mp 141–142 °C. Anal. Calcd for $C_{28}H_{42}N_4O_8$: C, 59.77; H, 7.52; N, 9.96. Found: C, 59.98; H, 7.21; N, 9.96.

5-Hexadecanoyl-*N,N'*-dimethylbarbituric Acid (2d). This compound was prepared in a manner similar to that described above for 7. Colorless crystals were obtained in 96% yield, mp 68–69 °C after recrystallization from hexane. Anal. Calcd for $C_{22}H_{38}N_2O_4$: C, 66.97; H, 9.71; N, 7.10. Found: C, 66.92; H, 9.71; N, 7.07.

Conversion of 8 to Eicosanedioic Acid. Compound 8, 0.50 g (0.88 mmol), was refluxed with 2.0 g of KOH in 10 mL of ethylene glycol under a nitrogen atmosphere for 1 day. The ethylene glycol was distilled off under reduced pressure and 15 mL of a 30% solution of HBr in acetic acid added to the residue. The mixture was refluxed for 1 day, filtered while hot, rinsed with 5 mL of hot acetic acid, and diluted with 65 mL of water. The dark colored crude product was removed by filtration and washed with water to give 0.22 g, mp 108–115 °C. Recrystallization from acetic acid afforded 90 mg (30% yield) of pure product as colorless crystals, mp 121–123 °C (lit.[26] mp 122–123 °C), which was converted to the diethyl ester, mp 53–54 °C (lit.[26] mp 54.5–55 °C).

Acknowledgment. We are grateful for support from a Cottrell College Science Grant awarded by the Research Corporation.

Registry No. 1a, 64074-05-1; **1b**, 74965-86-9; **1c**, 74965-87-0; **2a**, 58713-10-3; **2b**, 74965-88-1; **2c**, 58713-08-9; **2d**, 74965-89-2; **3a**, 4139-73-5; **3b**, 4139-74-6; **3c**, 36953-87-4; **3d**, 74965-90-5; **4a**, 74965-91-6; **4b**, 74965-92-7; **4c**, 3709-38-4; **5a**, 1953-33-9; **5b**, 14077-80-6; **5c**, 1953-34-0; **5d**, 74965-93-8; **6a**, 6617-70-5; **6b**, 21315-30-0; **6c**, 74965-94-9; **6d**, 74965-95-0; **7**, 74965-96-1; **8**, 74965-97-2; **9**, 771-03-9; **10**, 50607-35-7; pentanoic acid, 109-52-4; 4-methylpentanoic acid, 646-07-1; 4-phenylbutanoic acid, 1821-12-1; sodium cyanoborohydride, 25895-60-7; acetic acid, 64-19-7; hexadecanedioic acid, 505-54-4; hexadecanedioic acid chloride, 34959-19-8; *N,N'*-dimethylbarbituric acid, 769-42-6; eicosanedioic acid, 2424-92-2; diethyl eicosanedioate, 42235-39-2.

Reaction of 3-Amino-2-benzoylcrotonate Esters with Phosgene

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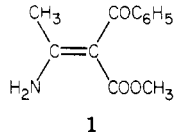
Received February 27, 1980

Phosgene, in the presence of 2,6-lutidine, reacts with alkyl esters of 3-amino-2-benzoylcrotonic acid to give as major products 1,3-oxazin-2-ones, formally derived from the reaction of 2 equiv of amino ester with 2 and 3 equiv of phosgene. Ethyl 3-amino-2-benzoyl-2-pentenoate reacts with phosgene–2,6-lutidine to give a 1,3-oxazin-2-one derived from the reaction of 1 equiv of phosgene and 1 equiv of amino ester. Diethyl 3-amino-2-benzoylglutaconate reacts with phosgene–2,6-lutidine to give both a "1:1" 1,3-oxazin-2-one and a 4-aminopyrone.

Some time ago, we reported that benzoyl chloride reacts with methyl 3-aminocrotonate to produce the C-benzoylated isomer 1.[1] Recently we examined the reaction



1

of 1 with phosgene to see if cyclic products could be obtained. In fact, phosgene reacts readily with an ether solution of 1 and 2,6-lutidine at room temperature to produce a complex mixture which was separated into an ether-soluble and an ether-insoluble fraction.

