TPS enol ether of 3-pentanone (4f): 7.4 g (73%); oil consisting of *E* and *Z* isomers; bp 120 °C (0.2 torr); NMR (partial) δ 4.63 (q, J = 6 Hz) and 4.55 (q, J = 6 Hz) *E* and *Z* vinyl H; IR 1670 cm^{-1} (C=C); mass spectrum, m/e 404 (M^+), 389, 347, 319, 303, 143, 75, 57; high-resolution mass spectrum, calcd m/e 404.3111, obsd m/e 404.3110.

TPS enol ether of 2,4-dimethyl-3-pentanone (4g): 10.3 g (95%); white crystals; mp 74-75 °C; NMR δ 7.26 (s, 2 H), 2.87 (m, 1 H, J = 6.6 Hz), 1.68 (s, 3 H), 1.66 (s, 3 H), 1.44 (s, 18 H), 1.30 (s, 9 H), 0.98 (d, 6 H, J = 6.6 Hz), 0.30 (s, 6 H); IR 1670 cm^{-1} (C=C); mass spectrum, m/e 432 (M^+), 417, 376, 319, 303, 263, 75; high-resolution mass spectrum, calcd m/e 432.3424, obsd m/e 432.3404.

TPS enol ether of 2,6-dimethyl-4-heptanone (4h): 9.9 g (86%); oil consisting of *E* and *Z* isomers; bp ~160 °C (0.2 torr); NMR (partial) δ 4.53 (d, J = 9.9 Hz) and 4.31 (d, J = 9.8 Hz), *E* and *Z* vinyl H; mass spectrum, m/e 460 (M^+), 445, 403, 321, 303, 247, 75, 57; high-resolution mass spectrum, calcd m/e 460.3737, obsd m/e 460.3743.

TPS enol ether of isobutyrophenone (4j): 9.5 g (81%); white crystals; mp 85-86 °C; NMR δ 7.2-7.4 (m, 7 H), 1.77 (s, 3 H), 1.67 (s, 3 H), 1.45 (s, 18 H), 1.29 (s, 9 H), 0.086 (s, 6 H); IR 1660 cm^{-1} (C=C); mass spectrum, m/e 466 (M^+), 451, 409, 353, 303, 205, 131, 75, 57; high-resolution mass spectrum, calcd m/e 466.3267, obsd m/e 466.3271.

Hydrolysis studies of **4b**, **5**, and **6** were conducted by dissolving 1 mmol of silyl enol ether in 2.5 mL of solution A, B, C, or D. After the indicated time, the standard, decane, was added, 10 mL of ether was used to extract the solution (except for solution D, which was analyzed directly), and the solution was washed with H_2O (1 × 5 mL), dried with $MgSO_4$, and analyzed by GLC.

Trityl Tetrafluoroborate Oxidation of 4b. A solution of **4b** (2.08 g, 5 mmol) in 2.5 mL of CH_2Cl_2 was added dropwise to a suspension of trityl tetrafluoroborate (1.80 g, 5.5 mmol) in 2.5 mL of CH_2Cl_2 over 1 min at 25 °C. After 10 min the reaction was quenched with 10 mL of water. The CH_2Cl_2 layer was dried ($MgSO_4$) and the internal standard, *n*-hexadecane, was added. GLC analysis (4 ft × 0.25 in. column packed with 15% Carbowax 20M terephthalate on Chromsorb W) showed cyclohexenone (91%) and cyclohexanone (6%).

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Registry No. **3**, 79746-31-9; **4a**, 79746-32-0; **4b**, 79746-33-1; **4c**, 79746-34-2; **4d**, 79746-35-3; **4e**, 79746-36-4; (*E*)-**4f**, 79746-37-5; (*Z*)-**4f**, 79746-38-6; **4g**, 79746-39-7; (*E*)-**4h**, 79746-40-0; (*Z*)-**4h**, 79746-41-1; **4i**, 79746-42-2; **4j**, 79746-43-3; **5**, 6651-36-1; **6**, 62791-22-4; acetophenone, 98-86-2; cyclopentanone, 120-92-3; cyclohexanone, 108-94-1; 2,6-dimethylcyclohexanone, 2816-57-1; cycloheptanone, 502-42-1; cyclooctanone, 502-49-8; 3-pentanone, 96-22-0; 2,4-dimethyl-3-pentanone, 565-80-0; 2,6-dimethyl-4-heptanone, 108-83-8; isobutyrophenone, 611-70-1; cyclohexenone, 930-68-7; dichlorodimethylsilane, 75-78-5; 2,4,6-tri-*tert*-butylphenol, 732-26-3.

