

Elaref S. Ratemi, Nivedita Namdev and Martin S. Gibson*

Department of Chemistry, Brock University,
St. Catharines, Ont., Canada L2S 3A1

Received April 20, 1993

3-Substituted 2(1*H*)-pyridones are produced from reaction of 4-(4-morpholino)-3-pentenone **1** with each of the following carbon acids: cyanoacetamide, malononitrile, cyanothioacetamide, acetylacetamide, benzoyl-acetonitrile. Reaction of ethyl 3-(4-morpholino)-2-butenate **2** with cyanoacetamide gives the corresponding hydroxypyridone. Pyrimidines are formed by reaction of **1** and of **2** with benzamidine and with *S*-benzylthio-urea; in the last case, the eliminated morpholine displaces the benzylthio group to give the final product.

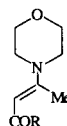
J. Heterocyclic Chem., **30**, 1513 (1993).

Introduction.

An interesting idea is explored in a new "3 + 3" pyridine synthesis [1] from primary enamionitriles and unsaturated ketones, namely that elimination of hydrogen cyanide can provide an alternative to oxidation or disproportionation in the path to the pyridine. In this synthesis, the pyridine nitrogen is supplied by the enamine, and the loss of hydrogen cyanide is mandated by substituent choice in the enamionitrile. We have been interested in a parallel route to pyridine derivatives, in which the group to be eliminated is contained in the unsaturated carbonyl component, as a result of observing formation of a highly substituted 2(1*H*)-pyridone from the reaction of 1,1-dipiperidinoethene with cyanoacetamide under basic conditions [2]. This reaction evidently involved Michael addition of the cyanoacetamide anion to the intermediate unsaturated carbonyl compound, followed by loss of piperidine and ring closure. We noted later that Kochetkov [3] had reacted 4-dimethylamino-3-butenone with cyanoacetamide in aqueous solution to obtain 3-cyano-6-methyl-2(1*H*)-pyridone and, while this reaction might have involved prior hydrolysis, were encouraged to pursue this approach further. In this paper, we examine the reactions of two push-pull alkenes, 4-(4-morpholino)-3-pentenone (**1**) and ethyl 4-(4-morpholino)-2-butenate (**2**), with various nitrogen-containing carbon acids and with amidines as sources of pyridine and pyrimidine derivatives.

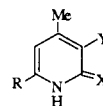
Results and Discussion.

Compound **1**, behaving as the Michael acceptor [2], reacted with cyanoacetamide in ethanol containing sodium ethoxide to give **3** in 54% yield. However, better yields were obtained by reacting the two components in aqueous acetic acid; the solution is buffered by release of morpholine as the reaction proceeds. Compound **3** was formed under similar conditions when malononitrile was used in place of cyanoacetamide. Compound **1** reacted very quickly with cyanothioacetamide in aqueous acetic acid to give **4**, and with acetylacetamide and benzoylacetonitrile to give **5** and **6**, respectively.



1: R = Me

2: R = OEt



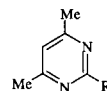
3: R = Me; X = O; Y = CN

4: R = Me; X = S; Y = CN

5: R = Me; X = O; Y = COMe

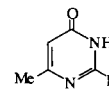
6: R = Me; X = O; Y = C(=O)Ph

7: R = OH; X = O; Y = CN



8: R = Ph

9: R = -SCH₂Ph



10: R = Ph

11: R = 4-morpholino

Compound **2** reacted with cyanoacetamide in ethanolic sodium ethoxide to give **7**. This compound has been formulated as the dihydroxypyridine [4], but tautomerism with either of two hydroxypyridones is possible. Compound **7** was also isolated from reaction of these two components in glacial acetic acid or, less satisfactorily, in *ca* 10% aqueous acetic acid under conditions otherwise similar to those used for the preparations of **3-6**. When the reaction was conducted in *ca* 5% aqueous acetic acid, an adduct of **7** and morpholine (possibly a dihydropyridine) was obtained. The FAB mass spectrum of this adduct showed a peak at *m/z* 238 (adduct + H⁺), but the EI mass spectrum (like the pmr and cmr spectra) was a composite of the spectra of **7** and morpholine. The adduct was converted into **7** under conditions used for the other preparations of **7**. A similar adduct was formed from reaction of **2** with cyanothioacetamide in 5% aqueous acetic acid, but no such adduct was observed in the reaction of **1** with cyanoacetamide.

