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J. Org. Chem., Just Accepted Manuscript • Publication Date (Web): 10 Oct 2018

Downloaded from http://pubs.acs.org on October 10, 2018

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Photoiodocarboxylation of Activated C=C Double Bonds with CO₂ and Lithium lodide

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ABSTRACT: The photolysis at 254 nm of lithium iodide and olefins 1 carrying an electron-withdrawing Z-substituent in CO_2 -saturated (1 bar) anhydrous acetonitrile at room temperature, produces the atom efficient and transition metal-free photoiodocarboxylation of the C=C double bond. The reaction proceeds well for terminal olefins 1 to form the new C-I and C-C σ -bonds at the α and β -positions of the Z-substituent, respectively, and is strongly inhibited by polar protic solvents or additives. The experimental results suggest that the reaction channels through the radical anion $[CO_2^-]$ in acetonitrile, yet involves different intermediates in aqueous medium. The stabilizing ion-quadrupole and electron donor-acceptor interactions of CO₂ with the iodide anion play a crucial role in the reaction course as they allow CO₂ to penetrate the solvation shell of the anion in acetonitrile, but not in water. The reaction paths and the reactive intermediates involved under different conditions are discussed.

Introduction

The necessary transition from petroleum and natural gas to renewable feedstocks for sustainable chemical production¹ has turned the research on the capture and functionalization of carbon dioxide (CO₂) into a major innovation arena.² The use of CO₂ as a renewable C1feedstock has evolved along three main avenues, namely: i) synthesis of carbamates and carbonates by reaction with amines, alcohols or epoxides;³ ii) reduction of CO₂ to CO, formic acid and its derivatives, methanol or methane;4 iii) CO₂-fixation through the formation of a kinetically and thermodynamically stable C-C σ-bond.^{5,6} While the CO₂capture into carbonic acid derivatives and the CO₂reduction to give useful fuels have become well developed research areas,^{3,4} the carboxylation of organic substrates under atmospheric CO₂ and mild conditions has proven more challenging.5,6 Recently, photoinduced electron transfer reactions, generally coupled to transition metal catalysis, have emerged as a powerful approach to C-C σ bond-forming reactions with CO₂, which has provided suitable CO₂-fixation procedures.⁶

The reactivity pattern of CO_2 , as determined by its structure and bonding, is the basis of CO_2 capture and functionalization methodologies (Figure 1).^{7-11,12} The strong quadrupole moment of CO_2 ,⁹ with positive charge density localized at the carbon atom, and its Lewis acid and weakly basic character,¹³ determine the ability of CO_2 to coordinate Lewis bases¹⁴ and metal complexes,¹² and to react with nucleophilic species.³⁻⁵ This reactivity scope further expands through the single electron reduction of



Figure 1. Data on CO₂ and $[CO_2^{--}]$.⁷⁻¹¹ α_e : bond angle, R_e: bond length, PA: proton affinity, QM: quadrupole moment, DM: dipole moment; E^o_{red} : standard reduction potential *vs*. SCE in water.

 CO_2 , which turns it into a strong reductant $[E^{\circ}_{red}(CO_2/CO_2^{--}) = -2.14 V vs. SCE]$,¹⁰ a nucleophilic radical¹⁵ and a Lewis base.¹¹ The application of these properties to synthesis requires suitable reaction conditions to generate the radical anion $[CO_2^{--}]$ and to channel it towards products, while avoiding its deactivation and the side reactions of the ensuing reactive intermediates. Our recent report on the transition metal-free iodide-photocatalyzed reduction of CO_2 to formic acid with thiols¹⁶ has revealed that the photolysis of the iodide anion in the presence of CO_2 provides a suitable entry to the chemistry of the radical anion $[CO_2^{--}]$ in the absence of transition metals. These results prompted us to further explore the photochemistry of the iodide anion and CO_2 in the presence of olefins.

Herein we report that the photolysis at 254 nm of CO_2 saturated acetonitrile solutions of lithium iodide (LiI) and olefins carrying electron-withdrawing substituents, at both room temperature and atmospheric pressure, produces the α -iodo- β -carboxylation of the C=C double bond (Equation 1). The scope of the reaction and the involved reactive intermediates are discussed.

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Results

The photoiodocarboxylation reaction. Reactions were performed by irradiating 0.04 M solutions of substrates 1 and lithium iodide (1:LiI 1:1) in anhydrous acetonitrile- d_3 saturated with CO₂ (1 bar) with a 36 W low pressure mercury lamp ($\lambda = 254$ nm) at room temperature for 3 h. The initial CO₂ concentration, estimated from the solubility reported for carbon dioxide (1 atm) in propionitrile at 25°C, was 0.245 M (initial molar ratio 1:CO₂ 1:3.5).¹⁷ The reaction mixtures were dark yellow suspensions, with variable amounts of solid. Aliquots of the decanted solutions and solid residues were analyzed by ¹H NMR spectroscopy in acetonitrile-*d*₃ and D₂O, with *tert*butanol used as the external standard. Substrate conversions and product yields were determined from the integrals of their NMR signals and those of the external standard. The results were confirmed in a series of identical experiments in which the reaction mixtures were diluted with a known amount of water to obtain a homogeneous solution, and were analyzed by ¹H NMR with tert-butanol as the external standard. The results are shown in Table 1. Preparative experiments were performed in anhydrous acetonitrile as described above, and reaction mixtures were decanted at o°C. Solid residues were isolated, washed with acetonitrile, dried under vacuum and characterized. Detailed experimental procedures and spectra are included in the Experimental Section and Supplementary Material.

The photolysis ($\lambda = 254$ nm) of LiI and activated alkenes 1 in acetonitrile saturated with CO₂ at atmospheric pressure and room temperature led to the addition of the iodine atom and CO_2 to the α and β -positions of the substituted C=C double bonds, respectively (Table 1). No polycarboxylation products were found in the reaction mixtures. Adducts 2 underwent the partial elimination of hydrogen iodide to give unsaturated compounds 3 under our reaction conditions,²⁷ or by standing for long periods in aqueous medium. The extent of these side processes depended on the substrate structure (Table 1). The iodocarboxylation adducts 2 from acrylic acid derivatives 1a-c were partially converted into the corresponding anhydrides in aqueous medium. The efficiency of the photochemical reaction was hampered by the insolubility of the reaction products in acetonitrile.

Photoiodocarboxylation was efficient for the unsaturated substrates carrying electron withdrawing substituents **1a-h** (Entries 1-8, Table 1), with conversions within the 53-86% range, to give carboxylated products **2** and **3** as the major products (over 90 % in most of these cases). Allyl acrylate (**1e**) reacted exclusively at the carbonyl-substituted C=C double bond to give **2e** (84 %) and **3e** (14 %) as the only products (Entry 5, Table 1). Acrylic acid (1h) also gave 2-iodopropanoic acid (4a) (37 %) (Entry 8, Table 1).

Methacrylamide (**ii**) reacted efficiently under our reaction conditions, and reached 68 % conversion (Entry 9, Table 1). The reaction products readily decomposed in aqueous solution in this case. Thus the reaction mixture was analyzed by dissolving the solid materials with an equimolar amount of trifluoroacetic acid and analyzing the homogeneous solution by NMR with *tert*-butanol as the external standard. The dehydrohalogenation reaction took place in the α -methyl group to exclusively give lithium 3-carbamoylbut-3-enoate (**3i**).

The substrates **1** carrying substituents at the β -position reacted less efficiently. Thus the substrate conversion found for crotononitrile (**1j**) (mixture *E*:*Z* 1.9:1), the most reactive substrate in this series, was 58 %, but was only 20-30 % for (*E*)-crotonamide (**1k**), methyl (*E*)-crotonate (**1l**) and methyl (*E*)-3-methoxyacrylate (**1m**). Adducts **2j-m** (mixtures of diastereomers, 1.8:1, 11:1, 4:1 and 2.1:1, respectively) were the major products in all cases (Runs 10-13, Table 1). Substrates **1j-m** underwent isomerization under these reaction conditions since the unreacted materials were found as *E*:*Z* mixtures from 1:1 to 1.5:1. Dehydrohalogenation product **3j** was found as *E*:*Z* 1.9:1 (Entry 10, Table 1).

2-Cyclopentenone (**1n**) converted only 24 % to give carboxylation products **2n** (67 %) and **3n** (13 %) (Entry 14, Table 1), although other cyclic substrates with endocyclic C=C double bonds, like 2-cyclohexenone (**10**), *N*,*N*-dimethyluracil (**1p**), and maleic anhydride (**1q**), were unreactive under our standard reaction conditions (Entries 15-17, Table 1). Dimethyl maleate (**1r**) exclusively underwent isomerization to give dimethyl fumarate (Entry 18, Table 1).

Styrene (**1s**) gave lithium cinnamate (**3s**) as the only product, with 68 % conversion and a mass balance as low as 44 % (Entry 19, Table 1). Isoprene (**1t**) reacted efficiently, but no identifiable products were found (mass balance 23 %) (Entry 20, Table 1). Simple alkenes were non-reactive under our reaction conditions.

