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# One-Pot Protocol for Synthesis of α-Organosulfonyloxy Ketones from Secondary Alcohols Using Hypervalent Iodine(V)–Mediated Oxidations

**Swapnil S. Deshmukh, Sameerana N. Huddar, and Krishnacharya G. Akamanchi**
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**Abstract:** α-Tosyloxy ketones and α-mesyloxy ketones were directly prepared from alcohols in one pot by treatment with hypervalent iodine(V) reagents in combination with p-toluenesulfonic acid and methanesulfonic acid, respectively, in moderate to good yields. Reactions were also feasible under solvent-free conditions.

**Keywords:** Alcohols, Dess–Martin periodinane, hypervalent iodine(V) reagents, organosulfonic acids, α-organosulfonyloxy ketones, solvent-free reaction condition

The α-organosulfonyloxy ketones are useful intermediates in the synthesis of a variety of biologically important heterocyclic ring systems such as thiazoles, imidazoles, oxazoles, pyrazines, pyrazoles, lactones, benzofurans, benzopyrazines, benzooxazines, benzothiazines, imidazo[2,1-*b*] thiazoles, and thiazolo[3,2-*a*] benzimidazoles.[1–3] α-Organosulfonyloxy ketones are also useful intermediates for α-azidation of ketones.[3d]

Hypervalent iodine reagents are extensively used in organic synthesis because these reagents are mild, nonmetallic, and highly selective oxidants. Development of new methodologies using these reagents is of current

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interest.[4] Our group has recently reported hypervalent iodine(V) reagents for α-tosyloxylation of carbonyl compounds, including ketones.[5]

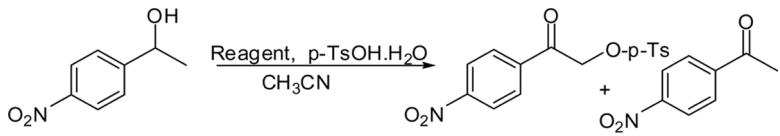
In continuation of our efforts to develop of useful synthetic methodologies of hypervalent iodine(V) reagents, especially *o*-iodoxybenzoic acid (IBX), Dess–Martin periodinane (DMP), and $HIO_3$, we report here a one-pot synthesis of α-organosulfonyloxy ketones starting from alcohols using DMP in combination with organosulfonic acids. One-pot transformations offer a number of advantages, such as the time–cost benefits gained by avoiding isolation, handling, and chromatography of intermediates, as well as fewer workup steps.

Oxidation of alcohols to ketones is a fundamental organic transformation for which a number of reagents and reagent systems are available,[6] whereas only a few methods are available for direct α-organosulfonyloxylation of ketones.[7] Combining these two steps in a one-pot synthesis has great practical advantages, and we report one such development using hypervalent iodine(V) reagents.

Some hypervalent iodine(III) reagents are known to promote direct conversion of alcohols to α-tosyloxy ketones. Among them are poly (4-hydroxytosyloxyiodo)styrenes,[8a] iodosylbenzene, 4-methyl-1-idosylbenzene, 3-(trifluromethyl)-1-idosylbenzene, (diacetoxyiodo)benzene, 4-methyl-1-(diacetoxyiodo)benzene, and 3-(trifluromethyl)-1-iodosylbenzene in combination with p-toluenesulfonic acid monohydrate.[8b]

For developing the protocol, 1-(4-nitrophenyl)ethanol (**1a**) was chosen as a model substrate, and studies were carried out using 3 equiv

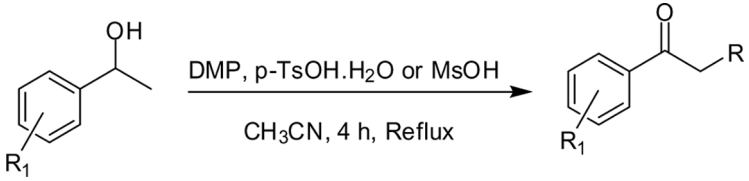
**Table 1.** α-Tosyloxylation using hypervalent iodine(V) reagents[a]