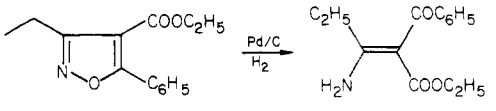
The ether-insoluble material (50% of the mass balance) was fractionally crystallized from glacial acetic acid to give two compounds in a 4:1 ratio. The major component was a yellow solid, mp 192 °C [UV ($CHCl_3$) λ_{max} 353 nm (ϵ_{max} 36 445)], which exhibited a carbonyl stretching absorption at 1775 cm^{-1} characteristic of 1,3-oxazin-2-one.[2] Its empirical formula of $C_{26}H_{22}N_2O_8$ (high-resolution mass spectrum and elemental analysis) corresponded to a product of the reaction of 2 equiv of 1 and 2 equiv of phosgene. In addition to the 1775-cm^{-1} absorption and an ester carbonyl band at 1740 cm^{-1}, an infrared absorption band was present at 1667 cm^{-1}, typical of the benzoyl group of starting material 1. The ^1H NMR spectrum indicated one allylic methyl group, two dissimilar methoxy groups, one vinyl hydrogen, and two dissimilar amide protons. Two kinds of aromatic resonances were present. One was the typical 3:2 multiplet pattern centered at δ 7.5 and 8.3

(1) R. T. Buckler, H. E. Hartzler, and B. M. Phillips, *J. Med. Chem.*, 18, 509 (1975).

(2) L. Kozeski, *Tetrahedron*, 32, 1299 (1976).

(3) The oxazine 12 exhibited only bonded NH in the IR spectrum and the position of its vinyl proton in the ^1H NMR spectrum (δ 5.22) was exactly the same as that in 4. On this basis we assign *Z* stereochemistry to the side chains of both 4 and 12.

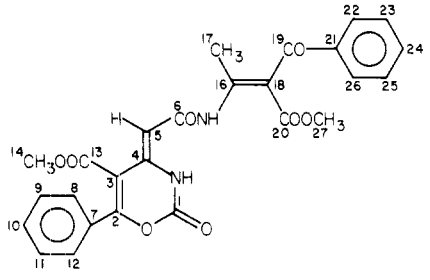
(4) Prepared by first heating 24 g (0.1 mol) of ethyl 3-pyrrolidin-1-ylcinnamate, 10.7 g (0.12 mol) of 1-nitropropane, and 26.2 g (0.22 mol) of phenyl isocyanate in benzene/triethylamine [G. Stork and J. E. McMurry, *J. Am. Chem. Soc.*, 89, 5461 (1967)] to give 4-carbethoxy-3-ethyl-5-phenylisoxazole (ii): b.p. 108–118 °C (0.1 mmHg); IR (CCl_4) 1720 cm^{-1} (CO); ^1H NMR (CCl_4) δ 1.3 (t, J = 8 Hz, 3 H, CH_2CH_3), 1.35 (t, J = 6 Hz, 3 H, OCH_2CH_3), 2.95 (q, J = 8 Hz, 2 H, CH_2CH_3), 4.3 (q, J = 6 Hz, 2 H, OCH_2CH_3), 7.3–8.0 (m, 5 H, C_6H_5); exact mass calcd for $C_{14}H_{15}NO_3$ *m/e* 245.105 10, found 245.106 22. Hydrogenation of 10.4 g of ii (Pd/C, 50 psig, EtOH) gave a quantitative yield of ethyl 3-amino-2-benzoylpent-2-enoate (iii) as a clear oil: IR ($CHCl_3$) 3470 (NH), 1700–1600 (CO's); ^1H NMR ($CDCl_3$) δ 0.7 (t, J = 8 Hz, 3 H, OCH_2CH_3), 1.3 (t, J = 8 Hz, 3 H, CH_2CH_3), 2.62 (q, J = 8 Hz, 2 H, CH_2CH_3), 3.9 (q, J = 8 Hz, 2 H, OCH_2CH_3), 7.2–8.0 (m, 5 H, C_6H_5); exact mass calcd for $C_{14}H_{17}NO_3$ *m/e* 247.120 74, found 247.124 17.



ii iii

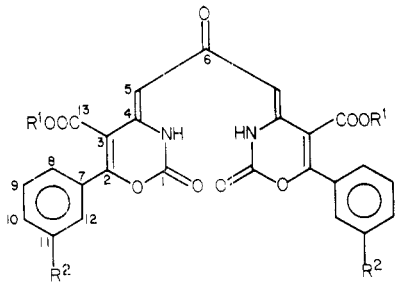
0022-3263/80/1945-4608$01.00/0

($CDCl_3$), characteristic of a benzoyl group; the other was a five-proton singlet at δ 7.4, characteristic of an unconjugated phenyl group. The ^{13}C NMR spectrum confirmed the presence of 26 carbon atoms (see paragraph at the end of the paper about Supplementary Material). From this information we assigned the structure of the major component of the ether-insoluble fraction as the 1,3-oxazinylidin-2-one **2**.