Control experiments. The reaction of methyl acrylate (1a) and CO_2 with potassium iodide (KI) in acetonitrile (Entry 21, Table 1) gave results similar to those found with Lil (Entry 1, Table 1).

The photoiodocarboxylation reactions of acrylamide (**1b**) and acrylic acid (**1h**), KI and CO₂ in D₂O were performed following the experimental procedure described above (Entries 22 and 23, Table 1). The substrate 1 concentration was 0.01 M in these cases, as solubility in water reported for CO₂ at atmospheric pressure and room temperature was 0.035 M (molar ratio 1:CO₂ 1:3.5).²⁸ The reaction mixtures were analyzed by ¹H NMR, with *tert*-butanol used as the external standard.

The reaction of acrylamide (**1b**) in aqueous solution proceeded with low substrate conversion (13 %) to give carboxylation products **2b** (40 %) and **3b** (60 %) and a quantitative mass balance (Entry 22, Table 1). Conversely,

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acrylic acid (1h) underwent complete conversion (>99 %)

Table 1. Photoiodocarboxylation of activated olefins 1 with LiI or LiK, and carbon dioxide.^{*a*}

| | | | R'wy | H hv 254 nm | |) ∕س ^ر ⊕ R'س | | R'√ | Н | | |
|-----|----|------------------------|----------|--|----------------------------|---------------------------------|-----------------|--------------------------|------------------------|----|-----|
| | | | z ⊥ 1 | $\begin{array}{c} \text{CO}_2, \text{ LII} \\ \text{R} 3 \text{ h, r.t.} \end{array}$ | | + z | R 3 | z A | 4 | | |
| Run | 1 | Z | R | R ['] | E _{red} o | Condi. | Conv. | Product distribution (%) | | | MB |
| | | | | | $(V)^b$ | | (%) | 2 | 3 (E/Z) | 4 | (%) |
| 1 | 1a | COOCH ₃ | Н | Н | -2.10 ¹⁸ | Stand. | 86 | 72 | 22 (1:1.5) | 6 | 90 |
| 2 | ıb | CONH ₂ | Н | Н | -2.01 ¹⁹ | Stand. | 86 | 90 | 10 (1:1.1) | | 91 |
| 3 | 10 | $CON(CH_3)_2$ | Н | Н | | Stand. | 68 | 69 | 27 (1.5:1) | 4 | 85 |
| 4 | ıd | CN | Н | Н | -2.14 ¹⁸ | Stand. | 83 ^c | 84 | 14 (1:2) | | 93 |
| 5 | 1e | COOAllyl | Н | Н | | Stand. | 52 | 84 | 14 (1.9:1) | 2 | >99 |
| 6 | ıf | COCH ₃ | Н | Н | -1.91 ²⁰ | Stand. | 60^d | 64 | 20 (E) | | 97 |
| 7 | ıg | SO ₂ Ph | Н | Н | -1.49 ²¹ | Stand. | 86 ^e | 64 | 30 (1:1) | 1 | 66 |
| 8 | ıh | СООН | Н | Н | -1.76 ¹⁹ | Stand. | 60 | 52 | 11 (1:1.7) | 37 | 74 |
| 9 | 11 | CONH ₂ | CH3 | Н | | Stand. ^f | 68 | 37 | 59 ^{<i>g</i>} | 4 | 80 |
| 10 | ıj | CN | Н | CH ₃ | -2.55 ²² | Stand. | 58 | 79^h | 21 (1.9:1) | | 77 |
| 11 | ık | CONH ₂ | Н | CH ₃ | -2.74 ²³ | Stand. | 30 | 99 ⁱ | | | 81 |
| 12 | ıl | COOCH ₃ | Н | CH ₃ | -2.41 ¹⁸ | Stand. | 28 | 99 ^j | | | 63 |
| 13 | ım | COOCH ₃ | Н | OCH ₃ | -2.6718 | Stand. | 20 | 99 ^k | | | 96 |
| 14 | ın | COCH ₂ - | Н | -CH ₂ - | -2.23 ²⁰ | Stand. | 24 | 67 | 33 | | 83 |
| 15 | 10 | COCH ₂ - | Н | -(CH ₂) ₂ - | -2.17 ²⁰ | Stand. | 13 | | | | 87 |
| 16 | 1p | CON(CH ₃)- | Н | -N(CH ₃)CO- | -2.0624 | Stand. | | | | | 96 |
| 17 | ıq | COO- | Н | -CO- | -0.98 ²⁵ | Stand. | | | | | 98 |
| 18 | ır | COOCH ₃ | Н | COOCH ₃ | -1.84 ¹⁸ | Stand. | 68 ¹ | | | | >99 |
| 19 | 15 | Ph | Н | Н | -2.60 ²⁶ | Stand. | 68 | | >99 | | 44 |
| 20 | ıt | CH=CH ₂ | CH3 | Н | -2.70 ²⁶ | Stand. | 77 | | | | 23 |
| 21 | 1a | COOCH ₃ | Н | Н | -2.10 ¹⁸ | KI | 73 | 70^m | 25 (1.7:1) | 5 | 82 |
| 22 | ıb | CONH ₂ | Н | Н | -2.01 ¹⁹ | D ₂ O/KI | 13 | 40 | 60 (1:1.7) | | >99 |
| 23 | ıh | СООН | Н | Н | -1.76 ¹⁹ | D ₂ O/KI | >99 | <1 | | | <1 |
| 24 | 1a | COOCH ₃ | Н | Н | -2.10 ¹⁸ | H_2O^n | 6 | 63 | 37 (1.3:1) | | >99 |
| 25 | 1a | COOCH ₃ | Н | Н | -2.10 ¹⁸ | CH ₃ OH ^o | | | | | 93 |
| 26 | 1a | COOCH ₃ | Н | Н | -2.10 ¹⁸ | 90 min | 66 | 84^p | 11 (1.1:1) | 5 | 91 |
| 27 | 1a | COOCH ₃ | Н | Н | -2.10 ¹⁸ | LiI 10% | 18 | 66^q | 30 (1:1.6) | 4 | 85 |
| 28 | 1a | COOCH | Н | Н | -2.10 ¹⁸ | LiI 30% | 53 | 64 ^r | 31 (1:1.4) | 5 | 80 |

^{*a*} Standard procedure (Stand.): the reactions were performed by irradiating CO₂-saturated (1 bar) acetonitrile- d_3 solutions of 1 and LiI (1 equiv.), with a low pressure mercury lamp, for 3 h at room temperature; data from the ¹H NMR analyses of the decanted solution, and of the dried solid in D₂O, with *tert*-butanol as external standard. MB: Mass balance. ^{*b*} Data *vs*. SCE, in acetonitrile or dimethylformamide. ^{*c*} 2 % Lithium succinate derivative. ^{*d*} 16 % Lithium succinate derivative. ^{*e*} 5 % Lithium succinate derivative. ^{*f*} Analysis of the homogeneous solution after addition of CF₃COOH. ^{*g*} Lithium 3-carbamoylbut-3-enoate (3i), from deshydrohalogenation at the CH₃ group. ^{*h*} 2j: 1.8:1 mixture of diastereomers; 1j: starting material *E:Z* 1.9:1, unreacted material *E:Z* 1.5:1. ^{*i*} 2k: 11:1 mixture of diastereomers; starting material (*E*)-1k, unreacted material *E:Z* 1:1.1. ^{*j*} 2l: 4:1 mixture of diastereomers; starting material (*E*)-1l, unreacted material *E:Z* 1:1.1. ^{*k*} 2m: mixture of diastereomers 2.1:1; starting material *E*, unreacted material *E:Z* 1.6:1. ^{*l*} Starting material (*Z*)-1r; unreacted material *E:Z* 2.1:1. ^{*m*} 2m 58 %, anhydride 12 %. ^{*n*} CH₃CN:H₂O 5:1; 2a 27%, anhydride 36%. ^{*o*} CH₃CN:CH₃OH 1:3 v:v. ^{*p*} 2a 44 %, anhydride 40 %. ^{*q*} 2a 34 %, anhydride 32 %. ^{*r*} 2a 43 %, anhydride 21 %. under the same conditions, yet no detectable products were found in the reaction mixtures, which suggested the involvement of radical side reactions (mass balance <1 %) (Entry 23, Table 1). The reactions performed in acetonitrile with water or methanol as cosolvents were also much less efficient than the reactions in acetonitrile (<6 % conversion) (Entries 24 and 25, Table 1).

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The irradiation of the acetonitrile- d_3 solutions of methyl acrylate (**1a**), LiI and CO₂ for 90 min (Entry 26, Table 1) led to a lower conversion of **1a** (66 %), a slightly better mass balance, and a higher yield of iodocarboxylation adduct **2a** in relation to unsaturated derivatives **3a** than the reactions performed for 3 h (Entry 1, Table 1). This result suggests that iodocarboxylation adduct **2** may undergo photochemical dehydrohalogenation under our reaction conditions.²⁷

This side reaction was also evident in the reactions of methyl acrylate (1a) and CO₂ performed with 10% and 30% Lil (Entries 27 and 28, Table 1). The conversion of 1a reached 18 % and 53 %, respectively, and gave higher amounts of unsaturated products 3a compared to our standard reaction conditions (Entry 1, Table 1). The fact that carboxylation products 2a and 3a formed in larger amounts than expected for the starting LiI in these experiments suggested the possibility of designing an iodide-photocatalyzed carboxylation of substrates 1, which would proceed through the photoiodocarboxylation of 1, followed by the photodeshydrohalogenation²⁷ of adduct 2 to give unsaturated carboxylation product 3 and to deliver the iodide anion back to the solution.

