operating at 70 eV. ^1H NMR and ^{13}C NMR spectra were run on a Hitachi R-90H spectrometer. Analytical GLC was performed on a Shimadzu GC-8A chromatograph with an FID (OV-1) column. Elemental analyses were performed by the section on elemental analysis in our department.

Methyloxirane, ethyloxirane, 2,2-dimethyloxirane, and phenyloxirane were purchased and freshly distilled from CaH_2. Diphenylketene, phenylethylketene,[22] oxetane,[23] 2-phenyloxetane,[24] Ph_4SbI, Ph_4SbBr, Ph_4SbCl,[25] and Ph_3SbI_2[26] were prepared according to published procedures. Vinyloxirane was obtained from the reaction of NaOH with 1-bromo-3-buten-2-ol,[27] which was prepared from butadiene by a reported procedure.[28] 2-Methyl-2-vinyloxirane was obtained in a similar manner to that of vinyloxirane.

General Procedure. To a solution of the oxirane or oxetane (3 mmol) and Ph_4SbI (1) (0.17 g, 0.3 mmol) in dry benzene (5 mL) was added the ketene (3 mmol) with stirring under dry nitrogen. The resulting mixture was heated at 45 °C. The end of reaction was monitored by the disappearance of the infrared absorption band due to ketene (2100 cm^{-1}). Yields of products were monitored by GLC or ^1H NMR (internal standard was 1,1,2,2-tetrachloroethane). Isolation of **2** and **4** was carried out in the following manner: The solvent was removed under reduced pressure, and the residue was chromatographed over silica gel (benzene), yielding nearly pure product. Recrystallization using benzene/hexane or distillation gave a pure product. Products **3** and **5** were isolated as already reported.[6]

3,3,4-Triphenyloxolan-2-one (2d): mp 114–115 °C; IR (KBr) 1760 cm^{-1} (C=O); ^1H NMR ($CDCl_3$) δ 4.40–4.80 (m, 3 H), 6.60–7.75 (m, 15 H); ^{13}C NMR ($CDCl_3$) δ 50.66 (d), 62.12 (s), 69.81 (t), 127.03 (d), 127.52 (d), 127.74 (d), 128.28 (d), 128.41 (d), 128.56 (d), 128.89 (d), 129.20 (d), 129.54 (d), 136.55 (s), 139.75 (s), 139.99 (s), 177.22 (s). Anal. Calcd for $C_{22}H_{18}O_2$: C, 84.05; H, 5.77. Found: C, 83.73; H, 5.70.

3-Ethyl-3,4-diphenyloxolan-2-one (2e): mp 63 °C; IR (KBr) 1770 cm^{-1} (C=O); ^1H NMR ($CDCl_3$) δ 0.70 (t, 3 H, J = 7.0 Hz), 1.40–1.90 (m, 2 H), 3.86 (t, 1 H, J = 5.8 Hz), 4.20–4.75 (m, 2 H), 6.60–7.70 (m, 10 H); ^{13}C NMR ($CDCl_3$) δ 8.15 (q), 25.60 (t), 53.52 (d), 55.84 (s), 69.62 (t), 126.85 (d), 127.07 (d), 127.49 (d), 127.77 (d), 128.04 (d), 128.41 (d), 136.64 (s), 138.56 (s), 178.17 (s). Anal. Calcd for $C_{18}H_{18}O_2$: C, 81.17; H, 6.81. Found: C, 80.95, H, 6.80.

3,3-Diphenyl-4-vinyloxolan-2-one (2f): mp 148 °C; IR (KBr) 1770 cm^{-1} (C=O); ^1H NMR ($CDCl_3$) δ 3.85–4.20 (m, 2 H), 4.25–4.50 (m, 1 H), 5.00–5.45 (m, 3 H), 6.85–7.70 (m, 10 H); ^{13}C NMR ($CDCl_3$) δ 48.55 (d), 59.65 (s), 68.31 (t), 119.56 (t), 125.63 (d), 125.91 (d), 127.52 (d), 128.22 (d), 128.89 (d), 133.01 (d), 138.19 (s), 140.08 (s), 177.31 (s). Anal. Calcd for $C_{18}H_{16}O_2$: C, 81.80; H 6.10. Found: C, 81.74; H, 6.06.