2

The minor component **3** of the ether-insoluble fraction also displayed an infrared stretching absorption at 1780 cm^{-1} characteristic of a 1,3-oxazin-2-one. It was a deep yellow solid, mp 254 °C [UV ($CHCl_3$) λ_{max} 415 nm (ϵ_{max} 58320)]. Its empirical formula of $C_{27}H_{20}N_2O_9$ (high-resolution mass spectrum and elemental analysis) corresponded to structure **2** plus an additional molecule of CO, suggesting it to be the product of the further reaction of **2** with phosgene. However, **2** could not be induced to react with phosgene even under forcing conditions. Unfortunately, **3** was too insoluble to allow its NMR spectrum to be taken. In order to obtain a more soluble analogue, *tert*-butyl 3-amino-2-(3-bromobenzoyl)crotonate (**4**) was prepared and reacted with phosgene–2,6-lutidine. This reaction gave **5**, the 3-bromo *tert*-butyl ester analogue of **2**, and a smaller amount of a high-melting yellow solid **6**.



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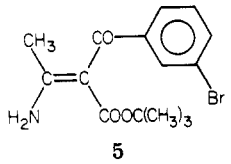

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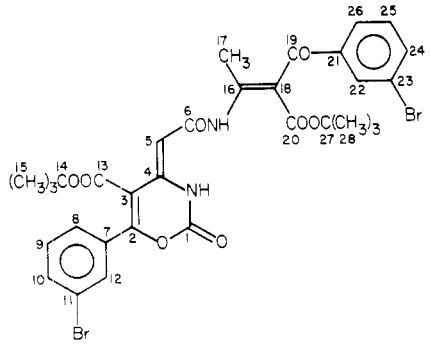
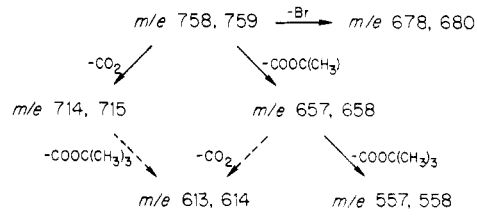


3, $R^1 = CH_3$; $R^2 = H$

6, $R^1 = C(CH_3)_3$; $R^2 = Br$

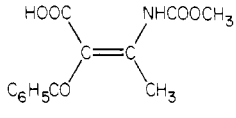
The ^1H NMR spectrum of **6** exhibited singlets for *tert*-butyl, vinyl, and NH protons, and its ^{13}C NMR showed only 15 unique carbons out of a total of 33 present. The IR displayed no benzoyl carbonyl stretching frequency. These findings led us to the assignment of a symmetrical diketone structure for **3** and **6**.

Scheme I. Major Fragments of 6

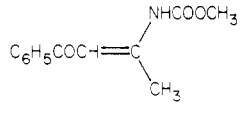


The mass spectrum (field desorption) of **6** exhibited a pattern consistent with the presence of two bromine atoms. Intense parent ions occurred at *m/e* 756 ($^{79,79}Br$), 758 ($^{79,81}Br$), and 760 ($^{81,83}Br$) along with the corresponding protonated parent ions *m/e* 757, 759, and 761. Other major fragmentations of **6** are shown in Scheme I and consist of loss of Br (*m/e* 80), CO_2 (*m/e* 44), and (*tert*-butyloxy)carbonyl (*m/e* 101). The observation that loss of CO_2 occurs independently of loss of (*tert*-butyloxy)carbonyl in the parent ion and possibly from fragment *m/e* 657, 658 lends support to the assignment of two distinct COO and $COOC(CH_3)_3$ groupings in 6.