In order to test the feasibility of the dehydrohalogenation reaction²⁷ under our reaction conditions, we carried out the photolysis of iodocarboxylation adducts 2b and 2d from acrylonitrile (1b) and acrylamide (1d) in an inert atmosphere. The results are shown in Table 2. The reactions in aqueous medium were very efficient to give ca. 1:1 mixtures of 1 and 3 (Entries 1 and 2, Table 2). No 2hydroxysuccinic acid derivatives **5** from the photosolvolysis of the C-I σ -bond²⁷ were observed as products under these conditions. The reactions in anhydrous acetonitrile were inefficient due to the low solubility of adducts 2 in this medium. However, the addition of acetic acid to improve the solubility of 2 in acetonitrile (Entries 3 and 4, Table 2) led to significant amounts of 2-hydroxypropanoic acid derivatives 5, which indicated the opening of alternative reaction paths under these conditions.

These results showed that the iodide photocatalyzed carboxylation of substrates 1 may indeed be feasible, provided that iodocarboxylation adduct 2 was soluble in the reaction medium. The remarkable sensitivity of the photoiodocarboxylation reaction to polar protic solvents prevented an iodide photocatalyzed process from being implemented for the carboxylation of substrates 1 under our reaction conditions.

The results in Table 1 show that the photoiodocarboxylation of acrylic acid (1h) produced

significant amounts of 2-iodopropanoic acid (4h) (Entry 8, Table 1). Minor amounts of products 4 were also found in the reactions of methyl

Table 2. Photolysis of the iodocarboxylation adducts 2.^a

| z | 0 ⁰ Li | ⊕ <u>hv 254 ni</u> 3 h, r.t. | $\xrightarrow{m} z \xrightarrow{H} z$ | _н `н | | Li⊕ ⁺ z | СН ₃ Он 5 |
|-----|-------------------|---------------------------------|---------------------------------------|-----------------|-----------------|-------------------|-----------------------------------|
| Run | 2 | Solv. | Conv. | Prod. distribu. | | (%) | MB |
| | | | (%) | 1 | 3 (E:Z) | 5 | (%) |
| 1 | 2b | D₂O | 95 | 52 | 48 (1:1.6) | | 80 |
| 2 | 2d | D₂O | 90 | 59 | 41 (1.5:1) | | 68 |
| 3 | 2b | ACN, AA | 90 | 15 | 54 (1:1.4) | 31 | 53 |
| 4 | 2d | ACN, AA | 86 | 5 | 51 <i>(1:1)</i> | 45 | 83 |

^{*a*} Reactions performed by irradiating solutions of **z** in D₂O or in mixtures of acetonitrile- d_3 (ACN) and acetic acid (AA) (100 equiv), with a low pressure mercury lamp (35 W), for 3 h at room temperature; data from the ¹H NMR analyses of the solutions, with *tert*-butanol as external standard.

acrylate (1a), *N*,*N*-dimethylacrylamide (1c), allyl acrylate (1e), methyl phenyl sulfone (1g) and methacrylamide (1i) (Table 1). These results prompted us to explore the impact of excess acetic acid (10 equiv) on the reactions of methyl acrylate (1a), acrylamide (1b), acrylonitrile (1d), and (*E*)-crotonamide (1k), with LiI in anhydrous acetonitrile, both saturated with CO_2 and in an argon atmosphere. The reaction mixtures were analyzed by ¹H NMR. Table 3 provides the results.

The reactions with excess acetic acid run in a CO₂ atmosphere (Entries 1, 3, 7 and 9, Table 3) led to lower substrate 1 conversions than under our standard reaction conditions (Table 1), which agrees with the negative impact of the polar protic additives in the photoiodocarboxylation reactions. The major products were the corresponding hydrohalogenated derivatives 4 from methyl acrylate (1a), acrylamide (1b), acrylonitrile (1d), and (E)-crotonamide (1k), accompanied by small amounts of carboxylation products 2 and 3. The reaction of (E)-crotonamide $(\mathbf{1k})$ led to the isomerization of the starting material (Entry 9, Table 3). These results indicate that the formation of hydrohalogenated product **4h** from acrylic acid **(1h)** (Entry 8, Table 1) derives from the acidic character of substrate 1h. The formation of products 4 in other cases can be attributed to the presence of acidic impurities in the reaction medium.

Conversely, the reactions performed in an inert atmosphere produced the corresponding lactic acid derivatives **5** as the only products, with substrate conversions lower than for the reactions run with CO_2 and with satisfactory mass balances (Entries 2, 4, 8, Table 3). *(E)*-Crotonamide (**1k**) underwent isomerization under these conditions.

The reactions of acrylamide (**1b**) in the presence of excess acetic acid were also performed in aqueous solution with KI (Entries 5 and 6, Table 3). The reactions underwent similar substrate conversions to those found in acetonitrile, yet no significant products were detected in the reaction mixture.

Table 3. Reactions in the presence of excess acetic acid.^{*a*}

| R' _{by} H | hv, CH ₃ C 3 h | | C C Li + | | `o [⊖] Li | R'\ + | | |
|--------------------|---------------------------------|----------------------------------|-----------------|----------|-----------------------|----------|-------|------|
| 1 | 011, | 2 | 1 | 2 H 3 | | 2 | 4 | 2 OF |
| Run | 1 | Cond. ^a | Conv. | Proc | d. dis | tribu. | . (%) | MB |
| | | | (%) | 2 | 3 | 4 | 5 | (%) |
| 1 | 1a | CO ₂ | 43 | 8 | 14 | 78 | - | 86 |
| 2 | ıa | Ar | 23 | - | - | - | 100 | 84 |
| 3 | ıb | CO2 | 46 | 34^b | 13 | 53 | - | 75 |
| 4 | ıb | Ar | 19 | - | - | - | 100 | 85 |
| 5 | ıb | CO ₂ / | 45 | <1 | - | - | - | 55 |
| | | D ₂ O/KI ^c | | | | | | |
| 6 | ıb | Ar/ | 25 | | | | | 75 |
| | | D ₂ O/KI ^c | | | | | | |
| 7 | ıd | CO2 | 63 | 14 | 37 | 47 | 2 | 84 |
| 8 | ıd | Ar | 33 | - | - | - | 100 | 81 |
| 9 | ık | CO2 | 18^d | 27 | - | 73 | - | 93 |
| 10 | ık | Ar | 20 ^e | - | - | - | 100 | 81 |

^{*a*} Reactions were performed by irradiating acetonitrile- d_3 of **1** ([**1**] = 0.04 M) LiI or KI (1 equiv.), and acetic acid (AA) (10 equiv.) saturated with CO₂ (1 bar) or argon (Ar), with a low pressure mercury lamp, for 3 h at room temperature; data from the ¹H NMR analyses of the reaction mixtures, with *tert*butanol as external standard; MB: mass balance. ^{*b*} Adduct **2b** 10%, anhydride 24 %. ^{*c*} Substrate concentration [**1**] = 0.01 M. ^{*d*} Starting material (*E*)-**1k**; unreacted material *E:Z* 1.9:1. ^{*e*} Starting material (*E*)-**1k**; unreacted material *E:Z* 2.1:1.

UV spectra. The UV spectra of LiI (5.34 x 10⁻⁵ M) and methyl acrylate (1a) (1.0 x 10⁻³ M) in anhydrous acetonitrile (Figure 2A) showed that the main absorption at 254 nm corresponded to the charge transfer to the solvent (CTTS) band of the iodide anion ($\lambda_{max} = 247.2 \text{ nm}$).²⁹ This band did not significantly change upon the addition of increasing amounts of acrylonitrile (1j) (up to 1.7 x 10⁻² M) (Fig. 2B), methyl acrylate (1a), and acrylamide (1b) to the acetonitrile solution of LiI. The complete set of UV spectra can be found in the Supplementary Material.

