was purified by preparative liquid chromatography (C-18 reverse phase, 20% methanol–water) to afford **20** as a white powdery solid (60%): mp 210–213 °C; IR (KBr) ν_{max} 1790, 1680, 1547, 1290, 1262, 1191, 1050 cm^{-1}; ^{1}H NMR (Me_2SO-d_6) δ 3.90 (s, 3, OCH_3), 4.33 (dq, 1, $^3J_{HF}$ = 6.1, $J_{2,3}$ = 2.5 Hz, H-2), 4.37 (s, 2, $ClCH_2$-), 4.91 (dd, 1, J = 2.5, 8 Hz, H-3), 7.41 (s, 1, thiazole proton), 9.57 (d, 1, J = 8 Hz, NH), 12.84 (br s, 1, -HN-thiazole); ^{19}F NMR (Me_2SO-d_6) δ −72.0 (d, $^3J_{HF}$ = 6.14 Hz, CF_3); mass spectrum (positive ion FAB, glycerol matrix), calcd for $C_{12}H_{11}ClF_3N_5O_7S_2Na$ (M + H) 515.9631 (found 515.9595). Anal. Calcd for $C_{12}H_{10}ClF_3N_5O_7S_2Na$: C, 27.94; H, 1.95; N, 13.58. Found: C, 28.11; H, 2.24; N, 13.88.

Sodium *cis,rac*,(*Z*)-3-[[[2-[(Chloroacetyl)amino]-4-thiazolyl](methoxyimino)acetyl]amino]-2-(trifluoromethyl)-4-oxo-1-azetidinesulfonate (18). This compound was prepared by application of the preceding method utilizing the appropriate azetidinone, **15**. Purification was accomplished by preparative liquid chromatography (C-18 reverse phase, 20% methanol–water) to afford **18** as a white lyophilized powder (62%): mp 181–184 °C; IR (KBr) ν_{max} 1792, 1685, 1551, 1290, 1273, 1190, 1172, 1055 cm^{-1}; ^{1}H NMR (Me_2SO-d_6) δ 3.87 (s, 3, OCH_3), 4.40 (s, 2, $ClCH_2$), 4.58 (dq, 1, $^3J_{HF}$ = 6.5, $J_{2,3}$ = 5.5 Hz, H-2), 5.56 (dd, 1, $J_{2,3}$ = 5.5, J = 8.5 Hz, H-3), 7.35 (s, 1, thiazole proton), 9.63 (d, 1, J = 8.5 Hz, NH), 12.94 (s, 1, thiazole-NH-); ^{19}F NMR (Me_2SO-d_6) δ −67.8 (d, $^3J_{HF}$ = 6.5 Hz, CF_3); mass spectrum (positive ion FAB, glycerol matrix), calcd for $C_{12}H_{11}ClF_3N_5O_7S_2Na$ (M + H) 515.9631 (found 515.9621). Anal. Calcd for $C_{12}H_{10}ClF_3N_5O_7S_2Na$ (0.5 H_2O): C, 27.46; H, 2.11; N, 13.34. Found: C, 27.50; H, 2.17; N, 13.49.

