

SYNLETT Spotlight 421

This feature focuses on a reagent chosen by a postgraduate, highlighting the uses and preparation of the reagent in current research

Ethyl 2-Diazoacetoacetate

Compiled by Flaviana Rodrigues Fintelman Dias

Flaviana Rodrigues Fintelman Dias was born in Muriaé, Brazil in 1985. She received her pharmacy degree from Universidade Federal Fluminense (UFF), Niterói, Brazil in 2010. She is currently in the final stages of her M.Sc. studies under the supervision of the Professors Anna Claudia Cunha and Vitor Francisco Ferreira in organic chemistry at Universidade Federal Fluminense. Her research interests are focused on the design and synthesis of new bioactive compounds, such as quinone and 1,2,3-triazole derivatives. By using ethyl 2-diazoacetoacetate and *para*-substituted aromatic hydrazine hydrochlorides several 1,2,3-triazoles have been prepared.

Instituto de Química, Universidade Federal Fluminense, UFF, CEP 24020-141 Niterói, Rio de Janeiro, Brazil
E-mail: flaviana15@yahoo.com.br



Introduction

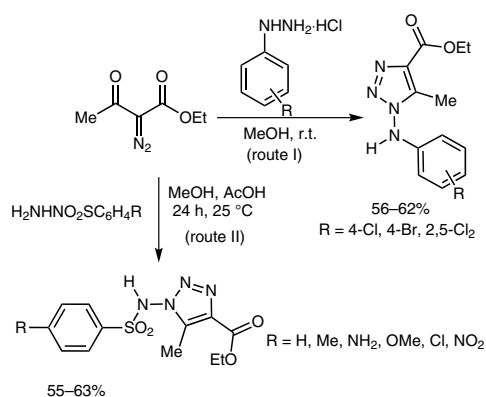
α -Diazoacetyl compounds have attracted great attention because of their versatile, synthetically useful transformations.¹ Their most important reactions are those that involve loss of molecular nitrogen induced by thermolytic, catalytic, and photolytic conditions.^{1,2}

Conventional synthetic methods for diazo carbonyl compounds include diazotization of amines, dehydrogenation of hydrazones and diazo transfer reactions.³ The diazo

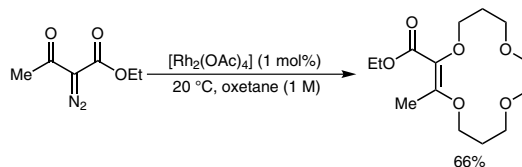
transfer donor is invariably a sulfonyl azide such as tosyl azide, *p*-carboxylbenzenesulfonyl azide, *p*-dodecylbenzenesulfonyl azide and methanesulfonyl azide. This Spotlight focusses on ethyl diazoacetoacetate, a yellow oil (1.131 g/mL at 25 °C).³ The general method for the construction of this reagent involves diazo-transfer reaction to the α -methylene position of ethyl acetoacetate in the presence of a base such as Et₃N.⁴

Abstracts

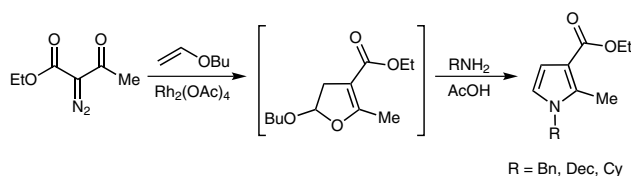
(A) Cunha and co-workers^{5,6} showed that ethyl 2-diazoacetoacetate undergoes reaction with different phenylhydrazine hydrochlorides (route I) or arylsulfonylhydrazides (route II) to yield the corresponding 1,2,3-triazole derivatives in good yield. The intramolecular 1,5-electrocyclization of β -substituted- α -diazoacetyl compounds represents an efficient and flexible method for preparing various substituted 1,2,3-triazoles from easily available, properly functionalized carbonyl compounds and amine derivatives. The *N*-amino triazoles are easily converted into the corresponding 5-methyl-1*H*-[1,2,3]-triazole-4-carboxylic acid hydrazides, that exhibited in vitro antiplatelet profile against human platelet aggregation using arachidonic acid, adrenaline and ADP as agonists.⁵ The 1-arylsulfonylamino-5-methyl-1*H*-[1,2,3]-triazole-4-carboxylic acid ethyl esters were able to neutralize the hemolytic property of *L. muta* crude venom.⁶



