Tetrahedron Letters No. 2, pp 89 - 92.
©Pergamon Press Ltd. 1979. Printed in Great Britain.

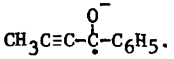
0040-4039/79/0108-0089$02.00/0

III. SILYLATION STUDIES OF SOME CONJUGATED ACETYLENE COMPOUNDS: LITHIUM DIISOPROPYLAMIDE AS BASE, NUCLEOPHILE AND ELECTRON TRANSFER REAGENT

C. Celia Shen and C. Ainsworth*
Department of Chemistry, San Francisco State University
San Francisco, California 94132, U.S.A.

In a preceding communication we reported that the alkylation/silylation of 2-butynoic acid (tetrolic acid) could be regiospecifically controlled by choice of strong base to produce α or γ-alkylation products. In the immediately preceding communcation related 2-alkynoic acids were found to undergo isomerization-alkylation or addition-cleavage reactions. These interesting results prompted us to study the silylation of systems related to 2-alkynoic acids, including conjugated acetylenic ketones, anhydrides, esters and nitriles (Table I, 1-6). Such systems treated with lithium diisopropylamide (LDA) and chlorotrimethylsilane (CTMS) have been found to undergo a variety of reactions including regiospecific alkylation (route I), electron transfer reduction (route II) and 1,4-conjugative addition (route III). The last two reactions are of particular interest since LDA is currently in favor as a strong base because it is largely devoid of side reactions.[1]

In contrast to 2-butynoic acid which with LDA gave both α and γ-silylation, the ester 1 gave only the α-product 7[2]: $H^1NMR(CDCl_3)$ δ0.16(S,9H), 3.3(S,2H), 3.7(S,3H); IR(neat) 1970(C=C=C), 1730 cm^{-1}(C=O); mass spectrum m/e (rel intensity) 170(M^+, 0.3), 155(51.8), 127(100), 73(7.8). However, the yield was relatively low (vide infra). 1-Phenyl-2-butyn-1-one (2)[3] with LDA and CTMS gave no α or γ-silylation product nor any corresponding cumulenic product. Surprisingly, the silylated reduction compound 8[4] was the major product formed. The reaction mixture of 2 and LDA was not the typical yellow color of other anion forming reactions but it was purple which is associated with radical anion intermediates. We thus propose that LDA in this reaction is acting as an electron transfer agent[5a] and that the phenyl group stabilizes the intermediate[5b]



$CH_3C{\equiv}C{-}\overset{O^-}{\underset{\bullet}{C}}{-}C_6H_5$.

The products from the reaction of the mixed anhydride 3[6] were trimethylsilyl benzoate in 70% yield and the volatile product 2-butynal which was isolated in poor yield. The yield is not surprising since it seems likely that under the basic reaction conditions self-condensation of 2-butynal would take place. The formation of this aldehyde is also best explained in terms of

Table I

2-Butynoic Acid and Related Conjugated Acetylenic Compounds Treated with LDA and CTMS[a]

Compound	Product	Route	Yield, %[a]
$CH_3C\equiv C-CO_2Me$ (1)	$CH_2=C=C(SiMe_3)CO_2Me$ (7)	I	40[b]
$CH_3C\equiv CCOC_6H_5$ (2)	$CH_3C\equiv CCH(C_6H_5)OSiMe_3$ (8)	II	71
$CH_3C\equiv CCO_2COC_6H_5$ (3)	$CH_3C\equiv CCHO + C_6H_5CO_2SiMe_3$	II	70[c]
$C_6H_5C\equiv CCO_2Me$ (4)	$C_6H_5(isoPr_2N)C=CHCONisoPr_2$ (9)[d]	III	45
$CH_3C\equiv C-C\equiv N$ (5)	complex products[e]		
$CH_3(C\equiv C)_2CO_2H$ (6)	polymer		

a. Experimental conditions and procedures similar to those recorded in preceding communications.

b. Use of HMPA as cosolvent did not improve the yield.

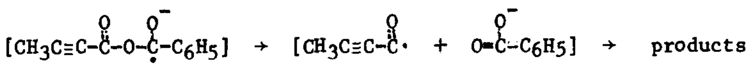
c. Refers to trimethylsilyl benzoate.

d. See ref. 8.

e. See text.

---

a radical anion mechanism.[7]



$$[CH_3C\equiv C-\overset{O}{\overset{\|}{C}}-O-\underset{\bullet}{\overset{O^-}{C}}-C_6H_5] \rightarrow [CH_3C\equiv C-\overset{O}{\overset{\|}{C}}\cdot + O=\overset{O^-}{C}-C_6H_5] \rightarrow \text{products}$$

The reaction product from methyl phenylpropiolate (4) and LDA (1.1 equiv) at -78° for 1 hr was treated directly with aqueous ammonium chloride and gave the addition compound 9, as major product.[8] A similar nucleophilic addition[11] in the methyl tetrolate reaction may account for the low yield of 7. The carboxylate charge is most likely responsible for decreasing such an addition when the starting material is the carboxylic acid. 9: H^1NMR($CDCl_3$) δ1.25(d,12H,J=7Hz), 1.4(d,12H,J=7Hz), 3.3-4.8(m,4H), 5.4(S,1H), 7.1(m,3H), 7.3(m,2H); IR(neat) 1680(C=O), 1610, 1590 cm^{-1}(phenyl and C=C); mass spectrum m/e (rel intensity) 330(M^+,23), 160(67), 118(100), 100(31), 91(52).