These pyridone-forming reactions seem to be quite tolerant of conditions which may range from basic to acidic. We note that ring closure occurs preferentially *via* the carboxamide and thiocarboxamide groups when in competition with a cyano group, but that otherwise a cyano group

is incorporated as C2 of the pyridone in these syntheses. This route to pyridines takes advantage of reactive centre differentiation in push-pull alkenes and may in principle be extended by using other push-pull alkene/carbon acid combinations [2]. Such an approach to pyridines supplements syntheses in which a variety of push-pull alkenes, including primary enamionitriles [1,5], have been used as nucleophilic rather than electrophilic reagents [6].

In the foregoing experiments, molecules such as cyanoacetamide provide two donor centres for the construction of the pyridine ring, raising the question of whether a general pyrimidine synthesis might be carried out along similar lines. We found that **1** reacts with benzamidine and with *S*-benzylthiourea to give **8** and **9** respectively, while **2** and benzamidine give **10**. These reactions presumably involve Michael addition of the amidine to **1** or **2** via one nitrogen atom, with ring closure via the other. Morpholine is eliminated as in the previous pyridine syntheses. We noted with interest that **2** reacted with *S*-benzylthiourea to give **11**. The liberated morpholine is evidently displacing the *S*-benzyl group at C2 in the intermediate pyrimidine in this case. Such a nucleophilic substitution would be facilitated by the carbonyl group at C4. Since the amine liberated depends on the push-pull alkene employed, this reaction may have value for preparing specific 2-substituted pyrimidines.

EXPERIMENTAL

Melting points (°C) were determined on an Electrothermal melting point apparatus and are uncorrected. The ir spectra (potassium bromide discs, maxima in cm⁻¹) were recorded on an Analect FX 6260 FTIR spectrophotometer. Pmr and cmr spectra (peaks in ppm; exchangeable protons identified by use of deuterium oxide) were recorded on a Bruker AC200 spectrometer operating at 200 MHz (tetramethylsilane as the internal standard) and at 50 MHz (solvent as the internal standard) respectively. Mass spectra were recorded on an AEI MS30 double beam mass spectrometer interfaced to a Kratos DS 55 data system or a Kratos Concept 1S double focussing mass spectrometer, with glycerol or *m*-nitrobenzyl alcohol used as the matrix for FAB spectra. Thin layer chromatography (tlc) was performed on Merck silica gel 60F 254 slides.

For preparation of **1**, mp 45-46° (lit [7] mp 46-47°), the reaction time was shortened to 17 hours on the basis of pmr monitoring of the reaction [7]. The distilled compound, containing a trace of morpholine, was used for most reactions. For the preparation of **2**, 85% formic acid was used as catalyst in place of *p*-toluenesulfonic acid; the reaction time was 8 hours [7].

Benzamidine hydrochloride hydrate (moles of water unspecified) and *S*-benzylthiourea hydrochloride (hygroscopic) were commercial samples, and were used in excess of amounts calculated for anhydrous compounds.

General Procedures for 2(1*H*)-Pyridones.

(A) A solution or suspension of **1** or **2** (25 mmoles) and the carbon acid (25 mmoles) in glacial acetic acid (0.5-1.0 ml) and water (20 ml) was boiled under reflux (time and % yield in parentheses)

and then cooled. The product was filtered off and dried.

(B) A stirred solution of **1** or **2** (7.5 mmoles) and the carbon acid (7.5 mmoles) in absolute ethanol (75 ml) containing sodium ethoxide (from 12-20 mg-atoms of sodium) was boiled under reflux (time and % yield in parentheses). The solution was then concentrated *in vacuo* and cooled. The solid was collected, dissolved in water, and the solution was acidified to pH 3 by the addition of concentrated hydrochloric acid. The product was filtered off and dried.

3-Cyano-4,6-dimethyl-2(1*H*)-pyridone **3**.

This compound, prepared (method A) from **1** and cyanoacetamide (1.5 hours, 91%) or malononitrile (3 hours, 75%), crystallized from ethylene glycol as needles, mp 287-288° (lit [8] mp 288-289°); ir: 3280, 3130 (NH), 2203 (CN), 1650 (CO), and 1608 (C=C); pmr (DMSO-*d*₆): 2.23 (s, 3H, CH₃), 2.30 (s, 3H, CH₃), 6.16 (s, 1H, 5-H), and 12.3 (br s, 1H, NH, exchangeable); JMOD cmr (DMSO-*d*₆): 18.7 (4-CH₃), 20.5 (6-CH₃), 99.1 (C3), 107.3 (C5), 115.9 (CN), 151.0 (C4), 160.2 (C6), and 160.8 (C2) [5,9]; EI ms: *m/z* (%) 148 (M⁺, 100), 120 (22), and 119 (85); hrms: Calcd. for C₈H₈N₂O: 148.0637. Found: 148.0628.

