Tetrahedron Letters, Vol.22, No.38, pp 3703 - 3706, 1981
Printed in Great Britain

0040-4039/81/383703-04$02.00/0

SYNTHESIS AND CHARACTERIZATION OF STABLE N-PHTHALIMIDYL-2,3-BUTADIENOATES

F. G. Kathawala*, H. F. Schuster and M. J. Shapiro

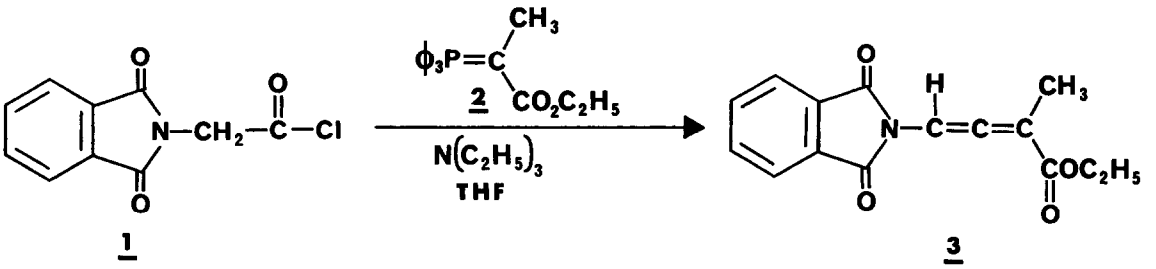
Preclinical Research Department, R&D,
Sandoz, Inc., East Hanover, New Jersey 07936

SUMMARY: A variety of stable, crystalline N-phthalidmidyl-2,3-butadienoates were synthesized via a Wittig reaction of the acid chloride with ethyl-2-(triphenyl-phosphoranylidene)-propionate. Both proton and ^{13}C-nmr are used to confirm the allene structure.

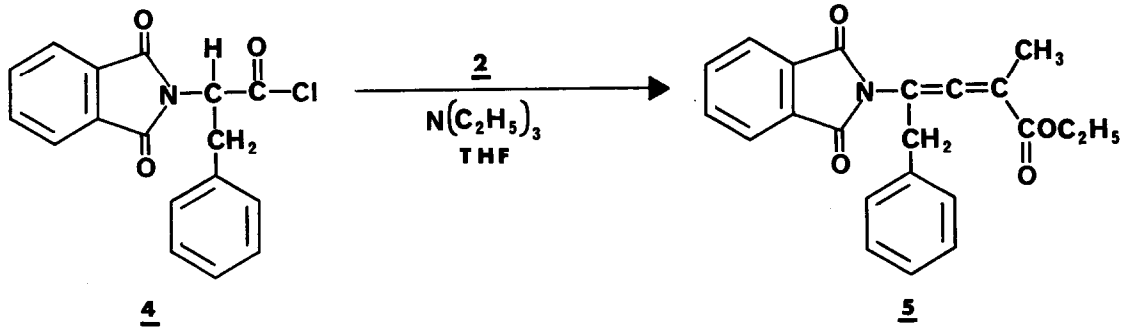
N-Acylamino-1,2-dienes are virtually unknown. The alkylation of 2-pyrrolidinone with propargyl bromide in the presence of base did not give the expected 1-(2-propargyl)-2-pyrrolidinone but gave instead 1-(1,2-propadienyl)-2-pyrrolidinone, the structure of which was well supported by experimental and spectral data.[1] In developing a highly stereoselective method for preparing (1Z, 3E)-1-trichloroacetamido-13-dienes, Overman, et al, [2] have demonstrated the intermediacy of the thermally labile N-trichloroacetamido-1,2-dienes by direct isolation, although the yields were in the order of 16-19%. Wender[3] in an in vitro analogy for suicide enzyme inhibition has reported the conversion of a propargylamine to the novel allenylimine. However, no experimental data and characterization of the product was provided.

Since not many well characterized N-acylamino-1,2-dienes have been hitherto reported, we wish to describe the synthesis and isolation in good yields of N-phthalimidyl-2,3-butadienoates and their characterization through spectral data. Synthetic approach to these 2,3-dienes involved the use of the Wittig reaction of an acid chloride with a phosphorane, which has been well documented as a method of preparing a variety of allenic esters.[4]

Reaction of the acid chloride of N-phthaloyl glycine (1)[5] with ethyl 2-(triphenyl phosphoranylidene)-propionate (2) in the presence of triethylamine in tetrahydrofuran at room temperature for 15 hours results after chromatographic separation in the isolation of beautifully crystalline ethyl 2-methyl-4-phthalimidyl-2,3-butadienoate (3).[6,7]



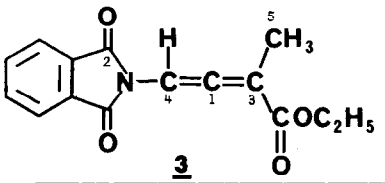
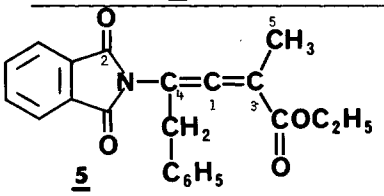
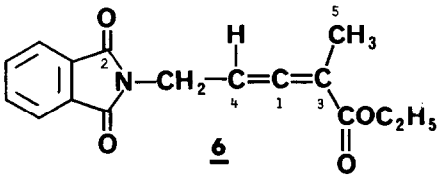
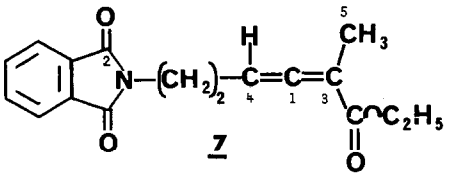
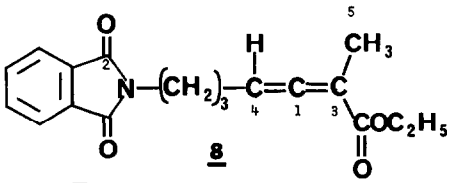
Similarly from acid chloride (4), ethyl 4-benzyl-4-phthalimidly-2-methyl-2, 3-butadienoate (5) was prepared in 52% yield.



