Syntheses of β-hydroxy-α-amino esters and non-proteinogenic α-amino acids from Morita-Baylis-Hillman adducts.

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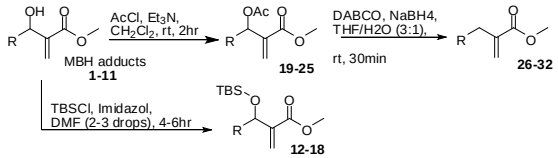
INTRODUCTION

β-hydroxy-*α*-amino esters are found in various bioactive natural.[1] On the other hand non proteinogenic amino acids play a vital role in the syntheses of various bioactive compounds and drugs. For example "DOPA" is employed against Parkinson's disease.[2] Thus, both of their biological and synthetic role make them attractive for synthetic and medicinal community. Thus the goal of our work is a diastereoselective syntheses of the *β*-hydroxy-*α*-amino esters, non-proteinogenic amino acids including racemic "DOPA" from MBH adducts.

RESULTS AND DISCUSSION

Our work begins with preparation of MBH adducts **1-11**.[3] Then the adducts **1-7,** were silylated to give products **12-18** and the adducts **3, 4, 6 and 8-11** were acetylated[2] to give products **19-25**. The later (**19-25**) were deacetylated to provide metacrylate derivatives **26-32** (Table 1).

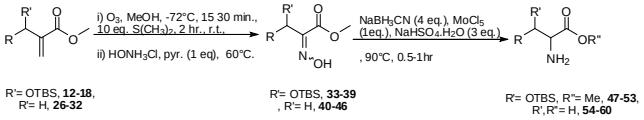
Table 1. Syntheses of silylated and deacetylated adducts.



MBH Adduct	Silylated MBH, %	MBH Adduct	Acet. MBH, %	Prod. %
1, 6-Br-Piperonyl	**12**, 92	**3,** 4-^{t}Bu-Ph	**19**, 81	**26**, 94
2, 4-OMe-Ph	**13**, 91	**6,** 3-Cl-Ph	**20**, 92	**27**, 95
3, 4-^{t}Bu- Ph	**14**, 90	**8,** 4-Cl-Ph	**21**,75	**28**, 93
4, Ph	**15**, 93	**9,** 4-Br-Ph	**22**, 87	**29**, 94
5, Ethyl	**16**, 85	**10,** 3,4,5-OMe-Ph	**23**, 71	**30**, 90
6, 3-Cl-Ph	**17**, 94	**4,** Ph	**24**, 70	**31**, 93
7, 4-NO_2-Ph	**18**, 95	**11,**Piperonyl	**25**, 75	**32**,89

Subsequently, Ozonolysis[3] and Oximation[4] of compound **12-18** and **26-32** gave oximes **33-39** and **40-46**, respectively. These oximes were reduced[5] to provide β-hydroxy-amino-esters **47-53** in high diastereoselectivity (*anti*:*syn* >95:5) and aminoesters **54-60,** respectively (Table 2).

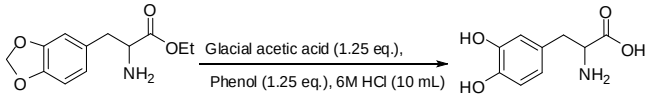
Table. 2. Preparation of oximes, amino esters and amino acids.



Cpds	Oxime, %	Amino* ester,%	Cpds	Oxime ,%	Amino acid,%
12	**33**, 92	**47,** 88	**26**	**40**, 94	**54**, 64
13	**34**, 91	**48,** 95	**27**	**41**, 95	**55**, 65
14	**35**, 90	**49,** 93	**28**	**42**, 91	**56**, 61
15	**36**, 93	**50,** 93	**29**	**43**, 90	**57**, 63
16	**37**, 85	**51,** 91	**30**	**44**, 94	**58**, 64
17	**38**, 94	**52,** 96	**31**	**45**, 92	**59**, 59
18	**39**, 95	**53,** 80	**32**	**46**, 88	**60**, 52

*The diastereoselectivity was determined by analysis of H^1 NMR of the crude reaction mixture

The above methodology allowed us to develop an efficient preparation of the DOPA (scheme 1).



60

DOPA, **61**, yield (63%)

Scheme 1. Preparation of DOPA **61**

CONCLUSION

We prepared *anti*-β-hydroxy-α-aminoesters **47-53**, amino acids **54-60** and DOPA **61 using a new apparoach**.

ACKNOWLEDGEMENTS

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