The stepwise pressurization with CO_2 from 1 to 10 bar of a 3.26 x 10⁻⁵ M solution of LiI in anhydrous acetonitrile at room temperature ([CO_2] = 4 M at 10 bar and 25 °C) produced increasing bathochromic shifts of the CTTS band of iodide (Figure 2C), which overcame the blue shifts associated with the changes in density and pressure.³⁰ The CTTS band shift showed neither transient band changes nor isosbestic points. The UV spectra of 5.34 x 10⁻⁵ M acetonitrile solutions of the LiI saturated with CO_2 (1 bar) at 22 °C, 0 °C and -20 °C displayed the bathochromic shifts promoted by the increasing CO_2 concentration in the solution at these temperatures (Figure 2D), as well as the characteristic hypsochromic shift of the CTTS band of iodide associated with lowering temperature.²⁹⁻³³



Figure 2. A) UV spectra of LiI (5.34×10^{-5} M) (red line) and methyl acrylate (**1a**) (1.0×10^{-3} M) (black line) in anhydrous acetonitrile (ACN). B) Changes in the UV spectra of LiI (5.34×10^{-5} M) in ACN (black line) upon addition of acrylonitrile (**1d**) (from 5.55×10^{-3} M to 1.5×10^{-1} M). C) Changes in the UV spectra of LiI (3.26×10^{-5} M) in ACN (black line) upon pressurization with CO₂ from 1-10 bar (*ca.* 0.25-4 M). D) Changes in the UV spectra of LiI (5.34×10^{-5} M) in ACN at 22 °C, o °C and -20 °C (black lines), upon saturation with CO₂ (1 bar). E) Changes in the UV spectra of LiI (5.34×10^{-5} M) in ACN (black line), upon addition of water (from 5.5×10^{-2} M to 5.5×10^{-1} M). F) Changes in the UV spectra of LiI (3.26×10^{-5} M) in water (black line), upon pressurization with CO₂ from 1-10 bar.

Conversely, the CTTS band of LiI in acetonitrile underwent progressive hypsochromic shifts upon the stepwise addition of water³⁴ (Figure 2E). Remarkably, the progressive pressurization from 1-10 bar with CO₂ at room temperature of a 3.26 x 10⁻⁵ M aqueous solution of LiI (λ_{max} = 227.0 nm) did not significant displace the CTTS band (Figure 2F).

Discussion

The photolysis of LiI and activated olefins 1 in the CO₂saturated anhydrous acetonitrile led to the iodocarboxylation of the C=C double bond, with the formation of new C-I and C-C σ -bonds at the α and β positions of the electron-withdrawing substituent, respectively (Equation 1, Table 1). This reaction course

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indicates the involvement of electron transfer processes and radical-ion intermediates.35 As the main absorption at 254 nm corresponded to the iodide anion (Figure 2A), the reaction would initiate with a photoinduced electron transfer from iodide to some reducible species in solution. Two alternative reaction paths (Scheme 1) differing in the actual electron acceptor may account for the photoiodocarboxylation reaction, namely the reduction of the C=C double bond and the capture of the substrate radical anion $[1^{-}]$ by CO₂ (path a, Scheme 1), or the reduction of CO₂ [E^o_{red}(CO₂/CO₂⁻⁻) -2.14 and -2.21 V vs. SCE in water¹⁰ and dimethylformamide,³⁶ respectively] and the addition of the radical anion [CO₂^{...}] to the activated C=C double bond of substrate 1 (path b, Scheme 1), followed in both cases by the non-rate-determining coupling of the distonic radical anion [I⁻⁻] with the iodine atom to give iodocarboxylation adduct 2.

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Scheme 1. Starting hypothesis for the competitive reaction paths towards photoiodocarboxylation adducts 2.



The competition of CO_2 and substrates 1 as electron acceptors was also discussed in relation to the electrocarboxylation of substituted alkenes,^{5e} which was proposed to proceed through either path *a* or *b* (Scheme 1) depending on the standard reduction potentials of the CO₂.^{5e, 37} substrate and Notwithstanding, the photoiodocarboxylation of the substituted alkenes 1 described herein takes place through a photoinduced electron transfer step which concomitantly delivers an iodine atom to the solution,³⁸ so that the actual reaction paths could also depend on additional factors. The inhibition of the reaction by polar protic solvents or additives (Entries 22-25, Table 1, and Table 3), which should actually facilitate the intermediacy of radical anions, and the singular features of the CTTS spectra under conditions (Figure 2), are remarkable different observations that merit further consideration. The experimental results and data available on the different elementary steps of these reactions are discussed in the paragraphs below.

The electron transfer step. The irradiation of the CTTS band of the iodide anion is known^{29,39} to generate a short-lived excited state that either deactivates back to the ground state or evolves through solvent reorganization to a photodetached electron that is in close proximity to the iodine atom, held in a diffuse orbital bound by the combined electrical fields of the solvent molecules and the

counterion.^{29,39} The photodetached electron can either recombine with the iodine atom in the geminate pair or be scavenged by electron acceptors in solution. Both the CTTS band energy and bandwidth depend on the distinct stabilization exerted by the solvent on the ground and the excited state, the variety of configurations available for the solvent molecules in the solvation shell, and the solvent structure.^{29,39} The strong sensitivity of CTTS bands to the structure and composition of the solvent has been applied to explore the microscopic structure of solvent mixtures, and the preferential solvation phenomena.⁴⁰

The blue shift of the CTTS band of lithium iodide in acetonitrile observed upon the addition of water (Figure 2E) has been attributed^{29,39,40} to the progressive water enrichment of the solvation shell of the iodide anion, driven by the stronger ion-dipole and hydrogen-bonding interactions provided by water compared to those exerted by the polar, aprotic and less structured acetonitrile. These interactions stabilize the ground state of the iodide anion better than the more diffuse CTTS excited state. The weaker impact observed for H-bond donors like acetic acid and acrylamide (**1b**) (the spectra are shown in the Supplementary Material) could be attributed to the solute association.

Accordingly, the progressive displacement of the CTTS band of the iodide anion in acetonitrile observed upon the intake of CO_2 into the solution (Figures 2C,D) discloses the progressive penetration of CO_2 molecules into the solvation shell of the iodide anion, devoid of efficient solvation in the polar non protic acetonitrile, to provide stabilizing ion-quadrupole and electron donor-acceptor interactions. The formation of clusters $[Hal(CO_2)_n]^-$ in the gas phase,⁴¹ and the ionization of the sensitive alkyl halides in supercritical CO_2 ,⁴² are further examples of the ability of CO_2 to coordinate halide anions. The bathochromic shift of the CTTS band observed under these conditions suggests that CO_2 stabilizes the CTTS excited state better than the ground state.

The insensitivity to CO_2 of the CTTS band of aqueous LiI (Figure 2F) revealed that CO_2 is unable to compete with the ion-dipole and H-bonding interactions provided by the water molecule to the iodide anion. Therefore, the results suggest that CO_2 displaces the solvent from the cybotactic region of the iodide anion in acetonitrile, but not in water.

The addition of methyl acrylate (1a), acrylamide (1b), and acrylonitrile (1d) to the acetonitrile solutions of lithium iodide did no significantly modify the CTTS band of the iodide anion (Figure 2B), which indicates the absence of significant ion-molecule interactions in these cases.

Substrates **1** and CO₂ are competitive scavengers of the photodetached electron from the iodide anion (E°_{red} (aq/ e^{-aq}) = -3.11 V vs. SCE)¹⁰ under our standard conditions, according to the data reported on the standard reduction potentials (Table 1)¹⁸⁻²⁶ and the rate constants for the reaction with hydrated electrons (3.1 x 10¹⁰ M⁻¹ s⁻¹ and 7.7 x 10⁹ M⁻¹ s⁻¹, for **1b** and CO₂, respectively).^{43,44} The rate constants reported for selected reactions of acrylamide (**1b**) from pulse radiolysis studies^{45,46} are shown in Scheme

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2. However, CO_2 has a singular competitive advantage over substrates 1 in acetonitrile solution as it actually resides in the solvation shell of the iodide anion. Indeed the effective molarity of the reactants held in the proximity of its reaction partner by non-covalent intermolecular forces could reach values as high as 10⁶ M,⁴⁷ which is a key factor in enzyme catalysis commonly applied to control chemical reactivity.

Conversely, polar protic solvents or additives displace the $\rm CO_2$ molecules from the solvation shell of the iodide anion

Scheme 2. Selected rate constants reported for acrylamide (1b) from pulse radiolysis studies.



Ox: 2-sulfoanthraquinone (E^{o}_{red} = -0.634 vs SCE).^{45,46}

and, thereby, hinder the formation of the radical anion $[CO_2^{--}]$. Water and methanol do not scavenge hydrated electrons efficiently (1.9 x 10¹ M⁻¹ s⁻¹, and < 1 x 10⁻⁴ M⁻¹ s⁻¹, respectively),⁴³ yet unionized acetic acid and the $[H_3O^+]$ ions do (2.0 x 10⁸ M⁻¹ s⁻¹ and 1.9 x 10¹⁰ M⁻¹ s⁻¹, respectively),⁴³ and these reactions deliver H-atoms⁴³ to the solution. Therefore, the data set discussed in this section suggests that the photolysis of the CO₂-saturated solutions of LiI and substrates 1 preferentially channels through the radical anion $[CO_2^{--}]$ in acetonitrile, but involves different reactive species in aqueous medium.

The carboxylation step. The radical anions $[CO_2^{--}]$ and $[1^{--}]$ are strong reductants that undergo electron transfer reactions with oxidants at rates close to diffusion $[0.7-5 \times 10^9 \text{ M}^{-1} \text{ s}^{-1}, \text{ for different species } [1^{--}],^{45} \text{ and } 0.33 \times 10^{10} \text{ M}^{-1} \text{ s}^{-1}, \text{ for [CO}_2^{--}]^{48}$, in the reaction with 2-sulfoanthraquinone (E^o = -0.634 V vs. SCE)] (Scheme 2). Therefore, the photoinduced electron transfer reaction will not proceed towards the iodocarboxylation adducts 2 unless the ensuing steps are efficient enough to compete with the electron transfer to the oxidizing iodine species in the reaction medium (Scheme 1).

