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A Convinent Route for Synthesis of New Stable 1, 4- Diionic Compounds from Three Component Reactiones of 4,4,4-Trifluoro-1-thiophen-2-yl-butan-1,3-dione, Dialkyl Acetylenicesters and Azines

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ABSTRACT

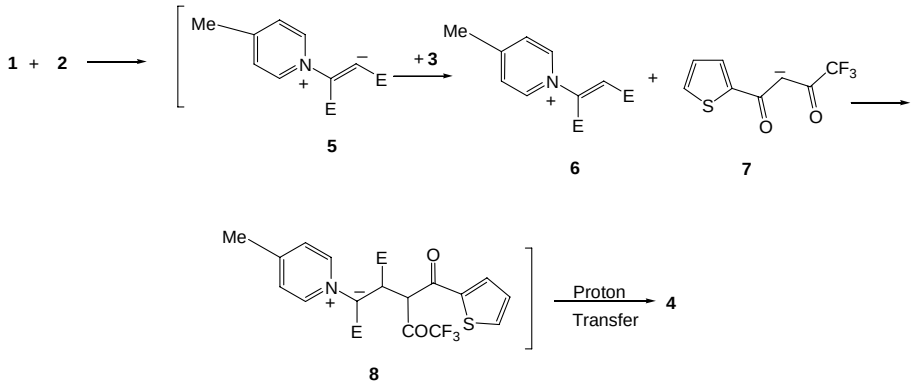
Multicomponent reactions involving azines (4-methylpyridine, isoquinoline and N-methyl imidazole) and acetylenic ester were undertaken in the presence of CH compound such as 2-furoyl trifluoroacetone(4,4,4-trifluoro-1-thiophen-2-yl-butan-1,3-dione) to generate enaminoesters as stable 1,4-diionic compounds in high yields.

Key words: Azine, 1,4- diionic compounds, 4,4,4-Trifluoro-1-thiophen-2-yl-butan-1,3-dione, Enaminoester.

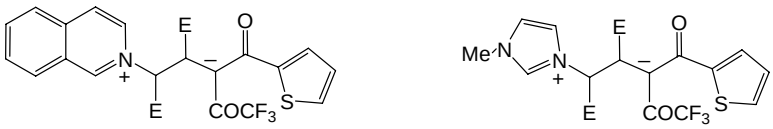
INTRODUCTION

Multicomponent reactions (MCRs) have attracted considerable attention in organic synthesis as they can produce the target products in a single operation without isolating the intermediates, thus reducing reaction times and energy consumption. MCRs have merits over conventional linear type syntheses in several aspects including simple procedures, possible structural variations, and rapid access to complex molecules. Therefore, discovery and development of new MCRs is highly desirable.These reactions have gained more use in synthetic organic chemistry[1-3]. Among these reactions are the Ugi and Passerini reactions, and more recently the synthesis of phosphorous yields and phosphonate esters[1,4-9,11-14] which have been intensively studied in recent years. Heterocyclic rings are present as fundamental components in the skeleton of more than half of the biologically active compounds produced by nature[15]. The isoquinoline moiety and its derivatives are found in drugs such as papaverine, an opium alkaloid that is used as a nonspecific smooth muscle relaxant and also as a vasolidator[16,18-21]. In addition, papaveraldine and benzo[c] phenathridine alkaloids,

including nitidine and anguinarine, have been attractive to synthetic organic chemists and biochemists over the last two decades since such compounds have shown interesting biological properties[22]. Molecules that contain a phenanthridine core have been found useful in many research areas[23] with applications as drugs[24], dyes[25], and molecular probes, DNA targeting agents[26]. As previously reported[27], the reaction between pyridine 1, isoquinoline and N-metyl imidazole with dialkyl acetylenedi- carboxylate 2 (DMAD and (DEAD) led to the formation of a new 1,4- diionic esters on the pyridine, isoquinoline and N-metyl imidazole core. In the current work, we wish to describe new three-component reactions as an efficient synthetic route of compounds 4, 10 and 12 using pyridine, isoquinoline and N-metyl imidazole (Schemes 1 and 2).



Scheme 1.



10	E	Yield (%)
a	CO_2Me	86
b	CO_2Et	92

12	E	Yield (%)
a	CO_2Me	88
b	CO_2Et	87

Scheme 2.

RESULTS AND DISCUSSION

The reactions between pyridine, isoquinoline and N-metyl imidazole with the Michael acceptor dimethyl cetylene- dicarboxylate [9,15,20,22,27] in the presence of CH acid (2-furoyl trifle -oroacetone) were carried out in dichloromethane and finished after approximately 5min at room tempera -ture. On the basis of well-established chemistry of nitrogen nucleophiles[1,7,10,17,24], reactions between pyridine, isoquinoline and N-metyl imidazole and dialkyl acetylenedicar -boxylate in the presence of 2-furoyl trifluoroacetone lead to 1,4-diionic compounds. To explain the outcome of these reactions we postulate the reaction mechanism of these reactions is driven from the initial addition of pyridine, isoquinoline and N-metyl imidazole in synthesis to the acetylenic ester followed by the addition of the CH 1, 3-dicarbonyl compound to form enaminoesters. The structures of compounds 4a–b, 10a-b and 12a–b were confirmed by ^{1}H NMR, ^{13}C NMR and IR. (See "Experimental section"). In short, we have developed a new multicomponent reaction method to access a novel class of stable 1, 4-diionic compounds.