3-Ethyl-3-phenyl-4-vinyloxolan-2-one (2g): bp 63 °C (0.01 mmHg); IR (neat) 1770 cm^{-1} (C=O); ^1H NMR ($CDCl_3$) δ 0.65–1.20 (m, 3 H), 1.80–2.20 (m, 2 H), 3.15–3.50 (m, 1 H), 3.95–4.50 (m, 2 H), 5.05–5.45 (m, 2 H), 5.70–6.15 (m, 1 H), 7.05–7.65 (m, 5 H); ^{13}C NMR ($CDCl_3$) δ 8.55 (q), 25.69 (t), 51.85 (d), 54.71 (s), 69.07 (t), 119.44 (t), 126.82 (d), 127.71 (d), 128.59 (d), 132.61 (d), 138.93 (s), 178.26 (s). Anal. Calcd for $C_{14}H_{16}O_2$: C, 77.75; H, 7.46. Found: C, 77.99; H, 7.27.

3,3-Diphenyloxan-2-one (4a):[6] mp 116 °C; IR (KBr) 1730 cm^{-1} (C=O); ^1H NMR ($CDCl_3$) δ 1.88 (m, 2 H), 2.62 (t, 2 H, J = 7.5 Hz), 4.22 (t, 2 H, J = 7.5 Hz), 7.22 (m, 10 H).

3-Ethyl-3-phenyloxan-2-one (4b): bp 77 °C (0.01 mmHg); IR (neat) 1720 cm^{-1} (C=O); ^1H NMR ($CDCl_3$) δ 0.82 (t, 3 H, J = 8.5 Hz), 1.70–2.20 (m, 6 H), 3.70–4.40 (m, 2 H), 7.15–7.45 (m, 5 H); ^{13}C NMR ($CDCl_3$) δ 9.00 (q), 19.62 (t), 27.79 (t), 34.30 (t), 51.86 (s), 67.71 (t), 126.17 (d), 128.82 (d), 140.76 (s), 174.81 (s). Anal. Calcd for $C_{13}H_{16}O_2$: C, 76.44; H, 7.90. Found: C, 76.00; H, 7.92.

3,3,4-Triphenyloxan-2-one (4c-1): mp 161 °C; IR (KBr) 1720 cm^{-1} (C=O); ^1H NMR ($CDCl_3$) δ 2.39 (dd, 2 H, J = 10.5 and 15.5 Hz), 3.92–4.55 (m, 3 H), 6.40–7.85 (m, 15 H); ^{13}C NMR ($CDCl_3$) δ 27.88 (t), 46.63 (d), 61.97 (s), 66.45 (t), 126.33 (d), 126.79 (d), 127.64 (d), 128.16 (d), 129.02 (d), 130.30 (d), 140.21 (s), 140.91 (s), 141.88 (s), 172.59 (s). Anal. Calcd for $C_{23}H_{20}O_2$: C, 84.12; H, 6.14. Found: C, 84.08; H, 6.16.

3,3,6-Triphenyloxan-2-one (4c-2): mp 162 °C; IR (KBr) 1720 cm^{-1} (C=O); ^1H NMR ($CDCl_3$) δ 1.51–1.55 (m, 2 H), 2.69–2.93 (m, 2 H), 5.40 (dd, 1 H, J = 6.5 and 11.0 Hz), 7.19–7.50 (m, 15 H); ^{13}C NMR ($CDCl_3$) δ 28.49 (t), 32.79 (t), 57.37 (s), 82.06 (d), 125.78 (d), 127.28 (d), 127.43 (d), 128.35 (d), 128.47 (d), 140.08 (s), 142.28 (s), 142.68 (s), 171.96 (s). Anal. Calcd for $C_{23}H_{20}O_2$: C, 84.12; H, 6.14. Found: C, 84.42; H, 6.21.