Compound **3** was also prepared by method B from **1** and cyanoacetamide (3 hours, 54%).

3-Cyano-4,6-dimethyl-2(1*H*)-pyridinethione **4**.

This compound, prepared (method A) from **1** and cyanothioacetamide (3 hours, 98%), crystallized from ethanol as fine yellow crystals, mp 259-260° (lit [10] mp 264° dec after sintering at 250°); ir: 3180 (NH), 2217 (CN), 1611 (C=C), and 1205 (CS); pmr (deuteriochloroform/DMSO-*d*₆, 1:1): 1.39 (s, 6H, 2CH₃), 5.63 (s, 1H, 5-H), and 11.17 (br s, 1H, NH, exchangeable); pmr (pyridine-*d*₅): 2.00 (s, 3H, CH₃), 2.05 (s, 3H, CH₃), and 5.96 (s, 1H, 5-H) [11]; cmr (deuteriochloroform/DMSO-*d*₆, 1:1): 19.4 (4-CH₃), 24.0 (6-CH₃), 105.6 (C3), 114.1 (C5), 121.9 (CN), 151.6 (C4), 158.4 (C6), and 161.7 (C2); EI ms: *m/z* (%) 164 (M⁺, 100), 120 (46), and 119 (39); hrms: Calcd. for C₈H₈N₂S: 164.0408. Found: 164.0412.

3-Acetyl-4,6-dimethyl-2(1*H*)-pyridone **5**.

This compound, prepared (method A) from **1** and acetylacetamide (45 hours, 59%), crystallized from ethanol as needles, mp 216-217° (lit [12] mp 215-216°); ir: 3340 w, 3280, 3130 (NH), 1686 (CO) and 1650 (CO); pmr (deuteriochloroform): 2.27 (s, 3H, CH₃), 2.31 (s, 3H, CH₃), 2.95 (s, 3H, CH₃ of acetyl), 5.97 (s, 1H, 5-H), and 12.96 (br s, 1H, NH; exchangeable); cmr (deuteriochloroform): 18.7 (4-CH₃), 20.7 (6-CH₃), 31.6 (CH₃ of acetyl), 110.1 (C3), 125.8 (C5), 146.7 (C4), 154.0 (C6), 164.0 (C2), and 202.1 (CO); EI ms: *m/z* (%) 165 (M⁺, 79), 150 (100), and 122 (10); hrms: Calcd. for C₉H₁₁NO₂: 165.0789. Found: 165.0752.

3-Benzoyl-4,6-dimethyl-2(1*H*)-pyridone **6**.

This compound, prepared (method A) from **1** and benzoylacetonitrile (43 hours, 67%), crystallized from benzene as light yellow crystals, mp 227-229° (lit [13] mp 234°); ir: 1690 (CO), and 1645 (CO); pmr (deuteriochloroform): 2.11 (s, 3H, CH₃), 2.32 (s, 3H, CH₃), 6.09 (s, 1H, 5-H), and 7.49 (m, 5H, phenyl protons), and 11.9 (br s, 1H, NH, exchangeable); EI ms: *m/z* (%) 227 (M⁺, 26), 226 (73), 198 (29), 105 (61), and 77 (100); hrms: Calcd. for C₁₄H₁₃NO₂: 227.0946. Found: 227.0988 (Sample incompletely characterized).

3-Cyano-6-hydroxy-4-methyl-2(1*H*)-pyridone **7**.

