Stereospecific Intermolecular Interception of sp^2 Carbanion Intermediates in Nucleophilic Addition to Alkynes

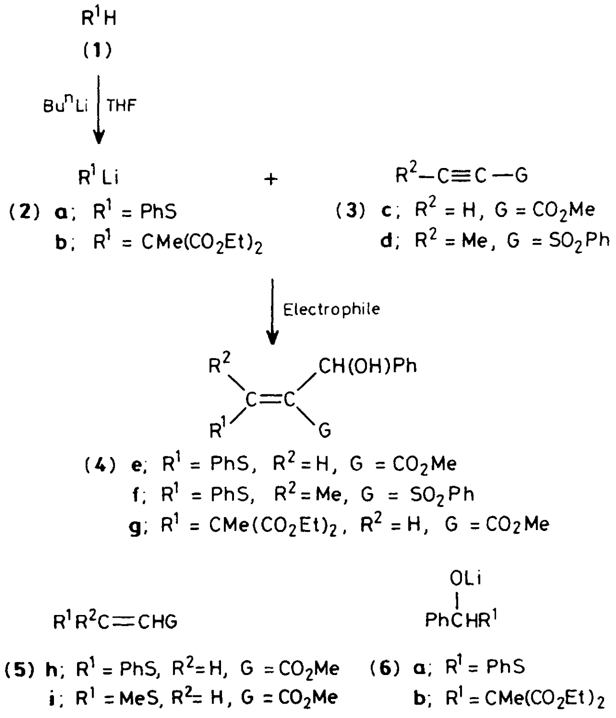
Adrian Bury, Sushama D. Joag, and Charles J. M. Stirling*

Department of Chemistry, University College of North Wales, Bangor LL57 2UW, U.K.

Addition of sulphur and carbon nucleophiles to methyl propiolate and to phenyl prop-1-ynyl sulphone in the presence of benzaldehyde gives adducts incorporating the three components with a predominantly *E*-disposition of nucleophile and incorporated benzaldehyde.

Nucleophilic addition to alkynes is a very familiar reaction but examples in which the electrophilic component of the nucleophile–electrophile partnership is other than a proton are rare. *Intra*molecular trapping of the sp^2 carbanions presumed to be formed is well known[1] and leads to cyclic products. Some examples of *inter*molecular trapping involving vinyl–copper intermediates[2] and vinyl-lithium–*N,N,N',N'*-tetramethylethylenediamine complexes[3] obtained from acetylenes have been reported and sp^2 carbanions have been trapped intermolecularly by polyfluorinated aromatic and heterocyclic electrophiles.[4] Trapping of sp^2 carbanions formed in simple Michael-type reactions has, however, remained unexplored except for the low-yield alkylations giving mixtures of products reported by Kon in the 1930's.[5]

We now report on trapping of carbanions formed in additions of two types of nucleophile to electrophilic alkynes. We reasoned that, for success in such a simple system, a highly reactive electrophile capable of diverting sp^2 carbanions from further Michael additions leading to polymeric products was required. In addition to such high reactivity, however, was the requirement that the reaction of the external electrophile with the nucleophile involved in the Michael addition must be reversible. This requirement dictated the need for an electrophile undergoing nucleophilic addition and not (irreversible) substitution. In the first instance we chose benzaldehyde but we also have briefly examined benzophenone and dimethyl disulphide as electrophilic trapping agents.



Scheme 1

Additions of the lithium salts of benzenethiol (**2a**) and of diethyl methylmalonate (**2b**) to alkynes (**3c**) and (**3d**) in the presence of electrophiles have been examined. Typically, the salts (**2**) were generated by addition of butyl-lithium (0.015 mol) to the conjugate acids (**1**) (0.015 mol) in dry tetrahydrofuran under argon at 0 °C. The solutions were cooled and a mixure of alkyne (**3**) (0.01 mol) and benzaldehyde (0.05 mol) was injected, maintaining the temperature close to -20 °C (30—40 min). After 5 min, injection of saturated aqueous ammonium chloride at -10 °C with subsequent extraction ($CHCl_3$) and flash chromatography gave the products in Table 1.

The reactions are stereoselective; *Z*-adducts (**4**) were at least 83% of the adduct mixtures. Conditions have not been optimised; we used 4 molar excesses of electrophile, and higher yields, particularly of adducts (**4f**) and (**4g**), can probably be obtained by using even larger excesses.

The structure of *Z*-adduct (**4e**) was unambiguously determined from the *X*-ray crystal structure† (Figure 1) and the 400 MHz ^1H n.m.r. spectrum. Those of adducts (**4f**) and (**4g**), formed with 100% stereospecificity, followed from nuclear Overhauser effect measurements. By contrast, Corey and his group have observed rapid equilibration of vinyl–copper derivatives.[2a]

Separate experiments showed that adduct (**4e**) did *not* arise by deprotonation of simple (proton-trapped) adduct (**5h**) which is an accompanying product, nor did adduct (**4e**) arise by nucleophilic addition to the simple adduct (**5h**) with interception by the electrophile and subsequent elimination.

