bulb-to-bulb distillation (180 °C, 0.5 mm) gave 260 mg (96%) of **24** as an 8:1 mixture of *Z*/*E* isomers, which could be separated by PTLC (silica gel, 8:1 CH_2Cl_2–Et_2O). Major *Z* isomer: ^1H NMR ($CDCl_3$) δ 0.83 (t, 3 H), 0.88 (s, 9 H), 1.27 (br 12 H), 2.23 (s, 2 H), 2.25–2.65 (m, 2 H), 5.91 (t, *J* = 7.3 Hz, 1 H). The olefinic proton in the minor (lower R_f) *E* isomers appears as a triplet at δ 6.95. Anal. Calcd for $C_{16}H_{30}O_2$: C, 75.53; H, 11.89. Found: C, 75.65; H, 11.73.

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Registry No. **5**, 110875-05-3; **6**, 111-14-8; **7**, 1561-11-1; **8**, 1118-47-4; **9**, 501-52-0; **10**, 35329-50-1; **11**, 591-80-0; **12**, 86146-09-0; **13**, 1115-16-8; **14**, 140-77-2; **15**, 110875-06-4; **16**, 110875-07-5; **17**, 58888-90-7; **18**, 110875-08-6; **19**, 606-83-7; **20**, 66270-63-1; **21**, 76346-98-0; **22**, 110875-09-7; **23**, 3302-09-8; (*Z*)-**24**, 110875-10-0; (*E*)-**24**, 110875-11-1; PhMgBr, 100-58-3; *sec*-BuMgCl, 15366-08-2; *n*-BuMgCl, 693-04-9; *t*-BuMgCl, 677-22-5; (*E*)-1-hexenyllithium, 62839-68-3; cyclopentylmagnesium bromide, 33240-34-5; 2-dithianyllithium, 36049-90-8; (bromovinyl)trimethylsilane, 13683-41-5; dithiane, 505-23-7; (trimethylsilyl)magnesium bromide, 49750-22-3; nonanal, 124-19-6; vinyllithium, 917-57-7; vinylmagnesium bromide, 1826-67-1.

Synthesis of α-Keto Esters via Palladium-Catalyzed Double Carbonylation

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In recent years, increasing importance has been placed on the utilization of carbon monoxide for organic synthesis.[1] Of particular industrial value are those reactions in which more than one unit of carbon monoxide are incorporated in the products. One reaction of considerable interest in this field is the direct reductive carbonylation of carbon monoxide with the chief aim being the synthesis of C_2 oxygenates such as ethylene glycol, ethanol, and/or acetic acid.[2] The alternative copolymerization of carbon monoxide with olefins also seems to be of great promise.[3] Another of industrial potential is the cobalt[4] or palladium[5-7] catalyzed double carbonylation of organic halides leading to the formation of α-keto acid derivatives, which are useful starting materials for α-amino acids and others.

Table I. Steric Effect of Alcohols on the Reaction Rate[a]

ROH	total yield,[b] % $PR_3 = PPh_3$	$PPh_2(o\text{-}MeC_6H_4)$
MeOH	67	
EtOH	51	70
i-PrOH	17	33
t-BuMeCHOH	4	9
t-BuOH	0	

[a] $PdCl_2(PR_3)_2$ (0.02 mmol), PhI (2.2 mmol), ROH (2.5 mmol), NEt_3(2.5 mmol), benzene (2.5 mL), *p*(CO) = 150 atm at room temperature, 80 °C, 14 h. [b] $PhCOCO_2R$ + $PhCO_2R$.

Table II. Effect of Alcohols on Keto Ester Synthesis[a]

ROH	selectivity,[b] %	total yield,[c,d] %
MeOH	0	83
EtOH	13	92
n-BuOH	32	90
i-BuOH	40	77
t-$BuCH_2OH$	51	98
i-PrOH	37	99
$C_6H_{11}OH$[e]	41	97
sec-BuOH	26	99
t-BuOH	0	24
$PhCH_2OH$	0	95
PhMeCHOH	12	100
PhOH	0	94

[a] $PdCl_2(PPh_3)_2$ (0.038 mmol), PhI (4 mmol), ROH (1 mL), NEt_3 (5 mL), *p*(CO) = 150 atm at room temperature, 120 °C, 10 h. [b] 100 × $PhCOCO_2R$/($PhCOCO_2R$ + $PhCO_2R$). [c] $PhCOCO_2R$ + $PhCO_2R$. [d] Conversions were 100% except the case of *t*-BuOH (54%). [e] Cyclohexanol.

We recently reported the first example of a palladium complex catalyzed double carbonylation of halides in the presence of primary or secondary amines that affords α-keto amides in good yields (eq 1).[5a,b] Our continuous

$$ArX + CO + HNu \rightarrow ArCOCONu\ (+\ ArCONu) \qquad (1)$$

(HNu: R_2NH, RNH_2, ROH, H_2O)

and comprehensive research on the double carbonylation has revealed that α-keto esters can also be synthesized from organic halides and alcohols in the presence of tertiary amines.[6a,b] However, the selectivities for the double carbonylation were usually lower than those observed in the α-keto amide synthesis, so that the reaction recipe should be more strictly specified for the α-keto ester synthesis. We now report the full details of the influence of the various reaction parameters that affect the selec-

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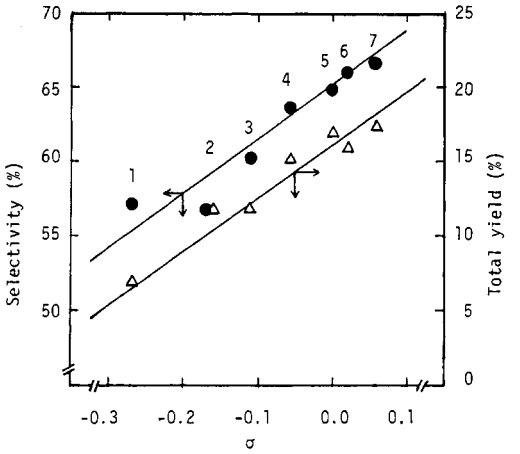

Figure 1. Electronic effect of para-substituted triarylphosphines. Reaction conditions: $PdCl_2(PR_3)_2$ (0.02 mmol), PhI (2.2 mmol), *i*-PrOH (2.5 mmol), NEt_3 (2.5 mmol), benzene (2.5 mL), $p(CO)$ = 150 atm at room temperature, 80 °C, 14 h. PR_3: 1, P(*p*-$MeOC_6H_4)_3$; 2, P(*p*-$MeC_6H_4)_3$; 3, $PPh(p\text{-}MeC_6H_4)_2$; 4, PPh_2(*p*-MeC_6H_4); 5, PPh_3; 6, P(*p*-$PhC_6H_4)_3$; 7, P(*p*-$FC_6H_4)_3$. σ: Hammett's sigma value. σ for $P(p\text{-}XC_6H_4)_nPh_{3-n}$ = $^1/_3[n\sigma_p(X) + (3-n)\sigma_p(H)]$.

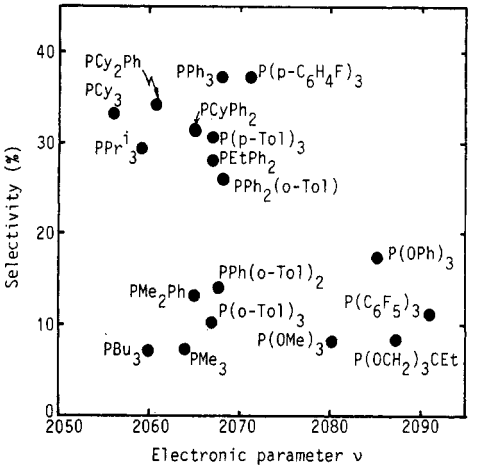

Figure 2. Electronic effect of phosphine ligands on the selectivity. Reaction conditions: $PdCl_2(PR_3)_2$ (0.04 mmol), PhI (4.0 mmol), *i*-PrOH (1 mL), NEt_3 (5 mL), $p(CO)$ = 150 atm at room temperature, 120 °C, 10 h. Cy: cyclohexyl. Tol: MeC_6H_4.

tivity as well as the reaction rate.