(B) Lacour et al.⁷ have reported that the unusual rhodium(II)-catalyzed condensation of oxetane with ethyl 2-diazoacetoacetate gives exclusively a rare type of functionalized 15-membered polyether macrocycle.



(C) Ferreira and co-workers⁸ used the rhodium-catalyzed decomposition of α -diazo- β -ketoester in the presence of butyl vinyl ether to produce ethyl 5-butoxy-2-methyl-4,5-dihydrofuran-3-carboxylate. The reaction of this intermediate with an excess of primary amine in the presence of glacial acetic acid afforded the corresponding substituted 4-acyl-2-methyl-1*H*-pyrrole in good yield.



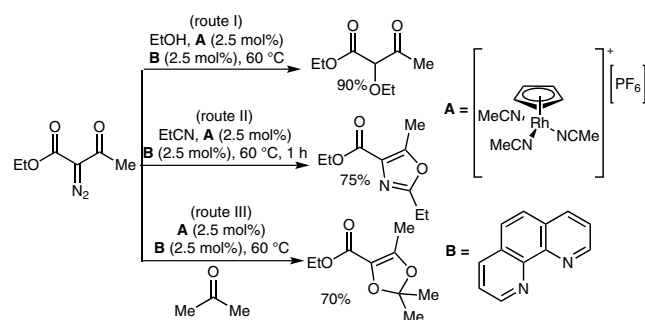
SYNLETT 2013, 24, 0397–0398

Advanced online publication: 08.01.2013

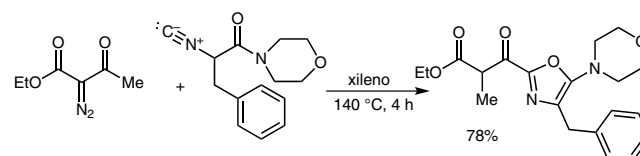
DOI: 10.1055/s-0032-1317879; Art ID: ST-2012-V0427-V

© Georg Thieme Verlag Stuttgart · New York

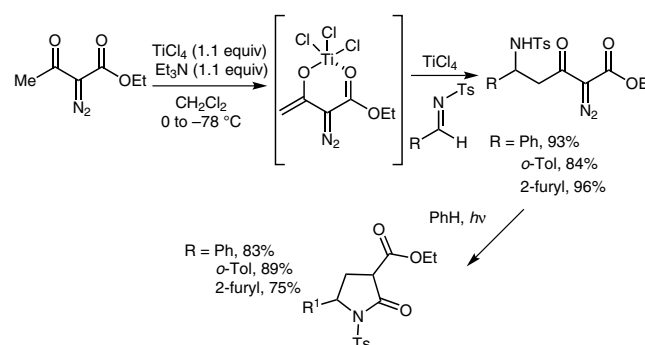
(D) $[\text{CpRu}(\text{CH}_3\text{CN})_3][\text{PF}_6]$ and a diimine ligand catalyze the decomposition of ethyl 2-diazoacetoacetate leading to the O–H insertion (route I) and condensation (routes II and III) products with nitriles and ketones.⁹



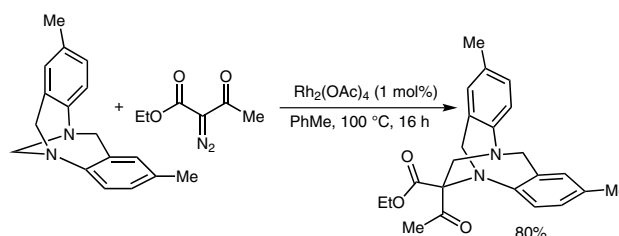
(E) The reaction of ethyl 2-diazoacetoacetate with α -isocyanoacetamides provided the corresponding polysubstituted 5-aminooxazoles in moderate to good yield. In the mechanism suggested by Yu and co-workers,¹⁰ ethyl 2-diazoacetoacetate is transformed into a ketene through the Wolff rearrangement. This intermediate reacts with isocyanoacetamide to produce the nitrilium intermediate that is cyclized to the 2-keto-5-aminooxazole.