2-(Diphenylmethylene)-4-methyl-1,3-dioxolane (3a):[6] mp 88–89 °C; IR (KBr) 1660 cm^{-1} (C=C); ^1H NMR ($CDCl_3$) δ 1.42 (d, 3 H, J = 7.5 Hz), 3.82 (t, 1 H, J = 6.0 Hz), 4.38 (dd, 1 H, J = 6.0 Hz), 4.70 (m, 1 H), 7.00–7.40 (m, 10 H).

2-(Diphenylmethylene)-4-ethyl-1,3-dioxolane (3b):[6] mp 57–58 °C; IR (KBr) 1660 cm^{-1} (C=C); ^1H NMR ($CDCl_3$) δ 1.00 (t, 3 H, J = 7.5 Hz), 1.50–1.90 (m, 2 H), 3.90 (t, 1 H, J = 6.5 Hz), 4.30 (t, 1 H, J = 6.5 Hz), 4.30–4.60 (m, 1 H), 7.00–7.40 (m, 10 H).

2-(Diphenylmethylene)-3,3-dimethyl-1,3-dioxolane (3c):[6] mp 98–100 °C; IR (KBr) 1660 cm^{-1} (C=C); ^1H NMR ($CDCl_3$) δ 1.15 (s, 3 H), 1.45 (s, 3 H), 4.00 (d, 2 H, J = 5.5 Hz), 7.00–7.40 (m, 10 H).

2-(Diphenylmethylene)-3-phenyl-1,3-dioxolane (3d):[6] bp 132 °C (0.01 mmHg); IR (KBr) 1660 cm^{-1} (C=C); ^1H NMR ($CDCl_3$) δ 4.10 (t, 1 H, J = 7.5 Hz), 4.60 (t, 1 H, J = 7.5 Hz), 5.50 (t, 1 H, J = 7.5 Hz), 7.00–7.40 (m, 15 H).

2-(Diphenylmethylene)-1,3-dioxane (5a):[6] mp 80–81 °C; IR (KBr) 1640 cm^{-1} (C=C); ^1H NMR ($CDCl_3$) δ 1.95–2.25 (m, 2 H), 4.15 (t, 4 H, J = 6.5 Hz), 7.10–7.40 (m, 10 H).

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Registry No. **1**, 13903-91-8; **2d**, 117040-43-4; **2e**, 117040-44-5; **2f**, 117040-45-6; **2g**, 117040-46-7; **3a**, 109911-27-5; **3b**, 109911-28-6; **3c**, 109911-29-7; **3d**, 95025-62-0; **3f**, 117040-47-8; **3h**, 117040-50-3; **4a**, 68319-09-5; **4b**, 68319-11-9; **4c-1**, 117040-48-9; **4c-2**, 117040-49-0; **5a**, 94029-61-5; HMPA, 680-31-9; Ph_4SbBr, 21450-52-2; Ph_4SbCl, 19638-17-6; Ph_3SbI_2, 1538-60-9; Bu_2SnI_2, 2865-19-2; $BrCH_2CH(OH)CH{=}CH_2$, 64341-49-7; $Ph_2C{=}C{=}O$, 525-06-4; $PhEtC{=}C{=}O$, 20452-67-9; 2-methyloxirane, 75-56-9; 2-ethyloxirane, 106-88-7; 2,2-dimethyloxirane, 558-30-5; 2-phenyloxirane, 96-09-3; 2-vinyloxirane, 930-22-3; 2-methyl-2-vinyloxirane, 1838-94-4; oxetane, 503-30-0; 2-phenyloxetane, 4436-23-1.

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On the Condensation of 2,4-Dioxocarboxylates (β-Acylpyruvates) with Urea. An Example of the Utility of Selective Heteronuclear $^{13}C(^1H)$ NOE Difference Spectroscopy in Structure Elucidation†