Iodine atoms are not expected to play a key role in the photoiodocarboxylation reaction as they react with excess iodide anion with a rate constant of $2.5 \pm 0.4 \times 10^{10} \text{ M}^{-1} \text{ s}^{-1}$ to give the radical anion $[I_2^{--}]$, which is able to produce additional negatively charged species under our reaction conditions.^{49,50} However, we will herein consider the iodine atoms as actual intermediates for simplicity reasons.

Pulse radiolysis studies in aqueous medium have shown that the radical anion $[CO_2^{--}]$ adds to acrylamide **1b** (path b, Scheme 1) with a second-order rate constant of $(4 \pm 1) \times$ 10⁷ M⁻¹ s⁻¹ without any significant competition of electron transfer (Scheme 2).⁴⁶ The addition of the radical anion $[CO_2^{--}]$ to methyl acrylate (**1a**) has also been demonstrated in hydrated clusters in the gas phase.⁵² This reaction proceeds with the rehybridization of only the β-carbon atom of substrate **1** as the radical anion $[CO_2^{--}]$ already has a bent structure. Hence, the intermediacy of the distonic radical anion [I⁻⁻] in the formation of the iodocarboxylation adducts **2** in acetonitrile (Table 1) agrees well with the chemistry reported for the radical anion $[CO_2^{--}]$ in aqueous medium.^{46,52}

Conversely, no data on the reaction of the substrate radical anion [1⁻⁻] with CO₂ (path a, Scheme 1) are reported in the literature. Notwithstanding, it is known53 that radical anions [1b⁻⁻] and [1h⁻⁻] from acrylamide (1b) and acrylic acid (1h) in aqueous medium undergo reversible and diffusion-controlled protonation at the oxygen atom $(pK_a 7.9 \text{ and } 7.0, \text{ for } [\mathbf{1bH}] \text{ and } ([\mathbf{1hH}] \text{ respectively}), \text{ but}$ irreversible pH-dependent β-protonation with pseudofirst-order rate constants at pH 7 of 1.4 x 105 s⁻¹ and 4.0 x 104 s⁻¹, respectively (Scheme 2).⁵³ The different magnitudes of these rate constants have been attributed to the energy penalty posed by the rehybridization of the terminal carbon atom in the irreversible β-protonation step.⁵³ Accordingly, the reaction of the substrate radical anion [1-] with CO₂ to give the distonic radical anion [I⁻⁻] (path a, Scheme 1), which requires the rehybridization of both reaction partners, is not expected to compete efficiently with the proton transfer from the solvent in aqueous medium.

It is noteworthy that all the steps proposed for the photoiodocarboxylation reaction (Scheme 1), except the capture of CO₂ by the radical anion [1⁻⁻], have been proven efficient in aqueous medium, even the addition of $[CO_2^{--}]$ to 1.^{45,46,48,52,54}. Therefore, the formation of the radical anion $[CO_2^{--}]$ in water is probably marginal under our reaction conditions, otherwise the photoiodocarboxylation adduct would also be produced in this medium.

The distonic radical anion $[I^-]$. The impact of the solvent on the photoiodocarboxylation reaction could alternatively be attributed to the fragmentation of the distonic radical anion $[I^-]$ to give $[CO_2^-]$ and 1 (path b, Scheme 1). This decarboxylative process, which has been disclosed in the ion cyclotron mass spectrometry study of the addition of $[CO_2^-]$ to methyl acrylate (1a) in hydrated clusters in the gas phase,⁵² could be more efficient in water than in acetonitrile given the better solvation of the radical anion $[CO_2^-]$ in the polar protic solvent. In other words, the carboxylation equilibrium could be strongly displaced to the left-hand side in aqueous medium (path b, Scheme 1).

The results in Table 2 provide information on the reactivity of the intermediate [I⁻⁻]. Indeed the photolysis of iodocarboxylation adducts **2b** and **2d** in water (Table 2), which proceeds through the radical pair [I⁻, I⁻],²⁷ gave a *ca*.

1:1 mixtures of starting materials **1b** and **1d**, and maleic and fumaric acid derivatives **3b** and **3d** (Table 2). These results establish that, first, the addition of the radical anion $[CO_2^{--}]$ to the substrates **1** is reversible, in agreement with the conclusions drawn from the ion cyclotron mass spectrometry study;⁵² and second, the radical anion $[I^{--}]$ undergoes irreversible H-atom transfer to the iodine atom to give the unsaturated products **3** (path b, Scheme 3), in competition with decarboxylative fragmentation followed by electron transfer from $[CO_2^{--}]$ to the iodine atom to give the starting materials (path a, Scheme 3).

Scheme 3. Reaction paths proposed for the distonic radical anion [I⁻⁻].^{27,52}



The photolysis of acrylic acid (**1h**), KI and CO_2 in aqueous medium (Entry 23, Table 1) gave neither iodocarboxylation adducts **2h**, nor maleic and fumaric acids **3h**, which should accompany the decarboxylative fragmentation of the intermediate [Ih^{...}]. The reaction of acrylamide (1b) under the same conditions (Entry 22, Table 1) gave only a small amount of **3b**, which indicates that the fragmentation of [**Ib**^{..}] back to the starting materials does not play a key role in preventing this reaction, otherwise the low substrate conversion would be accompanied by a greater formation of **3b** than that actually found. Similar results were found for the photoiodocarboxylation reaction of methyl acrylate (1a) when water and methanol were used as cosolvents (Entries 24 and 25, Table 1). Therefore, neither the photolysis of iodocarboxylation adduct 2 nor an unfavorable carboxylation equilibrium, satisfactorily accounts for the failure of the photoiodocarboxylation reaction in polar protic media.

Impact of acids on the reaction course. The results in Table 3 revealed that the presence of excess acetic acid in the reaction medium actually opens up alternative paths in the photoiodocarboxylation reaction. The reactions took place with low substrate conversions (Table 3), as expected from the partial displacement of CO_2 from the solvation sphere of the iodide anion by the polar protic additive. Notwithstanding, CO_2 still competed with acetic acid for the photodetached electron to eventually give significant amounts of carboxylation products **2** and **3** (Entries 1, 3, 7 and 9, Table 3).

The formation of 2-iodopropanoic acid derivatives 4 under these conditions (Table 3) could be tentatively accounted for by two alternative reaction paths (Scheme 4). The first proceeds through one electron reduction of 1 and β -protonation of the radical anion $[1^{-1}]^{53}$ (path a, Scheme 4), and the second through one electron reduction of the carboxylic acid moiety⁴³ coordinated to the iodide anion, and addition of the resulting H-atom to the C=C double bond of 1 (path b, Scheme 4),⁴³ followed in both cases by coupling of the resulting C-radical [II⁻] with the iodine atom. Note that these reaction paths require that either the substrate 1 (path a, Scheme 4) or the carboxylic acid (path b, Scheme 4) efficiently compete with CO₂ as electron acceptors in the electron transfer step, which contradicts some of the observations discussed above.

Scheme 4. Possible reaction paths leading to the hydrohalogenated products 4 in the presence of acids.



The most salient feature in Table 3 is, however, the formation of 2-iodopropanoic acid derivatives 4 as the major product in a CO_2 atmosphere, but of lactic acid derivatives 5 in an inert atmosphere, which indicates the involvement of different intermediates for each reaction condition. Indeed if substrate 1 was able to compete with acetic acid and CO_2 for the photodetached electron, and if the radical anion [1⁻⁻] gave 2-iodopropanoic acid derivatives 4 through path a in Scheme 4, then the reaction in an inert atmosphere would also produce 4. The same conclusion would apply if acetic acid competed with CO_2 and substrate 1 as an electron acceptor to give H-atoms, which would lead to 4 through path b in Scheme 4. The reaction paths towards lactic acid derivatives 5 will not be discussed herein.

Actually, the results in Table 3 show that products 4 arise only when CO₂ and acetic acid are both present in the reaction medium, which reveals that the radical anion $[CO_2^{--}]$ is involved in the reaction path to 4. Since pulse radiolysis studies55,na,b have established that the radical anion $[CO_2^{--}]$ does not generate H-atoms even at pH < 3, the formation of 4 under these conditions is better accounted for through the radical anion intermediate [1⁻⁻] (path a, Scheme 4), generated by electron transfer from the radical anion [CO₂^{...}] to 1. ⁵⁶ Accordingly, the radical anion [CO2"] would react with substrates 1 through either addition to the C=C double bond to give [I⁻⁻], or electron transfer to give [1⁻⁻], which agrees with its dual character as a nucleophilic radical¹⁵ and a strong reductant. The fact that the electron transfer step from $[CO_2^{-1}]$ to 1 went unnoticed in acetonitrile under our standard reaction conditions suggests that the radical anion [1-] most probably deactivates through electron transfer to the oxidizing iodine species.

