–959, 2004

Mild Diazo Transfer Reaction Catalyzed by Modified Clays

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ABSTRACT

A very mild method for the preparation of various 2-diazo-1,3-carbonyl compounds in the presence of environmentally attractive solid acids such as clays in a heterogeneous manner in moderate to good yield is reported.

Key Words: Diazo compounds; Heterogeneous catalysts; Clay catalyst; Smectite; Atapulgite; Vermiculite.

The chemistry of diazo compounds is an intensively developing area of organic chemistry, which includes diazo dicarbonyl compounds that are important intermediates and have been exploited in synthetic organic

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DOI: 10.1081/SCC-120028368 0039-7911 (Print); 1532-2432 (Online)

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chemistry for the synthesis of a variety of complex molecules.[1] Base-catalyzed transfer of the diazo moiety to a methylene group adjacent to one or more electron-withdrawing groups is a well established and powerful synthetic tool. The most known protocol involves the reaction of an alkyl or arylsulfonyl azide with the methylene group[2,3] usually named diazo transfer reaction (the reaction described here, a transfer of an intact diazo moiety to an anionic site, is labelled as diazo transfer reaction to distinguish it from diazotization, a process in which the N—N bond is created in the reaction[4]). Several diazo transfer reagents based on these sulfonyl azides have been used for preparing diazo compounds, (for the use of sulfonyl azides as diazo-transfer reagents, see Ref.[5]) but some of then are potentially hazardous due to their propensity for explosive decomposition under various reaction conditions (e.g. tosylazide). In addition, several author have found that formylation and benzoylation followed by diazo transfer are useful processes to diazo synthesis.[6,7]

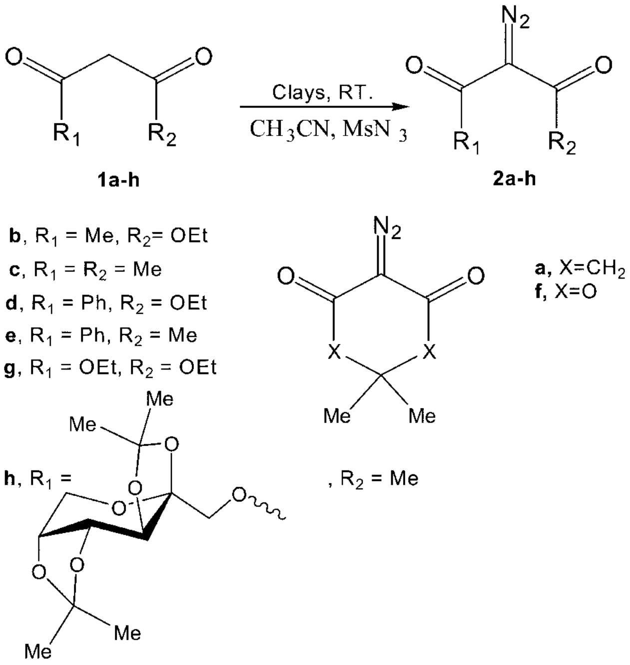
Base-catalyzed diazo transfer reactions are catalyzed mainly by alkyl amines, but other solid bases such KF-alumina have been reported.[8]

Due to environmental demands, there has been considerable interest in developing new catalysts for organic reactions based on inorganic solids, which can be recovered and reused again.

In this regard, layered clay catalysts have received increasing attention in many areas of organic chemistry, including organic synthesis,[9–12] mainly due to their chemo- and regio-selective properties, availability, low cost, mild reaction conditions, nonvolatility, noncorrosiveness, easy recovery, and reuse.[13] Indeed, we recently reported a mild and efficient transesterification process using three natural clays, which are very appropriate to be used in reactions involving carbohydrate derivatives without their degradation.[14]

Herein, we wish to report our studies on the reaction of 1,3-dicarbonyl compounds with mesyl azide to produce several 2-diazo-1,3-dicarbonyl compounds by using three natural clays previously treated with sodium hydroxide.[15] The advantage of mesyl azide is that it is easily separated from the desired product upon washing the organic phase with 10% aqueous NaOH solution. Several other variations conditions were examined with a view to simplifying product isolation. To the best of our knowledge, there is no report of diazo transfer reaction using clays as catalyst.

In the general reaction procedure an excess of clay (1.5 w/w) and mesyl azide with an excess of 1.5 mmol was used for the 1,3-dicarbonyl compounds (**1a–h**) in acetonitrile at room temperature (Sch. 1). The time of the reaction varied from 3–72 hr (see Table 1) depending on the 1,3-dicarbonyl compounds, but was less dependent of sulfonyl azide. The diazo compounds were purified by column chromatography and identified by spectroscopic methods. In some experiments the pure products (entries 8, 9, 10, 12, 13) were



Scheme 1.

obtained by simple remove the excess of the starting materials. This protocol worked well for each of the examples tried so far (Table 1).