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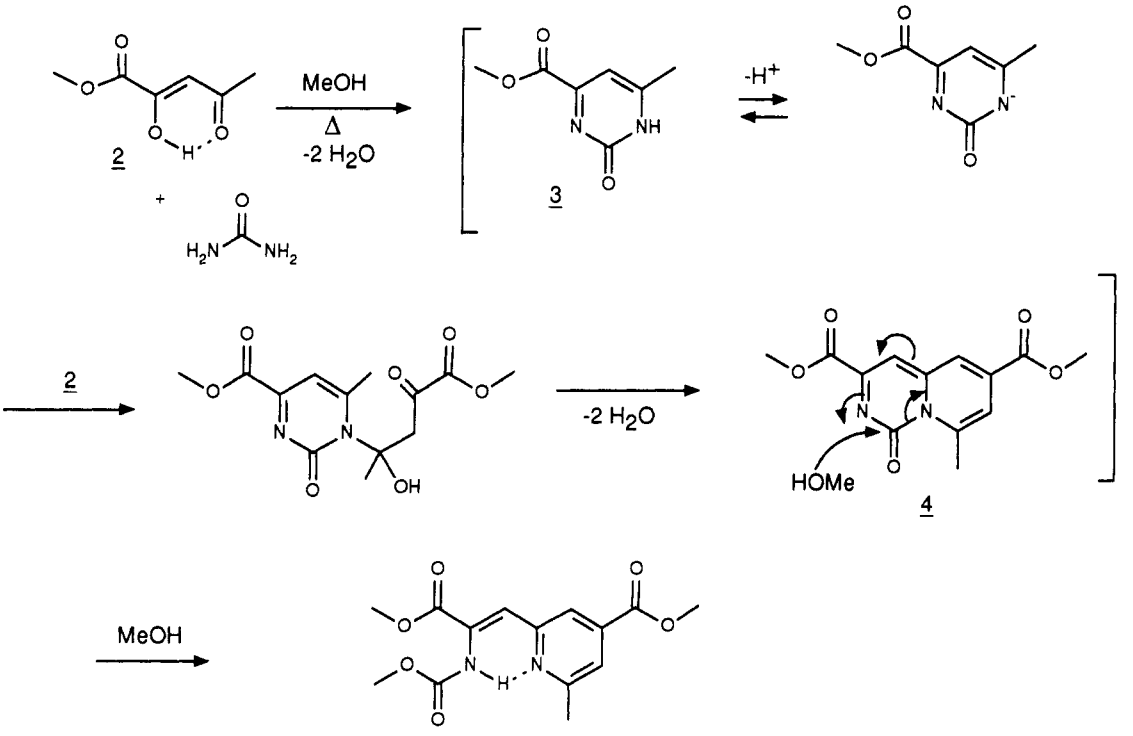
In the course of exploring the chemistry of 2,4-dioxocarboxylic esters[1] (β-acylpyruvates, $ROC(O)C(O)CH_2C(O)R'$, **1**), we investigated some condensation reactions with two- and three-atom units to form heterocycles. The utility

† Dedicated to Professor Edward C. Taylor, Princeton University, Princeton, NJ, on the occasion of his 65th birthday.

0022-3263/88/1953-5977$01.50/0

Scheme I



of 2,4-dioxocarboxylic acid derivatives as heterocycle synthons had been exemplified previously by reactions forming pyrazoles,[2] isoxazoles,[3] pyridines,[4] pyrimidines,[5] and condensed heterocyclic systems.[6] In particular, precedent existed for the condensation of 1, R′ = Ar, *t*-Bu, with urea to give 2-pyrimidinones.[5] We were therefore surprised that the reaction of methyl 2,4-dioxopentanoate (**2**) with urea (1:1) in refluxing methanol did not provide the anticipated pyrimidinone **3**; rather, the sole isolable product (23% yield) proved to be a highly yellow-fluorescent (long-wavelength UV light) 2:1 adduct incorporating 1 equiv of solvent methanol (**5**) as evidenced by spectroscopic and elemental analysis. Adjusting the reaction stoichiometry to 2:1 accordingly increased the yield of **5** (Experimental Section). The structure of the adduct proved difficult to assign via conventional spectroscopic techniques due to the large number of quaternary carbons present. Therefore the emerging technique of selective heteronuclear $^{13}C(^1H)$ NOE difference spectroscopy[7] was applied to determine connectivity information between quaternary carbons and nearby protons.