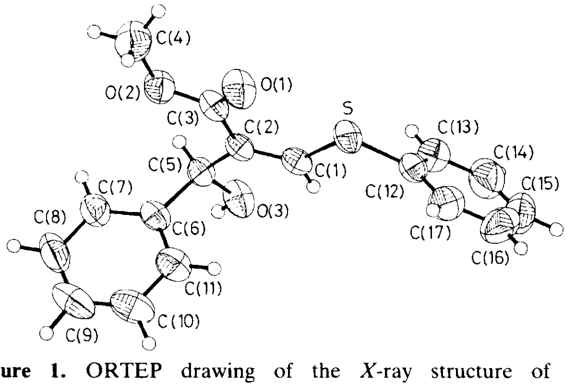


Figure 1. ORTEP drawing of the *X*-ray structure of (*Z*)-$PhSCH{=}C(CO_2Me)CH(OH)Ph$ (**4e**).

---

† *Crystal data:* $C_{17}H_{16}O_3S$, $M = 300$, monoclinic, space group $P2_1/c$, $a = 7.301(1)$, $b = 18.987(8)$, $c = 11.249(2)$ Å, $\beta = 92.88(1)°$, $U = 1557.4$ Å^3, $Z = 4$, $F(000) = 632$, Mo-K_α radiation, $\lambda = 0.71069$ Å, $\mu = 1.72$ cm^{-1}; $1.5 \leqslant \theta \leqslant 23°$, 2160 independent reflections, 1864 with $I \geqslant 1.5\sigma(I)$ used, direct methods, SHELX-84, $R = 0.032$, $R_w = 0.030$. The atomic co-ordinates for this work are available on request from the Director of the Cambridge Crystallographic Data Centre, University Chemical Laboratory, Lensfield Rd., Cambridge CB2 1EW. Any request should be accompanied by the full literature citation for this communication.

Table 1. Nucleophile–alkyne–electrophile adducts.

Nucleophile or Li salt	Alkyne	Electrophile	Adduct	% Yield	% *Z*-isomer
(**2a**)	(**3c**)	PhCHO	(**4e**)	84[a,b]	83[c]
(**2a**)	(**3d**)	PhCHO	(**4f**)	48[d]	100
(**2b**)	(**3c**)	PhCHO	(**4g**)[e,f]	47[e]	?
(**2b**)	(**3d**)	PhCHO	[g]	—	—
MeS^-	(**3c**)	MeSSMe	(**5i**)	82	[h]
(**2a**)	(**3c**)	$Ph_2C=O$	[i]	—	[h]
(**7**)[j]	(**3c**)	PhCHO	[i]	—	—

[a] M.p. 87 °C (from Et_2O–hexane); M^+, m/z 300. [b] (*Z*)-$PhSCH=CHCO_2Me$ (12%) also isolated. [c] (*E*)-Isomer (^1H n.m.r.) present in crystallisation mother liquors. [d] M.p. 132 °C (from Et_2O–hexane). [e] Adduct (**5g**) (20%) also isolated. [f] M.p. of phenylurethane 96—97 °C. [g] Mixtures of adducts (**4**) and (**5**). [h] Both isomers. [i] Complex product mixtures. [j] (**7**) = (*E*)-*p*-$MeC_6H_4SO_2CH=CHCH_2^-$.

Treatment of salts (**2a**) and (**2b**) with benzaldehyde in dimethyl sulphoxide showed (^1H n.m.r.) complete conversion into the adducts (**6a**) and (**6b**).

Attempts to use dimethyl disulphide and benzophenone as trapping electrophiles failed, nor was an adduct obtained with the anion of allyl *p*-tolyl sulphone which has been reported[6] to react efficiently in Michael reactions. One step joining of thiolate anions, activated alkenes, and carbonyl compounds has been reported earlier.[7]

The simplicity of these reactions yielding tri- and tetra-substituted functionalised alkenes has obvious synthetic potential; we are further examining the range of nucleophile, alkyne, and trapping electrophile that can be used.

We thank the S.E.R.C. for access to the *X*-ray crystal (Queen Mary College) and high field n.m.r. (Warwick) services and express our gratitude to Drs. M. B. Hursthouse and O. W. Howarth respectively.

Received, 12th August 1985; Com. 1206

References

1 J. I. Diekstein and S. I. Miller, in 'Chemistry of the Carbon Carbon Triple Bond,' ed. S. Patai, Wiley, New York, 1978, vol. 2, p. 813.

2 (a) E. J. Corey and J. A. Katzenellenbogen, *J. Am. Chem. Soc.*, 1969, **91**, 1851; (b) J. B. Siddall, M. Biskup, and J. H. Fried, *ibid.*, p. 1853.

3 J. E. Mulraney and D. J. Newton, *J. Org. Chem.*, 1969, **34**, 1936; L. I. Olsson and A. Claesson, *Tetrahedron Lett.*, 1974, 2161.

4 W. T. Flowers, R. N. Haszeldine, and P. G. Marshall, *Chem. Commun.*, 1970, 371; R. D. Chambers, W. K. R. Musgrave, and S. Partington, *ibid.*, 1970, 1050; R. D. Chambers, W. K. R. Musgrave, S. Partington, and D. B. Speight, *J. Chem. Soc., Perkin Trans. 1*, 1974, 2673.

5 E. H. Farmer, S. C. Ghosal, and G. A. R. Kon, *J. Chem. Soc.*, 1936, 1804.

6 B. M. Trost and N. R. Schmuff, *J. Am. Chem. Soc.*, 1985, **107**, 396.

7 T. Shono, Y. Matsumura, S. Kashimura, and K. Hatanaka, *J. Am. Chem. Soc.*, 1979, **101**, 4752.