We have found that the overall yield for diazo transfer reaction ranged from fair to good for all three clays with MsN_3 and TsN_3, but was a little better with smectite. A good yield for the diazo **2b** and **2c** was expected with smectite, since (a) **1b** and **1c** have a very acidic methylene group and, (b) smectite have high contents of Al_2O_3 (ca 20%), then more basic. However, the products were obtained in low yield (entry 7). We speculated that this low yield could be related with adsorption of the products on the surface of the clays. To overcome this problem the usual work up was changed to a filtration followed by several washing the clay with CH_2Cl_2. With this work up the products were obtained in higher yields (entries 8, 9, 10). Some degradations products of the carbohydrate moiety of **1h** were observed during the reactions with these clays. However, it was possible to isolate the desired diazo **2h** in moderate yield (entries 23–25).

The clays were obtained from Bravo farm,[16] Boa Vista district, Paraíba, Brazil. They were ground to 0.150 mm. Their specific surface areas were

Table 1. Compounds **1a–h** prepared by using modified clays.

Entry	β-Ketoesters	Clay[a]	Diazo	(%)	Time (h)
1	**1a**	Esmectite	**2a**	84[b] (85)[c] (86)[d]	3
2	**1a**	Atapulgite	**2a**	85[b] (88)[c] (79)[d]	3
3	**1a**	Vermiculite	**2a**	85[b] (90)[c] (88)[d]	3
4	**1b**	Esmectite	**2b**	82[b]	24
5	**1b**	Atapulgite	**2b**	77[b]	24
6	**1b**	Vermiculite	**2b**	82[b]	24
7	**1c**	Esmectite	**2c**	23[b]	48
8	**1c**	Esmectite	**2c**	95[b]	48
9	**1c**	Atapulgite	**2c**	96[b]	48
10	**1c**	Vermiculite	**2c**	95[b]	48
11	**1d**	Esmectite	**2d**	80[b]	48
12	**1d**	Atapulgite	**2d**	90[b]	48
13	**1d**	Vermiculite	**2d**	97[b]	48
14	**1e**	Esmectite	**2e**	79[b] (81)[d]	24
15	**1e**	Atapulgite	**2e**	87[b] (78)[d]	24
16	**1e**	Vermiculite	**2e**	86[b] (80)[d]	24
17	**1f**	Esmectite	**2f**	85[b] (80)[d]	48
18	**1f**	Atapulgite	**2f**	84[b] (81)[d]	48
19	**1f**	Vermiculite	**2f**	87[b] (85)[d]	48
20	**1g**	Esmectite	**2g**	55[b]	72
21	**1g**	Atapulgite	**2g**	60[b]	72
22	**1g**	Vermiculite	**2g**	62[b]	72
23	**1h**	Esmectite	**2h**	54[b]	48
24	**1h**	Atapulgite	**2h**	55[b]	48
25	**1h**	Vermiculite	**2h**	52[b]	48

[a] Clay treated with NaOH.
[b] Yield using MsN_3.
[c] Yield reusing the clay recovered.
[d] Yield using TsN_3.

measured by the BET-method[17] before pretreatment and activation: smectite 68.88 m^2/g, atapulgite 49.30 m^2/g, and vermiculite 119.67 m^2/g. Percent composition of clays were determined by x-ray powder diffraction.[14]

In summary, we have detailed a procedure that does allow the preparation of 2-diazo-1,3-dicarbonyl compounds using clay minerals as catalyst. The advantages of this clay-catalyzed procedure are many. First, the clay are natural materials commercially available in bulk. Second, it can be easily recovered and used again without losing its catalytic activity. Third, it provides the advantage of product isolation by filtration the catalyst. Finally, it is an environmentally safe alternative to existing bases.

EXPERIMENTAL

Melting points were observed on a Fischer Jones and are uncorrected. Analytical grade solvents were used. Methanol was distilled before being used. Column chromatography was performed on silica gel 60 (Merck 70–230 mesh). Infrared spectra were recorded on a Perkin-Elmer FT-IR Spectrum One spectrophotometer calibrated relative to the 1601.8 cm^{-1} absorbance of polystyrene. Ultraviolet (UV) spectra were obtained on Schimadizu spectrophotometer. Wavelengths and are in nm and ε in mol cm^{-1}. NMR spectra were recorded on a Varian Unity Plus VXR (300 MHz) equipment in $CDCl_3$ solutions and tetramethylsilane was used as the internal standard ($\delta = 0$ ppm).

The clays were prepared by a procedure described in the literature, which involves a reflux with NaOH for 8 h filtration and heating in a oven at 100°C for 2 hr.[15]

Typical Procedure

To a stirred solution of the 1,3-dicarbonyl compounds **1** and mesyl azide (1.5 mmol) in 5 mL of distilled acetonitrile was added the clay (1.5 w/w). The mixture was stirred for 3–72 hr (see Table) at room temperature, filtrated and diluted with CH_2Cl_2 (50 mL). The organic solution was washed with aqueous solution of NaOH (10% w/w), dried over anhydrous $MgSO_4$ and concentrated under reduced pressure producing the diazo compounds **2** described in Table 1.