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In aqueous medium, however, carboxylic acids release into the solution [H₃O⁺]-ions which react efficiently with hydrated electrons (2.3 x 10¹⁰ M⁻¹ s⁻¹).^{43,57} The reaction, then, probably channels through the radical intermediates generated from the addition of H-atoms to 1, which proceeds in aqueous medium with rate constants of 3.3 x 10^{10} M⁻¹ s⁻¹ and 1.8×10^{10} M⁻¹ s⁻¹ for **1h** and **1b**, respectively (Scheme 2).⁴³ Indeed the photolysis of acrylic acid (1h) with KI and CO₂ in water failed to give products from the β protonation of the radical anion [1h^{--]53} and proceeded with a low mass balance (Entry 23, Table 1), suggesting radical side processes. Non-acidic acrylamide (1b) did not undergo such a destructive reaction under the same conditions (Entry 22, Table 1), but it did in the presence of acetic acid (Entries 5 and 6, Table 3). These data suggest that the radical anion [1⁻⁻] either does not form in aqueous medium or deactivates through electron transfer to the oxidizing iodine species.50

The scope of the reaction. Scheme 5 summarizes the major features of the photoiodocarboxylation reaction in anhydrous acetonitrile discussed herein, namely: i) CO₂ is the main electron acceptor in the photoinduced electron transfer from the iodide anion; ii) the radical anion [CO,⁻⁻] reacts with substrate 1 through either reversible addition to the C=C double bond to give the distonic radical anion [I⁻⁻] or electron transfer to give [1⁻⁻]; iii) the intermediate [I⁻⁻] reacts with the iodine atom through either radical coupling to give adduct 2 or H-atom transfer to give unsaturated carboxylation product 3; iv) the radical anion [1⁻] either deactivates back to 1 through electron transfer to an oxidizing iodine species or, in the presence of acids, undergo irreversible β -protonation and coupling of the resulting C-radical [II-] with the iodine atom to give product 4. However, the reaction in aqueous medium channels through alternative intermediates because CO₂, unable to displace water from the solvation sphere of the iodide anion, loses its competitive advantage as an electron acceptor. The results obtained for the different substrates 1 (Table 1) can now be discussed in light of the reaction paths outlined in Scheme 5.

Scheme 5. Reaction paths proposed for the photoiodocarboxylation reaction in anhydrous acetonitrile.



The nucleophilic radical anion [CO,"] efficiently adds to substrates 1 with reduction potentials that fall within the range of *ca*. -2.50 to -2.00 V *vs*. SCE (Table 1). For substrates 1 with a reduction potential less negative than -2.00 V, the reaction channels preferentially through electron transfer (Scheme 5), as shown by the isomerization of dimethyl [(Z)-1r] observed under maleate the photoiodocarboxylation conditions (Entry 18, Table 1), and in agreement with the results from the pulse radiolysis studies on dimethyl maleate $[(Z)-\mathbf{1r}]$ and dimethyl fumarate $[(E)-\mathbf{1r}]$.⁵⁷ The absence of polycarboxylation¹⁸ products from the reaction of [CO₂⁻⁻] with unsaturated product 3 under our reaction conditions (Table 1) is the result of this unproductive path. The insolubility of lithium carboxylates 2 and 3 in acetonitrile contributes to prevent further carboxylation or photolysis reactions of these products under our reaction conditions.

For substrates 1 with similar or more negative reduction potentials than for CO_2 , the reaction course depends on the efficiency of the carboxylation step, and the competitive reactions of the distonic radical anion [I⁻], i.e. fragmentation back to the reactants, and coupling or deshydrohalogenation with the iodine atom (Scheme 5).

Table show The results in 1 that the photoiodocarboxylation is more efficient for acrylic acid derivatives 1a-e than for crotonic acid derivatives 1j-l and, in general, for substrates 1 with substituents at the β position. This observation cannot only be attributed to the more negative reduction potentials of substrates 1 with electron-releasing substituents at β-position because cyclopentenone (1n), cyclohexenone (1p), and N,Ndimethyluracil (10), with reduction potentials that fall within the optimal range, do not react significantly under our conditions (Entries 14-16, Table 1). Instead these results evidence that the addition of [CO,"] to substrates 1 is sensitive to steric hindrance at the β-position.^{15b,c}

The approach trajectory of $[CO_2^{--}]$ towards 1 aligns the C_{β} -CO₂ σ -bond parallel to the *p* orbital of the α -carbon radical [I⁻⁻] in the plane perpendicular to the C=C double bond,^{15b,c,58} which is the optimal orientation for the reverse reaction. The steric or electronic factors that prevent the intermediate [I⁻⁻] to escape this reactive conformation are expected to favor the path back to the starting materials. Moreover, the carboxylation reaction occurs with rehybridization of the β -carbon atom of 1, and those factors that prevent this geometrical change are expected to hinder the formation of the new C-C σ -bond. The restricted conformational mobility of the cyclic distonic radical anions [In-o⁻⁻] would then contribute to the poor performance of substrates **1n-o**, regardless of their favorable reduction potentials (Table 1).

The isomerization of the unreacted substrates observed for the crotonic acid derivatives **1j-l**, with more negative standard reduction potentials than CO_2 (Table 1), could be attributed to the contributions made from the reversible formation of the distonic radical anion [I⁻]⁵² and electron transfer from [CO_2^{-}]. The isomerization of *(E)*crotonamide (**1k**) observed in the presence of acetic acid under inert atmosphere (Entry 10, Table 3) suggests that the addition to the C=C double bond of intermediate Hatoms may also be reversible.

The reactions of the radical anion $[I^-]$ with the iodine atom are crucial for the formation of carboxylation products 2 and 3 (paths a and b, Scheme 5). The coupling of these intermediates, though not rate-determining, is sensitive to steric and electronic factors, as indicated by the remarkable diastereselectivity observed for substrates 1j-l, whose intermediates [Ij-l⁻⁻] have stereogenic β-carbon atoms (Table 1). The H-atom transfer from [I⁻] to the iodine atom is less favorable as it involves the breaking of a C_{B} -H bond, which has to be aligned in parallel to the *p* orbital holding the unpaired electron in order to be activated.^{27,58} With methacrylamide (11) (Entry 9, Table 1), the H-atom transfer occurred preferentially from the α methyl group of [Ii⁻], which provides stereoelectronically and statistically more favored C-H σ -bonds than the β carbon atom. The trends on the selectivity for this reaction are, however, obscured by the possible isomerization of products 3 through reversible electron transfer, the photolysis of adducts 2 under our reaction conditions,²⁷ the impact of the α -substituents on the lability of the C-I σ bond of adduct 2, and the possible formation of transient carbocation intermediates by electron transfer from [I⁻⁻] to the iodine atom.²⁷ For instance, the reaction of styrene (1s) gave only unsaturated carboxylation product 3s with a low mass balance (Entry 19, Table 1). In this case, the labile benzylic C-I σ -bond of adduct **2s** could open up alternative polar or radical reaction paths and lead to alternative products or polymeric materials.

Finally, it is worth mentioning that ion pairing could be a significant factor for the reactions carried out in acetonitrile. For instance, the interactions of the lithium cation with the polar and ionic groups of the negatively charged intermediates could impact the electron capture by CO_2 , the conformational equilibrium of the intermediates [I⁻], the carboxylation step and the coupling of [I⁻] with the iodine atom. The change of Lil to KI did not significantly alter the reaction course (Entries 1 and 21, Table 1), but this issue deserves a detailed study, which is beyond the scope of the present work.

Conclusions

The photolysis at 254 nm of the CO₂-saturated acetonitrile solutions of LiI and olefins 1 carrying an electron withdrawing Z-substituent led to the addition of iodine and CO₂ to the C=C double bond. This reaction proceeded efficiently with terminal C=C double bonds to give new C-I and C-C σ -bonds at the α and β -positions of the Z-substituent, respectively. The UV spectra of the reaction components under different conditions have revealed that CO₂ is able to penetrate the solvation sphere of the iodide anion in acetonitrile, but not in water, as the intermolecular ion-quadrupole interactions provided by CO₂ to the halide anion cannot successfully compete with H-bonding. This fact determined the negative impact of polar protic solvents on reaction efficiency. This transformation has been interpreted in terms of a photoinduced electron transfer reaction from the iodide anion to reducible species in solution, which leads to different reactive intermediates, depending on the reaction conditions. The results suggest that the reactions in acetonitrile involve the radical anion $[CO_2^{--}]$ as a key intermediate, which reacts with substrate 1 through reversible addition or electron transfer, depending on the reduction potential and the steric hindrance at the βposition of 1. Conversely, CO_2 is not an efficient electron acceptor in water and the reaction proceeds through alternative paths, which probably involve H-atoms as intermediates.

In summary, the present report describes the transition metal-free and atom-efficient photoiodocarboxylation of activated olefins 1 with CO_2 and LiI in acetonitrile, and discusses the reaction course and the reactive intermediates involved.