The ether-soluble fraction from the reaction of**1** with phosgene–2,6-lutidine amounted to 8% of the theoretical mass balance (the rest was tar). From this we obtained a 1% recovery of unreacted **1** and two new compounds in a ratio of 10:1. The major component of this fraction was separated by extraction with aqueous $NaHCO_3$ and identified as (*Z*)-2-benzoyl-3-[(carbomethoxy)amino]crotonic acid (**7**) (elemental analysis, mass spectrum, ^1H and ^{13}C NMR, and IR spectra). The minor component was determined to be 3-[(carbomethoxy)amino]crotonophenone (**8**), the decarboxylation product of **7**.



7



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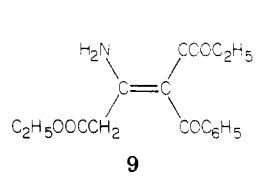
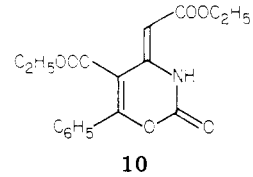
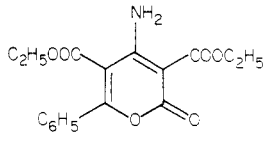
Next we examined the reaction of diethyl 3-amino-2-benzoylglutaconate (**9**) with phosgene–2,6-lutidine. A mixture resulted from which compounds **10** and **11** were



9



10



11

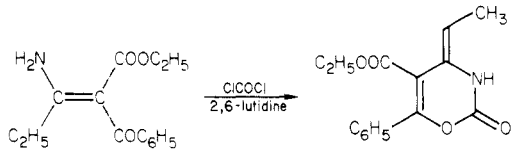
separated by silica gel chromatography. The less polar compound **10** (30% yield) was a yellow solid [UV ($CHCl_3$) λ_{max} 320 nm (ϵ_{max} 19967)] whose IR spectrum ($CHCl_3$) exhibited the 1,3-oxazinone CO band at 1775 cm^{-1} together with both bonded and non-bonded ester carbonyls at 1735 and 1725 cm^{-1}.[5] Its ^1H NMR spectrum ($CDCl_3$) displayed an NH singlet at δ 11.0, a vinyl H at δ 5.23, two dissimilar ethoxy groups, and a phenyl singlet at δ 7.5. This evidence, together with the empirical formula of $C_{12}H_{17}NO_6$ (high-

(5) L. J. Bellamy, "Infrared Spectrs of Complex Molecules", 3rd ed., Chapman & Hall, Ltd., London, 1975, p 204.

resolution mass spectrum and elemental analysis), was compatible with 4-(carbethoxy-methylene)-5-carbethoxy-3,4-dihydro-6-phenyl-2*H*-1,3-oxazin-2-one (**10**).

The second-eluted compound, **11** (15% yield), was a white solid [UV ($CHCl_3$) λ_{max} 290, 320 nm (ϵ 8508, 8207)] having the same empirical formula as **10**. Its IR spectrum exhibited a carbonyl band at 1775 cm^{-1}, suggestive of a 2-pyrone,[6] and an ester band at 1690 cm^{-1}. The ^1H NMR spectrum displayed a two-proton NH_2 singlet at δ 9.8, no vinyl hydrogen, two dissimilar ethoxys, and a phenyl multiplet centered at δ 7.8. This suggested **11** to be 4-amino-3,5-bis(carbethoxy)-6-phenyl-2*H*-pyran-2-one.

In contrast to **1**, the reaction of ethyl 3-amino-2-benzoylpent-2-enoate (**12**) with phosgene was sluggish;



12 **13**

mostly unreacted **12** was recovered after 5 days at room temperature. However, a small amount of a pale yellow solid **13** was isolated [UV ($CHCl_3$) λ_{max} 310 nm (ϵ_{max} 7434)] that possessed CO bands at 1765, 1725, and 1715 cm^{-1}. The ^1H NMR spectrum ($CDCl_3$) in addition to one ethoxy group showed an allylic methyl doublet at δ 1.7 coupled to a vinyl H multiplet centered at δ 4.8 (J = 7 Hz), a phenyl multiplet centered at δ 7.45 and a one proton NH singlet at δ 8.35. This and the elemental analysis were consistent with 5-carbethoxy-4-ethylidine-3,4-dihydro-6-phenyl-2*H*-1,3-oxazin-2-one.