2-Diazo-5,5-dimethyl-cyclohexane-1,3-dione (2a)

Obtained in 85% (546 mg) yield from 542 mg (4.17 mmol) of **1a** as a yellow solid. m.p. 108–109°C (lit.[5h] 107–109°C). IR (film) $\nu_{máx}$ (cm^{-1}): 1671 (C═O); 2146 and 2188 (N_2); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 1.13 (3H, s, CH_3), 2.45(2H, s, CH_2).

2-Diazo-3-oxobutyric Acid Ethyl Ester (2b)

Obtained in 80% (480 mg) yield from 500 mg (3.85 mmol) of **1b** as a yellow oil.[18] IR (film) $\nu_{máx}$ (cm^{-1}): 1660 and 1720 (C═O), 2139 (N_2); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 1.1 (3H, t, $J = 7.2$ and 14.4 Hz, CH_3), 4.31 (2H, q, $J = 7.2$ and 14.4 Hz, CH_2), 2.48 (3H, s, CH_3).

3-Diazo-2,4-pentadione (2c)

Obtained in 95% (598 mg) yield from 500 mg (5 mmol) of **1c** as a yellow liquid.[5h] IR (film) $\nu_{máx}$ (cm^{-1}): 1667 (C═O), 2127 (N_2); IV (film) $\nu_{máx}$ (cm^{-1}): 1660 and 1720 (C═O); 2139 (N_2); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 2.44 (3H, s, CH_3).

3-Phenyl-2-diazomalonic Acid Ethyl Ether (2d)

Obtained in 90% (490 mg) yield from 480 mg (2.5 mmol) of **1d** as a liquid.[5h] IR (film) $\nu_{máx}$ (cm^{-1}) 1629 and 1725 (C═O), 2142 (N_2); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 1.26 (3H, t, $J = 7.2$ and 14.4 Hz, CH_3), 4.26 (2H, q, $J = 7.2$ and 14.4 Hz, CH_2), 7.40–7.64 (5H, m).

2-Diazo-1-phenyl-butane-1,3-dione (2e)

Obtained in 86% (485 mg) yield from 486 mg (3 mmol) of **1e** as a solid. m.p. 60–62°C (lit.[5i] 60–61°C). IR (film) $\nu_{máx}$ (cm^{-1}) 1653 and 1623 (C═O), 2115 (N_2); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 2.58 (3H, s, CH_3), 7.47–7.67 (5H, m).

2,2-Dimethyl-4,6-diketo-5-diazo-1,3-dioxane (2f)

Obtained in 85% (433 mg) yield from 432 mg (3 mmol) of **1f**. m.p. 94–96°C (lit. 94–95°C[19]); IR (film) $\nu_{máx}$ (cm^{-1}) 1724 (C═O), 2183 (N_2); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 1.73 (3H, s, CH_3).

2-Diazomalonic Acid Diethyl Ether (2g)

Obtained in 60% (335 mg) yield from **1g** (480 mg, 3 mmol) as an oil.[5i,8] IR (film) $\nu_{máx}$ (cm^{-1}): 1735 (C═O), 2138 (N_2); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 1.29 (3H, t, $J = 7.5$ and 14.4 Hz, CH_3), 4.21 (2H, q, $J = 6.9$ and 14.4 Hz, CH_2).

2-Diazo-3-oxo-butyric Acid 1,2 : 3,4-Di-*O*-isopropylidene-D-fructopyranosyl Ester (2h)

Obtained in 55% (296 mg) yield from **1h** (500 mg, 1.45 mmol) as an light yellow oil. IV (film) $v_{\text{máx}}$ (cm^{-1}): 1722 and 1661 (C═O), 2141 (N_2); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 1.35 (6H, s, CH_3), 1.48 (3H, s, CH_3), 1.55 (3H, s, CH_3), 2.51 (3H, s, CH_3), 4.78 (1H, d, $J = 12.9$ Hz, CH_3); 3.92 (1H, dd, $J = 12.9$; 1.5 Hz, CH_3), 4.27 (1H, dd, $J = 1.5$ and 7.5 Hz, H-5), 4.62 (1H, dd, $J = 2.7$ and 8.1 Hz, H-4), 4.30 (1H, d, $J = 2.7$ Hz, H-3), 4.2 (2H, d, $J = 11.7$ Hz, H-1).

ACKNOWLEDGMENTS

Fellowships granted to RSR by CAPES and M.C.B.V.S. and V.F.F. by CNPq (Brazil) are gratefully acknowledged. This work was partially supported by CNPq (National Council of Research of Brazil) and FAPERJ.

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Received in the USA October 4, 2003

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