Sodium *trans,rac*,(*Z*)-3-[[(2-Amino-4-thiazolyl)(methoxyimino)acetyl]amino]-2-(trifluoromethyl)-4-oxo-1-azetidinesulfonate (22). To a stirred solution of the chloroacetyl-protected aminoazetidinone, **20**, (0.112 g, 0.22 mmol) in water (4 mL) at 5 °C was added sodium methyldithiocarbamate[19] (0.0323 g, 0.22 mmol). After being stirred at room temperature for 2 h, the mixture was purified by preparative liquid chromatography (C-18 reverse phase, 100% water) to afford, after lyophilization, the title compound **22** (0.052 g, 55%) as a white powder: mp 252–255 °C; IR (KBr) ν_{max} 3440, 3340, 1792, 1673, 1617, 1533, 1392, 1290, 1272, 1189, 1125, 1053 cm^{-1}; ^{1}H NMR (Me_2SO-d_6) δ 3.84 (s, 3, OCH_3), 4.32 (dq, 1, $^3J_{HF}$ = 6.8, $J_{2,3}$ = 2.5 Hz, H-2), 4.87 (dd, 1, $J_{2,3}$ = 2.5, J = 8.5 Hz, H-3), 6.69 (s, 1, thiazole proton), 7.17 (br s, 2, NH_2), 9.46 (d, 1, J = 8.5 Hz, NH); ^{19}F NMR (Me_2SO-d_6) δ −72.05 (d, $^3J_{HF}$ = 6.8 Hz, CF_3); mass spectrum (positive ion FAB, glycerol matrix,) calcd for $C_{10}H_9F_3N_5O_6S_2Na_2$ (M + Na) 461.9742 (found 461.9716). Anal. Calcd for $C_{10}H_9F_3N_5O_6S_2Na{\cdot}2H_2O$: C, 25.43; H, 2.77; N, 14.82. Found: C, 25.65; H, 2.44; N, 14.35.

Sodium *cis,rac*,(*Z*)-3-[[(2-Amino-4-thiazolyl)(methoxyimino)acetyl]amino]-2-(trifluoromethyl)-4-oxo-1-azetidinesulfonate (21). This was prepared by removal of the chloroacetyl protecting group from **18** as outlined for the corresponding trans analogue. Purification by preparative liquid chromatography (C-18 reverse phase, 100% water) followed by lyophilization afforded the desired amino compound **21** (62%) as a white powder: mp 249–252 °C; IR (KBr) ν_{max} 3400, 1790, 1680, 1620, 1530, 1395, 1290, 1270, 1190, 1145, 1053, cm^{-1}; ^{1}H NMR (Me_2SO-d_6) δ 3.98 (s, 3, OCH_3), 4.52 (dq, 1, $^3J_{HF}$ = 6.9, $J_{2,3}$ = 5.5 Hz, H-2), 5.50 (dd, 1, $J_{2,3}$ = 5.5, J = 8.5 Hz, H-3), 6.57 (s, 1, thiazole proton), 7.14 (br s, 2, NH_2), 9.45 (d, 1, J = 8.5 Hz, -CONH-); ^{19}F NMR (Me_2SO-d_6) δ −68.81 (d, $^3J_{HF}$ = 6.9 Hz, CF_3); mass spectrum (positive ion FAB, glycerol matrix), calcd for $C_{10}H_{10}F_3N_5O_6S_2Na$ (M + H) 439.9922 (found 439.9893). Anal. Calcd for $C_{10}H_9F_3N_5O_6S_2Na{\cdot}2.5H_2O$: C, 24.80; H, 2.91; N, 14.46. Found: C, 24.68; H, 2.90; N, 14.34.

Stability Studies on 19 and Its Nonfluorinated Analogue. Deuterated "biological buffer solution" was prepared in D_2O essentially as described in the literature,[21] being 0.27 M in Na_2DPO_4 and 0.065 M in KD_2PO_4. The buffer had a pD of 7.4. Solutions containing 15 μmol of the appropriate β-lactam in 0.5 mL of deuterated buffer were maintained in NMR tubes at 37 °C. The fluorinated compound **19** was monitored by ^{19}F NMR whereas the nonfluorinated analogue was followed by monitoring the CH_3 group shift by ^{1}H NMR.

Acknowledgment. We are grateful to Dr. D. Pruess (Microbiology Department) and Drs. J. Christenson and G. Beskid (Chemotherapy Department) for in vitro antibacterial testing. We thank the personnel of the Physical Chemistry Department, Hoffmann-La Roche Inc., Nutley, NJ, for spectroscopic and microanalytical data.

