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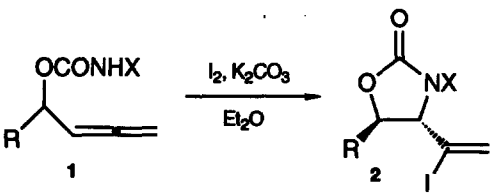
A NOVEL REARRANGEMENT OF TERTIARY α-ALLENIC ALCOHOL CARBAMATES. PREPARATION OF 2-*O*-CARBAMOYL-4,4-DISUBSTITUTED-1,3-BUTADIENES

Richard W. Friesen,*‡ Aleksandra E. Kolaczewska and Nina Khazanovich
Department of Chemistry, University of Toronto, Lash Miller Chemical Laboratories,
80 St. George St., Toronto Ontario, Canada M5S 1A1

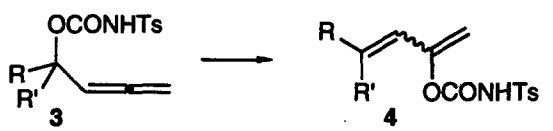
Abstract: Treatment of a variety of tertiary α-allenic alcohols with N-tosyl isocyanate results in a facile and novel rearrangement reaction that provides isolable 2-*O*-carbamoyl-4,4-disubstituted-1,3-butadienes in a stereoselective manner.

We have previously reported that the N-tosyl and N-trichloroacetyl carbamates of secondary α-allenic alcohols **1** undergo an electrophile induced cyclofunctionalization reaction in the presence of iodine to provide cyclic trans urethanes **2** in a highly diastereoselective manner (eq 1).[1] We wished to study the corresponding

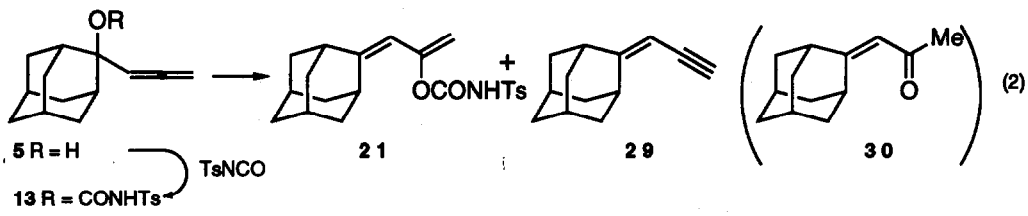


(1)

reactions of tertiary α-allenic alcohol carbamates in an effort to determine what effect an additional alkyl substituent at the allenic position would have on the stereochemical outcome of the cyclization reaction. Unexpectedly, the N-tosyl carbamate derivatives of these tertiary α-allenic alcohols **3** could not be isolated upon treatment of the alcohols with N-tosyl isocyanate. Rather, a facile rearrangement to produce 2-*O*-carbamoyl-4,4-disubstituted-1,3-butadienes **4**[2] was observed. In this paper we describe our results dealing with this novel rearrangement reaction of tertiary α-allenic alcohol carbamates.



Our initial investigations were carried out on the adamantanone derived α-allenic alcohol **5** (eq 2).[3] The allenic alcohol **5** was treated with TsNCO in $CDCl_3$ (deacidified by shaking with Na_2CO_3 followed by filtration through basic alumina) and the reaction progress was monitored by ^1H NMR spectroscopy at room temperature. After 3 minutes, the alcohol **5**[4] had been completely converted into the corresponding allenic carbamate **13**. After a further 5 minutes, new proton resonances were observed[4] and were assigned to the vinyl protons of the



enol carbamate **21**. These resonances continued to grow in intensity until, after 3.75h, the resonances due to the allenic carbamate **13** were absent. Also apparent were resonances corresponding to a second product, identified as the enyne **29**.[4] The enyne **29** could be easily isolated from the reaction mixture by flash column chromatography on silica gel (19 %). However, the enol carbamate **21** proved to be much more labile. Only small amounts of this compound (~20 %) could be isolated by this purification method since facile hydrolysis to the corresponding methyl enone **30** occurred upon chromatography and/or concentration of the apparently pure enol carbamate fractions obtained from chromatography.[5] The ^1H resonances corresponding to **30** were not observed in the crude reaction mixture. Prewashing the column with Et_3N did not result in any improvement in the isolated yield of **21**. Fortunately, isolation of **21** by radial chromatography[6] proved to be very facile. The isolated product exhibited spectral and physical data characteristic of the proposed enol carbamate **21**.[7] The same reaction could be carried out in CH_2Cl_2 (monitoring by TLC) without any significant difference in isolated yields of products.