Results

(a) Influence of the Nature of Alcohols. In the double carbonylation reaction of aryl halides using secondary amines as nucleophiles, the reaction rate and the selectivity toward keto amides depended much on the bulkiness of amines. Thus, dipropylamine gave the best results, and the use of either smaller or larger amines resulted in the decrease of selectivity[5a,d] (the ratio of keto amide to the sum of the keto amide and the amide formed as a byproduct). The steric factor of nucleophiles was also important in the reaction with primary amines.[5b]

As was observed in these reactions, the effect of the bulkiness of alcohols was also quite large in the keto ester synthesis. The reaction rate was markedly influenced by the bulkiness of alcohols.[8] The higher rate was observed when the smaller alcohol was used (Table I). As Table II shows, there was an optimum size of nucleophiles in regard to selectivities: In the series of primary alcohols, the order of the selectivities was the same as that of the bulkiness of the alcohols: *t*-$BuCH_2OH$ > *i*-BuOH > *n*-BuOH > EtOH > MeOH. However, for the reaction with secondary or tertiary alcohols used as the nucleophiles, the selectivity decreased according to the order of bulkiness; *t*-BuOH gave only the monocarbonylated product.

Electronic character of the alcohols cannot be neglected, either. Thus, phenol or benzyl alcohol did not give double carbonylated products, even though their bulkiness was not so different from those of cyclohexyl and isobutyl alcohols, respectively. However, when α-phenethyl alcohol was used, the keto ester was, albeit in a low yield, obtained, probably due to the increased steric bulk endowed with α-methyl group.

(b) Influence of the Catalyst Ligands. In the keto amide synthesis, moderately basic monophosphines like $PPhMe_2$ or diphosphines such as 1,4-bis(diphenylphosphino)butane and 1,4-bis(dicyclohexylphosphino)butane were the ligands of choice for obtaining high selectivities. However, considered as a whole, the ligand effect on the selectivities was rather small, and a high selectivity was readily achieved even without phosphine ligands employed. On the other hand, in the present keto ester synthesis, the nature of phosphine ligand played a decisive role.

In order to estimate the performance of the ligands from the electronic aspect, the reactions with para-substituted triphenylphosphine palladium complexes used as the catalysts were examined for the combination of iodobenzene and 2-propanol. The results illustrated in Figure 1 show that a fast reaction and a high selectivity for the keto ester were realized when electron-withdrawing groups were bound at the para position of the phosphines. As for other various phosphines, the sum of the yield of the keto ester and ester in the reaction of iodobenzene with 2-propanol in triethylamine solvent under the conditions of 150 atm, 120 °C for 10 h increased as follows: PMe_2Ph (5.5%) < PBu_3 (12.0%) < PMe_3 (50.6%) < $PEtPh_2$ (58.0%) < $P(OMe)_3$ (86.8%) < $P(OPh)_3$ (93.6%) < P(*i*-Pr)$_3$, P(c-$C_6H_{11})_3$, PPh_3 (over 95%). Although deviations were observed because of the difficulty in evaluating the electronic effect separately from the steric one, the tendency was that phosphines having alkyl groups, which were capable donors, gave lower reaction rate than those with aryl or alkoxy groups. High reaction rates obtained by P(*i*-Pr)$_3$ and P(c-$C_6H_{11})_3$ compared with other alkylphosphines would be due to their large steric bulkiness, which cause the dissociation at this temperature, making a vacant coordination site during the reaction. On the other hand, any correlation between the electronic parameters (ν)[9] of various phosphines and selectivities for double carbonylation was hardly found from the scattered plots shown in Figure 2. It turned out that the results should be estimated from the steric aspect. Thus, if the selectivities are plotted against the cone angles[9] of the phosphines used (Figure 3), one can easily recognize the significant correlation among those with optimum values around 140–170°. The use of less or more congested phosphines resulted in inferior selectivities. Similar correlations of the selectivities with the cone angles were also obtained for other alcohols as illustrated in Figure 4. It is interesting to note that the steric effect of the ligands was dependent on the bulkiness of the alcohols; the optimum cone angle has a propensity to shift to smaller values as the bulkiness of alcohols increased. Considering

(8) The sum of the yield of keto ester and ester (total yield) was used as an index of reaction rate. The total yields were almost the same as the conversions of aryl iodides.

(9) Tolman, C. A. *Chem. Rev.* **1977**, *77*, 313.

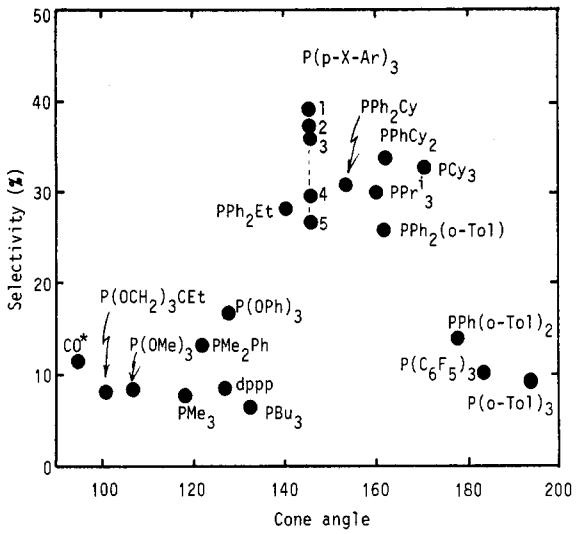

Figure 3. Steric effect of phosphine ligands on the selectivity. Reaction conditions: $PdCl_2(PR_3)_2$ (0.04 mmol), PhI (4.0 mmol), *i*-PrOH (1 mL), NEt_3 (5 mL), $p(CO)$ = 150 atm at room temperature, 120 °C, 10 h. X: 1, Ph; 2, F; 3, H; 4, Me; 5, MeO. *$PdCl_2(PhCN)_2$. Cy: cyclohexyl. Tol: MeC_6H_4. dppp: 1,3-bis(diphenylphosphino)propane.

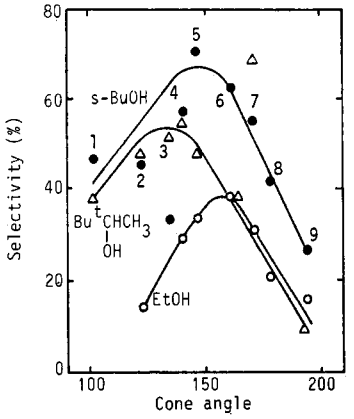

Figure 4. Steric effect of phosphine ligands on the selectivity. Reaction conditions: $PdCl_2(PR_3)_2$ (0.02 mmol), PhI (2.2 mmol), ROH (2.5 mmol), NEt_3 (2.5 mmol), benzene (2.5 mL), $p(CO)$ = 150 atm at room temperature, 80 °C, 14 h. PR_3: $P(OCH_2)_3CEt$; 2, PMe_2Ph; 3, $PPh_2(OEt)$; 4, $PEtPh_2$; 5, PPh_3; 6, $PPh_2(o\text{-Tol})$; 7, $P(Cy)_3$; 8, $PPh(o\text{-Tol})_2$; 9, $P(o\text{-Tol})_3$.

the results mentioned above as a whole, the dominant effects of the ligands on the selectivities may be attributed to the steric factor rather than the electronic one, although the latter also plays a minor role. Some deviant plots observed in Figures 3 and 4 may be due to the neglection of the minor electronic effect.