A solution of **2** (9.95 g, 50 mmoles) and cyanoacetamide (4.20 g, 50 mmoles) in glacial acetic acid (30 ml) was refluxed for 42 hours. When cool, the mixture was neutralized by addition of 50% aqueous sodium hydroxide solution. The solid that separated was filtered off, washed with methanol, and dried. Crystallization from absolute ethanol gave **6** as a white powder (4.1 g, 55%), mp 314-318° dec (lit [4] mp 314-315°) [tlc (ethanol) showed a single component (R_f 0.51)]; ir: 3420 br (OH), 3230, 3100 (NH), 2203 (CN), 1650 (CO) and 1608 (C=C); pmr (DMSO- d_6): 1.95 (s, 3H, CH₃), 4.96 (s, 1H, 5-H), and 9.69 (br s, 2H, OH/NH, exchangeable); cmr (deuteriochloroform/DMSO- d_6 , 1:1): 19.0 (CH₃), 74.6 (C3), 97.6 (C5), 119.6 (CN), 152.3 (C4), 163.3 and 163.7 (C6 and C2); EI ms: m/z (%) 150 (M^+ , 100) and 122 (62); FAB ms: m/z 151 ($M+H^+$).

Compound **7** was also prepared from **2** and cyanoacetamide by method A using 10% aqueous acetic acid (4 hours, 20%) and by method B (23 hours, 29%).

Reaction of **2** with (a) Cyanoacetamide, (b) Cyanothioacetamide in 5% Acetic Acid.

(a) A solution of **2** (9.95 g, 50 mmoles) and cyanoacetamide (4.20 g, 50 mmoles) in glacial acetic acid (1 ml) and water (20 ml) was refluxed for 16 hours. When cool, the solution was brought to pH 7 by addition of 0.1M sodium hydroxide solution. Concentration at 50° *in vacuo* gave a solid (8.26 g, 70%) that crystallized from absolute ethanol to give light brown shiny crystals of the adduct, mp 235-238° [tlc (ethanol) showed a single component (R_f 0.34)]; ir: 3400 w, 3230 sh, 3080, 2205, 1650, and 1600; pmr (DMSO- d_6): 1.97 (s, 3H, CH₃), 3.12 (t, 4H, CH₂NCH₂), 3.76 (t, 4H, CH₂OCH₂), 4.97 (s, 1H, 5-H), 8.76 (br s, 2H, exchangeable), and 10.1 (br s, 1H, exchangeable); JMOD cmr (DMSO- d_6): 19.0, 41.6 (CH₂NCH₂), 61.9 (CH₂OCH₂), 75.4, 98.0, 119.4, 152.6, 163.3, and 163.9; FAB ms: m/z (%) 238 ($M+H^+$, 11) and 88 (morpholine + H^+ , 100).

The adduct (0.5 g, 2 mmoles) was refluxed for 16 hours in glacial acetic acid (1 ml) and water (10 ml). Adjusting the pH of the solution to 9 by adding 1M sodium hydroxide solution and then refrigerating overnight gave **7** as a crystalline solid (0.21 g, 66%), mp 300°, identified by comparison with the previous sample.

(b) In an analogous experiment, a suspension of **2** (1.99 g, 10 mmoles) and cyanothioacetamide (1.00 g, 10 mmoles) in glacial acetic acid (0.5 ml) and water (10 ml) was refluxed for 48 hours. A similar workup gave a solid (1.0 g, 40%) that crystallized from absolute ethanol to give fine pale yellow crystals of the corresponding adduct, mp 220-222° [tlc (ethanol) indicated one component (R_f 0.56)]; ir: 3450 br, 2440, 2202, and 1629 br (CO and C=C); pmr (DMSO- d_6): 2.01 (s, 3H, CH₃), 3.13 (t, 4H, CH₂NCH₂), 3.77 (t, 4H, CH₂OCH₂), 5.41 (s, 1H, 5-H), 8.77 (br s, 2H, exchangeable), and 10.4 (br s, 1H, exchangeable); JMOD cmr (deuteriochloroform/DMSO- d_6 , 1:1): 19.6 (CH₃), 42.1 (CH₂NCH₂), 62.2 (CH₂OCH₂), 93.8 (C3), 105.6 (C5), 119.0 (CN), 151.3 (C4), 161.8 (C6), and 174.0 (C2); FAB ms: m/z (%) 254 ($M+H^+$, 6) and 88 (morpholine + H^+ , 100).

4,6-Dimethyl-2-phenylpyrimidine **8**.