Table I. Crystal Parameters for 5

molecular formula	$C_{14}H_{16}N_2O_6$
formula weight	308.3 g
crystal color	yellow
crystal size	0.22 × 0.25 × 0.25 mm
a	7.965 (2) Å
b	8.224 (2) Å
c	12.378 (4) Å
α	103.22 (2)°
β	103.66 (2)°
γ	98.27 (2)°
V	750.1 (4)Å^3
Z	2
space group	$P\bar{1}$
d(calcd)	1.37 g/cm^3
F(000)	324 e$^-$
μ(Cu Kα)	9.3 cm^{-1}
crystal system	triclinic

Analogous to the commonly used $^1H(^1H)$ NOE experiment, selective $^{13}C(^1H)$ NOE experiments measure signal enhancements from those carbons close to the proton(s) being selectively saturated by a small radio-frequency (rf) field. NOEs are not observed for directly attached carbons since only the ^{12}CH signal is irradiated with the low power used. The NMR pulse sequence used for this technique is diagrammed below.

(1) For the sake of convenience, the keto nomenclature for **1**, **2**, and **6** is used throughout the text of this paper even though the α-enol is the exclusive form in solution and the solid state. Cf.: Haider, A.; Wyler, H. *Helv. Chim. Acta* **1983**, *66*, 606. Sheldrick, W. S.; Trowitzsch, W. *Z. Naturforsch., B: Anorg. Chem., Org. Chem.* **1983**, *38B*, 220. Battesti, P.; Battesti, O.; Selim, M. *Bull. Soc. Chim. Fr.* **1974**, 2214.

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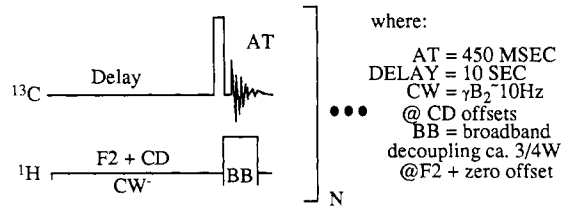


A list of proton irradiation frequencies is created in a CD list and incremented after N steps. In a series of irradiation frequencies, one off-resonance frequency is used as the control. NOE difference (NOED) spectra generated for **5** together with the NOE pathways are shown in Figure 1. From the NOED data all of the necessary connectivities could be made. The negative NOEs observed occur in those cases where three spins are involved in dipolar interaction, e.g., $H_3H_7C_7$. Saturation of the proton farthest from the carbon atom in such a system leads to a negative NOE. This effect is well established for $^1H(^1H)$ NOE studies[7e] and has also been reported in $^{13}C(^1H)$ NOE experiments.[7d]

Ultimately structure **5** was confirmed by single-crystal X-ray analysis (supplementary material), thereby validating the selective heteronuclear $^{13}C(^1H)$ NOED technique as well. A summary of the X-ray data for **5** is given in Table I.

The proposed reaction mechanism for the formation of **5** is outlined in Scheme I. An initially formed pyrimidinone **3** condenses[5d] with the γ-carbonyl[8] of a second molecule of **2**, generating the unstable pyridopyrimidine **4**, which solvolyzes to the methyl carbamate **5**. The regiochemistry of the ester and methyl groups on the pyridine ring and the stereochemistry of the double bond are established by bicyclic intermediate **4**. Note that the pyridine ring nitrogen and the carbamate C(=O)N moiety are derived from urea; the carbamate OMe is derived from solvent methanol. Attempted catalysis by base (NaOMe) or reaction in the absence of alcohol (*N*-methylpyrrolidinone solvent) inhibited the desired reaction with formation of polymeric byproducts. Addition of powdered dehydrated 3-Å molecular sieves did not improve the yield of **5**.

The generality of this condensation reaction was explored briefly. In theory, complex isonicotinates of type **7** should be preparable in one step from the readily available[9] 2,4-dioxocarboxylates **6** and urea (Scheme II). Unfortunately in practice, aside from **2**, only cyclic 2,4-dioxocarboxylates (**6**, R = Et, R^1,R^2 = $(CH_2)_n$, n = 2, 3) provided any of the isonicotinates **7**. Ethyl 2,4-dioxohexanoate[4] yielded no identifiable products when refluxed with urea in EtOH. The requisite esters **6** could not be obtained from 1,3-diphenylacetone or 3-pentanone and diethyl oxalate; lactones were the sole products obtained.[10] Thus, only a limited entry to isonicotinates of type **7** exists via this methodology; however, for those specific cases to which it is applicable, an exceedingly efficient route for the synthesis of rather complex pyridine derivatives of type **7** is now available.