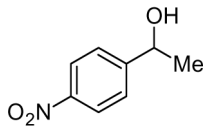
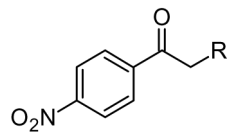
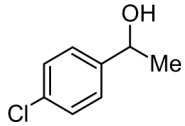
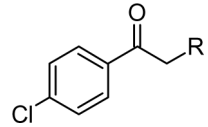
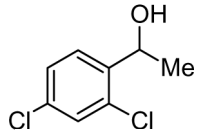
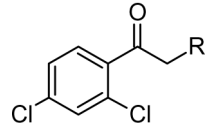
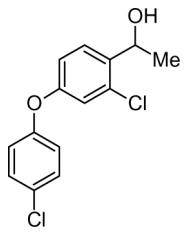
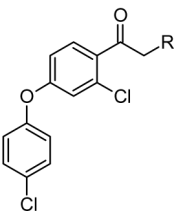
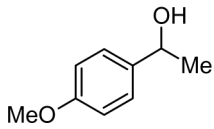
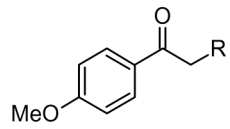



| Entry | Reagent | Conditions | Yield (%)[b] | |
|---|---|---|---|---|
| | | | **1b** | **1c** |
| 1 | DMP | rt, 12 h | Nil | 45 |
| 2 | DMP | Reflux, 4 h | 92 | Nil |
| 3 | IBX | Reflux, 4.5 h | 75 | 10 |
| 4 | $HIO_3$ | Reflux, 12 h | 25 | 35 |

[a]Reactions were carried on a 5-mmol scale and with 3 equiv of reagents.
[b]Isolated yields using column chromatography.

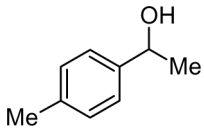
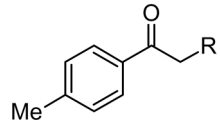
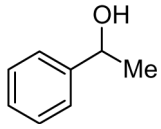
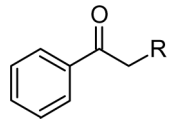
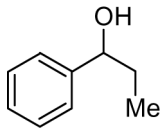
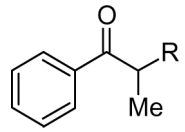
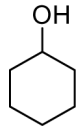
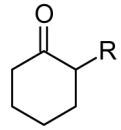
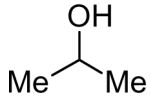
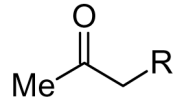
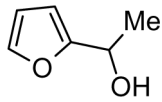
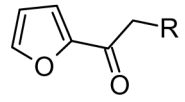
**Table 2.** DMP-mediated direct conversion of secondary alcohols to α-organosulfonyloxy ketones[a]




| Entry | Substrate | Product | Yield (%)[b,c] R=O-p-Ts | Yield (%)[b,c] R=OMs |
|---|---|---|---|---|
| 1 |  |  | 92 | 88 |
| 2 |  |  | 82 | 80 |
| 3 |  |  | 80 | 77 |
| 4 |  |  | 73 | 71 |
| 5 |  |  | 76 | 73 |

(*Continued*)

**Table 2.** Continued

| Entry | Substrate | Product | Yield (%)[b,c] R=O-p-Ts | Yield (%)[b,c] R=OMs |
|---|---|---|---|---|
| 6 |  |  | 77 | 74 |
| 7 |  |  | 89 | 86 |
| 8 |  |  | 75 | 72 |
| 9 |  |  | 68 | 64 |
| 10 |  |  | 82 | 77 |
| 11 |  |  | 81 | 71 |

[a]Reactions were carried out on a 5-mmol scale in $CH_3CN$ at reflux temperature with DMP (3 equiv) and organosulfonic acid (3 equiv).

[b]Products were characterized by $^1H$ NMR, IR, and physical constants.

[c]Isolated yields were determined using column chromatography.

of DMP and 3 equiv of p-toluenesulfonic acid monohydrate in acetonitrile. When the reaction was carried out at room temperature for 12 h, only 1-(4-nitrophenyl)ethanone (**1c**) was obtained (Table 1, entry 1). However, when the reaction was conducted at reflux temperature, it proceeded smoothly, and 2-(4-nitrophenyl)-2-oxo-ethyl-4-methanebenzene sulfonate (**1b**) was obtained in 92% yield in 4 h (Table 1, entry 2). Other hypervalent iodine(V) reagents such as IBX and $HIO_3$ were also found to

be viable, and α-sulfonyloxylated compound (**1b**) was obtained in 75% and 25% yields respectively with isolation of intermediate ketone in the range of 10–35% yield (Table 1, entries 3 and 4).

