"PUSH-PULL-ACETYLENES" AS VERSATILE INTERMEDIATES
IN HETEROCYCLIC SYNTHESIS +

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Phosgene and oxalyl chloride add to "push-pull-acetylenes" (1) to give excellent yields of highly reactive adducts of type (3) and (4). A variety of specifically substituted heterocyclic compounds, like pyrazolo-oxazinones (6), pyrazoles (7), oxazinones (9), (10), (12) and (13) or furanones, e.g., (21) and (22) (Table I), can be synthesized taking advantage of the bifunctionality of these adducts. From the acetylenes (1) and phenylhydrazine the isomeric pyrazoles (25) and (26) as well as pyrazolones (27) and (28) (Table I) are obtained due to their ambident electrophilic reactivity.

Acetylenes, having both electron-donating (push) and electron-accepting (pull) groups (1) directly linked to the triple bond are versatile intermediates in organic synthesis 1,3,4,5,6. They are readily available from the correspondingly substituted olefins (2) on a preparative scale in high yields by a simple one pot bromination and dehydrobromination sequence 1a,2.

+ Dedicated with best wishes to Dr. Ken'ichi Takeda on the occasion of his 70th birthday.

— 1921 —
The acetylenes (1), as highly reactive nucleophilic and electrophilic triple bond systems\(^{1a}\), are known to undergo with great facility cycloadditions to isolated, conjugated or cumulated multiple bonds. Among these (1) have been reacted with diphenylketene\(^{1a},3\), azides\(^{1a},4\), diazomethane\(^5\), phenyl-\(^{1a},3\) and carbonylisocyanates\(^6\) to give specifically substituted cyclobutenone, oxete, 1,2,3-triazole, pyrazole, 2-quinolone and 1,3-oxazinone derivatives in high yields.

According to their spectroscopic properties the acetylenes (1) show a similar mutual conjugation between the push- and pull-groups across the triple bond as in the olefins (2) and may be therefore regarded as ethynylogous amides, urethanes and ureas. However, on the contrary to (2), which behave as vinylogous amides, urethanes and ureas in acylation and alkylation, the acetylenes (1) react with carboxylic acid chlorides under addition to the triple bond to give excellent yields of adducts of the type (3) and (4).
In particular the phosgene adducts (3) are extremely reactive, as indicated by their violent reactions with water and methanol to form malonic acid derivatives, and very useful as bifunctional reagents for the synthesis of heterocycles. Because of their bifunctionality, they react with various potential 1,2- and 1,3-bifunctional nucleophiles under formation of 5- and 6-membered ring systems.

From (3c) and hydrazine, a 1,2-bifunctional nucleophile, one obtains, presumably through the intermediacy of the pyrazole (5), the new pyrazolo-oxazinone (6) in 64% yield, whereas with phenylhydrazine the pyrazole (7) is the final stage as expected.
The capability of the phosgene adducts (3) to yield 6-membered ring systems with 1,3-bifunctional nucleophiles is clearly demonstrated by their smooth reaction with benzamide and urethane, which leads to the oxazinones (9), (10), and (12).
The formation of these compounds deserves further comment. Due to the liberation of hydrogen chloride during the course of the reaction the initially formed oxazinones (8) suffer rearrangement to (9) or in the case of (11) dealkylation to (12), whereas (10) is stable towards acids under the reaction conditions. These assumptions have been totally confirmed by the independent synthesis of (8), (10), and (11) from (1) and the corresponding carbonyl isocyanates by a 2+4-cycloaddition reaction and treatment of the resulting cycloadducts with hydrogen chloride under precisely the same conditions as employed above.

The two most obvious pathways for the fascinating acid-catalyzed rearrangement of 6-dimethylamino-oxazinones (8) into 5-dimethylcarbamyl-oxazinones (9), which proceeds in almost quantitative yield under the strict exclusion of water, are shown in scheme 1.

Path 1, which shows similarities to the α-acyl-lactone-rearrangement, is based on a thermodynamically controlled O-protonation of (8) followed by a ring opening of the aza-pyrylium salt (14). Recyclization of the thus formed N-acyl-nitrilium derivative (15) would give (9).

Path 2, which bears some resemblance to the rearrangement of 3-chloro-3-dimethylaminopropenal into 3-chloro-N,N-dimethylacrylamide, implies a kinetically controlled N-protonation of (8) accompanied by a ring cleavage of (16) to form the ketene-iminium ion (17). Isomerisation of the oxete intermediate (18) derived from (17) would then lead to the 8-chloro-acryl derivative (19), a reactive precursor for (9).
Scheme 1

Path 1

Path 2

- HCl

- HCl

- HCl

\( X \) | \( a \) | \( b \)
---|---|---
\( H \) | \( \text{CH}_3 \) |
The dealkylation product (12) undergoes smooth methylation by diazomethane in methanol under exclusive formation of (13) in 96% yield.