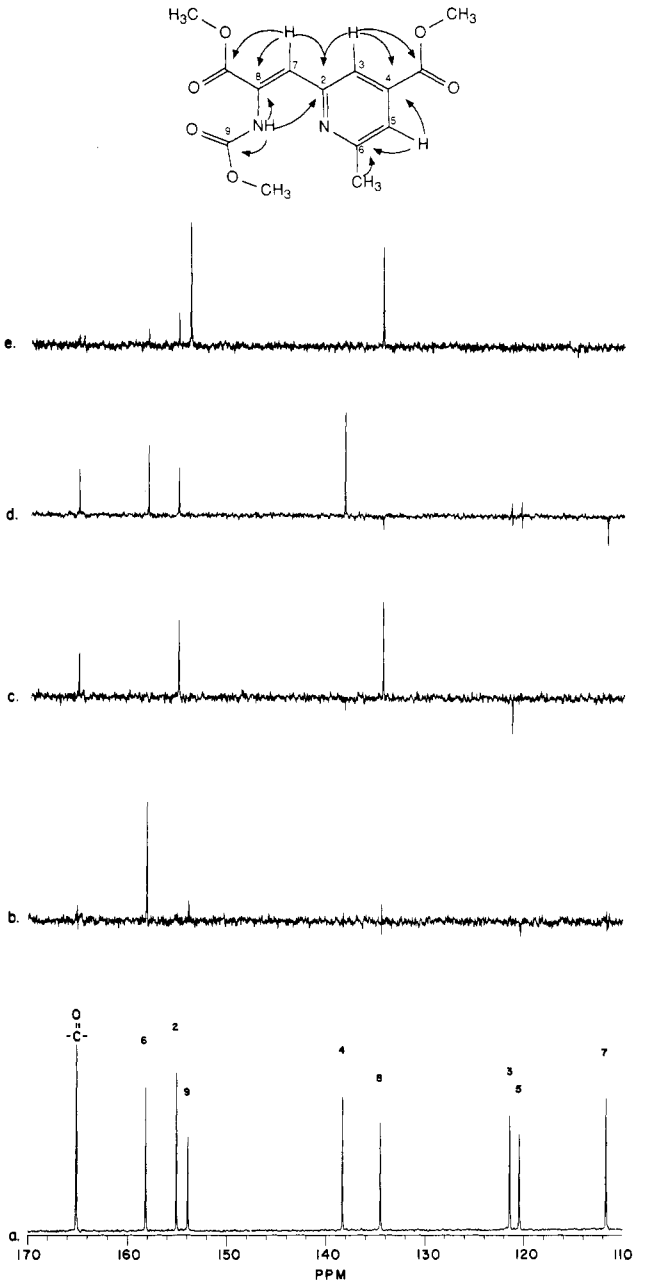
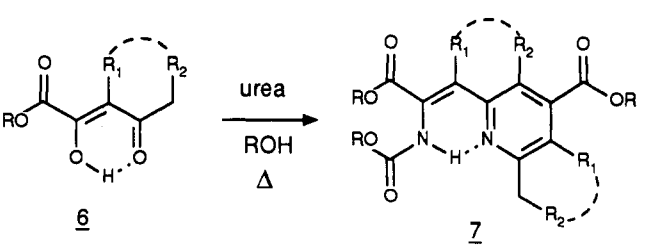


Figure 1. (a) Proton-decoupled ^{13}C spectrum of **5** (75 mg in 0.5 mL of $CDCl_3$); (b) $^{13}C(^1H)$ NOED spectrum irradiating the 6-CH_3 protons; (c) $^{13}C(^1H)$ spectrum with H-7 irradiated; (d) $^{13}C(^1H)$ NOED spectrum with H-3 and H-5 irradiated; and (e) $^{13}C(^1H)$ NOED spectrum with the NH proton irradiated. Total experiment time was approximately 12 h.