For establishing general utility of this protocol, DMP was chosen as oxidant, and the results are shown in Table 2.

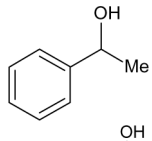
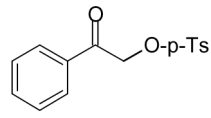
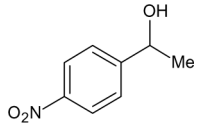
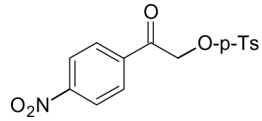
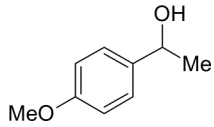
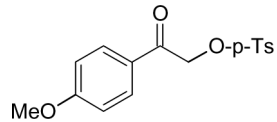
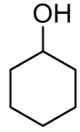
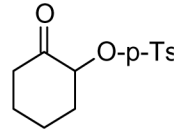
As illustrated in Table 2, the reactivity profile of the substituted alcohols was remarkable. The reaction was also facile with cyclohexanol, isopropanol, and heterocyclic alcohol such as 1-(furan-2-yl)ethanol, and in all cases corresponding α-organosulfonyloxy ketones were obtained in moderate to good yields (Table 2, entries 9–11).

As solvent-free reactions are of current interest,[9] the reaction was also carried out under solvent-free conditions, and results are summarized in Table 3. The reaction is viable; however, yields were found to be comparatively less.

In conclusion, a one-pot protocol has been developed for synthesis of α-organosulfonyloxy ketones starting from corresponding alcohols using hypervalent iodine(V) reagents, especially DMP, in combination with organosulfonic acids. The reaction is also viable under solvent-free conditions.



**Table 3.** DMP-mediated solvent-free α-organosulfonyloxylation[a]

| Entry | Substrate | Product | Yield[b] (%) |
|---|---|---|---|
| 1 |  |  | 65 |
| 2 |  |  | 59 |
| 3 |  |  | 51 |
| 4 |  |  | 38 |

[a]Reactions were carried out under solvent-free conditions on a 5-mmol scale with DMP (3 equiv) and organosulfonic acid (3 equiv) at rt.

[b]Corresponding ketones were recovered in the range of 20–40%.

## α-ORGANOSULFONYLOXYLATION: GENERAL PROCEDURE

Alcohol (5 mmol) was added in one portion to a stirred suspension of Dess–Martin periodinane (15 mmol) and organosulfonic acid (15 mmol) in $CH_3CN$ (20 mL), and the reaction mixture was refluxed for 4 h. Solvent was removed under reduced pressure, and the residue obtained was diluted by adding $CHCl_3$ (60 mL) and washed with saturated solution of $NaHCO_3$ ($2 \times 35$ mL) and brine (60 mL). The organic layer was dried over anhydrous $Na_2SO_4$ and concentrated under reduced pressure to give crude α-organosulfonyloxylated product. Pure product was obtained after column chromatography ($SiO_2$, mesh size 60–120, eluent, ethyl acetate–hexane, 15:85).

## SOLVENT-FREE α-ORGANOSULFONYLOXYLATION: GENERAL PROCEDURE

DMP (15 mmol) and p-toluenesulfonic acid monohydrate (15 mmol) were gently ground for 15 min using pestle and mortar. The resulting reaction mixture was washed with diethyl ether and dried under a strong vacuum to afford solid reagent, which was slowly added in portions to alcohol (5 mmol). An exotherm was observed. Stirring continued for 30 min, and $CHCl_3$ (30 mL) was added. The slurry was filtered, and the filtrate was washed with a saturated solution of $NaHCO_3$ ($2 \times 35$ mL) and brine (60 mL). The organic layer was dried over anhydrous $Na_2SO_4$ and concentrated under reduced pressure to give crude α-organosulfonyloxylated product. Pure product was obtained after column chromatography ($SiO_2$, mesh size 60–120, eluent, ethyl acetate–hexane, 15:85).