A mixture of **1** (4.57 g, 25 mmoles), benzamidine hydrochloride hydrate (4.87 g), and anhydrous sodium acetate (5.08 g, 62 mmoles) in glacial acetic acid (25 ml) was refluxed for 4.5 hours. The suspension was filtered while hot, and the filtrate was left to

cool. The crystalline deposit (mp 84°) was filtered off, and the mother liquor was neutralized to pH 7 by addition of 1M sodium hydroxide solution, whereupon a further quantity of crystals separated. The two crystalline deposits were identical (tlc) and were combined. Crystallization from benzene gave **8** (1.5 g, 33%), mp 80-84° (lit [8] mp 81-83°); pmr (deuteriochloroform): 2.52 (s, 6H, 2CH₃), 6.91 (s, 1H, 5-H), 7.44 (t, 3H, phenyl protons), and 8.41 (d, 2H, phenyl protons); JMOD cmr (deuteriochloroform): 24.1 (CH₃), 117.9 (C5), 128.1, 128.3, 130.2 (unsubstituted phenyl carbons), 138.1 (substituted phenyl carbon), 164.1 (C2), and 166.6 (C4 and C6) [14]; EI ms: m/z (%) 184 (M^+ , 100), 169 (25), and 103 (46); hrms: Calcd. for C₁₂H₁₂N₂: 184.1000. Found: 184.1004.

2-Benzylthio-4,6-dimethylpyrimidine **9**.

A mixture of **1** (5 ml, *ca* 25 mmoles) and S-benzylthiourea hydrochloride (5 g) was refluxed for 5.5 hours. When cool, the supernatant liquid was drained from the greasy solid, and the liquid was refrigerated. A waxy solid, mp 54-56°, separated. Crystallization from ethanol and lengthy cooling gave **9** (1.4 g, 24%) as needles, mp 63° (lit [15] mp 64.5-65°); pmr (acetone- d_6): 2.30 (s, 6H, 2CH₃), 4.32 (s, 2H, CH₂), 6.74 (s, 1H, 5-H), and 7.20-7.38 (m, 5H, phenyl protons); JMOD cmr (acetone- d_6): 23.8 (CH₃), 35.4 (CH₂), 116.7 (C5), 127.9, 129.3, 130.0 (unsubstituted phenyl carbons), 139.7 (substituted phenyl carbon), 168.2 (C4 and C6), and 171.0 (C2); EI ms: m/z (%) 230 (M^+ , 100), 197 (76), 108 (50), and 91 (79); hrms: Calcd. for C₁₃H₁₄N₂S: 230.0878. Found: 230.0867.

Trituration of the greasy solid (see above) with cold ethanol gave colorless needles, identified (pmr spectrum) as morpholine hydrochloride.

6-Methyl-2-phenyl-4(3H)-pyrimidone **10**.

A mixture of **2** (5.0 ml, *ca* 25 mmoles) and benzamidine hydrochloride hydrate (3.9 g) was simmered under reflux for 5.5 hours. When cool, the solid (700 mg, 15%) that separated was filtered off and crystallized from ethanol to give **10** (400 mg, 9%) as shiny fluffy crystals, mp 220° (lit [16] mp 218-221°); ir: 3200 br (NH) and 1674 (CO); pmr (deuteriochloroform/DMSO- d_6): 2.38 (s, 3H, CH₃), 6.25 (s, 1H, 5-H), 7.46-8.18 (m, 5H, phenyl), and 10.1 (br s, 1H, NH, exchangeable); JMOD cmr (deuteriochloroform/DMSO- d_6): 23.7 (CH₃), 110.6 (C5), 127.5, 128.4, 131.4 (unsubstituted phenyl carbons), 132.0 (substituted phenyl carbon), 156.3 (C6), 164.2 (C2), and 165.0 (C4); EI ms: m/z (%) 186 (M^+ , 100), 158 (21), 104 (65), 83 (38), and 77 (30); hrms: Calcd. for C₁₁H₁₀N₂O: 186.0793. Found: 186.0789.

6-Methyl-2-(4-morpholino)-4(3H)-pyrimidone **11**.

A mixture of **2** (5 ml, *ca* 25 mmoles) and S-benzylthiourea hydrochloride (5.1 g) was simmered for 6 hours. Cooling gave a gummy solid that was dissolved in hot absolute ethanol. The crystals (mp 215-225°) obtained on chilling were collected and recrystallized from ethanol to give **11** as light yellow crystals (1.6 g, 33%), mp 240° (lit [17] mp 239-243°); ir: 3320-3180 (NH) and 1690 (CO); pmr (deuteriochloroform): 2.20 (s, 3H, CH₃), 3.77 (s, 8H, morpholino H, partially resolved to d on addition of deuterium oxide), and 5.66 (s, 1H, 5-H); JMOD cmr (deuteriochloroform): 24.0 (CH₃), 45.1 (CH₂NCH₂), 66.7 (CH₂OCH₂), 100.8 (C5), 153.5 (C6), 166.1 (C2), and 166.9 (C4); EI ms: m/z (%) 195 (M^+ , 47), 165 (25), 164 (63), 150 (35), 138 (70), and 110 (100); hrms: Calcd. for C₉H₁₃N₃O₂: 195.1007. Found: 195.1021.