Experimental Section

Melting points were obtained by using a Thomas-Hoover capillary melting point apparatus and are uncorrected. NMR spectra were obtained by using a Nicolet NT 300 (300 MHz, ^1H; 75 MHz,

(8) Preferential or exclusive reaction at the γ-carbonyl of 2,4-dioxocarboxylates has been reported in some instances.[3,6a,b] Presumably this is due to the α-enol form predominating.

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^{13}C) spectrometer using Me_4Si as internal standard and $CDCl_3$ as solvent. $^{13}C(^1H)$ NOED experiments were performed as described in the literature[7] as modified in the pulse-sequence diagram (*vide supra*). Mass spectrometry was performed on either an MAT 212 or MAT 311A spectrometer. "Chromatography" refers to the flash column chromatography technique[11] over EM silica gel 60 (0.040–0.063 mm).

Methyl (*Z*)-2-[3-Methoxy-2-[(methoxycarbonyl)amino]-3-oxo-1-propenyl]-6-methyl-4-pyridinecarboxylate (5). A solution of 15.5 g (108 mmol) of methyl 2,4-dioxopentanoate and 3.40 g (56.6 mmol) of urea in 200 mL of absolute MeOH was refluxed for 4 days. The dark solution was evaporated to dryness and the solid residue chromatographed by using 10% Et_2O/CH_2Cl_2 as eluent, affording 10.5 g (63.3%) of bright yellow solid. Recrystallization from 100 mL of MeOH gave 6.7 g (40% overall yield) of bright yellow crystals: mp 134.5–7.5 °C; UV (MeOH) λ_{max} 334 (ϵ 1.30 × 10^4), 274 (1.78 × 10^4), 219 nm (sh) (1.27 × 10^4); IR (KBr) 1730 (CO) and 1715 (CO), 3400 cm^{-1} (NH); EIMS 308 (M^+), 277, 249, 216, 205, 190 (base peak); ^{13}C NMR ($CDCl_3$) δ 24.14 (6-CH_3), 52.33, 52.43, 52.52 ($CH_3OC(O)$), 111.45 (C-7), 120.25 (C-5), 121.11 (C-3), 134.32 (C-8), 138.13 (C-4), 153.71 (C-9), 154.90 (C-2), 157.97 (C-6), 164.88 and 164.91 (3 carbons, $CH_3OC(O)$); ^1H NMR ($CDCl_3$) all singlets δ 11.32 (NH), 7.58 (pyridine 3-H, 5-H), 6.28 (vinyl 7-H), 3.95 and 3.89 (ester methyls), 3.78 (carbamate methyl), 2.65 (pyridine 6-Me). Anal. Calcd for $C_{14}H_{16}N_2O_6$, MW 308.29: C, 54.54; H, 5.23; N, 9.09. Found: C, 54.30, 54.06; H, 4.98, 5.20; N, 8.96, 9.17.

Crystals of **5** suitable for X-ray analysis were grown by vapor diffusion[12] of water vapor into a methanol solution of **5**.

Ethyl (*Z*)-3-[2-ethoxy-1-[(ethoxycarbonyl)amino]-2-oxoethylidene]-1,2,3,5,6,7-hexahydrodicyclopenta[*b*,*e*]pyridine-8-carboxylate (7a), R = Et, R^1,R^2 = CH_2CH_2, was prepared from **6a** and urea in absolute EtOH in an analogous manner to give a 72.6% yield of amber waxy solid with a characteristic orange fluorescence (long-wavelength UV) after chromatography using 5% Et_2O/CH_2Cl_2 as eluent: mp 63–73 °C; EIMS 402 (M^+); exact mass calcd for $C_{21}H_{26}N_2O_6$ 402.1791, found 402.1787; ^1H NMR ($CDCl_3$) δ 10.95 (br s, 1, NH), 4.6–4.0 (m, 6, (O)$COCH_2$), 3.4–2.8 (m, 6, CH_2), 2.6–1.6 (m, 4, CH_2), 1.5–1.1 (m, 9, (O)$COCH_2CH_3$).