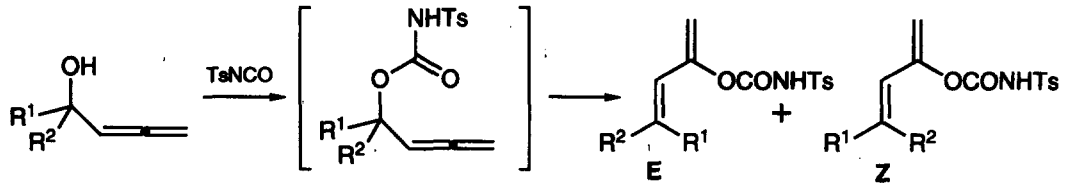
The preparation of **21** represents a novel and potentially synthetically useful synthesis of enol carbamates. There have been relatively few reports of the synthesis of the enol carbamate moiety and these procedures are quite different from the method described above.[2] In addition, most of these methods introduce the carbamate function as a tertiary nitrogen ($OCONR_2$).

In order to probe the scope of the rearrangement process, the same reaction sequence was then applied to a variety of tertiary α-allenic alcohols. The alcohols **6-12**[3] (in $CDCl_3$) were treated with TsNCO and the rearrangement reaction was monitored by ^1H NMR spectroscopy in order to determine the reaction conditions required for rearrangement (Table 1). Again, the enol carbamates **22-28** were observed to be formed following a rapid conversion of the alcohols **6-12** into the intermediate allenic carbamates **14-21**. Separate experiments in CH_2Cl_2 yielded isolable enol carbamates **22-28**. The reaction conditions required for rearrangement, the isolated yields of the enol carbamates and the ratio of isomers produced in the rearrangement reaction are shown in Table 1. Although we have not isolated the enynes corresponding to **29** from the crude reaction mixtures of these latter examples, products having ^1H resonances characteristic of these compounds were observed in each of the ^1H NMR spectra of the crude reaction mixtures. These byproducts account for approximately 10-20% (*in situ* yield) of the reaction mixture.

In all cases for which geometric isomers are expected (entries 4-8), the major rearranged product corresponds to the isomer in which the sterically smaller substituent on the internal double bond is cis to the enol carbamate moiety. The olefin geometry was easily established by suitable difference nOe experiments. For example, irradiation at the resonance frequency of the vinyl proton in **28E** (δ 5.53) resulted in an enhancement of the methyl signal of the ^{t}Bu group (δ 1.01), indicating their cis relationship about the double bond.[8]

The stereochemical outcome of the rearrangement reaction of the tertiary α-allenic alcohol carbamates **16-20** can be rationalized based on an analysis of the steric interactions in chair transition states similar to those of a

Table 1. Preparation of Dienol Carbamates 21-28 from Tertiary α-Allenic Alcohols 5-12

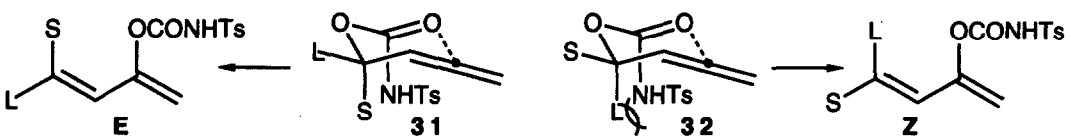


5-12 13-20 21-28

Entry	Alcohol (Carbamate)	R^1	R^2	Reaction Conditions (Time, Temperature)[a]	Isolated Yield, %[b]	Ratio E:Z[c]
1	**5 (13)**	adamantyl		3.75 h, rt	**21** 80	---
2	**6 (14)**	-$(CH_2)_5$-		2 h, 35°C	**22** 62	---
3	**7 (15)**	n-Pr	n-Pr	2 h, rt	**23** 78	---
4	**8 (16)**	Me	n-Bu	3 h, rt	**24E/24Z** 87	2.3:1
5	**9 (17)**	Me	i-Bu	1 h, rt	**25E/25Z** 75	1.8:1
6	**10 (18)**	Me	i-Pr	2 h, rt	**26E/26Z** 77	6.5:1
7	**11 (19)**	Me	Ph	0.75 h, rt	**27E** 64	20:1
8	**12 (20)**	n-Pr	t-Bu	4 h, 35°C	**28E** 74	>50:1

[a]Determined from ^1H NMR experiments in $CDCl_3$. [b]Isolated yield of chromatographically purified product from reactions carried out in CH_2Cl_2. These rather labile compounds[5] were characterized by ^1H and ^{13}C NMR, IR and high resolution mass spectroscopy. For entries 4, 5 and 6, the isomers were not separated. [c]Determined from integration of the ^1H NMR spectra of the crude reaction mixtures and were consistent with those observed in the purified mixtures of isomers.

concerted [3,3] sigmatropic rearrangement.[9] The energetically more favourable process to provide the E-isomer would occur via a transition state derived from **31** in which the sterically larger (L) and smaller (S) substituents adopt equatorial and axial orientations, respectively, on a chair like conformer. In the alternative conformer **32** leading to the Z-isomer, the L substituent experiences a destabilizing 1,3-diaxial interaction that would make this pathway energetically less favourable. An observable solvent effect on the rate of the rearrangement (the



rearrangement becomes more rapid in solvents of increasing polarity), suggests that there is a degree of ionic character in the transition state.[10] In CD_2Cl_2 at room temperature, the allenic carbamate **13** rearranged to the dienol carbamate **21** in 1.75h, while rearrangement in $CDCl_3$ and CCl_4 required 3.75h and 4.75h, respectively, under otherwise identical reaction conditions.