(c) Ligand Dissociation and the Influence of the Addition of Phosphine. While the data shown in Figure 4 was collected, it was recognized that the use of bulky phosphines like *o*-tolylphosphines, $P(o\text{-Tol})_nPh_{3-n}$ (n = 1–3), facilitated the reaction as compared with that of triphenylphosphine (Figure 5). This phenomenon was not distinct in the reactions effected under more severe conditions for a longer period like the ones shown in Figure 3. To consider the steric and electronic aspects separately, the reactions in the presence of *p*-tolylphosphines, $P(p\text{-Tol})_nPh_{3-n}$ (n = 1–3), were compared with those of *o*-tolylphosphines. The comparison is illustrated in Figure 6. Since the electronic parameter of $P(o\text{-Tol})_nPh_{3-n}$ is the same as that of $P(p\text{-Tol})_nPh_{3-n}$,[9] the difference in the reactivity between them can be ascribed to the steric effect. As the number of *p*-tolyl groups (n) increased, the sum of

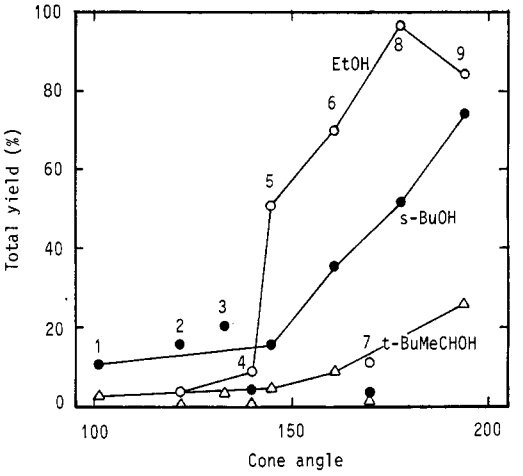

Figure 5. Steric effect of phosphine ligands on the reaction rate. Reaction conditions: $PdCl_2(PR_3)_2$ (0.02 mmol), PhI (2.2 mmol), ROH (2.5 mmol), NEt_3 (2.5 mmol), benzene (2.5 mL), $p(CO)$ = 150 atm at room temperature, 80 °C, 14 h. PR_3: 1, $P(OCH_2)_3CEt$; 2, PMe_2Ph; 3, $PPh_2(OEt)$; 4, $PEtPh_2$; 5, PPh_3; 6, $PPh_2(o\text{-Tol})$; 7, $P(Cy)_3$; 8, $PPh(o\text{-Tol})_2$; 9, $P(o\text{-Tol})_3$.

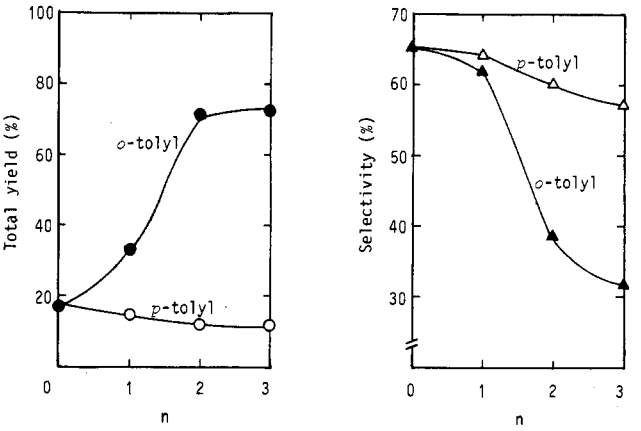

Figure 6. Steric and electronic effect of triarylphosphines. Reaction conditions: $PdCl_2[P(MeC_6H_4)_nPh_{3-n}]_2$ (0.02 mmol), PhI (2.2 mmol), *i*-PrOH (2.5 mmol), NEt_3 (2.5 mmol), benzene (2.5 mL), $p(CO)$ = 150 atm at room temperature, 80 °C, 14 h.

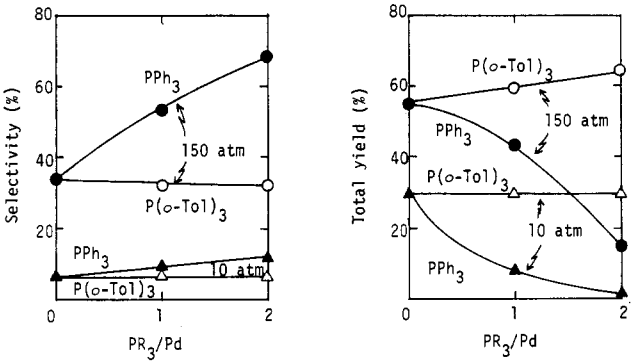

Figure 7. Effect of addition of $P(o\text{-Tol})_3$ and PPh_3 to $PdCl_2$. Reaction conditions: $PdCl_2$ (0.03 mmol), PhI (2.2 mmol), *i*-PrOH (2.5 mmol), NEt_3 (2.5 mmol), benzene (2.5 mL), 80 °C, 14 h.

the yield of the keto ester and the ester slightly reduced (vide supra). This trend is entirely different from that observed for *o*-tolylphosphine series. In regard to the selectivities, both series of phosphines exhibited descending trends, the influence of *o*-tolylphosphine being enormous as compared with the corresponding para isomers. Considering the large cone angles of *o*-tolylphosphines, it seems conceivable that these phosphines easily dissociate under carbon monoxide of high pressures; the palladium catalyst

Table III. Effect of Excess Amount of Triphenylphosphine on Keto Ester Synthesis

ROH	PPh_3/Pd	yield, % $PhCOCO_2R$	yield, % $PhCO_2R$	selectivity, %
MeOH[a]	2	16.1	51.3	24
	4	7.8	11.1	41
	6	5.0	4.7	52
EtOH[b]	0	11.4	54.8	17
	2	15.2	21.0	42
	4	5.0	4.3	54
	6	4.2	3.0	59
	10	2.5	1.2	68
sec-BuOH[b]	0	17.3	46.5	27
	1	21.5	17.6	55
	2	12.7	5.1	71
	3	4.6	3.1	60
	4	2.3	2.1	51
	6	1.3	1.4	47
	10	0.6	1.2	35

[a] $PdCl_2(PPh_3)_2$ (0.02 mmol), PhI (2.2 mmol), ROH (2.5 mmol), NEt_3 (2.5 mmol), benzene (2.5 mL), p(CO) = 150 atm at room temperature, 80 °C, 14 h. [b] $PdCl_2$ (0.03 mmol), the other conditions were the same as noted in *a*.

is free from phosphines while it is working. As a matter of fact, addition of tri-*o*-tolylphosphine to the palladium chloride catalyst caused little change in both the reaction rate and the selectivity as compared with the reaction catalyzed by palladium chloride alone, while the addition of triphenylphosphine enhanced the selectivity at the expense of the reaction rate (Figure 7). From the results mentioned above, it may safely be concluded that the low selectivities exhibited by P(*o*-Tol)$_2$Ph, P(*o*-Tol)$_3$, and presumably also P(C$_6$F$_5$)$_3$ may be due to the participation of phosphine-free species generated through the ligand dissociation. Weak donor ability of these phosphines may also be another reason for easy dissociation to occur, since strong electron donation may result in strong coordination. This may be supported by the fact that tricyclohexylphosphine, a bulky but capable donor, did not facilitate, but rather hampered the reaction in spite of its large cone angle (Figure 5).

Since the phosphine–palladium complexes $PdCl_2(PR_3)_2$ exerted higher selectivities than $PdCl_2$ or $PdCl_2(PhCN)_2$ in general, the influence of the ratio PPh_3/Pd was examined (Table III). The formation of both the keto ester and the ester were suppressed a great deal according to the increase of the PPh_3/Pd ratio. However, it may be worth noting from the synthetic viewpoint that even small alcohols like methanol and ethanol can give high selectivities if excess phosphine is used, though the reaction is slow. In other words, in the reaction with small alcohols, the suppression of the formation of ester is larger than that of the keto ester.

(d) Influence of the Pressure of Carbon Monoxide and the Reaction Temperature. The influence of the CO pressure is illustrated in Figure 8. As in the keto amide synthesis, higher pressure was favorable for both the reaction rate and the selectivity,[10] although a much higher pressure was necessary to get a high selectivity than in the keto amide synthesis.

In regard to the reaction temperature, an analogous trend to the keto amide synthesis was observed, although the influence was more profound. Figure 9 shows that the selectivity markedly decreased as the temperature became higher.

(10) Yamamoto et al. reported the opposite effect of CO pressure on the selectivity in the system with tricyclohexylphosphine as a ligand. See ref 6d.