Mechanism of Formation of 2, 3, and 7. Compound **1** reacts with phosgene–2,6-lutidine to give both the *E* and *Z* isocyanates **14**, which do not readily interconvert. The *E* isocyanate probably cyclizes to the oxazine **15**. Since neither **15** nor its tautomer could be detected in the reaction mixture, it must react further with starting material to give **2** or with its precursor to give **3** (Scheme II).

The crotonic acid **7** must arise from the *Z* isocyanate **14** by rearrangement of the methoxy group to give **16** followed by addition of H_2O.

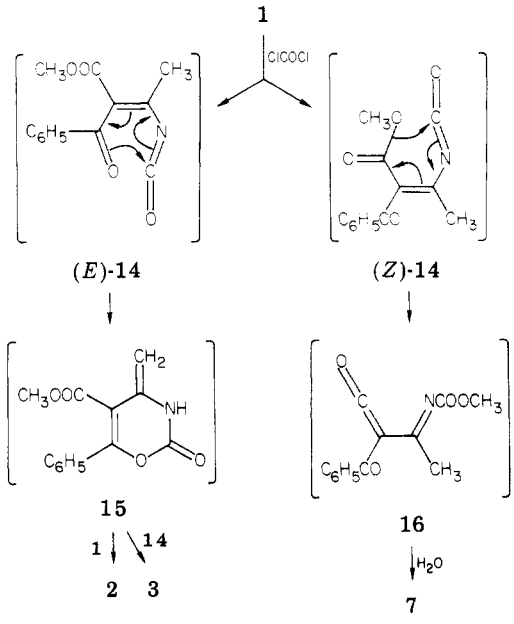
In contrast to **1**, the amino esters **9** and **12** give rise to oxazines **10** and **13**, which are the products of the reaction of 1 equiv of phosgene with 1 equiv of ester. No "2:2" products analogous to **2** or **3** were detected. This is perhaps due to steric hindrance to attack of the corresponding isocyanate intermediates on the substituted methylene groups of **10** and **13**.

Experimental Section

Mass spectra were taken on an Associated Electronic Industries MS 902. ^1H and ^{13}C NMR were taken on a Varian T 60 A or XL-100 spectrometer. Melting points are uncorrected.

Oxazines 2 and 3. A mixture of 55 g (0.25 mol) of methyl 3-amino-2-benzoylcrotonate (**1**),[1] 62 g (0.6 mol) of 2,6-lutidine, and 1 L of anhydrous ether was cooled to 0 °C while being stirred. A solution of 30 g (0.3 mol) of phosgene in 200 mL of anhydrous ether was added dropwise over a period of 1 h. After an additional three h at 0 °C, the reaction was allowed to warm to room temperature and stir for 3 days during which time a heavy yellow precipitate formed. The reaction was mixed with 750 mL of H_2O to dissolve the coprecipitated lutidine hydrochloride and then filtered. The yellow precipitate was recrystallized from methanol and then from acetic acid to give 2.8 g of the ketone **3** as fine yellow crystals: mp 254 °C dec; IR (KCl) 1780 (CO), 1728 (ester CO), 1720 cm^{-1} (ketone CO); exact mass calcd for $C_{27}H_{20}N_2O_9$ m/e 516.1167 (M^+), found 516.1227.

Scheme II



Dilution of the acetic acid filtrate with H_2O gave 20 g of **2**: mp 191–192 °C; IR ($CHCl_3$) 1775 (CO), 1725 (CO, ester), 1665 cm^{-1} (CO, ketone); ^1H NMR ($CDCl_3$) δ 2.35 (s, 3 H, CH_3). Anal. Calcd for $C_{26}H_{22}N_2O_8$: C, 63.67; H, 4.52; N, 5.71. Found: C, 63.54; H, 4.53; N, 5.61.