Allenic structures of both (3) and (5) are supported by proton nmr. Allene (3) shows the characteristic allenic proton (C-4) quartet at δ 7.11 (J=3Hz) as well as the methyl doublet at δ 2.00 (J=3Hz). The only characteristic signal for the allenic structure of (5) is the methyl singlet at δ 1.95. It is important to note that neither (3) nor (5) exhibits in its infrared spectrum absorption at 1960-1970 cm^{-1} characteristic of the allenic bond. Since the proton nmr was considered insufficient to support the allenic structures of (3) and (5), further supportive evidence was sought using ^{13}C nmr. For the purpose of obtaining model compounds for this spectral approach, three additional compounds: ethyl 2-methyl-4-(phthalimidylmethyl)-, 2-methyl-4-(phthalimidylethyl)-, and 2-methyl-4-(phthalimidylpropyl)-2,3-butadienoates, (6), (7) and (8), respectively, were synthesized in an analogous manner from their corresponding acid chlorides. The ^{13}C nmr data of compounds discussed is presented in the accompanying table. From this data, the allenic nature of all the compounds depicted is clearly established by the two high field chemical shifts for the terminal allenic carbons (C3 and C4) and the very low field chemical shift for the central carbon (C1), a result also observed by Overman.[2b]

Our success with the preparation of these allenes shows that a variety of N-acylamino-1,2-dienes of this sort can be easily prepared from a variety of desired acid chlorides or by altering the phosphoranes used.

The allenes described in the paper provide useful synthons for preparation of a variety of heterocyclic compounds.

Allene	^{1}H nmr (ppm) 60 MHZ (CDCl3)	^{13}C nmr (ppm) (XL-100)(CDCl3)	Infrared	Yield
 **3**	7.11 (1H,q J=3Hz) 2.55 (3H,d J=3Hz)	C1 206.366 C2 165.120 C3 104.952 C4 90.029 C5 16.311	1720 cm^{-1} (ester)	42
 **5**	3.91 (2H, s) 1.95 (3H, s)	C1 208.857 C2 166.119 C3 104.11* C4 101.951* C5 15.459	1778 cm^{-1} 1710 cm^{-1}	53
 **6**	5.48-5.80 (1H, m) 4.40 (2H,d J=6Hz) 1.76 (3H,d J=3Hz)	C1 210.029 C2 167.291 C3 98.824 C4 89.893 C5 14.607	1962 cm^{-1} (allene) 1770 1710	32
 **7**	5.30-5.68 (1H, m) 3.74-4.2 (4H,t-q) 1.70 (3H,d J=3Hz) 2.54 (2H,q J=7Hz)	C1 210.137 C2 167.932 C3 96.128 C4 89.984 C5 14.769	1960 cm^{-1} 1770 1710	84
 **8**	5.38-5.70 (1H, m) 3.78 (2H,t J=7Hz) 1.68-2.4 (4H, m) 2.79 (3H,d J=3Hz)	C1 210.047 C2 168.204 C3 96.456 C4 92.779 C5 15.161	1960 cm^{-1} 1770 1710	83

*Assignment may be reversed. All other assignment are based upon chemical shifts and peak intensities in the proton decoupled ^{12}C nmr spectrum.

REFERENCES AND EXPERIMENTAL NOTE

1. W. B. Dickinson and P. C. Lang, Tet. Lett (31) 3035 (1967).

2. a) L. E. Overman and L. A. Clizbe, J. Am. Chem. Soc. 98, 2352, 8295 (1976).
   b) L. E. Overman, C. K. Marlowe and L. A. Clizbe, Tet. Lett. (7) 599 (1979).
   c) L. E. Overman, Accts. of Chem. Res. 13, 218 (1980).

3. P. A. Wender and J. M. Schaus, J. Org. Chem. 43 (4) 702 (1978).

4. Von R. W. Lang and H. J. Hansen, Helv. Chim. Acta 63 438 (1980).

5. Prepared from phthalic anhydride and glycine in refluxing pyridine followed by treatment with thionyl chloride in toluene. General procedure used for all acid chlorides.

6. Experimental note: The following provides a general procedure for preparing N-phthalimidyl-2,3-butadienoates:

   A three-necked 500 ml round-bottomed flask equipped with addition funnel and gas inlet tube is charged with 24.0 g (66.3 mmole) ethyl 2-(triphenylphosphoranylidene)-propionate, 8.0 q (67 mmole) triethylamine and 350 ml dry tetrahydrofuran. Stir under nitrogen at room temperature, while the 66.3 mmole of the appropriate acid chloride in 35-50 ml tetrahydrofuran is added dropwise. The mixture is stirred at room temperature 12-15 hours under nitrogen, then filtered and the solvent removed under reduced pressure. The brown residue is dissolved in chloroform and chromatographed on a 2 x 24" silica gel column eluted with chloroform. An oil is usually isolated which is crystallized upon standing. Trituration is possible with 3:1/pentane:ether.

7. All products meet required elemental analysis for proposed structures.

(Received in USA 20 May 1981)