(F) Titanium(IV) enolates derived from ethyl 2-diazoacetoacetate add to TiCl_4 -activated *N*-tosylimines to give the δ -*N*-tosylamino substituted α -diazo- β -keto carbonyl compounds. The diazo decomposition of the addition product under irradiation affords γ -lactam derivatives in good yield.¹¹



(G) Lacour et al.¹² reported a one-step catalytic asymmetric synthesis of ethano-Tröger's base using ethyl 2-diazoacetoacetate and a rhodium(II)-catalyzed reaction. A new carbon quaternary stereogenic center was introduced. Ethano-Tröger's base exhibits chirality, being the first chiral compound with two bridgehead stereogenic nitrogen atoms in its structure.



References

- (1) (a) Ferreira, V. F. *Curr. Org. Chem.* **2007**, *11*, 177. (b) da Silva, F. C.; Jordao, A. K.; da Rocha, D. R.; Ferreira, S. B.; Cunha, A. C.; Ferreira, V. F. *Curr. Org. Chem.* **2012**, *28*, 224.
- (2) Ferreira, V. F.; Pereira, L. O. R.; de Souza, M. C. B. V.; Cunha, A. C. *Quím. Nova* **2001**, *24*, 540.
- (3) Ye, T.; McKervey, M. A. *Chem. Rev.* **1994**, *94*, 1091.
- (4) Chiara, J. L.; Suárez, J. R. *Adv. Synth. Catal.* **2011**, *353*, 575.
- (5) Campos, V. R.; Abreu, P. A.; Castro, H. C.; Rodrigues, C. R.; Jordão, A. K.; Ferreira, V. F.; de Souza, M. C. B. V.; Santos, F. C.; Moura, L. A.; Domingos, T. S.; Carvalho, C.; Sanchez, E. F.; Fuly, A. L.; Cunha, A. C. *Bioorg. Med. Chem.* **2009**, *17*, 7429.
- (6) Jordão, A. K.; Afonso, P. P.; Ferreira, V. F.; de Souza, M. C. B. V.; Almeida, M. C. B.; Beltrame, C. O.; Paiva, D. P.; Wardell, S. M. S. V.; Wardell, J. L.; Tiekink, E. R. T.; Damaso, C. R.; Cunha, A. C. *Eur. J. Med. Chem.* **2009**, *44*, 3777.
- (7) Rix, D.; Garrido, R. B.; Zeghida, W.; Besnard, C.; Lacour, J. *Angew. Chem. Int. Ed.* **2011**, *50*, 7308.
- (8) Da Silva, F. C.; Fonseca, M. G.; Rianelli, R. S.; Cunha, A. C.; de Souza, M. C. B. V.; Ferreira, V. F. *Beilstein J. Org. Chem.* **2008**, *4*, 45.
- (9) Austeri, M.; Rix, D.; Zeghida, W.; Lacour, J. *Org. Lett.* **2011**, *13*, 1394.
- (10) Wu, J.; Chen, W.; Hu, M.; Zou, H.; Yu, Y. *Org. Lett.* **2010**, *12*, 616.
- (11) Dong, C.; Deng, G.; Wang, J. *J. Org. Chem.* **2006**, *71*, 5560.
- (12) Sharma, A.; Guénee, L.; Naubron, J. V.; Lacour, J. *Angew. Chem. Int. Ed.* **2011**, *50*, 3677.