Oxazines 5 and 6. To a cold stirred solution of 24 g (0.07 mol) of **4**[1] and 18 g (0.17 mol) of 2,6-lutdine in 250 mL of anhydrous ether was added 8.4 g (0.08 mol) of phosgene in 50 mL of ether. After the mixture was stirred for 4 days at room temperature, water was added. The ether phase was separated, dried, and evaporated. The residue was extracted with eight 400-mL portions of boiling hexane. The extracts were pooled and evaporated, and the residue was recrystallized from methanol to give 6.8 g (27% yield) of oxazine **5** as fine yellow needles: mp 170–171 °C; IR ($CHCl_3$) 1780, 1725, 1660 cm^{-1} (CO's); ^1H NMR ($CDCl_3$) δ 1.30 and 1.50 (2 s, 9 H each, 2 $OC(CH_3)_3$), 2.45 (s, 3 H, CH_3), 5.30 (s, 1 H, vinyl), 7.2–8.0 (m, 8 H, 2 C_6H_4), 11.8 and 11.9 (2 s, 1 H each, 2 NH). Anal. Calcd for $C_{32}H_{32}Br_2N_2O_8$: C, 52.47; H, 4.40; N, 3.83. Found: C, 52.36; H, 4.41; N, 3.75.

The residue that was insoluble in boiling hexane was triturated with acetone to give a solid. Recrystallization from chloroform–methanol gave 400 mg of **6** as fine yellow needles: mp 233–235 °C dec; IR ($CHCl_3$) 1775 and 1725 cm^{-1} (CO); ^1H NMR ($CDCl_3$) δ 1.4 (s, 18 H, *tert*-butyl's), 5.45 (s, 2 H), 7.2–7.8 (m, 8 H, aromatic), 12.7 (s, 2 H, NH). Anal. Calcd for $C_{33}H_{30}Br_2N_2O_9$: C, 52.26; H, 3.99; N, 3.69. Found: C, 52.56; H, 4.03; N, 3.65.

2-Benzoyl-3-[(carbomethoxy)amino]crotonic Acid (7) and 3-[(Carbomethoxy)amino]crotonophenone (8). The ether filtrate from the reaction that produced **2** and **3** was evaporated to give an oil. It was triturated with 1 L of boiling pentane and the residue twice recrystallized from CCl_4 to give 4.3 g of **7** as white crystals: mp 156–157 °C dec; IR ($CHCl_3$) 3500 (NH), 3400–2400 (COOH), 750 cm^{-1} (CO); ^1H NMR ($CDCl_3$) δ 2.2 (s, 3 H, $C{=}CCH_3$), 3.7 (s, 3 H, OCH_3), 7.2–8.0 (m, 5 H, C_6H_5), 11.8 and 12.0 (2 s, 2 H, NH and COOH). Anal. Calcd for $C_{13}H_{13}NO_5$: C, 59.31; H, 4.98; N, 5.32; m/e 263.0793 (M^+). Found: C, 58.77; H, 4.89; N, 5.30; m/e 263.0784.

The pentane from the trituration step was evaporated to give an oil that was chromatographed on silica gel, eluting with benzene, to give 360 mg of **8** as a white solid: mp 81–83 °C; IR ($CHCl_3$) 1745 (CO), 1660 cm^{-1} (C=C); ^1H NMR ($CDCl_3$) δ 2.5 (s, 3 H, $C{=}CCH_3$), 3.7 (s, 3 H, OCH_3), 6.0 (s, 1 H, $COCH{=}C$), 7.4–8.1 (m, 5 H, C_6H_5), 12.0 (s, 1 H, NH); exact mass calcd for $C_{12}H_{13}NO_3$ m/e 219.0870 (M^+), found 219.0892.

Compound **8** could be produced by thermal decarboxylation of **7**. When 1 g of **7** was heated at 160 °C (0.05 mm) in a vacuum-distillation apparatus, 0.4 g of **8** collected and solidified in

(6) R. N. Jones, C. Angell, T. Itoh, and R. J. D. Smith, *Can. J. Chem.*, 37, 2007 (1959).

the receiver. It had mp 81–83 °C and was identical in all respects with the material described above.

Diethyl 3-Amino-2-benzoylglutaconate (9). A solution of 74 g (0.33 mol) of diethyl 3-aminoglutaconate and 36 g (0.33 mol) of 2,6-lutidine in 500 mL of THF was stirred at reflux while 47 g (0.33 mol) of benzoyl chloride was added dropwise over a 30-min period. After the mixture was heated overnight the solvent was evaporated and the residue partitioned between ether and H_2O. The ether phase was separated, dried, and evaporated to give an oily residue which was chromatographed on 400 g of Florisil. Elution with 6 L of 4:1 (v/v) pentane–benzene removed the N-benzoylated isomer. Further elution with 4 L of ether removed the C-benzoylated isomer **9**. Recrystallization from ethyl acetate–pentane gave 19 g (19% yield) of **9** as white crystals, mp 77 °C. Anal. Calcd for $C_{16}H_{19}NO_5$: C, 62.94; H, 6.27; N, 4.59. Found: C, 63.04; H, 6.37; N, 4.45.