Ethyl (*Z*)-4-[2-ethoxy-1-[(ethoxycarbonyl)amino]-2-oxoethylidene]-1,2,3,4,5,6,7,8-octahydro-9-acridinecarboxylate (7b), R = Et, R^1,R^2 = $CH_2CH_2CH_2$, was prepared from **6b**[9b] as above to give a 2.1% yield of an amber waxy low-melting solid: EIMS 430 (M^+); exact mass calcd for $C_{23}H_{30}N_2O_6$ 430.2104, found 430.2100; ^1H NMR δ 12.90 (br s, 1, NH), 4.6–4.0 (m, 6, (O)$COCH_2$), 3.1–2.2 (m, 8, CH_2), 2.2–1.6 (m, 6, CH_2), 1.6–1.2 (m, 9, (O)-$COCH_2CH_3$). The major product (18.2%) isolated from this reaction was a liquid dimer of **6b** of undetermined structure:[13] EIMS and CIMS 396 (M^+). Anal. Calcd for $C_{20}H_{28}O_8$: C, 60.59; H, 7.12; N, 0.00. Found: C, 60.10; H, 7.24; N, 0.00.

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Registry No. **2**, 39847-91-1; **5**, 117098-05-2; **6a**, 85258-72-6; **6b**, 117098-06-3; **7a**, 117098-07-4; **7b**, 117098-08-5; urea, 57-13-6.

Supplementary Material Available: Experimental details of crystal **5**, PLUTO-type drawing of **5**, labeled ORTEP drawing of **5**, stereoview of the unit cell packing diagram, tables of atomic coordinates and isotropic thermal parameters, bond lengths, bond angles, anisotropic thermal parameters, and H-atom coordinates and isotropic thermal parameters (11 pages). Ordering information is given on any current masthead page.

(11) Hostettmann, K.; Hostettmann, M.; Marstou, A. *Preparative Chromatography Techniques Applications in Natural Products Isolation*; Springer-Verlag: Berlin, 1986; pp 41–6.
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Convenient Method for the Recovery of Eicosapentaenoic Acid from Cod Liver Oil

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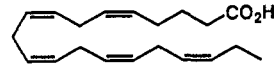
The marine-derived polyunsaturated fatty acids eicosapentaenoic acid (1) (EPA) and docosahexaenoic acid (2) (DHA) are currently of much interest due to the increasing evidence that points to a beneficial role of fish lipids in maintaining cardiovascular health.[1-3] We have recently reported a process for the extractive isolation of DHA from cod liver oil[4] that avoids the need for distillation or chromatography. We now describe in detail how EPA may be separated with similar ease from the residues remaining from the preparation of DHA.



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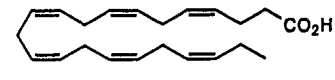

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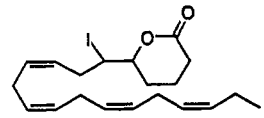

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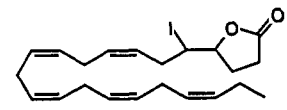

4

Following the selective conversion of DHA to iodo lactone 4,[4] extractive workup yielded an alkaline solution containing the unreacted fatty acids as a byproduct. Acidification and extraction gives a mixture of polyunsaturated fatty acids enriched in EPA. This mixture is subjected to iodolactonization in aqueous tetrahydrofuran using an excess of iodine and potassium iodide. Following extractive workup, a mixture of the iodo lactones **3** and **4**, derived from EPA and the residual DHA, is obtained. The ratio of **3** to **4** can be estimated from the ^1H NMR spectrum of the mixture by integration of the signals at 3.95 and 4.25 ppm, due to **3** and **4**, respectively. The mixture of **3** and **4** is then treated with iodotrimethylsilane, generated in situ from chlorotrimethylsilane and sodium iodide, using 1.4 equiv based on the amount of **3** present.[5] Selective cleavage of the iodo δ-lactone **3** in the presence of the iodo γ-lactone **4** occurs as a result of the greater stability of the γ-lactone system in **4**. As soon as most of the δ-lactone **3** has reacted (ca. 2 h at 22 °C), the reaction mixture is worked up to yield pure EPA. The procedure given below is well suited for the preparation of quantities of eicosapentaenoic acid.

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(6) This research was assisted financially by a grant from the National Institutes of Health.

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