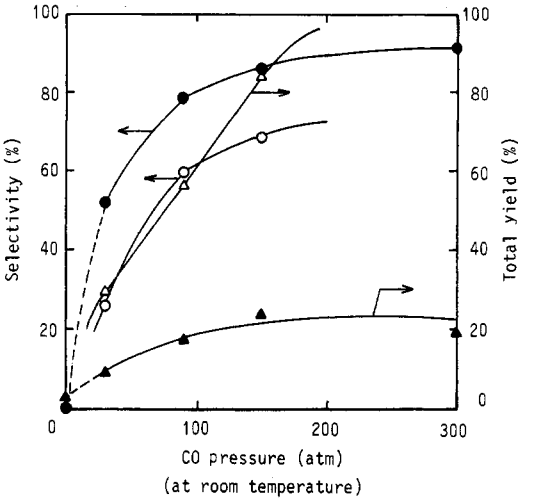

Figure 8. Effect of CO pressure. Reaction conditions: $PdCl_2(PPh_3)_2$ (0.038 mmol), PhI (4.0 mmol), ROH (1 mL), NEt_3 (5 mL), 60 °C, 24 h. The reaction at 1 atm was carried out in a glass flask with a balloon filled with CO. ● and ▲, *i*-PrOH; ○ and △, EtOH.

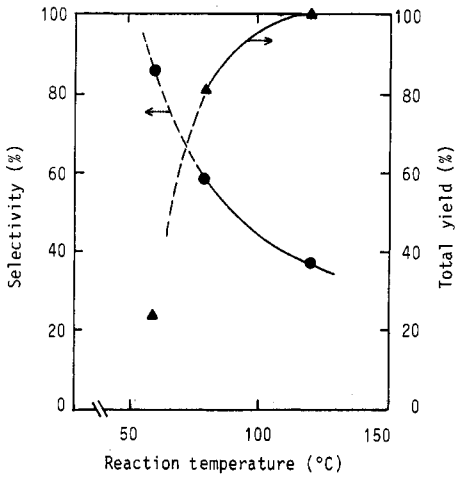

Figure 9. Effect of temperature. Reaction conditions: $PdCl_2(PPh_3)_2$ (0.038 mmol), PhI (4.0 mmol), *i*-PrOH (1 mL), NEt_3 (5 mL), p(CO) = 150 atm at room temperature, 10 h. The reaction at 60 °C was carried out for 24 h.

Table IV. Effect of Tertiary Amines on Keto Ester Synthesis[a]

amine	pK_a	selectivity, %	total yield, %
NEt_2Ph	6.6	0	8
NMe_3	9.9	28	69
$NMe(CH_2)_4$	10.5	39	39
NEt_3	10.7	70	27
NPr_3	10.7	28	14
NBu_3	10.9	27	11
NMe(*i*-Pr)$_2$		59	15
NEt(*i*-Pr)$_2$		15	5
$NMe(C_6H_{11})_2$		62	16
$NMe_2(C_6H_{11})$		58	26

[a] $PdCl_2(PPh_3)_2$ (0.12 mmol), PhI (4.3 mmol), *i*-PrOH (5 mmol), NR_3 (5 mmol), benzene (5 mL), p(CO) = 150 atm at room temperature, 80 °C, 14 h; C_6H_{11}, cyclohexyl.

(e) Effect of Tertiary Amines and Inorganic Bases. As summarized in Table IV, the nature of tertiary amines plays a significant role in the keto ester synthesis. In the reaction with *N*,*N*-diethylaniline, a less basic amine, the reactivity was low, and the keto ester was not formed at all. Keto esters were obtained only when the more basic amines were employed. Among trialkylamines of similar basicities, a descending trend of the reactivity was observed as the amines became more congested. As for the selec-

Table V. Effect of Solvents on Keto Ester Synthesis[a]

solvent	DN[b]	AN[b]	selectivity, %	total yield, %
hexane		0.0	41	4
benzene	0.1	8.2	64	26
CH_2Cl_2	0[c]	20.4	63	30
CH_3CN	14.1	19.3	51	49
THF	20.0	8.0	48	22
DMF	26.6	16.0	30	42
HMPA	38.8	10.6	20	34
NEt_3			72	14

[a] $PdCl_2(PPh_3)_2$ (0.06 mmol), PhI (4.3 mmol), *i*-PrOH (5 mmol), NEt_3 (5 mmol), solvent (5 mL), $p(CO)$ = 150 atm at room temperature, 80 °C, 20 h. [b] DN, donicity number; AN, acceptor number. [c] Value for 1,2-dichloroethane.

tivity, there existed an optimum size of amines. In the series of tri(primary alkyl)amines, triethylamine gave the best result, while the use of either smaller or larger amines resulted in poorer selectivities; among other trialkylamines having secondary alkyl groups bound to nitrogen, at least one of the remaining alkyl groups should be small (e.g. methyl) in order to obtain good selectivities. In many reactions like carbonylation of halides that liberate hydrogen halide during their progress, a tertiary amine added to the reaction system is prone to be regarded merely as a hydrogen halide scavenger. However, the results mentioned above cannot be understood from this simple idea. As was mentioned (vide supra), similar correlation of the bulkiness with both the rate and the selectivity was observed also for alcohols. Therefore, the steric effect of the amines may be rationalized by considering that tertiary amines are in the intimate proximity of the palladium catalyst molecule during the reaction, strongly interacting with alcohols.

Besides tertiary amines, performance of inorganic bases was examined with benzene, dimethylformamide, acetonitrile, or tetrahydrofuran as the solvent. When cesium fluoride was used as the base ($PdCl_2(PPh_3)_2$ 0.03 mmol, 17 h, the other conditions were the same as noted in Table IV), 33.8% of iodobenzene was consumed, and the ester, keto ester, and benzoyl fluoride[11] were formed in 5.6%, 3.6%, and 16.4% yields (based on the halide charged), respectively. In the reaction with lithium hydroxide monohydrate in benzene, benzoylformic acid (9.1%) was obtained together with benzoic acid (11.4%) and isopropyl benzoate (3.3%). The use of other inorganic bases (carbonate of Li, Na, and K and hydroxide of Na, K, and Cs) resulted in even worse selectivities for double carbonylation.

(f) Effect of Solvents. The solvent effect was studied for the reaction of iodobenzene and 2-propanol (Table V). The double carbonylation occurred in all the solvents, but was very slow in hexane, possibly because of its poor ability for dissolving the catalyst. Among the solvents examined, triethylamine gave the highest selectivity, although the direct comparison with the other solvents does not make sense, because of the difference in the amount of the base (e.g. triethylamine). The plots illustrated in Figure 10 indicate the negatively proportional relation of the selectivity with the solvent polarity, with the donicity number[12] (DN) as an index; solvents of higher DN promoted the ester formation.

(g) Reactions of Various Halides. The keto ester synthesis was applied to various organic halides (Table VI).

(11) The aroyl fluoride synthesis by the carbonylation of aryl halides will be published separately; Sakakura, T.; Chaisupakitsin, M.; Hayashi, T.; Tanaka, M. *J. Organomet. Chem.*, in press.
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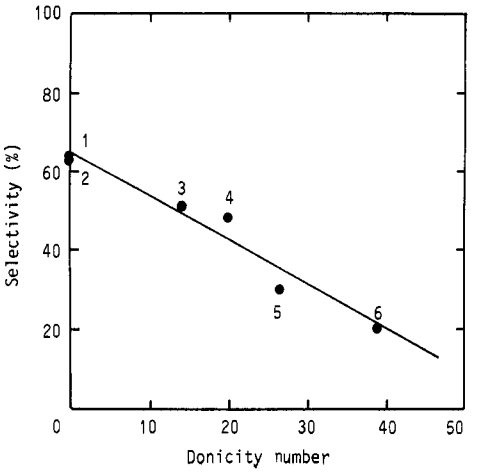
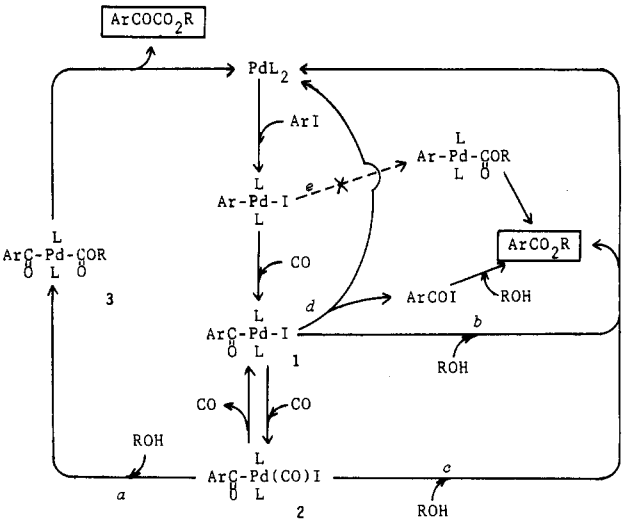


Figure 10. Effect of solvents on the selectivity. Reaction conditions were the same as noted in the footnote *a*, Table V. 1, benzene; 2, CH_2Cl_2; 3, CH_3CN; 4, THF; 5, DMF; 6, HMPA.