## SPECTRAL DATA FOR SELECTED α-ORGANOSULFONYLOXY KETONES FROM TABLE 2

### 2-(4-Nitrophenyl)-2-oxo-ethyl-4-methanebenzene-sulfonate (Entry 1)

Solid. Mp 130°C (lit.[8b] 130–131°C). IR (KBr): $\nu_{max} = 1180$, 1340, 1710 $cm^{-1}$. $^1H$ NMR (400 MHz, $CDCl_3$): δ 2.47 (s, 3 H), 5.25 (s, 2 H), 7.37 (d, $J = 8.3$ Hz, 2 H), 7.83 (d, $J = 8.3$ Hz, 2 H), 8.03 (d, $J = 8.9$ Hz, 2 H), 8.32 (d, $J = 8.9$ Hz, 2 H) ppm.

**2-(4-Chlorophenyl)-2-oxo-ethyl-4-methanebenzene-sulfonate (Entry 2)**

Solid. Mp 123°C (lit.[7a] 125°C). IR (KBr): $\nu_{max} = 1190, 1360, 1700\,cm^{-1}$. $^1H$ NMR (400 MHz, $CDCl_3$): δ 2.46 (s, 3 H), 5.21 (s, 2H), 7.35 (d, $J = 8.4$ Hz, 2 H), 7.45 (d, $J = 8.6$ Hz, 2 H), 7.80 (d, $J = 8.6$ Hz, 2 H), 7.84 (d, $J = 8.4$ Hz, 2 H) ppm.

**2-(2,4-Dichlorophenyl)-2-oxo-ethyl-methanesulfonate (Entry 3)**

Solid. Mp 87°C (lit.[5] 87°C). IR (KBr): $\nu_{max} = 1710\,cm^{-1}$. $^1H$ NMR (60 MHz,$CDCl_3$): δ 3.24 (s, 3H), 5.44 (s, 2H), 7.22–7.83 (m, 3H) ppm.

**2-[2-Chloro-4(4-chlorophenoxy)phenyl]-2-oxo-ethyl-methanesulfonate (Entry 4)**

White solid. Mp 118°C (lit.[5] 118–119°C). IR (KBr): $\nu_{max} = 1715\,cm^{-1}$. $^1H$ NMR (60 MHz, $CDCl_3$): δ 3.20 (s, 3H), 5.44 (s, 2H), 7.20–7.89 (m, 7H) ppm.

**2-(4-Methoxyphenyl)-2-oxo-ethyl-methanesulfonate (Entry 5)**

Solid. Mp 98 °C (lit.[5] 98°C). IR (KBr): $\nu_{max} = 1710\,cm^{-1}$. $^1H$ NMR (60 MHz, $CDCl_3$): δ 3.22 (s, 3H), 3.88 (s, 3H), 5.44 (s, 2H), 7.28 (d, $J = 7.8$ Hz, 2H), 7.74 (d, $J = 7.8$ Hz, 2H) ppm.

**2-Oxo-2-*p*-tolylethyl-methanesulfonate (Entry 6)[5]**

IR (KBr): $\nu_{max} = 1710\,cm^{-1}$. $^1H$ NMR (60 MHz, $CDCl_3$): δ 2.44 (s, 3H), 3.28 (s, 3H), 5.48 (s, 2H), 7.28 (d, $J = 8.33$ Hz, 2H), 7.77 (d, $J = 8.33$ Hz, 2H) ppm.

**2-Oxo-2-phenylethyl-methanesulfonate (Entry 7)**

Solid. Mp 76–77°C (lit.[3a] 76–78°C). IR (KBr): $\nu_{max} = 1725\,cm^{-1}$. $^1H$ NMR (60 MHz, $CDCl_3$): δ 3.20 (s, 3H), 5.43 (s, 2H), 7.12–8.12 (m, 5H) ppm.