Mild Conversion of Carboxamides and Carboxylic Acid Hydrazides to Acids and Esters

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A mild and selective conversion of unsubstituted carboxamides and carboxylic acid hydrazides to the corresponding acids and esters is brought about by the use of acidic resins. Application of the procedure to several carboxamides and carboxylic acid hydrazides is described.

Although unsubstituted carboxamides are readily prepared from the corresponding methyl or ethyl esters, the conversion of carboxamides to esters is often difficult. The existing methods for this transformation, or that to the carboxylic acid, usually call for treatment with strong acid or base under conditions generally incompatible with sensitive substrates.[1,2] Although amide hydrolysis via nitrosation has been carried out under neutral conditions,[4] often the use of strong proton[5] or Lewis acids[6] is required. Likewise, hydrolysis of carboxylic acid hydrazides usually requires strongly acidic or basic media, although mild conversions to acids and esters using copper compounds have recently been described.[7] Although ion-exchange resins have been used widely as catalysts in organic synthesis and particularly in hydrolysis reactions,[8] only a single report of amide hydrolysis promoted by a resin has appeared.[9] We now report that use of acidic resins provides a mild method for conversion of unsubstituted carboxamides and carboxylic acid hydrazides to the corresponding acid or ester.

The procedure consists of combining the amide or hydrazide with a 15-fold excess (by weight) or Amberlyst 15

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(10) Paulson, J. C.; Deatherage, F. E. *J. Am. Chem. Soc.* **1954**, *76*, 6198.

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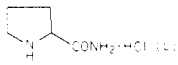
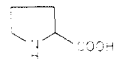
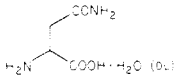
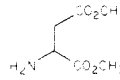
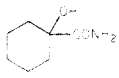
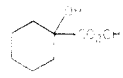
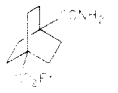
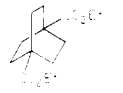
Table I. Conversion of Carboxamides and Carboxylic Acid Hydrazides to Acids and Esters

substrate	product	resin[a]	solvent	temp, °C	time, h	% yield[b]
$PhCONH_2$[c]	$PhCO_2CH_3$	A	CH_3OH	60	96	70
$PhCH_2CONH_2$[c]	$PhCH_2COOH$	A	H_2O	100	4	89
$PhCH{=}CHCONH_2$	$PhCH{=}CHCO_2CH_3$	A	CH_3OH	60	144	62
DL-$PhCONHC(CH_3)HCONH_2$	$PhCONHC(CH_3)HCO_2CH_3$	A	CH_3OH	60	24	89
				20	168	83
L-$PhtNC(CH_2Ph)HCONH_2$[d]	$PhtNC(CH_2Ph)HCO_2CH_3$	A	CH_3OH	60	144	87
		B			18	86
		C			24	91
	$PhtNC(CH_2Ph)HCO_2Et$	A	EtOH	60	144	84
$CH_2{=}CH(CH_2)_8CONH_2$	$CH_2{=}CH(CH_2)_8CO_2CH_3$	A	CH_3OH	60	48	94
$CH_2(CONH_2)_2$	$CH_2(CO_2CH_3)_2$	A	CH_3OH	60	24	63
$N{\equiv}CCH_2CONH_2$[c]	$N{\equiv}CCH_2CO_2CH_3$	A	CH_3OH	60	18	85
		A	H_2O	100	72	90
		A	CH_3OH	60	96	77
DL-Gly-Asn	Gly-Asp	A	H_2O	100	24	95
		A	CH_3OH	60	48	63
		B	EtOH	75	120	66
$PhCONCH_3$		A, B, C	CH_3OH	60	168	NR[e]
$PhCONHNH_2$	$PhCO_2CH_3$	A	CH_3OH	60	24	68
$PhCONHCH_2CONHNH_2$	$PhCONHCH_2CO_3CH_3$	A	CH_3OH	60	20	78
DL-CBZ-Val-Tyr-$NHNH_2$	CBZ-Val-Tyr-OCH_3	A	CH_3OH	60	2	62

