

A FACILE SYNTHESIS OF FUNCTIONALIZED NOVEL MONOCYCLIC
TRANS- β -LACTAMS

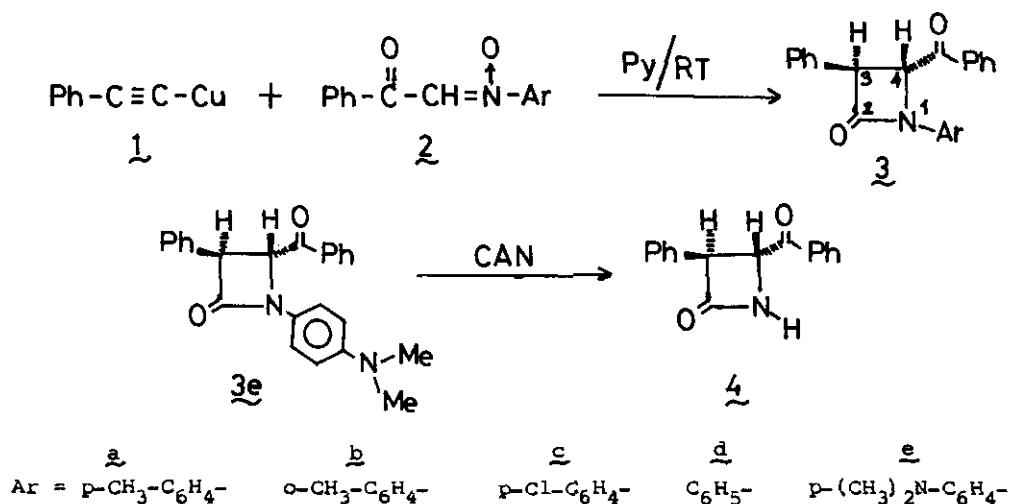
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Abstract - Treatment of copper acetylide (1) with aroyl-N-aryl nitron (2) afforded a novel class of 4-aroyl functionalized monocyclic trans- β -lactams (3). Oxidative N-dearylation of 3e with ceric ammonium nitrite (CAN) gave N-unsubstituted trans- β -lactam (4) in good yield.

Among the several antibacterial classes of compounds, the group of β -lactam antibiotics had been the major target of molecular manipulations^{1,2}. The discovery of highly potent broad spectrum antibiotic thienamycin and monobactam has clearly revealed that the presence of 6-amido side chain and fused thiazole ring of β -lactam is not absolute requirement for biological activity³. Also despite intense work in this area there still remains much to be learned about the fundamental factors that influence their antibacterial action and in particular about the structural and conformational requirement for activity⁴. Several synthetic routes^{5,6} for the preparation of monocyclic β -lactams and their conversion⁷ to bicyclic or polycyclic β -lactams including naturally occurring hydroxypenamams have been reported. The substituent at the 4-position of monobactam contributes substantially to the biological properties of β -lactams⁸. In this communication we wish to report a facile synthesis of monocyclic trans- β -lactam bearing a readily pliable carbonyl group at 4-position and conversion of the N-aryl substituted β -lactam to N-unsubstituted derivative via oxidative N-dearylation with CAN.

To a solution of copper acetylide (1) (prepared in situ⁹) in pyridine was added a solution of benzoyl-N-tolynitron¹⁰ (2a) in pyridine at room temperature and the whole mixture was magnetically stirred overnight. After acidification, extraction with chloroform and subsequent workup afforded

trans-1-tolyl-3-phenyl-4-benzoylazetidin-2-one (3a) in 88% yield as the sole product, mp 190°C ; MS m/z 341 (M^+ , 15%), 208 (100%), 133 (68%) ; IR $\nu_{\max}$ (KBr) 1750 (C=O), 1695 (C=O) cm^{-1} ; ^1H NMR (100MHz, CDCl_3) δ : 2.31(s, 3H), 4.40(d, 1H, $J=3\text{Hz}$, H-3), 5.37(d, 1H, $J=3\text{Hz}$, H-4), 7.15-7.89(m, 14H).



Table

Compound	Yield %	Mp °C	IR $\nu_{\max}$ cm^{-1}	^1H NMR (CDCl_3/TMS) δ ppm.	MS m/z (%)
3b	82	235-236	1750, 1695	2.40(s, 3H, 4.20(d, 1H, $J=3\text{Hz}$), 5.25(d, 1H, $J=3\text{Hz}$), 7.10-7.80(m, 14H).	341(15), 208(100), 133(68).
3c	80	185-186	1750, 1695	4.28(d, 1H, $J=3\text{Hz}$), 5.37(d, 1H, $J=3\text{Hz}$), 7.10-8.10(m, 14H).	361(18), 228(100), 133(62).
3d	86	188-189	1750, 1695	4.28(d, 1H, $J=3\text{Hz}$), 5.37(d, 1H, $J=3\text{Hz}$), 7.27-7.93(m, 15H).	327(20), 194(100), 133(60).
3e	85	197-198	1745, 1690	2.90(s, 6H), 4.17(d, 1H, $J=3\text{Hz}$), 5.17(d, 1H, $J=3\text{Hz}$), 7.20-7.90(m, 14H).	370(14), 237(100), 133(65).
4	80	227-228	3300, 1775, 1680	4.00(d, 1H, $J=3\text{Hz}$), 4.65(d, 1H, $J=3\text{Hz}$), 7.00-7.85(m, 11H).	251(35), 133(100), 118(45).

All the products gave satisfactory microanalytical data.

The configuration of the β -lactam ring was confirmed as trans arrangement on the basis of lower coupling constant values of H-3 and H-4 protons (3Hz) in NMR spectrum as the cis- β -lactam protons give higher values of coupling constants¹¹. The support for the β -lactam structure to 3a is further enhanced by the characteristic mass spectral data where the molecular ion peak at m/z 341 is followed by fragmentation ion peak at m/z 208 (base peak) appeared due to the loss of isocyanate fragment ($Ar-N=C=O$). Similarly compounds (2b-e) reacted with (1) to give trans- β -lactam (3b-e) in excellent yields (Table). Attempted conversion of compounds (3a-d) with CAN in acetonitrile-water to N-unsubstituted β -lactam was unsuccessful. Only when azetidinone (3e) was employed N-dearylation in 80% yield was obtained.

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