Thus, we have demonstrated that the N-tosyl carbamate derivatives of tertiary α-allenic alcohols **3** undergo a novel and facile stereoselective rearrangement reaction to provide dienol carbamates **4**. The reactions of this

functional group remain relatively unexplored and investigations into the reactivity and synthetic utility of compounds such as **4** are being actively pursued in our laboratories.

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References

‡ Present address: Merck Frosst Centre for Therapeutic Research, PO Box 1005, Pointe Claire-Dorval, Quebec, Canada, H9R 4P8

1. (a) Friesen, R.W. *Tetrahedron Lett.* **1990**, *31*, 4249. (b) Friesen, R.W.; Kolaczewska, A.E. *J. Org. Chem.* **1991**, *56*, 4888.
2. For previous syntheses of enol carbamates (vinyl carbamates), see: (a) Reaction of alkylidenecarbenes with isocyanates; Stang, P.J. *J. Org. Chem.* **1981**, *46*, 4585. (b) Trapping of enolates with carbamyl chlorides; De Cusati, P.F.; Olofson, R.A. *Tetrahedron Lett.* **1990**, *31*, 1405. Sengupta, S.; Snieckus, V. *J. Org. Chem.* **1990**, *55*, 5680 and references cited therein. (c) Lithiation and trapping of the carbamates of homoallylic alcohols; Hoppe, D. *Angew. Chem. Int. Ed. Engl.* **1984**, *23*, 932. (d) Reaction of 2° amines, CO_2 and terminal alkynes with ruthenium catalysts; Mahe, R.; Sasaki, Y.; Bruneau, C.; Dixneuf, P.H. *J. Org. Chem.* **1989**, *54*, 1518 and references cited therein.
3. Prepared from the lithium acetylide of THP-protected propargyl alcohol and the appropriate ketone by the method of: Cowie, J.S.; Landor, P.D.; Landor, S.R. *J. Chem. Soc., Perkin Trans. 1* **1973**, 720.
4. Vinyl proton resonances: ^{1}H NMR (200 MHz, $CDCl_3$) δ **5**: 4.85 (d, 2H, J = 6.8 Hz), 5.45 (t, 1H, J = 6.8 Hz); **21**: 4.78 (m, 2H), 5.46 (s, 1H); **29**: 2.89 (d, 1H, J = 2.3 Hz), 5.14 (d, 1H, J = 2.3 Hz).
5. We have found that simply concentrating pure samples of the enol carbamates results in a facile hydrolysis of the labile enol carbamate moiety to provide the corresponding methyl enones. As a result, characterization of these compounds must be done rapidly immediately after their purification.
6. 1 or 2 mm disks of silica gel (Merck, TLC grade with gypsum binder and fluorescent indicator).
7. The enol carbamate **21** exhibited: colorless oil; characterisitc resonances ^{1}H NMR (200 MHz, $CDCl_3$) δ 2.30 (s, 1H), 2.44 (s, 3H), 3.02 (s, 1H), 4.78 (m, 2H), 5.46 (s, 1H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 105.3, 111.1, 129.3, 130.4, 136.0, 146.0, 149.1, 151.7, 157.2; IR (neat) 3255, 1771, 1665, 1609 cm^{-1}; HRMS calcd for $C_{21}H_{25}O_4NS$ (M^+): 387.1504; Found: 387.1482.
8. Other nOe experiments: irradiated vinyl resonance - resonance enhanced; **24E**: 5.48 - 1.99 (CH_2); **25E**: 5.43 - 1.83 (CH_2); **26E**: 5.48 - 2.24 (CH); **27E**: 5.97 - 7.73 (Ar)
9. For examples of other sigmatropic rearrangements of allene derivatives, see: (a) Hopf, H. In *The Chemistry of the Allenes*; Landor, S.R., Ed.; Academic Press: London, 1982; Vol. 2, Chapter 4.2. (b) Huntsman, W.D. In *The Chemistry of Functional Groups: The Chemistry of Ketenes, Allenes and Related Compounds*, Patai, S., Ed.; John Wiley & Sons: New York, 1980; Part 2, Chapter 15.
10. Alternatively, the rearrangement may be occurring by the formation of a tight ion pair that subsequently collapses to form the enol carbamate. The corresponding rearrangements of the secondary α-allenic alcohol carbamates **1** could not be carried out, even under forcing conditions, further suggesting that there is at least a degree of ionic character in the transition state.

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