Scheme I



Chlorobenzene did not react under the present reaction conditions, because of the low reactivity in oxidative addition to palladium(0) species. Bromobenzene reacted but resulted in low selectivity because a higher reaction temperature and a lower CO pressure than in the case of iodobenzene was necessary for the occurrence of the reaction at a moderate rate.

The electronic effect of substituents on aromatic ring was studied with various para-substituted iodobenzenes. Electron-withdrawing substituents accelerated the reaction, as was reported in the keto amide synthesis.[5d] Since oxidative addition of aryl iodides is not considered to be the rate-determining step, the positive effect of electron-withdrawing groups on the rate may be due to the increase of electrophilicity of aroyl intermediates.

A heteroaromatic iodide, 2-iodothiophene, gave a good selectivity for double carbonylation. A heteroaromatic bromide and an alkenyl iodide also could be transformed into keto esters, though the selectivities were poor. In the reaction of benzyl chloride, the keto ester was not detected.

Discussion

In the keto amide synthesis via the palladium-catalyzed double carbonylation of aryl halides, the keto amide was proven to be formed through reductive elimination from the aroyl carbamoyl complex (eq 2).[13] The mechanism

$$ArCO\text{–}[Pd]\text{–}CONR_2 \rightarrow ArCOCONR_2 \quad (2)$$

Table VI. Keto Ester Synthesis from Various Organic Halides[a]

ArX	T, °C	time, h	conversion, %	yield,[e] % $ArCOCO_2R$	yield,[e] % $ArCO_2R$	selectivity, %
PhI[b]	60	24	26	20	3	86
PhBr[c]	100	120	80	16	64	20
p-NCC_6H_4I	80	12	100	48	43	53
p-(i-Pr)$O_2CC_6H_4I$	80	12	79	39	38	50
p-ClC_6H_4I	80	12	42	18	19	49
PhI	80	12	27	15	8	65
p-MeC_6H_4I	80	12	39	17	15	54
p-$MeOC_6H_4I$	80	12	39	28	9	76
p-$MeOC_6H_4I$[b]	60	48	45	(30)	(4)	88
2-iodothiophene[b]	60	48	73	62	6	91
5-bromothiazole[b]	100	50	100	(16)	(51)	24
PhCH=CHI[b]	rt	94	100	8	(60)	12
$PhCH_2Cl$[d]	120	48	37	0	19	0

[a] $PdCl_2(PPh_3)_2$ (0.0188 mmol), ArX (1 mmol), i-PrOH (0.5 mL), NEt_3 (2.5 mL), $p(CO)$ = 150 atm at room temperature. [b] $PdCl_2(PPh_3)_2$ (0.038 mmol), ArX (4 mmol), i-PrOH (1 mL), NEt_3 (5 mL), $p(CO)$ = 150 atm at room temperature. [c] $p(CO)$ = 30 atm at room temperature, the other conditions were the same as b. [d] Dicyclohexylmethylamine was used instead of NEt_3 to avoid the quaternization of the amine. The other conditions were the same as b. [e] GC yields. The figures in parentheses are isolated yields.

involving successive insertion of two CO molecules (eq 3, ancillary ligands are not shown) was denied by the detailed

$$ArCOCO\text{-}[Pd] + HNR_2 \rightarrow ArCOCONR_2 \quad (3)$$

studies on the reactivity of benzoyl and phenylglyoxyl palladium complexes toward amine. Aroyl alkoxycarbonyl complex rather than arylglyoxyl complex was proposed also in the cobalt-catalyzed double carbonylation of aryl halides.[14] Judging from these precedents, there is no doubt about the intermediacy of the aroyl alkoxycarbonyl complex in the present system, as represented in the route a of Scheme I; (1) oxidative addition of ArI to Pd(0), (2) CO insertion to Ar–Pd bond, (3) formation of the aroyl alkoxycarbonyl complex (3) via the nucleophilic attack of the alcohol to coordinated CO, and finally (4) reductive elimination of the keto ester. The formation of the ester as a byproduct is attributable to the reaction of the alcohol with the aroyl palladium complexes (routes b and c) and/or, to some extent, to the formation of aroyl iodide followed by its reaction with the alcohol (route d). The mechanism via the aryl alkoxycarbonyl complex (route e) is not plausible, because our study on the reactivity of $PhPdI(PPh_3)_2$ and $PhCOPdI(PPh_3)_2$ with alcohols under CO revealed that CO insertion to the Ph–Pd bond was much faster than the nucleophilic attack of alcohol to coordinated CO.[15] Similar observation was also reported for trimethylphosphine–palladium complexes.[16] Thus, the selectivity toward keto ester must be determined at the steps after the aroyl palladium complex 1, mainly by the ratio $a/(b + c)$. Most of the effects of various reaction parameters on the reaction rate and on the selectivity for keto ester are explainable based on Scheme I as follows.

A large PR_3/Pd ratio suppressed the keto ester formation, especially when the PR_3/Pd ratio was larger than 2 (Table III). This is probably because excess PR_3 occupies the coordination site on palladium and interrupts the formation of the CO coordinated species 2 (vide infra). Ester formation was also markedly suppressed as the PR_3/Pd ratio increased, indicating that the dissociation of phosphine is a prerequisite for the alcoholysis of the aroyl complex 1. These effects are not due to the deceleration of oxidative addition of aryl halides to Pd(0), because similar effects of excess phosphine were observed in the reaction of $PhCOPdI(PPh_3)_2$.[15] The promoting effect of electron-withdrawing groups of para-substituted triphenylphosphine on the reaction rate (Figure 1) may be attributable to the easy dissociation of phosphines and/or the decrease of the electron density of the aroyl group of the complex 1. The effect on the selectivity, however, is not easy to explain at the moment.

The existence of optimum steric bulk of alcohol and tertiary amine for the selectivity can be rationalized as follows (Tables I, II, and IV). When the steric bulk of the alcohol or tertiary amine is small, the reaction between the aroyl palladium complex 1 and the alcohol (route b) is fast, resulting in high reaction rate and low selectivity. According to the increase of their bulkiness, the reaction (route b) becomes slow, and the CO-coordinated aroyl palladium complex 2 will have more chances to take part in the catalysis. At the same time, the increased steric bulk of the alcohol and amine renders the attack to the aroyl group of the complex 2 (route c) less favorable. Consequently, less hindered coordinated CO is preferentially attacked to give the aroyl alkoxycarbonyl complex 3, resulting in the increase of the selectivity, although the intrinsic difference of the electrophilicity between aroyl group and coordinated CO is not clear.[17] By the use of even bulkier alcohols or amines, the reaction of an alcohol with both an aroyl group and coordinated CO is heavily decelerated. Under these circumstances, the route d seems to be the main path to result in poor selectivity and low reaction rate.[18] Although optimum size was observed not only for alcohols and tertiary amines but also for phosphine ligands to achieve high selectivity (Figures 3 and 4), the low selectivities obtained by the use of small phosphines cannot be simply ascribed to the acceleration of route b, because the reaction rates were not changed so much in the region of cone angles 100°–140° (Figure 5). Anyhow, the lower steric hindrance around the palladium complexes makes it easy for an alcohol to attack the aroyl group rather than coordinated CO, leading to the lower selectivity. High reaction rates and low selectivities obtained in the systems with highly bulky phosphines are explainable by the acceleration of route b through their easy

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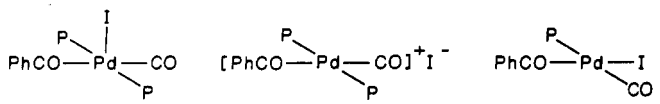
(18) Small amount of benzoyl iodide was detected when $PhPdI(PPh_3)_2$ and PhI were heated under CO. See ref. 15.

dissociation (Figures 5–7). These are the reasons why there are optima for the selectivity in the size of the alcohol, tertiary amine, and phosphine ligand.