Registry No. **2**, 372-31-6; (±)-**3**, 88968-78-9; **4**, 25597-16-4; **5**, 406-94-0; (±)-**6**, 88968-79-0; (±)-**7**, 88968-80-3; (±)-**8**, 88968-81-4; (±)-**9**, 88968-82-5; (±)-**11**, 88968-83-6; (±)-**12**, 88968-84-7; (±)-**13**, 88968-85-8; (±)-**14**, 88968-86-9; (±)-**15**, 88968-87-0; (±)-**16**, 88968-88-1; (±)-**17**, 89015-85-0; (±)-**18**, 88968-89-2; (±)-**19**, 88968-90-5; (±)-**20**, 89015-86-1; (±)-**21**, 88968-91-6; (±)-**22**, 89015-87-2; $CATOMCO_2H$, 64486-18-6; $PhOCH_2COCl$, 701-99-5.

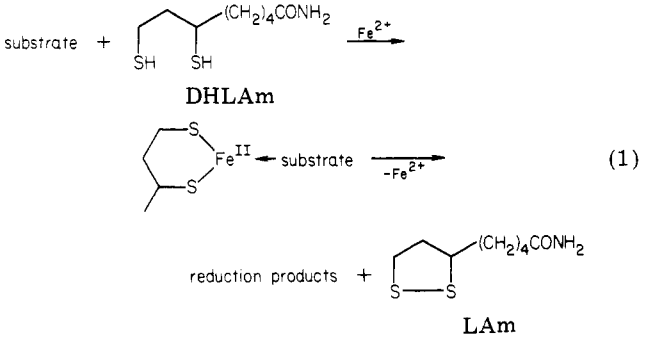
Selective Reduction of Monosubstituted Nitrobenzenes to Anilines by Dihydrolipoamide–Iron(II)

Masashi Kijima,* Yoko Nambu, Takeshi Endo, and Makoto Okawara

Research Laboratory of Resources Utilization, Tokyo Institute of Technology, Nagatsuta, Midori-ku, Yokohama 227, Japan

Received August 18, 1983

Lipoamide (LAm) works as a coenzyme in acyl transfer and redox reactions in living systems, undergoing the following redox reaction: LAm ⇌ dihydrolipoamide (DHLAm). We have recently reported[1,2] that hydroxylamine derivatives, azo-, azoxy-, and nitrobenzenes were reduced by DHLAm–Fe(II) through coordination of substrates to a complex of DHLAm–Fe(II) under weakly basic conditions as shown in eq 1. The peculiar reactivity of



(1)

DHLAm–Fe(II) is interesting in connection with electron transfer of iron–sulfur proteins such as ferredoxins.[3,4] In spite of extensive studies of iron–sulfur complexes as models for nonheme iron proteins, these complexes have not yet seen practical application in synthetic organic chemistry.

Because of the synthetic versatility of aryl nitro compounds, their direct reduction constitutes one of the best routes to the important aromatic amines. Reagents for the reduction of aromatic nitro compounds to the corresponding anilines by classical methods (catalytic hydrogenations, Clemmensen-type reductions, Birch reduction, metal (salts) reductions, etc.) are useful, but these methods have poor selectivity for some functional groups and usu-

(1) Nambu, Y.; Kijima, M.; Endo, T.; Okawara, M. *J. Org. Chem.* **1982**, *47*, 3066.
(2) Kijima, M.; Nambu, Y.; Endo, T.; Okawara, M. *J. Org. Chem.* **1983**, *48*, 2407.
(3) Valentine, R. C.; Mortenson, L. E.; Mower, H. F.; Jackson, R. L.; Wolfe, R. S. *J. Biol. Chem.* **1963**, *238*, 856.
(4) Wessels, J. S. C. *Biochim. Biophys. Acta* **1965**, *109*, 357.

0022-3263/84/1949-1434$01.50/0

Table I. Selective Reduction of Para-Substituted Nitrobenzenes by DHLAm-Fe(II)[a]

para substituent	aniline, %	para substituent	aniline, %
CN	94	H	40[b]
$COCH_3$	90	CH_3	35[b]
$OCOCH_3$	66	OCH_3	73[b]
Cl	58[b]	NH_2	77[b]

[a] Conditions: [DHLAm] = 200 mM, [Fe^{2+}] = 1 mM, [substrate] = 50 mM, 0.2 M carbonate buffer (pH 9.8)-EtOH (1:3), 50 °C, 15 h. [b] Isolated as trifluoroacetanilide.