[a] A = Amberlyst 15; B = Amberlyst XN-1010; C = Amberlite 120. [b] Yield of purified product. [c] One gram of amide was treated. [d] The amount of solvent was increased to 8 mL. [e] No reaction.

acidic resin[12] in water, methanol, or ethanol and warming the mixture at reflux. The product is isolated upon filtration to remove the resin and evaporation. In the case of substrates possessing a basic amine function, the product is washed from the resin with a mixture of the reaction solvent and pyridine or triethylamine. Results for several amides and hydrazides are shown in Table I.

Although Amberlyst 15 acidic resin was used for most reactions, both Amberlyst XN-1010 and Amberlite IR-120 resins[12] brought about faster conversions and were found more suitable for slow-reacting amides. However, even when the reactions proceeded slowly, the products isolated were very clean.[13] In most cases it was found to be convenient to run the reactions in a closed vessel (a flask with the cap wired on securely) at the reflux temperature of the solvent,[15] with the minimum amount of solvent necessary to cover the resin. In some cases, due to limited solubility, additional solvent was used.

The process is specific for unsubstituted carboxamides. Thus even an *N*-methyl substituent prevents the reaction from proceeding (see Table I). This, coupled with the mildness of the procedure, permits selective hydrolyses in the presence of other amides (including peptide bonds) and functional groups. Carboxylic acid hydrazides were consumed more rapidly than the corresponding amides, providing carboxylic acids or esters in good yields.

Experimental Section

The commercially available resins[12] were rinsed with methanol until the washes were neutral and then dried in vacuo. Unless otherwise noted, all compounds are known. Products of the reactions were identified by comparison TLC, IR, NMR, melting point) with authentic samples. Silica gel chromatography was performed on 1.0-mm silica gel plates (Analtech).

General Procedure. The amide or hydrazide (100 mg) and the resin (1.5 g) were combined with sufficient solvent (water, methanol, or ethanol) to cover the resin (~4 mL). For slightly soluble amides (Table I, footnote *d*) the volume of solvent was doubled. Gentle agitation was provided by a magnetic spinbar small enough to prevent powdering of the resin.[14] The flask was tightly stoppered and warmed to the reflux temperature of the solvent.[15] The progress of the reaction was monitored by TLC or GC. Removal of the resin by filtration and evaporation of the solvent provided the crude product, which was purified by silica gel chromatography or distillation. Amides possessing basic nitrogen atoms were used as the free bases or as the hydrochloride salts.[16] The product in these cases was recovered by collecting the resin in a column and eluting slowly with a mixture of the solvent and pyridine (20:1) or triethylamine (2:1). The progress of these reactions was followed by TLC by removing aliquots of the resin and eluting as described above. Representative examples are described below.

Methyl Cyanoacetate. Cyanoacetamide (1.0 g, 11.9 mmol) and Amberlyst 15 resin (15 g) were combined with methanol (40 mL), and the resulting mixture was stirred gently in a tightly capped flask at 60 °C for 18 h. The mixture was cooled and filtered, and the residue after concentration was distilled in a

(12) Amberlyst and Amberlite are registered trademarks of Rohm and Haas Co. The resins used (Rohm and Haas) were purchased from Aldrich Chemical Co.

(13) Due to the purity of the products isolated in all cases, many of the reaction times listed were not minimized.

(14) Powdering of the resin causes difficulties in the filtration; no increase in rate was observed when the resin was intentionally powdered prior to the reaction.

(15) The use of closed vessels was found to be convenient (and safe) for small volumes. For scale-ups a reflux condenser or slightly lower temperature should be used. In one case where the reaction flask ran dry, no reduction in yield resulted.

(16) When hydrochloride salts were used as substrates, some product was occassionally present in the supernatant and was recovered (as the hydrochloride salt) from neutral washes of the resin.

Kugelrohr apparatus, giving pure product (1.00 g, 10.1 mmol, 85%) as a colorless liquid.