Experimental Section

General. Lithium iodide (LiI) and potassium iodide (KI) were dried under vacuum for 3 h at 60 °C and stored in a desiccator. Solvents and reagents were degassed by standard freeze-pump-thaw procedures and stored under argon atmosphere. Carbon dioxide at 40 °C and 60 bar was passed through a Drierite® column prior to depressurizing and dosing into the reaction mixtures. The reactions were performed with a 45 cm long compact twin-tube low pressure mercury lamp (254 nm) Phillips TUV PL-L 36W/4P (power 36 W, UVC radiation 12 W). ¹³C NMR spectra for reaction products 2 in D₂O were recorded with the minimum acquisition times required for observing the signals, in order to minimize the decomposition of product 2. The UV spectra of the anhydrous acetonitrile solutions under argon or CO₂ atmosphere, and at different temperatures, were measured by using a fiber optic probe; the UV spectra under CO₂ pressure were measured on a 25 mL stainless steel view cell with sapphire windows (optical path 3.53 cm). HRMS measurements were carried out on a quadrupole-time of flight (Q-TOF) tandem mass spectrometer by using Electrospray (ESI) as ionization technique. The accurate mass measurements obtained

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from ESI in positive mode (ESI⁺) correspond to the protonated 2-substituted-2-iodocarboxylic acids (2HH⁺).

Photoiodocarboxylation reactions and control experiments. General procedures.

(A) Photolysis of lithium iodide, substrates 1, and CO₂ (Table 1). An acetonitrile- d_3 solution (3 mL) of lithium iodide (0.12 mmol) and methyl acrylate (1a) (0.12 mmol) was placed into a Suprasil[®] quartz test tube under CO₂ atmosphere. The tube was capped with a rubber septum, connected through a syringe needle to a CO₂-reservoir at ca. 20 psi, and cooled to 0 °C for 20 min under magnetic stirring. The quartz tube was firmly capped with a new rubber septum at o °C under CO₂ at atmospheric pressure, and fixed to a rotor unit. The sample was irradiated at 254 nm with a low-pressure mercury lamp (36 W) placed parallel 2 cm above the quartz tube, for 3 h, at room temperature under rotation and magnetic stirring. The reaction mixture was a dark yellow suspension which was allowed to decant at room temperature protected from the light. A o.8 mL aliquot of the supernatant was diluted with 0.1 mL of a 0.049 M acetonitrile- d_3 solution of *tert*-butanol as external standard, and the sample was analyzed by 'H-NMR. The remaining of the reaction mixture was evaporated to dryness under vacuum. The solid residue was dissolved in 0.8 mL of a 0.042 M solution of tertbutanol in water- d_2 , and the sample was analyzed by ¹H-NMR. The substrate conversion and the reaction products were quantified from both samples by comparing the integrals of their respective ¹H-NMR signals to those of the standard. The reaction products were identified as lithium 3-iodo-4-methoxy-4-oxobutanoate (2a), lithium (Z)- y (E)-4-metoxi-4-oxobut-2-enoato de litio [(Z)- and (E)-3a], and methyl 2-iodopropanoate (4a).

The results were confirmed with a series of identical experiments which were analyzed by diluting the reaction mixtures with 0.4 mL of ultrapure water. A 0.8 mL aliquot of the homogeneous solution was diluted with 0.1 mL of a 0.049 M acetonitrile- d_3 solution of *tert*-butanol as external standard. The samples were analyzed by 'H-NMR and the results compared with those obtained through procedure A. The samples showed variable amounts of 2-iodosuccinic anhydride.

The reactions in water were performed with 0.01 M solutions of KI and substrate 1 in water- d_2 , following the same procedures. An aliquot (0.8 mL) of the homogeneous reaction mixture was diluted with 0.1 mL of a 0.042 M water- d_2 solution of *tert*-butanol as external standard, and analyzed by ¹H NMR.

(B) <u>Preparative procedure</u>. An acetonitrile solution (6 mL) of lithium iodide (0.24 mmol) and methyl acrylate (1a) (0.24 mmol) was placed into a *Suprasil*[®] quartz test tube under CO₂ atmosphere. The tube was capped with a rubber septum, connected through a syringe needle to a CO₂-reservoir at *ca*. 20 psi, and cooled to 0 °C for 20 min under magnetic stirring. The quartz tube was firmly capped with a new rubber septum at 0 °C under CO₂ at atmospheric pressure, and fixed to a rotor unit. The sample was irradiated at 254 nm with a low-pressure mercury lamp (36

W) placed parallel 2 cm above the quartz tube, for 3 h, at room temperature under rotation and magnetic stirring. The reaction mixture was a dark yellow suspension which was allowed to decant for 30 min at 0 °C protected from the light. The supernatant solution was removed and the solid residue was washed with cold anhydrous acetonitrile (3 x 5 mL), at 0 °C and protected from the light. The final residue was dried under vacuum to give 57 mg (90 % yield) of crude lithium 3-iodo-4-methoxy-4-oxobutanoate (**2a**), with minor amounts of lithium (*E*)- and (*Z*)- 4-methoxy-4oxobut—2-enoate [(*Z*)- and (*E*)-**3a**].

(C) Photolysis of iodocarboxylation adducts 2 (Table 2). A water-*d*₂ solution (2.1 mL) of lithium 4-amino-3-iodo-4oxobutanonate (2b) (0.044 mmol) was placed into a Suprasil[®] quartz test tube under argon atmosphere. The tube was capped with a rubber septum, fixed to a rotor unit, and irradiated at 254 nm with a low-pressure mercury lamp (36 W) placed parallel 2 cm above the quartz tube, for 3 h, at room temperature under rotation and magnetic stirring. A 0.6 mL aliquot of the yellow solution was diluted with 0.2 mL of a 0.020 M water-*d*, solution of *tert*-butanol as external standard, and the sample was analyzed by 1H-NMR. The substrate conversion and the products distribution were determined from the integrals of their respective ¹H-NMR signals compared to those of the standard. The reaction products were identified as lithium (*Z*)- and (*E*)-4-amino-4-oxobut-2-enoate [(*Z*)- and (*E*)-3**b**], and acrylamide (1b).

The reactions in the presence of acetic acid were performed by irradiating acetonitrile- d_3 solutions (2.1 mL) of **2b** (0.044 mmol) and acetic acid (4.4 mmol), following the same procedure C. A 0.8 mL aliquot of the yellow solution was diluted with 0.1 mL of a 0.038 M acetonitrile- d_3 solution of *tert*-butanol as external standard, and analyzed by ¹H NMR.

(D) <u>Reactions in the presence of acetic acid (Table 3)</u>. An acetonitrile- d_3 solution (3 mL) of lithium iodide (0.12 mmol), methyl acrylate (1a) (0.12 mmol), and acetic acid (12 mmol) was placed into a *Suprasil*[®] quartz test tube under either argon or CO₂ atmosphere and irradiated, following the procedure A. The yellow reaction mixture was diluted with 0.2 mL of water- d_2 . A 0.8 mL aliquot of the homogeneous solution was diluted with 0.1 mL of a 0.035 M acetonitrile- d_3 solution of *tert*-butanol as external standard, and the sample was analyzed by ¹H NMR.

The reactions in aqueous medium were performed by irradiating a solution of acrylamide (**1b**) (0.03 mmol), potassium iodide (0.03 mmol) and acetic acid (0.3 mmol) in water- d_2 (3 mL), either under argon or saturated with CO₂, following the procedure A. A 0.8 mL aliquot of the homogeneous solution was diluted with 0.1 mL of a 0.020 M water- d_2 solution of *tert*-butanol as external standard, and the sample was analyzed by 'H NMR.

Lithium 3-iodo-4-methoxy-4-oxobutanoate (2a). AⁱH NMR (300 MHz, D₂O): δ 2.92 (dd, *J* = 6.3, 16.6 Hz, 1H), 3.14 (dd, *J* = 9.8, 16.6 Hz, 1H), 3.79 (s, 3H), 4.70 (dd, *J* = 6.3, 9.8 Hz, 1H). ¹³C {ⁱH} NMR (75 MHz, D₂O): δ 12.8, 43.1, 52.5, 173.8, 177.2. HRMS (ESI-Q-TOF) m/z: $[MH+H]^+$ Calcd for $C_5H_8IO_4$ 258.9467; Found 258.9462.

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Lithium 4-amino-3-iodo-4-oxobutanoate (**2b**). ¹H NMR (500 MHz, D₂O): δ . 2.87 (dd, *J* = 7.4, 16.3 Hz, 1H), 3.08 (dd, *J* = 8.3, 16.3 Hz, 1H), 4.71 (t, *J* = 7.9 Hz, 1H). ¹³C {¹H} NMR (125 MHz, D₂O): δ 17.1, 44.1, 176.8, 178.0. HRMS (ESI-Q-TOF) m/z: [MH+H]⁺ Calcd for C₄H₇INO₃ 243.9471; Found 243.9465.

Lithium 4-(dimethylamino)-3-iodo-4-oxobutanoate (**2c**). ¹H NMR (300 MHz, D₂O): δ 2.85-3.15 (m, 2H), 2.93 (s, 3H), 3.11 (s, 3H), 4.97 (dd, *J* = 6.5, 8.8 Hz, 1H). ¹³C {¹H} NMR (75 MHz, D₂O): δ 14.6, 36.4, 37.8, 44.4, 173.2, 178.4. HRMS (ESI-Q-TOF) m/z: [MH+H]⁺ Calcd for C₆H₁₁INO₃ 271.9784; Found 271.9778.