Table II. Control Experiment[a]

reducing agent, mM			
DHLAm	Fe^{2+}	substrate	% yield of aniline[b]
200	1	*p*-nitroacetophenone	85
200	0	*p*-nitroacetophenone	trace
0	300	*p*-nitroacetophenone	0
200	1	*p*-nitroanisole	70
200	0	*p*-nitroanisole	10
0	300	*p*-nitroanisole	1

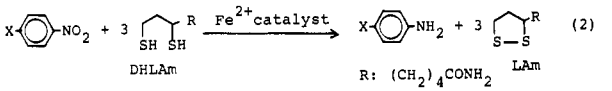
[a] Other conditions are the same as those in Table I. [b] Yields were determined by GLC.

ally require severe conditions. Reduction of nitrobenzenes under basic conditions often gives considerable quantities of N-coupling products.[5] However, as described earlier,[2] nitrobenzene was reduced to aniline without formation of any byproducts by DHLAm-Fe(II). Further, DHLAm-Fe(II) did not reduce many other functional groups (aldehyde, ketone, ester, and nitrile).[2]

In this paper, we describe the selective reduction of variously substituted nitrobenzenes to the corresponding anilines by DHLAm-Fe(II).

Results and Discussion

Various para-substituted nitrobenzenes were reduced by dihydrolipoamide (DHLAm) in the presence of a catalytic amount of ferrous ammonium sulfate in 0.2 M carbonate buffer (pH 9.8)–ethanol (1:3) at 50 °C for 15 h under an argon atmosphere. Anilines produced were usually isolated by column chromatography on silica gel. Unstable anilines were isolated as trifluoroacetanilides. LAm was obtained as an yellow crystal, and no other products were detected by TLC and GLC. The reaction proceeded according to eq 2. The results are summarized in Table I. Control

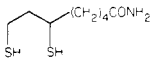
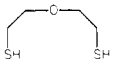
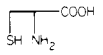


(2)

experiments carried out using *p*-nitroacetophenone and *p*-nitroanisole as substrates showed that very little, if any, reduction occurred with either DHLAm or ferrous ion alone (Table II). Therefore, the reduction might proceed by way of complex formation of nitro groups to DHLAm-Fe(II) complex as described in the previous report.[1]

It is noteworthy that aromatic nitro groups could be reduced selectively to amino groups by DHLAm-Fe(II) under slightly alkaline conditions without any reaction (reduction or hydrolysis) of other substituents (carbonyl, ester, cyano, and halogen). Even in the reduction of less reactive nitrobenzenes having electron-donating groups, anilines were obtained in high yields. This is presumably due to more effective coordination of the nitro group to the DHLAm-Fe(II) complex in these cases.

Table III. Reactivities of Thiols-Fe(II)[a]

thiol	anisidine,[b] %
	70
	67
PhSH	11
$PhCH_2SH$	1
	1
	67[c]
	87
	36

[a] Conditions are the same as those in Table I. [b] Determined by GLC. [c] 0.2 M carbonate buffer (pH 9.8)-EtOH (1:1).

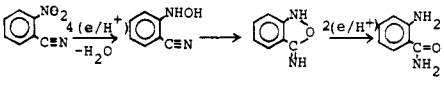
Table IV. Selective Reduction of Ortho-Substituted Nitrobenzenes by DHLAm-Fe(II)[a]

ortho substituent	aniline, %	ortho substituent	aniline, %
$COCH_3$	75	NH_2	97
CHO	67	CN	84[b]
OCH_3	81		

[a] Conditions: [DHLAm] = 200 mM, [Fe^{2+}] = 1 mM, [substrate] = 50 mM, 0.2 M carbonate buffer (pH 9.8)-EtOH (1:3), 50 °C, 15 h. [b] Product, anthranilamide.