Glycyl-DL-aspartic Acid. Glycyl-DL-asparagine (100 mg, 0.53 mmol) and Amberlyst XN-1010 resin (1.5 g) were combined with water (4 mL), and the mixture was heated in a closed flask (100 °C) for 72 h. The resin was collected in a small column and washed once with water. Elution with aqueous ammonia (0.5 N) and concentration provided glycyl-DL-aspartic acid (95.5 mg, 0.50 mmol, 95%) as a white foam.

Dimethyl DL-Aspartate. DL-Asparagine monohydrate (100 mg, 0.67 mmol) and Amberlyst 15 resin (1.5 g) were combined with methanol (4 mL), and the mixture was heated in a closed flask (60 °C) for 4 days. The resin was collected in a small column and the product eluted with a solution of methanolic ammonia (a saturated solution diluted with six volumes of methanol). Evaporation and purification of the residue on silica gel (1-mm plate, 20:1 CH_2Cl_2–CH_3OH) afforded dimethyl DL-aspartate (82.3 mg, 0.51 mmol, 77%) as a colorless oil.

***N*-Benzoylglycine Methyl Ester.** *N*-Benzoylglycinohydrazide (99.1 mg) and Amberlyst 15 resin (1.5 g) were combined with methanol (4 mL), and the mixture was heated in a closed flask (60 °C) for 20 h. After filtration and evaporation, the residue was purified by silica gel chromatography (1-mm plate, EtOAc), giving *N*-benzoylglycine methyl ester (77.7 mg, 0.40 mmol, 78%) as a colorless oil.

L-*N*-Phthaloylphenylalanine methyl ester was prepared by the general procedure and purified by chromatography on silica gel: NMR ($CDCl_3$) δ 3.50 (1 H, d, J = 9 Hz), 3.52 (1 H, d, J = 8 Hz), 3.72 (3 H, s), 5.08 (1 H, dd, J = 8, 9 Hz), 7.05 (5 H, s), 7.8 (4 H, m); IR ($CHCl_3$) 1770, 1735, 1710 cm^{-1}; mass spectrum, m/e 309 (M^+). Anal. Calcd for $C_{18}H_{15}NO_4$: C, 69.89; H, 4.89; N, 4.53. Found: C, 69.57; H, 5.08; N, 4.22.

L-*N*-Phthaloylphenylalanine ethyl ester was prepared by the general procedure and purified by chromatography on silica gel: NMR ($CDCl_3$) δ 1.22 (3 H, t, J = 7 Hz), 3.50 (1 H, d, J = 9 Hz), 3.53 (1 H, d, J = 7 Hz), 4.18 (2 H, q, J = 7 Hz), 5.07 (1 H, dd, J = 7, 9 Hz), 7.1 (5 H, s), 7.7 (4 H, m); IR ($CHCl_3$) 1770, 1735, 1710 cm^{-1}; mass spectrum, m/e 323 (M^+). Anal. Calcd for $C_{19}H_{17}NO_4$: C, 70.57; H, 5.30; N, 4.33. Found: C, 70.60; H, 5.32; N, 4.22.

DL-*N*-Benzoylalaninamide. A solution of DL-*N*-benzoylalanine methyl ester (1.0 g, 4.83 mmol) in ammonia-saturated methanol (20 mL) was allowed to stand for 48 h. The resulting crystalline product was collected (0.79 g, 85%) and washed with methanol: mp 231–233 °C; NMR (Me_2SO-d_6) δ 1.33 (3 H, d, J = 7 Hz), 4.42 (1 H, quintet, J = 7 Hz), 7.0 (1 H, br), 7.3–7.6 (4 H, m), 7.8–8.0 (2 H, m), 8.2–8.4 (1 H, br); IR (KBr) 3250, 3150, 1620, 1540 cm^{-1}; mass spectrum m/e 148 (P – $CONH_2$). Anal. Calcd for $C_{10}H_{12}N_2O_2$: C, 62.48; H, 6.29; N, 14.58. Found: C, 62.51; H, 6.23; N, 14.58.

