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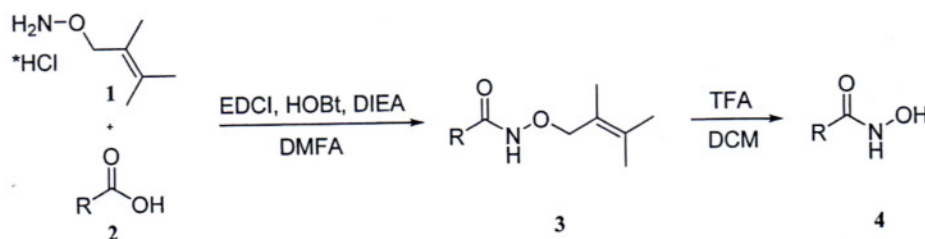


## METHYLPRENYL GROUP AS A NOVEL ACID-LABILE *O*-PROTECTING GROUP FOR HYDROXAMIC ACIDS

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Common methods for installation of hydroxamic acid functionality involve condensing of carboxylic acids with *O*-protected hydroxylamine followed by deprotection. Currently used protecting groups (such as THP, Bn, DMB, *t*Bu, Tr, TBDPS) are often unsuitable due to chemoselectivity problems and by-product formation in deprotection step.<sup>1</sup> Herein we present methylprenyl (2,3-dimethylbut-2-enyl) group as a novel *O*-protecting group for structurally different hydroxamic acids. *O*-Protected hydroxylamine **1** was synthesized and coupled with a range of carboxylic acids **2** to give *O*-methylprenyl protected hydroxamic acids **3**.



Stability of methylprenyl group in compound **3a** (R = 2-methylbenzyl) was examined under various reaction conditions typically used for deprotection. It was found that *O*-methylprenyl group in **3** is cleanly cleaved by TFA in DCM affording hydroxamic acids **4** in good to excellent yields (1. Scheme).

1.(a) Patel, D.V.; Young, M.G.; Robinson, S.P. et al. *J. Med. Chem.* **1996**, *29*, 4197; (b) Lienard, B.M.R.; Horsfall, L.E.; Galleni, M. et al. *Bioorg. Med. Chem. Lett.* **2007**, *17*, 964; (c) Ruda, G.F.; Wong, P.E.; Alibu, V.P. et al. *J. Med. Chem.* **2010**, *50*, 5752; (d) Wagner, S., Breyholz H.-J., Law M.P. et al. *J. Med. Chem.* **2007**, *50*, 5752; (e) Tommasi, R.A., Weiler S., McQuir L.W. et al; *Bioorg. Med. Chem. Lett.*, **2011**, *21*, 6440; (f) Oyere, A.K.; Chen, P.C.; Guerrant, W. et al. *J. Med. Chem.* **2009**, *52*, 456.