In order to investigate the reactivity of simple thiols in place of DHLAm, reduction of *p*-nitroanisole was attempted by using such thiols in the presence of a catalytic amount of ferrous ion. Results are summarized in Table III. Dithiols that can be oxidized easily to cyclic disulfides and monothiols that have other coordinating groups which form metal chelates showed high reactivities. These monothiols were oxidized to disulfides during the reduction of *p*-nitroanisole. In the case of cysteine, the oxidized reagent, cystine, was easily removed from the reaction mixture, which resulted in a simplified workup. It is interesting that cysteine, which plays an important role in the nonheme iron protein, showed high reactivity in the presence of ferrous ion.

Some ortho-substituted nitrobenzenes were also subjected to reduction by DHLAm-Fe(II), and the results are summarized in Table IV. Ortho-substituted (CHO, CH_3CO, CH_3O, NH_2) nitrobenzenes were reduced to the corresponding anilines selectively in high yield. However, *o*-nitrobenzonitrile was reduced to anthranilamide. Since *o*-nitrobenzonitrile was not hydrated by ferrous ion, and anthranilonitrile was not hydrated by DHLAm-Fe(II) or ferrous ion alone under the same reaction conditions, the reaction probably proceeds according to the following equation (eq 3), as also proposed[6] in the reduction of Raney Ni.



(3)

One application of the selective reduction of ortho-substituted nitrobenzenes might be in a preparation of quinoline. This reaction was attempted by using DHLAm

(5) Hutchins, R. O.; Lamson, D. W.; Rua, L.; Milewski, C.; Maryanoff, B. *J. Org. Chem.* **1971**, *36*, 803.

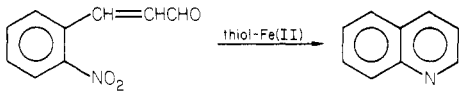
(6) Musso, H.; Schroder, H. *Chem. Ber.* **1965**, *98*, 1562.

Table V. Preparation of Quinoline from o-Nitrocinnamaldehyde by Thiols-Fe(II)[a]

thiol (mM)	Fe^{2+}, mM	time, h	quinoline,[b] %
DHLAm (200)	1	15	15
	50	15	29
cysteine (400)	1	6	76[c]

[a] Conditions: [o-nitrocinnamaldehyde] = 50 mM, 50 °C, 0.2 M carbonate buffer (pH 9.8)-EtOH (1:3). [b] Isolated by Kugelrohr distillation. [c] Buffer-EtOH (1:1).

or cysteine in the presence of a catalytic amount of ferrous ion (eq 4, Table V). DHLAm-Fe(II) gave quinoline in



(4)

thiol, DHLAm; cysteine

poor yield (15%) presumably due to addition of DHLAm to the C=C bond, whereas cysteine iron(II) gave quinoline in good yield (76%) even in the aqueous solvent (buffer-EtOH).

Selective reduction of nitrobenzenes by iron/HCl[7] or Fe^{2+}/NH_4OH[8] require severe conditions of temperature and pH. Reduction by $Fe_3(CO)_{12}$-MeOH[9] or phthalocyaninecobalt(I) anion[10] give good results in mild conditions, but the former complex is somewhat hazardous and the latter one has less reactivity and is not so simple to handle. Reduction of substituted nitrobenzenes by the present thiol-Fe(II) system under weakly alkaline conditions was found to be a simple and selective method.

Experimental Section

General Procedure and Materials. GLC analyses were carried out on a JEOL JGC-1100 gas chromatograph (10% SE-30, stainless steel column, N_2 carrier gas).

Dihydrolipoamide (DHLAm) was prepared as reported[2] earlier. Other chemicals used in this study were reagent grade; solvents were purified by the usual procedure.