10-Undecenamide. A solution of methyl 10-undecenoate (2.0 g, 10.0 mmol) in ammonia-saturated methanol (40 mL) was allowed to stand for 5 days. Recrystallization from ethyl acetate gave pure amide: mp 85–86 °C; 0.90 g (48%); NMR ($CDCl_3$) δ 1.2–1.9 (12 H, br s), 1.9–2.4 (4 H, m), 4.7–5.1 (2 H, m), 5.1–6.0 (3 H, m); IR ($CHCl_3$) 2940, 2860, 1660, 995, 915 cm^{-1}; mass spectrum, m/e 183 (M^+). Anal. Calcd for $C_{11}H_{21}NO$: C, 72.18; H, 11.55; N, 7.64. Found: C, 72.14; H, 11.79; N, 7.47.

Registry No. Methyl benzoate, 93-58-3; phenylacetic acid, 103-82-2; methyl cinnamate, 103-26-4; PhCO-DL-Ala-OMe, 38767-73-6; Pht-L-Phe-OMe, 14380-85-9; Pht-L-Phe-OEt, 50468-37-6; Methyl 10-undecenoate, 111-81-9; dimethyl malonate, 108-59-8; methyl cyanoacetate, 105-34-0; H-L-Pro-OH, 147-85-3; H-DL-Asp dimethyl ester, 40149-67-5; DL-Gly-Asp-OH, 79731-35-4; methyl 1-hydroxycyclohexanecarboxylate, 6149-50-4; diethyl 1,4-bicyclo[2.2.2]octanecarboxylate, 1659-75-2; *N*-benzoylglycine methyl ester, 1205-08-9; Cbz-L-Val-L-Tyr-OMe, 15149-72-1; benzamide, 55-21-0; phenylacetamide, 103-81-1; cinnamamide, 621-79-4; PhCO-DL-Ala-NH_2, 24250-70-2; Pht-L-Phe-NH_2, 21946-94-1; 10-undecenamide, 5332-51-4; malonamide, 108-13-4; 2-cyanoacetamide, 107-91-5; H-LPro-NH_2·HCl, 42429-27-6; H-DL-Asn-OH, 3130-87-8; DL-Gly-Asn-OH, 32729-21-8; 1-hydroxycyclohexanecarboxamide, 7500-69-8; ethyl 1-(aminocarbonylbicyclo[2.2.2]octane-4-carboxylate, 79663-72-2; *N*-methylbenzamide, 613-93-4; benzoic acid hydrazide, 613-94-5; 2-(benzoylamino)acetic acid hydrazide, 2443-68-7; Cbz-L-Val-L-Tyr-$NHNH_2$, 5992-90-5.

Reactivities of Aldehydes in Homogeneous Catalytic Hydrogenation with Cationic Rhodium Complexes

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Catalytic hydrogenation of several aldehydes with cationic rhodium complexes was investigated at 30 °C under atmospheric and 50-atm pressures of hydrogen. The catalytic activity was found to depend very much on the structure of the phosphorus ligands, PEt_3 exhibiting the highest activity among the ligands examined. The PPh_3 catalyst showed essentially no activity for aldehydes except for phenylacetaldehyde. The diphos catalyst was completely inactive for all the aldehydes examined. Although catalyst deactivation occurred in the early stages of the reactions under 1 atm of hydrogen for almost all the aldehydes examined, its extent depended very much on the substrate. Decarbonylation products were detected under the reaction conditions, suggesting the formation of carbonyl complexes as the reason for catalyst deactivation. A higher pressure of hydrogen, 50 atm, reduced to a great extent such catalyst deactivation. Selective hydrogenation of the unsaturated aldehyde, crotonaldehyde, yielding the corresponding unsaturated alcohol, was partially achieved, the yields being 4% and 13% under hydrogen pressures of 1 and 50 atm, respectively. The reactivities of aldehydes are discussed from the point of view of their coordination and hydrogenation mechanisms, in comparison with those of ketones and olefins.

Introduction

Hydrogenation of aldehydes with homogeneous catalysts has been extensively studied.[1,2] Although simultaneous decarbonylation often takes place even under mild reaction conditions,[3] a few catalysts have been reported to show the high catalytic activity at room temperature under atmospheric pressure of hydrogen.[2] It must be noted that $RuCl_2(PPh_3)_3$ was reported to hydrogenate aldehydes without decarbonylation at 50~70 °C under hydrogen

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