**1-Oxo-1-phenylpropan-2-yl-4-methanebenzene-sulfonate (Entry 8)**

Solid. Mp 68°C (lit.[7a] 68–69°C). IR (KBr): $\nu_{max} = 1170, 1370, 1700\,cm^{-1}$. $^1H$ NMR (400 MHz, $CDCl_3$): δ 1.60 (d, $J = 7.0$ Hz, 3H), 2.41 (s, 3H), 5.79 (q, $J = 7.0$ Hz, 1H), 7.29 (d, $J = 8.1$ Hz, 2H), 7.46 (t, $J = 7.2$ Hz, 2H), 7.60 (t, $J = 7.2$ Hz, 1H), 7.75 (d, $J = 7.2$ Hz, 2H), 7.88 (d, $J = 8.1$ Hz, 2H) ppm.

**2-Oxo-cyclohexyl-4-methylbenzenesulfonate (Entry 9)**

Solid. Mp 76°C (lit.[8a] 74–76°C) IR (KBr): $\nu_{max} = 1744\,cm^{-1}$. $^1H$ NMR (60 MHz, $CDCl_3$): δ 1.30–2.70 (m, 11H), 4.82 (s, 1H), 7.10 (d, 2H), 8.02 (d, 2H) ppm.

**2-Oxo-propyl-methanesulfonate (Entry 10)**

Oil.[3a] IR (neat): $\nu_{max} = 1738, 1367, 1187\,cm^{-1}$. $^1H$ NMR (60 MHz, $CDCl_3$): δ 2.20 (s, 3H), 3.16 (s, 3H), 4.37 (s, 2H) ppm.

**2-(Furan-2-yl)-2-oxo-ethyl-4-methanebenzenesulfonate (Entry 11)**

Solid. Mp 65°C (lit.[8a] 65–67°C). IR (KBr): $\nu_{max} = 1670\,cm^{-1}$. $^1H$ NMR (60 MHz, $CDCl_3$): δ 3.27 (s, 3H), 5.53 (s, 2H), 7.28–8.05 (m, 7H) ppm.

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## REFERENCES

1. (a) Tuncay, A.; Dustman, J. A.; Fisher, G.; Tuncay, C. I. Ultrasound-promoted hypervalent iodine reactions: (α-Tosyloxylation of ketones with [hydroxy (tosyloxy)iodo]benzene. *Tetrahedron Lett.* **1992**, *33*, 7647; (b) Moriarty, R. M.; Vaid, B. K.; Duncan, M. P.; Levy, S. G.; Prakash, O.; Goyal, S. A one-pot

synthesis of 2-amino- and 2-(arylamino)-substituted thiazoles and selenazoles using [hydroxy(tosyloxy)iodo]benzene, carbonyl compounds, and thioureas or selenoureas: A modification of the Hantzsch synthesis. *Synthesis* **1992**, 845; (c) Prakash, O.; Goyal, S. A new synthesis of 2-aroylcoumaran-3-ones by hypervalent iodine oxidation of 2-acetyl-phenyl benzoates using [hydroxy-(tosyloxy)iodo]benzene. *Synthesis* **1992**, 629.