Reduction of Monosubstituted Nitrobenzenes. Monosubstituted nitrobenzenes (0.25 mmol) and DHLAm (207 mg, 1 mmol) were put into a Schlenk tube which was degassed and replaced with argon gas. To the Schlenk tube were added ethanol (3.75 mL), 0.2 M Menzel carbonate buffer (Na_2CO_3-$NaHCO_3$, pH 9.8) (1.0 mL), and a 20 mM ferrous ammonium sulfate aqueous solution (0.25 mL), which were previously bubbled with argon, and the reaction mixture was allowed to stir in a water bath at 50 °C for 15 h under argon. After the reaction, ethanol was removed by evaporation and the aqueous residue was extracted with ether. The organic layer was dried with anhydrous magnesium sulfate and evaporated to give a mixture of LAm, DHLAm, starting material, and product. Monosubstituted anilines were separated by column chromatography on silica gel (benzene:ether = 4:1). The trifluoroacetanilides of unstable anilines were formed as described previously[2] and isolated by the same method as above. Anilines and trifluoroacetanilides obtained were identified by melting or boiling points and IR and NMR spectra of authentic samples: p-aminobenzonitrile, mp 84-85 °C (lit.[11] mp 85 °C); p-aminoacetophenone, mp 104-106 °C (lit.[12] mp 106 °C); methyl p-aminobenzoate, mp 100-102 °C (lit.[13] mp 112 °C); trifluoroacetamide, mp 86-87 °C (lit.[14] mp 88.5-90 °C); N,N'-bis(trifluoroacetyl)-p-phenylenediamine, mp 240-250 °C (lit.[14] mp 251 °C); p-methyltrifluoroacetanilide, mp 121-123 °C (lit.[15] mp 123-124.5 °C); p-methoxytrifluoroacetanilide, mp 110-112 °C (lit.[15] mp 111-112 °C); p-chlorotrifluoroacetanilide, mp 121-123 °C (lit.[15] mp 123-124.5 °C); o-aminobenzaldehyde, mp 35-36 °C (lit.[8] mp 38-39 °C); o-phenylenediamine, mp 99-100 °C (lit.[16] mp 99-101 °C); anthranilamide, mp 109-110 °C (lit.[6] mp 110.5-111.5 °C); quinoline; bp_5 90-100 °C (Kugelrohr) (lit.[17] bp_{14} 110-114 °C). IR and NMR spectra[18] of o-aminoacetophenone and o-anisidine coincided completely with those of authentic samples.

Reduction of p-Nitroanisole by Thiols-Fe(II). The reduction was carried out by the same method described above using thiols instead of DHLAm. After the reaction, the reaction mixture was extracted with ether, and the organic layer was dried with magnesium sulfate and evaporated. The residue was dissolved in 5 mL of chloroform. The yield of p-anisidine was determined by GLC analysis of the chloroform solution with n-decane as an internal standard.

Registry No. DHLAm, 3884-47-7; NC-p-$C_6H_4NO_2$, 619-72-7; $CH_3C(O)$-p-$C_6H_4NO_2$, 100-19-6; MeOC(O)-p-$C_6H_4NO_2$, 619-50-1; Cl-p-$C_6H_4NO_2$, 100-00-5; $PhNO_2$, 98-95-3; Me-p-$C_6H_4NO_2$, 99-99-0; MeO-p-$C_6H_4NO_2$, 100-17-4; NH_2-p-$C_6H_4NO_2$, 100-01-6; NH_2-p-C_6H_4CN, 873-74-5; NH_2-p-$C_6H_4C(O)CH_3$, 99-92-3; NH_2-p-$C_6H_4C(O)OMe$, 619-45-4; Cl-p-$C_6H_4NH_2$, 106-47-8; $PhNH_2$, 62-53-3; Me-p-$C_6H_4NH_2$, 106-49-0; MeO-p-$C_6H_4NH_2$, 104-94-9; NH_2-p-$C_6H_4NH_2$, 106-50-3; $HS(CH_2)_2O(CH_2)_2SH$, 2150-02-9; PhSH, 108-98-5; $HS(CH_2)_2NH_2$, 60-23-1; $HS(CH_2)_2CO_2Na$, 42267-40-3; NO_2-o-$C_6H_4C(O)CH_3$, 614-21-1; NO_2-o-C_6H_4CHO, 552-89-6; MeO-o-$C_6H_4NO_2$, 91-23-6; NO_2-o-$C_6H_4NH_2$, 88-74-4; NO_2-o-C_6H_4CN, 612-24-8; NH_2-o-$C_6H_4C(O)CH_3$, 551-93-9; NH_2-o-C_6H_4CHO, 529-23-7; NH_2-o-C_6H_4OMe, 90-04-0; NH_2-o-$C_6H_4NH_2$, 95-54-5; ferrous ammonium sulfate, 10045-89-3; cysteine, 52-90-4; anthranilamide, 88-68-6; o-nitrocinnamaldehyde, 1466-88-2; quinoline, 91-22-5.