Oxazine 10 and Pyrone 11. A solution of 6.1 g (0.02 mol) of diester **9** and 4.3 g (0.04 mol) of 2,6-lutidine in 100 mL of dry ether was cooled to 0 °C and combined with 2 mL of phosgene in 20 mL of ether. The reaction was allowed to stand for 15 days under an inert atmosphere. Water was added and the layers were separated. Evaporation of the ether layer gave an oil which was chromatographed on 1 kg of silica gel. The column was eluted with 19:1 (v/v) CCl_4–acetone and 20-mL fractions were collected. Fractions 228 to 252 were combined and evaporated, and the residue was recrystallized from ether–pentane to give 2 g (30% yield) of oxazinone **10** as yellow crystals: mp 97 °C; IR ($CHCl_3$) 1775, 1735, 1725 cm^{-1} (CO); ^1H NMR ($CDCl_3$) δ 1.04 and 1.30 (2 t, J = 8 Hz, 6 H, 2 OCH_2CH_3), 4.2 (2 q, J = 8 Hz, 4 H, 2 OCH_2CH_3), 5.23 (s, 1 H, vinyl), 7.5 (s, 5 H, C_6H_5), 11.0 (s, 1 H, NH). Anal. Calcd for $C_{17}H_{17}NO_6$: C, 61.61; H, 5.17; N, 4.23; m/e 331.1055 (M^+). Found: C, 61.40; H, 5.19; N, 4.23; m/e 331.1068.

Fractions 276 to 324 were pooled and evaporated, and the residue was recrystallized from ether–pentane to give 1 g (15% yield) of the pyrone **11** as white crystals: mp 87 °C; IR ($CHCl_3$) 3400, 3250 (NH_2), 1755–1690 cm^{-1} (CO's); ^1H NMR ($CDCl_3$) δ 0.8 (t, J = 8 Hz, 3 H, OCH_2CH_3), 1.4 (t, J = 7 Hz, 3 H, OCH_2CH_3), 3.95 (q, J = 8 Hz, 2 H, OCH_2CH_3), 4.39 (q, J = 7 Hz, 2 H, OCH_2CH_3), 7.4–8.2 (m, 5 H, C_6H_5), 9.8 (s, 2 H, NH_2). Anal. Calcd for $C_{17}H_{17}NO_6$: C, 61.61; H, 5.17; N, 4.23; m/e 331.1055 (M^+). Found: C, 61.32; H, 5.05; N, 4.08; m/e 331.1072.

5-Carbethoxy-4-ethylidine-3,4-dihydro-6-phenyl-2*H*-1,3-oxazin-2-one (13). A solution of 9.7 g (0.04 mol) of ethyl 3-amino-2-benzoylpent-2-enoate (**12**)[4] and 10.7 g (0.1 mol) of 2,6-lutidine in 200 mL of dry ether was combined at 0 °C with 4.5 g (0.045 mol) of phosgene in 30 mL of ether. The reaction was allowed to stand under an inert atmosphere for 5 days. Water was then added. The ether phase was separated, washed with dilute HCl, and filtered to give a dark oil that crystallized when triturated with MeOH. Recrystallization from ether gave 700 mg (7% yield) of oxazinone **13** as pale yellow crystals: mp 157–159 °C; IR ($CHCl_3$) 1765, 1750, 1725 cm^{-1} (CO); ^1H NMR ($CDCl_3$) δ 1.0 (t, J = 6 Hz, 2 H, OCH_2CH_3), 1.7 (d, J = 7 Hz, 3 H, $=CHCH_3$), 4.1 (q, J = 6 Hz, 2 H, OCH_2CH_3), 4.8 (q, J = 7 Hz, 1 H, $=CHCH_3$), 7.45 (m, 5 H, C_6H_5), 8.35 (s, 1 H, NH). Anal. Calcd for $C_{15}H_{15}NO_4$: C, 65.92; H, 5.53; N, 5.13. Found: C, 65.79; H, 5.57; N, 5.11.