High carbon monoxide pressure increases the concentration of the aroyl carbonyl complex **2** and improves the selectivity, whatever the real structure of the aroyl carbonyl complex may be (Figure 8). High reaction temperature was unfavorable to get good selectivity (Figure 9). This is probably due to the decrease in the concentration of **2**, resulting from the acceleration of route b and the shift of the equilibrium between **1** and **2** to the direction of carbon monoxide dissociation.

Polar solvents having high donicity numbers gave low selectivities (Table V, Figure 10). In these solvents, alcohols exhibit high nucleophilicity, owing to the increase in the ionicity of the O–H bonds resulting in the acceleration of route b. In addition, polar solvents enhance the ionicity of the Pd–I bond of the aroyl complex, which, in turn, raises the electrophilicity of the aroyl group. This may be another reason for low selectivity. The following observations support these rationalizations. The reaction of more acidic alcohols (e.g. C_2F_5OH) with $PhCOPdI(PPh_3)_2$ in the presence of triethylamine gave poorer selectivities than that of less acidic alcohols (e.g. C_2H_5OH). Substitution of sodium alkoxide for triethylamine decreased the selectivity.[15] Consequently, it can be concluded that increase in ionicity of O–H bonds of alcohols is unfavorable for double carbonylation. As for the effect of ionicity of the Pd–I bond, the reaction of $PhCOPd(PPh_3)_2(ClO_4)$ predominantly gave benzoate rather than phenylglyoxylate, when treated with 2-propanol and triethylamine under CO, whereas the similar reaction of $PhCOPdI(PPh_3)_2$ ended up in a much higher selectivity for phenylglyoxylate.[19]

There are three candidates for the structure of the aroyl carbonyl complex (**2**) responsible for the keto ester formation: the five coordinated complex **2a**, the cationic complex **2b**, which is formed via the dissociation of Pd–I bond, and the neutral carbonyl complex **2c** formed through the phosphine dissociation. Although the complex **2b** is



2a (configuration is not clear) **2b** **2c**

the postulated precursor for the keto amide,[5d,13b] its intermediacy as a solvent-separated ion pair in the keto ester formation is not probable, as judged from the solvent effect and/or the results of the reaction of perchlorate complex (vide supra).[19] The complex **2c** is not a good candidate either, because, in this model, it is difficult to explain the suppression of ester formation by the steric hindrance of phosphines, as well as the fact that keto ester synthesis was not accelerated so much when the PR_3/Pd ratio was less than 2 while ester formation was greatly enhanced. Considered as a whole, the five-coordinated complex **2a** and a contact ion pair of **2b** can be possible aroyl carbonyl complexes.

As compared with palladium-catalyzed keto amide synthesis, the keto ester synthesis was, in general, less selective.[5] This is because the reactivity of the amine toward aroyl carbonyl palladium complexes is quite different from that of the alcohol. In fact, the reaction of $PhCOPdI(PPh_3)_2$ with a secondary amine under CO resulted in the selective keto amide formation, while much ester was produced in the reaction with an alcohol and a tertiary amine.[5d,13b,19] The difference between the amine and the alcohol cannot be explained only by the difference of nucleophilicity, because the reaction with metal alkoxide, which is more nucleophilic than the alcohol itself, gave poorer selectivity than the alcohol. The reactivity of various nucleophiles toward acyl palladium species under CO is now under investigation.

Experimental Section

Infrared spectra were recorded on a JASCO A-302 spectrometer. ^1H NMR spectra were measured on a Hitachi R-40 (90 MHz) spectrometer in $CDCl_3$, with tetramethylsilane as an internal standard. Mass spectra were recorded on a Shimadzu QP-1000 (70 eV) GC–MS spectrometer. Microanalyses were performed by the Institute of Physical and Chemical Research.

Solvents, alcohols, tertiary amines, and aryl halides were dried by standard methods and distilled under nitrogen.

Pd catalyst: $PdCl_2$ was used as purchased. $PdCl_2(PhCN)_2$,[20] $PdCl_2(PPh_3)_2$,[21] $PdCl_2(PPh_2Et)_2$,[22] $PdCl_2(PPhMe_2)_2$,[23] $PdCl_2(Ph_2PCH_2CH_2CH_2PPh_2)$,[24] $PdCl_2[P(o\text{-}MeC_6H_4)_3]_2$,[25] $PdCl_2[P(p\text{-}FC_6H_4)_3]_2$,[25] $PdCl_2(PMe_3)_2$,[26] $PdCl_2(PBu_3)_2$,[27] and $PdCl_2[P(OCH_2)_3CEt]_2$[25] were prepared by the literature methods. $PdCl_2[P(p\text{-}MeOC_6H_4)_3]_2$[25] and $PdCl_2[PPh(p\text{-}MeC_6H_4)_2]_2$ were prepared by a modification of Negishi's method.[21] $PdCl_2[P(p\text{-}MeC_6H_4)_3]_2$,[28] $PdCl_2[PPh_2(p\text{-}MeC_6H_4)]_2$, $PdCl_2[PPh_2(o\text{-}MeC_6H_4)]_2$, $PdCl_2[PPh(o\text{-}MeC_6H_4)_2]_2$,[29] $PdCl_2[P(p\text{-}PhC_6H_4)_3]_2$, $PdCl_2[P(C_6F_5)_3]_2$,[30] $PdCl_2[P(i\text{-}Pr)_3]_2$,[31] and $PdCl_2[PPh_2(OEt)]_2$[32] were prepared by the reaction of $PdCl_2(PhCN)_2$ and corresponding tertiary phosphines or phosphinite.[24] The physical data of new compounds are as follows.

$PdCl_2[PPh(p\text{-}MeC_6H_4)_2]_2$: mp 107–110 °C. Anal. Calcd for $C_{40}H_{38}Cl_2P_2Pd$: C, 63.38; H, 5.05. Found: C, 63.41; H, 5.07.

$PdCl_2[PPh_2(p\text{-}MeC_6H_4)]_2$: mp 221–224 °C. Anal. Calcd for $C_{38}H_{34}Cl_2P_2Pd$: C, 62.53; H, 4.70. Found: C, 62.62; H, 4.71.

$PdCl_2[PPh_2(o\text{-}MeC_6H_4)]_2 \cdot {}^1/_2CHCl_3$: mp 275.5–278.5 °C. Anal. Calcd for $C_{38.5}H_{34.5}Cl_{3.5}P_2Pd$: C, 58.56; H, 4.40. Found: C, 58.28; H, 4.38.

$PdCl_2[P(p\text{-}PhC_6H_4)_3]_2$: mp 192.5–195.0 °C. Anal. Calcd for $C_{72}H_{54}Cl_2P_2Pd$: C, 74.65; H, 4.70. Found: C, 74.65; H, 4.92.

In the experiments in Figures 2 and 3, to examine the effect of $P(OMe)_3$, $P(OPh)_3$, $PPh_2(c\text{-}C_6H_{11})$, $PPh(c\text{-}C_6H_{11})_2$, and $P(c\text{-}C_6H_{11})_3$ as catalyst ligands, palladium complexes in situ generated from $[PdCl(\eta\text{-}C_3H_5)]_2$ and corresponding phosphines or phosphites were used.