2. (a) Prakash, O.; Saini, N.; Sharma, P. K. Hypervalent iodine reagents in the synthesis of heterocyclic compounds. *Synlett* **1994**, 221; (b) Varma, R. S.; Kumar, D.; Liesen, P. J. Solid state synthesis of 2-aroylbenzo[*b*]furans, 1,3-thiazoles, and 3-aryl-5,6-dihydroimidazo[2,1-*b*][1,3]thiazoles from α-tosyloxyketones using microwave irradiation. *J. Chem. Soc., Perkin Trans. 1* **1998**, 4093; (c) Koser, G. F. Oxysulfonylation of carbonyl compounds at the α-carbon. *Aldrichim. Acta* **2001**, *34*, 89; (d) Nicolaou, K. C.; Mantagnon, T.; Ulven, T.; Baran, P. S.; Zhong, Y. L.; Sarabia, F. Novel chemistry of α-tosyloxy ketones: Applications to the solution- and solid-phase synthesis of privileged heterocycle and enediyne libraries. *J. Am. Chem. Soc.* **2002**, *124*, 5718.
3. (a) Lodaya, J. S.; Koser, G. F. Direct α-mesyloxylation of ketones and β-dicarbonyl compounds with [hydroxy(mesyloxy)iodo]benzene. *J. Org. Chem.* **1988**, *53*, 210; (b) Prakash, O.; Pannu, K.; Prakash, R.; Batra, A. [Hydroxy(tosyloxy)iodo]benzene-mediated α-azidation of ketones. *Molecules* **2006**, *11*, 523; (c) Prakash, O.; Rani, N.; Goyal, S. Hypervalent iodine in the synthesis of bridgehead heterocycles: Novel and facile syntheses of 3-substituted-5,6-dihydroimidazo[2,1-*b*]thiazoles and 3-phenylthiazolo[3,2-*a*]benzimidazole from acetophenones using [hydroxy(tosyloxy)iodo]benzene. *J. Chem. Soc., Perkin Trans. 1* **1992**, 707.
4. (a) Ladziata, U.; Zhadankin, V. V. Hypervalent iodine oxidation of 1-phenyl-3-arylpyrazole-4-carboxaldehyde oximes: A facile and efficient synthesis of new 3,4-bis(1-phenyl-3-arylpyrazolyl)-1,2,5-oxadiazole-*N*-oxides. *Arkivoc* **2006**, *9*, 26; (b) Zhadankin, V. V.; Stang, P. Recent developments in the chemistry of polyvalent iodine compounds. *Chem. Rev.* **2002**, *102*, 2523; (c) Zhadankin, V. V. Benziodoxole-based hypervalent iodine reagents in organic synthesis. *Curr. Org. Synth.* **2005**, *2*, 221; (c) Fontaine, P.; Chiaroni, A.; Masson, G.; Zhu, J. One-pot three-component synthesis of α-iminonitriles by IBX/TBAB-mediated oxidative Strecker reaction. *Org. Lett.* **2008**, *10*, 1509.
5. Mahajan, U. S.; Akamanchi, K. G. A new application of hypervalent iodine ($\lambda^5$) reagents with organosulfonic acids for direct α-organosulfonyloxylation carbonyl compounds. *Synlett* **2008**, 987.
6. Trost, B. M. *Comprehensive Organic Chemistry*; I. Fleming (Ed.); Pergamon: Oxford, 1971; vol. 7, p. 251; (b) Larock, R. C. *Comprehensive Organic Transformation*; Wiley-VCH: New York, 1999**, p. 1234.**
7. (a) Khanna, M. S.; Garg, C. P.; Kapoor, R. P. α-Tosyloxylation of enolizable ketones using thallium(III) p-tolylsulphonate (TTS). *Tetrahedron Lett.* **1992**, *33*, 1495; (b) Oliver, R. S. J.; Killeen, N. M.; Knowles, D. A.; Yau, S. C.; Bagley, M. C.; Tomkinson, Nicholas, C. O. Direct α-oxytosylation of

carbonyl compounds: One-pot synthesis of heterocycles. *Org. Lett.* **2007**, *9*, 4009; (c) Creary, X.; Rollin, A. J. Reaction of α-keto triflates with sodium methoxide. *J. Org. Chem.* **1977**, *42*, 4226; (d) Charrlon, J. L.; Lai, H. K.; Lypka, G. N. Photoreactions of α-sulfonyloxyketones. *Can. J. Chem.* **1980**, *58*, 458.

8. (a) Nabana, T.; Togo, H. Reactivities of novel [hydroxy(tosyloxy)iodo]arenes and [hydroxy(phosphoryloxy)iodo]arenes for α-tosyloxylation and α-phosphoryloxylation of ketones. *J. Org. Chem.* **2002**, *67*, 4362; (b) Makoto, U.; Takahiro, N.; Togo, H. Novel oxidative α-tosyloxylation of alcohols with iodosylbenzene and *p*-toluenesulfonic acid and its synthetic use for direct preparation of heteroaromatics. *J. Org. Chem.* **2003**, *68*, 6424; (c) Lodaya, J. S.; Koser, G. F. Direct α-mesyloxylation of ketones and β-dicarbonyl compounds with [hydroxy(mesyloxy)iodo]benzene. *J. Org. Chem.* **1988**, *53*, 210.
9. (a) Yusubov, M. S.; Wirth, T. Solvent-free reactions with hypervalent iodine reagents. *Org. Lett.* **2005**, *7*, 519; (b) Toda, F.; Tanaka, K.; Sekikawa, A. Host–guest complex formation by a solid–solid reaction. *J. Chem. Soc., Chem. Commun.* **1987**, 279.