(7) Koopman, H. *Recl. Trav. Chim. Pays-Bas* **1961**, *80*, 1075.
(8) Smith, L. I.; Opie, J. W. "Organic Syntheses"; Wiley: New York, 1955; Collect. Vol. III, p 56.
(9) Landesberg, J. M.; Katz, L.; Olsen, C. *J. Org. Chem.* **1972**, *37*, 930.
(10) Eckert, H. *Angew. Chem., Int. Ed. Engl.* **1981**, *20*, 208.
(11) Watanabe, K. *Nippon Kagaku Zasshi* **1955**, *76*, 391.
(12) West, R. C.; Selby, S. M. "Handbook of Chemistry and Physics"; The Chemical Rubber Co.: Cleveland, OH, 1967.
(13) Riegel, E. R.; Buchwald, K. W. *J. Am. Chem. Soc.* **1929**, *51*, 484.
(14) Pailer, M.; Huebsch, W. J. *Monatsh. Chem.* **1966**, *97*, 1541.
(15) Bourne, E. J.; Henry, S. H.; Tatlow, C. M.; Tatlow, J. C. *J. Chem. Soc.* **1952**, 4014.
(16) Martin, E. L. "Organic Syntheses"; Wiley: New York, 1943; Collect. Vol. II, p 501.
(17) Clarke, H. T.; Davis, A. W. "Organic Syntheses"; Wiley: New York, 1932; Collect. Vol. I, p 478.
(18) (a) Pouchert, C. J. "The Aldrich Library of Infrared Spectra"; Aldrich, I.: Wisconsin, 1975; p 633, 767. (b) Pouchert, C. J.; Campbell, J. R. "The Aldrich Library of NMR Spectra"; Aldrich, Inc.: Wisconsin, 1974; Vol. V, p 45, Vol. VI, p 38.

Action of Diazomethane on (Z/E)-2-Methyl(or phenyl)-4-benzylidene-5(4H)-oxazolones

Carlos Cativiela, María D. Diaz de Villegas, José A. Mayoral, and Enrique Meléndez*

Department of Organic Chemistry, University of Zaragoza, Zaragoza, Spain

Received August 4, 1983

We have been interested in the synthesis of (Z/E)-2-methyl(or phenyl)-4-(α-arylethylidene)-5(4H)-oxazolones **5** and **6** for several years. Although earlier authors[1] found that acetophenones and hippuric acid could not condense under Plöchl-Erlenmeyer conditions, 2-phenyl derivatives were prepared[2] with moderate or low yields in acetic anhydride and lead acetate as isomeric mixtures with the Z isomer predominating. The pure isomers were obtained by crystallization or by suitable isomerization procedures. Attempts to prepare 2-methyl derivatives have been unsuccessful. On the other hand several workers[3] have in-

(1) Rao, Y. S. *J. Org. Chem.* **1976**, *41*, 722.
(2) Cativiela, C.; Meléndez, E. *Synthesis* **1978**, 832.

0022-3263/84/1949-1436$01.50/0