Keto Ester Synthesis. A typical procedure is as follows. Dichlorobis(triphenylphosphine)palladium (0.038 mmol), *p*-iodoanisole (4 mmol), 2-propanol (1 mL), and triethylamine (5 mL) were added to a 50-mL Schlenk-type stainless-steel autoclave under nitrogen. Carbon monoxide was charged up to 150 atm. After the reaction continued at 60 °C for 48 h, the reaction mixture was poured into ether and washed with dilute hydrochloric acid. The organic layer was dried over $MgSO_4$ and concentrated in vacuo. GC analysis of the resulting oil revealed that 2.21 mmol (55.3%) of *p*-iodoanisole remained unreacted. The oil was purified by preparative thin-layer chromatography (silica gel, hexane–ether,

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4:1) and afforded isopropyl *p*-methoxybenzoate (16.7 mg, 4.3%) and isopropyl *p*-methoxyphenylglyoxylate (134 mg, 30.1%).

α-Keto esters and esters thus obtained were characterized by ^{1}H NMR, IR, MS, and elemental analysis. Satisfactory data were obtained in all cases. Unless otherwise stated, the yield of keto ester and ester was estimated by GC analysis of reaction mixtures with an internal standard (based on halide charged). The spectral and analytical data of isolated keto esters are shown below.

Methyl phenylglyoxylate: IR (neat) 1735 (CO_2Me), 1687 (PhCO) cm^{-1}; NMR δ 3.97 (s, 3 H, Me), 7.4–8.2 (m, 5 H, Ph).

Ethyl phenylglyoxylate: IR (neat) 1737 (CO_2Et), 1685 (PhCO) cm^{-1}; NMR δ 1.41 (t, J = 7 Hz, 3 H, CH_3), 4.45 (q, J = 7 Hz, 2 H, CH_2), 7.4–8.2 (m, 5 H, Ph).

***n*-Butyl phenylglyoxylate**: IR (neat) 1733 (CO_2Bu), 1690 (PhCO) cm^{-1}; NMR δ 0.97 (t, J = 7 Hz, 3 H, CH_3), 1.15–2.0 (m, 4 H, CH_2CH_2), 4.41 (t, J = 7 Hz, 2 H, CH_2O), 7.4–8.2 (m, 5 H, Ph); MS, m/e (relative intensity) 206 (M^+, 0.2), 105 ($PhCO^+$, 100), 77 (Ph^+, 38).

Isobutyl phenylglyoxylate: IR (neat) 1733 (CO_2-*i*-Bu), 1688 (PhCO) cm^{-1}; NMR δ 1.00 (d, J = 7 Hz, 6 H, CH_3), 2.10 (m, 1 H, CH), 4.19 (d, J = 7 Hz, 2 H, CH_2), 7.4–8.15 (m, 5 H, Ph); MS, m/e (relative intensity) 206 (M^+, 0.2), 105 ($PhCO^+$, 100), 77 (Ph^+, 34).

***sec*-Butyl phenylglyoxylate**: IR (neat) 1741 (CO_2-*sec*-Bu), 1683 (PhCO) cm^{-1}; NMR δ 0.98 (t, J = 7 Hz, 3 H, CH_3CH_2), 1.38 (d, J = 6 Hz, 3 H, CH_3CH), 1.73 (m, 2 H, CH_2), 5.18 (m, 1 H, CH), 7.4–8.15 (m, 5 H, Ph); MS, m/e (relative intensity) 206 (M^+, 0.1), 105 ($PhCO^+$, 100), 77 (Ph^+, 45).

Neopentyl phenylglyoxylate: bp 86 °C (0.15 mmHg) (Kugelrohr); IR (neat) 1731 (CO_2R), 1685 (PhCO) cm^{-1}; NMR δ 1.00 (s, 9 H, *t*-Bu), 4.10 (s, 2 H, CH_2), 7.4–8.15 (m, 5 H, Ph); MS, m/e (relative intensity) 220 (M^+, 0.1), 105 ($PhCO^+$, 100), 77 (Ph^+, 30). Anal. Calcd for $C_{13}H_{16}O_3$: C, 70.88; H, 7.32. Found: C, 70.83; H, 7.34.

Cyclohexyl phenylglyoxylate: IR (neat) 1729 (CO_2R), 1686 (PhCO) cm^{-1}; NMR δ 1.0–2.3 (m, 10 H, $(CH_2)_5$), 4.9–5.3 (m, 1 H, CH), 7.3–8.2 (m, 5 H, Ph); MS, m/e (relative intensity) 105 ($PhCO^+$, 72), 83 ($C_6H_{11}^+$, 59), 77 (Ph^+, 34), 55 (100).

α-Phenethyl phenylglyoxylate: IR (neat) 1727 (CO_2R), 1682 (PhCO) cm^{-1}; NMR δ 1.70 (d, J = 7 Hz, 3 H, Me), 6.20 (q, J = 7 Hz, CH), 7.25–8.05 (m, 10 H, Ph); MS, m/e (relative intensity) 105 ($PhCO^+$, 100), 77 (Ph^+, 34).

Pinacolyl phenylglyoxylate: IR (neat) 1730 (CO_2R), 1690 (PhCO) cm^{-1}; NMR δ 0.97 (s, 9 H, *t*-Bu), 1.33 (d, J = 7 Hz, 3 H, Me), 5.03 (q, J = 7 Hz, 1 H, CH), 7.4–8.1 (m, 5 H, Ph).

Isopropyl phenylglyoxylate: IR (neat) 1724 (CO_2R), 1682 (PhCO) cm^{-1}; NMR δ 1.40 (d, J = 6 Hz, 6 H, Me), 5.33 (m, 1 H, CH), 7.3–8.1 (m, 5 H, Ph); MS, m/e (relative intensity) 192 (M^+, 0.3), 105 ($PhCO^+$, 100), 77 (Ph^+, 78).

Isopropyl [*p*-(isopropoxycarbonyl)phenyl]glyoxylate: bp 122 °C (0.1 mmHg) (Kugelrohr); IR (neat) 1728, 1721 (CO_2R), 1698 (ArCO) cm^{-1}; NMR δ 1.39 (d, J = 6 Hz, 6 H, Me), 1.42 (d, J = 6 Hz, 6 H, Me), 5.30 (m, 1 H, CH), 5.35 (m, 1 H, CH), 8.12 (d, J = 8 Hz, 2 H, Ar), 8.16 (d, J = 8 Hz, 2 H, Ar). Anal. Calcd for $C_{15}H_{18}O_5$: C, 64.74; H, 6.52. Found: C, 64.99; H, 6.62.

Isopropyl (*p*-chlorophenyl)glyoxylate: bp 74 °C (0.08 mmHg) (Kugelrohr); IR (neat) 1731 (CO_2R), 1688 (ArCO) cm^{-1}; NMR δ 1.40 (d, J = 6 Hz, 6 H, Me), 5.33 (m, 1 H, CH), 7.51 (d, J = 9 Hz, 2 H, Ar), 7.99 (d, J = 9 Hz, 2 H, Ar). Anal. Calcd for $C_{11}H_{11}ClO_3$: C, 58.29; H, 4.89. Found: C, 58.12; H, 4.85.

Isopropyl *p*-tolylglyoxylate: bp 136 °C (15 mmHg) (Kugelrohr); IR (neat) 1730 (CO_2R), 1680 (ArCO) cm^{-1}; NMR δ 1.40 (d, J = 6 Hz, 6 H, Me_2C), 2.43 (s, 3 H, MeC_6H_4), 5.33 (m, 1 H, CH), 7.33 (d, J = 8 Hz, 2 H, Ar), 7.92 (d, J = 8 Hz, 2 H, Ar). Anal. Calcd for $C_{12}H_{14}O_3$: C, 69.89; H, 6.84. Found: C, 69.69; H, 6.85.

Isopropyl *p*-anisylglyoxylate: bp 130 °C (0.1 mmHg) (Kugelrohr); IR (neat) 1727 (CO_2R), 1675 (ArCO) cm^{-1}; NMR δ 1.40 (d, J = 6 Hz, 6 H, Me_2C), 3.89 (s, 3 H, MeO), 5.32 (m, 1 H, CH), 6.98 (d, J = 9 Hz, 2 H, Ar), 8.00 (d, J = 9 Hz, 2 H, Ar). Anal. Calcd for $C_{12}H_{14}O_4$: C, 64.85; H, 6.35. Found: C, 64.67; H, 6.34.