Registry No. **1**, 21486-64-6; **2**, 74947-55-0; **3**, 74947-56-1; **4**, 74947-57-2; **5**, 74947-58-3; **6**, 74947-59-4; **7**, 74947-60-7; **8**, 74947-61-8; **9**, 74947-62-9; **10**, 74947-63-0; **11**, 74947-64-1; **12**, 74947-65-2; **13**, 74947-66-3; phosgene, 75-44-5; diethyl 3-aminoglutaconate, 54889-50-8; benzene chloride, 98-88-4; ethyl 3-pyrrolidin-1-ylcinnamate, 53256-23-8; 1-nitropropane, 108-03-2; phenyl isocyanate, 103-71-9; 4-carbethoxy-3-ethyl-5-phenylisoxazole, 74947-67-4; ethyl 3-amino-2-benzoylpent-2-enoate, 74947-68-5.

Supplementary Material Available: ^{13}C NMR data of oxazines **4**, **7**, and **8** (1 page). Ordering information is given on any current masthead page.

Regiochemical Control of the Addition of Aryl Selenols and Aryl Thiols to the Triple Bond of Arylpropiolates. Synthesis of Seleno- and Thioflavones and Seleno- and Thioaurones

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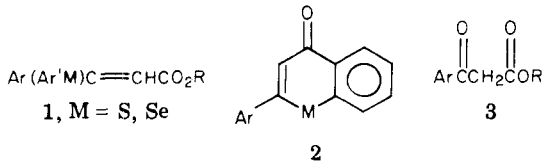
Received April 29, 1980

Addition of aryl selenols and aryl thiols to arylpropiolates under basic conditions followed by saponification gave exclusively β-substituted cinnamates of predominant Z stereochemistry. Neat solutions of aryl selenols or aryl thiols and arylpropiolates after saponification gave α-substituted cinnamates of presumed Z stereochemistry. The latter reactions are assumed to be radical additions. Cyclization of the cinnamates with phosphorus pentoxide–methanesulfonic acid gave seleno- and thioflavones and 2-arylidene-3-oxo-2*H*-benzo[*b*]selenophenes and -thiophenes.

β-(Arylthio)- and β-(arylseleno)cinnamates (**1**) are useful precursors of the corresponding thio- and selenoflavones (**2**).[1] Typically, the cinnamates **1** have been prepared by



condensing an appropriate β-keto ester (**3**) with the corresponding aryl thiol or aryl selenol.[1,2] Although β-keto esters are easily obtained,[3] the condensations frequently give poor yields. Similarly, subsequent cyclization of the cinnamates with hot polyphosphoric acid[4] or with aluminum chloride and the corresponding acid chloride[5] often

(1) (a) Bossert, F. *Angew. Chem., Int. Ed. Engl.* **1965**, *4*, 879. (b) Renson, M. *Bull. Soc. Chim. Belg.* **1964**, *73*, 483. (c) Bossert, F. *Justus Liebigs Ann. Chem.* **1964**, *680*, 40.

(2) Shultz, A. G.; Fu, W. Y.; Lucci, R. O.; Kurr, B. G.; Lo, K. M.; Boxen, M. *J. Am. Chem. Soc.* **1978**, *100*, 2140.

(3) Hauser, C. R.; Hudson, B. E. *Org. React.* **1942**, *1*, 266. Inglis, J. K. H.; Roberts, K. C. "Organic Syntheses"; Wiley: New York, 1944; Collect. Vol. 1, p 235. Royals, E. E. *J. Am. Chem. Soc.* **1948**, *70*, 489. Royals, E. E.; Hoppe, J. C.; Jordan A. D.; Robinson, A. G. *Ibid.* **1951**, *73*, 5857. Royals, E. E.; Turpin, D. G. *Ibid.* **1954**, *76*, 5452.

(4) Emmick, T. L.; Letzinger, R. L. *Org. Synth.* **1967**, *47*, 54. Hafner, K.; Kaiser, H. *Ibid.* **1964**, *44*, 101. Rawet, A.; Renson, M. *Bull. Soc. Chim. Belg.* **1966**, *75*, 260.

(5) Tolmachev, A. I.; Shulezhko, L. M.; Kisilenko, A. A. *Zh. Obshch. Khim.* **1967**, *37*, 367.

0022-3263/80/1945-4611$01.00/0