Acknowledgement.

We thank the Natural Sciences and Engineering Research Council of Canada for partial financial support.

REFERENCES AND NOTES

- [1] J. M. Robinson, L. W. Brent, C. Chau, K. A. Floyd, S. L. Gilham, T. L. McMahan, D. J. Magda, T. L. Motycka, M. J. Pack, A. L. Roberts, L. A. Seally, S. L. Simpson, R. R. Smith and K. N. Zalesny, *J. Org. Chem.*, **57**, 7352 (1992).
- [2] S. S. Gandhi and M. S. Gibson, *Can. J. Chem.*, **65**, 2717 (1987).
- [3] N. K. Kochetkov, *Izv. Akad. Nauk. SSSR, Otdel. Khim. Nauk*, **47** (1954); *Chem. Abstr.*, **49**, 6090 (1955).
- [4] T. R. Kasturi, V. K. Sharma and A. Srinivasan, *Tetrahedron*, **29**, 4103 (1973).
- [5] J. Světlik, I. Goljer and F. Tureček, *J. Chem. Soc., Perkin Trans. I*, 1315 (1990).
- [6] Cf. E. Hardegger and E. Nickles, *Helv. Chim. Acta*, **40**, 1016 (1957); A. Dornow and H. V. Plessen, *Chem. Ber.*, **99**, 244 (1966); German Patent 1,207,930 (1965); *Chem. Abstr.*, **64**, 9694 (1966); O. Makabe, Y. Murai and S. Fukatsu, *Heterocycles*, **13**, 239 (1979); T. Kato, H. Yamamaka and T. Hozumi, *Yakugaku Zasshi*, **91**, 772 (1971); *Chem. Abstr.*, **75**, 129623 (1971).
- [7] P. W. Hickmott and G. Sheppard, *J. Chem. Soc., Perkin Trans. I*, 1038 (1972). Hickmott and Sheppard reported that **1** undergoes self-condensation to give 2,6-dimethyl-4-(4-morpholino)acetophenone on prolonged refluxing in benzene. The same compound is apparently formed when **1** reacts with acetylacetone in aqueous acetic acid; a synthesis of substituted benzenes might be developed along these lines.
- [8] C. A. C. Haley and P. Maitland, *J. Chem. Soc.*, 3155 (1951) and references cited.
- [9] Cf. C. Peinador, V. Ojea and J. M. Quintela, *J. Heterocyclic Chem.*, **29**, 1693 (1992).
- [10] U. Schmidt and H. Kubitzek, *Chem. Ber.*, **93**, 1559 (1960).
- [11] Sensitivity of chemical shifts to solvent changes has been noted previously in the pyridine series; cf. T. Schaefer and W. G. Schneider, *J. Chem. Phys.*, **32**, 1224 (1960).
- [12] T. Kato and M. Noda, *Chem. Pharm. Bull. Japan*, **24**, 303 (1976).
- [13] H. Jahine, H. A. Zaher, A. A. Sayed and M. Seada, *J. Prakt. Chem.*, **316**, 337 (1974).
- [14] Cf. A. G. Martínez, A. Herrera, R. Martínez, E. Teso, A. García, J. Osío, L. Pargada, R. Unanue, L. Subramanian and M. Hanack, *J. Heterocyclic Chem.*, **25**, 1237 (1988).
- [15] J. E. Cranham, W. A. W. Cummings, A. M. Johnston and H. A. Stevenson, *J. Soc. Food Agr.*, **9**, 143 (1958); *Chem. Abstr.*, **52**, 11773e (1958).
- [16] A. Sitte and H. Paul, *Chem. Ber.*, **102**, 615 (1969); cf. A. Pinner, *Ber.*, **17**, 2519 (1884); *ibid.*, **18**, 760 (1885); *ibid.*, **22**, 1624 (1889).
- [17] B. Roth and L. A. Schlomer, *J. Org. Chem.*, **26**, 2659 (1963).