Isopropyl (*p*-cyanophenyl)glyoxylate: bp 106 °C (0.19 mmHg) (Kugelrohr); IR (neat) 2228 (CN), 1723 (CO_2R), 1692 (ArCO) cm^{-1}; NMR δ 1.42 (d, J = 6 Hz, 6 H, Me), 5.35 (m, 1 H, CH), 7.86 (d, J = 8.5 Hz, 2 H, Ar), 8.19 (d, J = 8.5 Hz, 2 H, Ar). Anal. Calcd for $C_{12}H_{11}NO_3$: C, 66.35; H, 5.10. Found: C, 65.99; H, 5.09.

Isopropyl 2-thienylglyoxylate: bp 122 °C (12 mmHg) (Kugelrohr); IR (neat) 1725 (CO_2R), 1657 (ArCO) cm^{-1}; NMR δ 1.39 (d, J = 6 Hz, 6 H, Me), 5.29 (m, 1 H, CH), 7.21 (dd, J = 4.8 and 4.0 Hz, 1 H, C_4H_3S), 7.83 (dd, J = 4.8 and 1.2 Hz, 1 H, C_4H_3S), 8.13 (dd, J = 4.0 and 1.2 Hz, 1 H, C_4H_3S). Anal. Calcd for $C_9H_{10}O_3S$: C, 54.53; H, 5.08. Found: C, 54.45; H, 5.10.

Isopropyl 5-thiazolylglyoxylate: bp 114 °C (10 mmHg) (Kugelrohr); IR (neat) 1720 (CO_2R), 1677 (ArCO) cm^{-1}; NMR δ 1.43 (d, J = 6 Hz, 6 H, Me), 5.30 (m, 1 H, CH), 8.91 (s, 1 H, C_3H_2NS), 9.13 (s, 1 H, C_3H_2NS). Anal. Calcd for $C_8H_9NO_3S$: C, 48.23; H, 4.55. Found: C, 48.00; H, 4.58.

Isopropyl β-styrylglyoxylate: bp 125 °C (0.05 mmHg) (Kugelrohr); IR (neat) 1724 (CO_2R), 1695 (RCO), 1665 (C=C) cm^{-1}; NMR δ 1.38 (d, J = 6 Hz, 6 H, Me), 5.23 (m, 1 H, CHO), 7.2–7.75 (m, 5 H, Ph), 7.32 (d, J = 16 Hz, 1 H, C=CH), 7.87 (d, J = 16 Hz, 1 H, C=CH). Anal. Calcd for $C_{13}H_{14}O_3$: C, 71.54; H, 6.47. Found: C, 71.38; H, 6.51.

Registry No. THF, 109-99-9; DMF, 68-12-2; HMPA, 680-31-9; dppp, 6737-42-4; $PdCl_2(PPh_3)_2$, 13965-03-2; *p*-$MeOC_6H_4CO_2Pr$-*i*, 6938-38-1; *p*-$MeOC_6H_4COCO_2Pr$-*i*, 101128-44-3; $PhCOCO_2Me$, 15206-55-0; $PhCOCO_2Et$, 1603-79-8; $PhCOCO_2Bu$, 5524-55-0; $PhCOCO_2Bu$-*i*, 31197-67-8; $PhCOCO_2Bu$-*sec*, 95653-53-5; $PhCOCO_2CH_2Bu$-*t*, 101128-42-1; $PhCOCO_2C_6H_{11}$, 61598-01-4; $PhCOCO_2CHMePh$, 93011-90-6; $PhCOCO_2Pr$-*i*, 31197-66-7; *p*-(*i*-Pr)$O_2CC_6H_4COCO_2Pr$-*i*, 111160-42-0; *p*-$ClC_6H_4COCO_2Pr$-*i*, 30565-44-7; *p*-$MeC_6H_4COCO_2Pr$-*i*, 101128-43-2; *p*-$NCC_6H_4COCO_2Pr$-*i*, 111160-43-1; $PhCH{=}CHCOCO_2Pr$-*i*, 111160-44-2; *p*-$MeOC_6H_4I$, 696-62-8; PhI, 591-50-4; *p*-(*i*-Pr)$O_2CC_6H_4I$, 111160-45-3; *p*-ClC_6H_4I, 637-87-6; *p*-MeC_1H_4I, 624-31-7; *p*-NCC_1H_4I, 3058-39-7; $PhCH{=}CHI$, 101349-79-5; *i*-PrOH, 67-63-0; MeOH, 67-56-1; EtOH, 64-17-5; BuOH, 71-36-3; *i*-BuOH, 78-83-1; *sec*-BuOH, 78-92-2; *t*-$BuCH_2OH$, 75-84-3; $C_6H_{11}OH$, 108-93-0; PhMeCHOH, 98-85-1; CO, 630-08-0; NEt_3, 121-44-8; *t*-BuOH, 75-65-0; $PhCH_2OH$, 100-51-6; PhOH, 108-95-2; *t*-BuMeCHOH, 464-07-3; PPh_3, 603-35-0; NEt_2Ph, 91-66-7; NMe_3, 75-50-3; $NMe(CH_2)_4$, 120-94-5; NPr_3, 102-69-2; NBu_3, 102-82-9; $NMe(i\text{-}Pr)_2$, 10342-97-9; $NEt(i\text{-}Pr)_2$, 7087-68-5; $NMe(C_6H_{11})_2$, 7560-83-0; $NMe_2(C_6H_{11})$, 98-94-2; CH_2Cl_2, 75-09-2; CH_3CN, 75-05-8; PhBr, 108-86-1; $PhCH_2Cl$, 100-44-7; $P(p\text{-}MeOC_6H_4)_3$, 855-38-9; $P(p\text{-}MeC_6H_4)_3$, 1038-95-5; $PPh(p\text{-}MeC_6H_4)_2$, 19934-95-3; $PPh_2(p\text{-}MeC_6H_4)$, 1031-93-2; $P(p\text{-}PhC_6H_4)_3$, 13885-05-7; $P(p\text{-}FC_6H_4)_3$, 18437-78-0; PCy_2Ph, 6476-37-5; PCy_3, 2622-14-2; $P(Pr\text{-}i)_3$, 6476-36-4; $PCyPh_2$, 6372-42-5; $PEtPh_2$, 607-01-2; $PPh_2(o\text{-}Tol)$, 5931-53-3; $P(OPh)_3$, 101-02-0; $PPh(o\text{-}Tol)_2$, 18803-09-3; PMe_2Ph, 672-66-2; $P(o\text{-}Tol)_3$, 6163-58-2; $P(C_6F_5)_3$, 1259-35-4; PBu_3, 998-40-3; PMe_3, 594-09-2; $P(OMe)_3$, 121-45-9; $P(OCH_2)_3CEt$, 111160-46-4; $PPh_2(OEt)$, 719-80-2; $PhCO_2Pr$-*i*, 939-48-0; *p*-(*i*-Pr)$O_2CC_6H_4CO_2Pr$-*i*, 6422-84-0; *p*-$ClC_6H_4CO_2Pr$-*i*, 22913-11-7; *p*-$MeC_6H_4CO_2Pr$-*i*, 19277-55-5; $PhCH_2CO_2Pr$-*i*, 4861-85-2; *p*-$NCC_6H_4CO_2Pr$-*i*, 29240-33-3; $PhCH{=}CHCO_2Pr$-*i*, 7780-06-5; pinacolyl phenylglyoxylate, 40121-97-9; isopropyl 2-thienylglyoxylate, 31697-81-1; isopropyl 5-thiazolylglyoxylate, 101128-45-4; 2-iodothiophene, 3437-95-4; 5-bromothiazole, 3034-55-7; pinacolyl alcohol, 464-07-3; hexane, 110-54-3; benzene, 71-43-2; isopropyl 2-thienecarboxylate, 111160-47-5; isopropyl 5-thiazolecarboxylate, 111160-48-6.

The Correct Structure of the Base $C_{12}H_{17}NO$, a Product of Cyclization of Tris(γ-chlorocrotyl)amine

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In 1948, one of us (M.H.) published a paper on the structure of an artifact resulting from the action of concentrated sulfuric acid on tris(γ-chlorocrotyl)amine (eq 1).[1]

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