In contrast to the phosgene adducts (3) the oxalyl chloride adducts (4) could not be isolated, except in the case of the adduct (4d), because of rapid intramolecular cyclizations. Thus one obtains from (1a) and oxalyl chloride after subsequent treatment of the initially formed cyclization product (20) with water and methanol the furanone (21) whereas in the case of (1c) the intramolecular cyclization of the adduct (4c) takes a somewhat different course yielding the dichlorofuranone (22) as a stable and nicely crystalline compound.
Contrary to ynamines "push-pull acetylenes" (1) undergo facile uncatalyzed additions of nucleophiles to the electrophilic triple bond\textsuperscript{1a,1b} like acetylene carbonyl compounds. In the case of bifunctional nucleophiles like hydrazine the reaction does not stop at the primary stage, but proceeds further even at low temperatures to give pyrazoles (23) and pyrazolones (24)\textsuperscript{1a}.

\[
\begin{align*}
\text{H} & \quad \text{N(CH}_3\text{)}_2 \\
\text{N} & \quad \text{H} \\
\text{23} & \quad \text{O} \\
\text{N} & \quad \text{H} \\
\text{24}
\end{align*}
\]

\[X = \text{H, CH}_3\]

However the structure of (23) and (24) allows no decision whether hydrazine attacks the triple bond or the deactivated carbonyl group first or even both at the same time. The reaction between (1) and substituted hydrazines like phenylhydrazine should give some insight into the course of the formation of (23), and (24). Treatment of the acetylenes (1) with phenylhydrazine at room temperature without solvent afforded the isomeric pyrazoles and pyrazolones, (25), (26), (27), and (28) respectively\textsuperscript{10}, indicating a primary addition of hydrazines to the triple bond as well as condensation with the carbonyl group of (1) followed by a ring closure of the intermediates (29), (30), (31), and (32).
\[ \text{1a, 1b} \]
\[ + \text{C}_6\text{H}_5\text{-NH-NH}_2 \]
\[ -\text{H}_2\text{O} \]
\[ \text{(CH}_3\text{)}_2\text{N-C} = \text{C} - \text{H} \quad \text{X} \]
\[ \text{29} \]
\[ \quad \text{(CH}_3\text{)}_2\text{N-C} = \text{C} - \text{C} \quad \text{X} \]
\[ \text{HN} - \text{N-C}_6\text{H}_5 \]
\[ \text{30} \]
\[ \quad \text{(CH}_3\text{)}_2\text{N-C} = \text{C} - \text{C} \quad \text{X} \]
\[ \text{HN} - \text{N-C}_6\text{H}_5 \]
\[ \quad \text{H} \quad \text{CH}_3 \]
\[ \text{26} \]
\[ \quad \text{X} \]
\[ \quad \text{a} \quad \text{b} \]
\[ \text{1c} \]
\[ + \text{C}_6\text{H}_5\text{-NH-NH}_2 \]
\[ -\text{CH}_3\text{OH} \]
\[ \text{(CH}_3\text{)}_2\text{N-C} = \text{C} - \text{H} \quad \text{COOCH}_3 \]
\[ \text{31} \]
\[ -\text{CH}_3\text{OH} \]
\[ \text{(CH}_3\text{)}_2\text{N} \quad \text{C}_6\text{H}_5 \quad \text{N} \quad \text{C}_6\text{H}_5 \quad \text{CO} \]
\[ \text{28} \]
\[ \text{(CH}_3\text{)}_2\text{N-C} = \text{C} - \text{C} \quad \text{X} \]
\[ \text{HN} - \text{N-C}_6\text{H}_5 \]
\[ \text{32} \]
\[ \text{(CH}_3\text{)}_2\text{N-C} = \text{C} - \text{C} \quad \text{X} \]
\[ \text{HN} - \text{N-C}_6\text{H}_5 \]
\[ \text{27} \]
<table>
<thead>
<tr>
<th>Compound</th>
<th>Yield [%]</th>
<th>mp/bp</th>
<th>$^1$H-NMR (in CDCl$_3$, $^6$TMS=0 ppm)</th>
<th>UV[$\lambda_{max}$ nm(log $\varepsilon$)]</th>
<th>IR[cm$^{-1}$, KBr]</th>
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<tbody>
<tr>