Other related conjugated systems that were studied included tetrolonitrile[12] ($CH_3C\equiv C-CN$,5) and 2,4-hexadiynoic acid[13] ($CH_3C{\equiv}CC{\equiv}CCO_2H$,6). Compound 5 and LDA gave a complex mixture of more than ten products which were not further pursued. Compound 6 unfortunately polymerized under the reaction conditions.

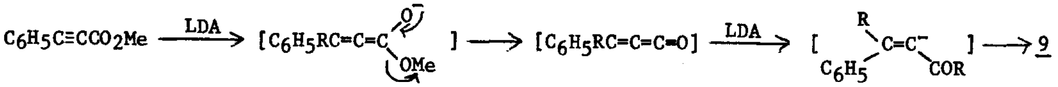
Interestingly, compound 5 with 1 equiv of BuLi-TMEDA at -100° followed by CTMS gave the trisily compound $(Me_3Si)_2C{=}C{=}C(SiMe_3)CN$ (10) which was isolated in 25% yield as colorless needles, mp 65-68°, $H^1NMR(CDCl_3)$ $\delta 0.18$ only, $IR(CHCl_3)$ 2200(C≡N), 1900 cm^{-1}(C=C=C). Use of 3 equiv of BuLi-TMEDA did not improve the yield of 10 but gave a mixture consisting of five products, none of which was compound 10. We thus conclude that polysilylation product 10 was formed through stepwise silylation.[14]

References:

1. (a) H. O. House, "Modern Synthetic Reactions" 2nd edition, W. A. Benjamin Inc., Menlo Park, California, 1972.
   (b) J. March, "Advanced Organic Chemistry", 2nd edition, McGraw-Hill, New York, N.Y., 1977.
   (c) A. I. Meyers and R. Gabel, J. Org. Chem., 42, 2653 (1977), recently reported that lithio amides displaced the methoxy group of 2-(o-methyoxyphenyl) oxaloline.
   (d) J. C. Herrman, G. R. Kieczykowski, and R. H. Schlessinger, Tetrahedron Lett., 2433 (1973).
2. M. W. Rathke and D. F. Sullivan, Tetrahedron Lett., 4249 (1972), reported the synthesis of methyl 2,3-butadienoate by a similar method.
3. A. G. Hortmann and R. L. Harris, J. Am. Chem. Soc., 93, 2477 (1971).
4. Identified by comparison with authentic sample.
5. (a) E. J. Panek and W. F. Carroll, Jr., Abstracts, 169th ACS National Meeting, Philadelphia, Pa., April, 1975, Organic Chemistry No. 20.
   (b) This intermediate by abstraction of a hydrogen atom (source not determined) is converted by CTMS to 8.
6. R. I. Yakhimovich and G. F. Dvorko, Zh. Org. Khim., 5, 1177 (1969).

7. Another pathway might involve nucleophilic attach of isoPr$_2$N$^-$ on the anhydride but N,N-diisopropyltetrolamide was not found.

8. The formation of 9 is visualized in the following way, where R = (iso Pr)$_2$N-



$$C_6H_5C\equiv CCO_2Me \xrightarrow{LDA} [C_6H_5RC=C=C(O^-)(OMe)] \longrightarrow [C_6H_5RC=C=C=O] \xrightarrow{LDA} [(R)(C_6H_5)C=C^-(COR)] \longrightarrow 9$$

The stereochemistry of 9 is assigned on the basis of the shift value of the alkene proton.[9] The above pathway is favored over direct amide formation because of the findings of Craig,[10] who observed cleavage of αβ-acetylenic esters and amides, which do not possess a γ-hydrogen, on treatment with amide ion.

9. (a) R. Huisgen, B. Giese and H. Huber, Tetrahedron Lett. 1833 (1967).
   (b) J. E. Dolfini, J. Org. Chem., 30, 2198 (1965).
   (c) J. Klein and N. Aminadar, J. Chem. Soc. C., 1380 (1970).

10. J. C. Craig and M. Moyle, J. Chem. Soc., 4402 (1963).

11. (a) LDA has been reported to act as a nucleophile adding conjugatively to ethyl crotonate — see ref. 1(d).
    (b) Amine addition to acetylenic esters has been investigated — see ref. 9a and references cited therein.

12. J. Sheridan and L. F. Thomas, Nature, 174, 798 (1954).

13. J. L. H. Allan, G. D. Meakins and M. C. Whiting, J. Chem. Soc., 1874 (1955).

14. G. A. Gornowicz and R. West, J. Am. Chem. Soc., 93, 1714 (1971), observed stepwise silylation in the polysilylation of acetonitrile.

(Received in USA 19 September 1978)