Lithium 3-cyano-3-*iodopropanoate* (*2d*). ¹H NMR (300 MHz, D₂O): δ 3.06 (qd, *J* = 7.2, 16.3 Hz, 2H), 4.70 (t, *J* = 7.2 Hz, 1H). ¹³C {¹H} NMR (75 MHz, D₂O): δ -10.3, 44.6, 121.1, 176.2. HRMS (ESI-Q-TOF) m/z: [MH+H]⁺ Calcd for C₄H₅INO₂ 225.9365; Found 225.9360.

Lithium 4-(allyloxy)-3-iodo-4-oxobutanoate (**2e**). 'H NMR (500 MHz, D₂O): δ 2.92 (dd, *J* = 16.6, 6.2 Hz, 1H), 3.14 (dd, *J* = 16.6, 10.0 Hz, 1H), 4.66-4.75 (m, 3H), 5.33 (d, *J* = 10.5 Hz, 1H), 5.45 (d, *J* = 17.3 Hz, 1H), 6.00 (ddd, *J* = 16.2, 10.7, 5.4 Hz, 1H). ¹³C {¹H} NMR (125 MHz, D₂O): δ 14.1, 44.1, 66.8, 118.7, 131.2, 173.4, 178.2. HRMS (ESI⁺): HRMS (ESI-Q-TOF) m/z: [MH+H]⁺ Calcd for C₇H₁₀IO₄ 284.9624; Found 284.9618.

Lithium 3-iodo-4-oxopentanoate (*af*). ¹H NMR (400 MHz, D₂O): δ 2.47 (s, 3H), 2.84 (dd, *J* = 16.5, 6.5 Hz, 1H), 3.09 (dd, *J* = 16.5, 9.2 Hz, 1H), 4.93 (dd, *J* = 9.1, 6.6 Hz, 1H). ¹³C {¹H} NMR (100.5 MHz, D₂O): δ 25.5, 25.8, 43.3, 178.5, 208.8. HRMS (ESI-Q-TOF) m/z: [MH+H]⁺ Calcd for C₅H₈IO₃ 242.9518; Found 242.9513.

Lithium 3-iodo-3-(phenylsulfonyl)propanoate (**2g**). ¹H NMR (400 MHz, D₂O): δ 2.80 (dd, *J* = 15.6, 10.9 Hz, 1H), 3.18 (dd, *J* = 15.6, 3.9 Hz, 1H), 5.55 (dd, *J* = 10.9, 3.9 Hz, 1H), 7.73 – 7.70 (m, 2H), 7.84 (t, *J* = 7.5 Hz, 1H), 7.99 (d, *J* = 7.6 Hz, 2H). ¹³C {¹H} NMR (100 MHz, D₂O): δ 37.7, 42.7, 129.4, 129.7, 134.8, 139.3, 175.2. HRMS (ESI-Q-TOF) m/z: [MH+H]⁺ Calcd for C₉H₁₀IO₄S 340.9344; Found 340.9339.

Lithium 3-*carboxy*-3-*iodopropanoate* (*ah*). ¹H NMR (500 MHz, D₂O): δ 2.81 (dd, *J* = 16.1, 9.1 Hz, 1H), 3.04 (dd, *J* = 16.1, 6.5 Hz, 1H), 4.51 (dd, *J* = 9.1, 6.5 Hz, 1H). ¹³C {¹H} NMR (125 MHz, D₂O): δ 23.2, 45.2, 178.7, 178.7. HRMS (ESI-Q-TOF) m/z: [M⁻] Calcd for C₄H₄IO₄ 242.9154; Found 242.9160.

Lithium 3-cyano-3-iodo-2-methylpropanoate (**2***j*, mixture of two diastereoisomers). 'H NMR (300 MHz, D₂O): δ 1.30 (d, *J* = 7.0 Hz, 3H), 1.35 (d, *J* = 7.1 Hz, 3H), 2.76 - 2.64 (m, 1H), 2.92 - 2.77 (m, 1H), 4.66 (d, *J* = 7.8 Hz, 1H), 4.75 (d, *J* = 6.1 Hz, 1H). '³C {'H} NMR (75 MHz, D₂O): δ 0.0, 1.6, 17.7, 18.1, 48.5, 49.8, 121.5, 121.6, 180.0, 180.3. HRMS (ESI-Q-TOF) m/z: [M⁻] Calcd for C₅H₅NO₂I 237.9365; Found 237.9371.

Lithium 4-amino-3-iodo-2-methyl-4-oxobutanoate (**2k**, mixture of two diastereoisomers). ¹H NMR (400 MHz, D₂O): δ 1.11 (d, *J* = 7.1 Hz, 3H), 1.30 (d, *J* = 7.2 Hz, 3H), 2.76 (dq, *J* = 10.5, 7.2 Hz, 1H), 4.35 (d, *J* = 11.6 Hz, 1H), 4.47 (d, *J* = 10.6 Hz, 1H). ¹³C {¹H} NMR (100 MHz, D₂O) (major diastereoisomer): δ 18.5, 28.5, 47.7, 177.0, 180.5. HRMS (ESI-Q-TOF) m/z: $[MH+H]^+$ Calcd for $C_5H_9INO_3$ 257.9627; Found 257.9622.

Lithium 3-iodo-4-methoxy-2-methyl-4-oxobutanoate (**2***l*, mixture of two diastereoisomers). 'H NMR (500 MHz, D₂O): δ 1.15 (d, *J* = 6.9 Hz, 3H), 1.33 (d, *J* = 7.2 Hz, 3H), 2.81 (dq, *J* = 10.7, 7.3 Hz, 1H), 3.75 (s, 3H), 3.79 (s, 3H), 4.48 (d, *J* = 10.8 Hz, 1H). ¹³C {¹H} NMR (125 MHz, D₂O) (major diastereoisomer): δ 17.9, 25.2, 47.8, 53.3, 174.9, 180.8. HRMS (ESI-Q-TOF) m/z: [MH+H]⁺ Calcd for C₆H₁₀IO₄ 272.9624; Found 272.9618.

Lithium 3-iodo-2,4-dimethoxy-4-oxobutanoate (2m, mixture of two diastereisomers). ¹H NMR (500 MHz, D₂O): δ 3.40 (s, 3H), 3.44 (s, 3H), 3.78 (s, 3H), 3.79 (s, 3H), 3.98 (d, J = 8.3 Hz, 1H), 4.63 (d, J = 8.3 Hz, 1H), 4.93 (d, J = 5.7 Hz, 1H). ¹³C {¹H} NMR (125 MHz, D₂O): δ 18.5, 53.68, 53.73, 57.6, 57.7, 58.3, 84.9, 85.0, 172.1, 175.3, 175.4. HRMS (ESI-Q-TOF) m/z: [MH+H]⁺ Calcd for C₆H₁₀IO₅ 288.9573, found 288.9573.

 $\begin{array}{l} Lithium (E)-4-methoxy-4-oxobut-2-enoate ((E)-3a) \left[2756-87-8 \right] .^{59} \ ^1\text{H} \ \text{NMR} \ (300 \ \text{MHz}, \ D_2\text{O}) : \delta \ 3.81 \ (\text{s}, \ 3\text{H}), \ 6.51 \ (\text{d}, \ 1\text{H}, \ ^3J = 16 \ \text{Hz}), \ 6.92 \ (\text{d}, \ 1\text{H}, \ ^3J = 16.0 \ \text{Hz}). \ ^{13}\text{C} \ ^{1}\text{H} \ \text{NMR} \ (75 \ \text{MHz}, \ D_2\text{O}) : \delta \ 52.9, \ 128.2, \ 141.3, \ 169.3, \ 173.4. \end{array}$

Lithium (Z)-4-methoxy-4-oxobut-2-enoate ((Z)-**3***a*) [3052-50-4].⁵⁹ ¹H NMR (300 MHz, D₂O): δ 3.74 (s, 3H), 5.87 (d, 1H, 3*J* = 12.1 Hz), 6.64 (d, 1H, 3*J* = 12.1 Hz). ¹³C {¹H} NMR (75 MHz, D₂O): δ 52.5, 118.8, 141.6, 168.4, 175.2.

Methyl 2-iodopropanoate (4a) [56905-18-1].⁶⁰ ¹H RMN (300 MHz, CD₃CN): δ 1.89 (d, 3H, ³*J* = 7.0 Hz), 3.68 (s, 3H), 4.57 (q, 1H, ³*J* = 7.0 Hz). ¹³C {¹H} NMR (75 MHz, CD₃CN): δ 14.0, 23.8, 53.4, 173.4.

ASSOCIATED CONTENT

Supporting Information. Details on the experimental setup, UV spectra, ¹H and ¹³C NMR spectra of the reaction products **2**, and ¹H NMR spectra of the reaction mixtures for the experiments reported in Tables 1-3. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interests.

ACKNOWLEDGMENT

Financial support from the Spanish Ministerio de Economía, Industria y Competitividad (CTQ2016-80503-P), and Fondos FEDER is gratefully acknowledged. We thank the SCSIE (Universidad de Valencia) for access to its instrumental facilities.

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SYNOPSIS TOC