<td>(6)</td>
<td>65</td>
<td>184-185°C</td>
<td>3.00 (s, 6H), 3.17 (s, 6H), 3.86 (s, 3H), 3.88 (s, 3H)</td>
<td>230 (4.37), 258 (4.30)</td>
<td>1712, 1715, 1690, 1605, 1572</td>
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<tr>
<td>(7)</td>
<td>57</td>
<td>130-131°C</td>
<td>2.97 (s, 6H), 3.95 (s, 3H), 7.20-7.60 (m, 3H), 7.70-8.00 (m, 2H), 8.94 (bs, 1H)</td>
<td>246 (4.36), 277 (4.01)</td>
<td>2400-3200, 1682, 1645, 1629</td>
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<tr>
<td>(12)</td>
<td>75</td>
<td>179-180°C</td>
<td>3.20 (s, 3H), 3.25 (s, 3H), 3.93 (s, 3H), 14.10 (s, 1H)</td>
<td>236 (3.96), 288 (4.42)</td>
<td>2300-3200, 1759, 1643, 1610, 1554</td>
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<tr>
<td>(13)</td>
<td>96</td>
<td>152°C</td>
<td>3.29 (s, 3H), 3.32 (s, 3H), 3.93 (s, 3H), 4.12 (s, 3H)</td>
<td>236 (3.84), 296 (4.31)</td>
<td>1772, 1702, 1620, 1520</td>
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<td>(21)</td>
<td>40</td>
<td>192-130°C</td>
<td>3.13 (s, 6H), 3.59 (s, 3H), 6.12 (s, 1H), 9.86 (bs, 1H)</td>
<td>278 (4.08)</td>
<td>3540, 2300-3400, 1782, 1705, 1692, 1600</td>
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<td>(22)</td>
<td>72</td>
<td>115-116°C</td>
<td>3.34 (s, 6H), 3.83 (s, 3H)</td>
<td>241 (3.89), 283 (4.27)</td>
<td>1722, 1694, 1630</td>
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<td>(25a)</td>
<td>24</td>
<td>155°C/10$^-3$ Torr</td>
<td>2.85 (s, 6H), 5.74 (d, J=2.6Hz, 1H), 6.95-7.65 (m, 5H), 7.58 (d, J=2.6Hz, 1H)</td>
<td>297 (4.19)</td>
<td>1602, 1562</td>
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<td>(25b)</td>
<td>36</td>
<td>145°C/10$^-3$ Torr</td>
<td>2.20 (d, J=1Hz, 3H), 2.84 (s, 6H), 5.58 (q, J=1Hz, 1H), 7.10-7.50 (m, 5H)</td>
<td>290 (4.10)</td>
<td>1597, 1588, 1567</td>
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<tr>
<td>(26a)</td>
<td>30</td>
<td>155°C/10$^-3$ Torr</td>
<td>2.49 (s, 6H), 5.75 (d, J=1.8Hz, 1H), 7.44 (d, J=1.8Hz, 1H), 7.10-7.50 (m, 3H), 7.65-7.85 (m, 2H)</td>
<td>246 (4.09)</td>
<td>2998, 1550, 1495</td>
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<td>(26b)</td>
<td>22</td>
<td>145°C/10$^-3$ Torr</td>
<td>2.25 (d, J=0.4Hz, 3H), 2.52 (d, 6H), 5.61 (q, J=0.4Hz, 1H), 7.12-7.52 (m, 3H), 7.60-7.85 (m, 2H)</td>
<td>250 (4.11)</td>
<td>1598, 1590, 1554</td>
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<tr>
<td>(27)</td>
<td>50</td>
<td>136-137°C</td>
<td>2.90 (s, 6H), 3.46 (s, 2H), 7.00-7.50 (m, 3H), 7.80-8.05 (m, 2H)</td>
<td>254 (4.25), 279 (3.83), 288 (3.78), 303 (3.57)</td>
<td>1690, 1612, 1590, 1484, 1426</td>
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<tr>
<td>(28)</td>
<td>40</td>
<td>150-151°C</td>
<td>2.57 (s, 6H), 5.13 (s, 1H), 7.20-7.60 (m, 5H), 9.93 (bs, 1H)</td>
<td>253 (4.25)</td>
<td>2300-3200, 1594, 1586, 1570, 1545, 1523, 1496</td>
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</tbody>
</table>

[a] 60 MHz; [b] CH$_3$OH; [c] CH$_2$Cl$_2$; [d] dioxane; [e] film; [f] CCl$_4$.  

Table 1
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REFERENCES:

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8 Suggested by Prof. Dr. R.B. Woodward to H.J. Gais, 1975.
10 In completion of previously reported results. See ref. 1a).

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