The present method not only offers the advantage of carrying out the reactions under

neutral conditions but also of mixing the reactants without any pre-activation. The simplicity and short time reaction of this procedure akes it an interesting alternative method in comparison to other approaches.

EXPERIMENTAL

Dialkyl acetylenedicarboxylates, 2-furoyl trifluoroacetone, pyridine, isoqui -noline and N-metyl imidazole, were obtained from Fluka or Merck comp -anies. Melting points were measured on an Electrothermal 9100 apparatus. IR spectra were recorded on a Shimadzu IR-460 spectrometer (pellets with KBr). ^{1}H NMR spectra were measured on a BRUKER DRX-500 AVANCE spect -rometer instrument with $CDCl_3$ as solvent.

General procedure for the preparation of compounds 4, 10, and 12

To a stirred solution of 1 and 3(each 2 mmol) in 10 mL of dry CH_2Cl_2 at 0°C dimethylacetylendicarboxylate (2 mmol) was added dropwise over 3 min. The reaction mixture was then allowed to warm up to room temperature and stirred for 2h. The solvent was removed under reduced pressure, and the residue was recrystallized from Et_2O to afford the pure title compounds.

1-(dimethyl succinate-3-[4-methylpyr -idinium-2-yl]-1-(2-thenoyl)-3,3,3-trifl -uoro-acetone-1-yl anion (4a)

Bone-like powder, m.p 116-118°C; yield: 0.71 g (72%). IR (KBr): 1730, 1628, 1579(C=O) cm^{-1}. ^{1}H-NMR: 2.18(s, Me), 3.57 (*s*, OMe), 3.88 (*s*, OMe), 4.79 (br. *d*, $^3J_{HH}$ = 9.1, CH), 6.24 (*d*, $^3J_{HH}$ = 9.1, CH), 7.21- 7.5-8.88 (*m*, 7 CH) ppm. ^{13}C-NMR: 28.4(33), 51.0(CH), 54.6 (OMe), 57.8(OMe), 73.9 (CH), 106.1 (C), 121.6 (*q*, $^1J_{CF}$ = 281.1, CF_3), 124.0 (2CH), 126.7 (CH), 138.2 (CH), 144.1 (CH), 148.6 (C), 149.2 (2 CH), 150.3 (CH), 168.5 (C=O), 169.8 (C=O), 172.4 (*q*, $^2J_{CF}$ = 22.8, CF_3C=O), 189.5 (C=O) ppm.

1-(diethyl succinate-3-4-methylpyridini -um-2-yl]-1-(2-thenoyl)-3,3,3-trifluoro-acetone-1-yl anion (4b)

Green yellow powder, m.p 108-109°C; yield: 0.78 g (71%). IR (KBr): 1748, 1644, 1579 (C=O) cm^{-1}. ^{1}H-NMR: 1.12 (*t*, $^3J_{HH}$ = 7.1, Me), 1.15(*t*, $^3J_{HH}$ = 7.1, Me), 2.12(s, Me),4.13 (*m*, OCH_2), 4.26(*m*, OCH_2), 4.65 (br. *d*, $^3J_{HH}$ = 9.0, CH), 6.16 (*d*, $^3J_{HH}$ = 9.0, CH), 6.95- 7.00-8.23(m,7H) ppm. ^{13}C-NMR: 14.5 (Me), 24.8 (Me), 58.4 (CH), 63.2 (OCH_2), 64.6 (OCH_2), 65.6 (CH), 108.1 (C$^-$), 122.7 (2CH), 133.2 (*q*, $^1J_{CF}$ = 179.2, CF_3), 138.5 (CH), 139.4 (CH), 141. 9 (CH), 143.6 (CH), 144.4 (CH), 145.9 (C), 146.7 (CH), 164.6 (C=O), 1676.3 (C=O), 172.2 (*q*, $^2J_{CF}$ = 27.0, CF_3C=O), 188.4 (C=O) ppm.

1-(dimethyl succinate-3-isoquionoliniu- m-2-yl)-1-(2-thenoyl)-3,3,3-trifluoro-acetone-1-yl anion (10a)

Yellow powder, m.p 130-131°C; yield: 0.77g (78%). IR (KBr): 1738, 1646, 1610 (C=O) cm^{-1}. ^{1}H-NMR: 3.60 (*s*, Me), 3.75 (*s*, Me), 4.96 (*q*, $^3J_{HH}$ = 7.1, OCH_2), 6.55 (*d*, $^3J_{HH}$ = 9.2, CH), 6.38 (*d*, $^3J_{HH}$ = 9.2, CH), 6.67- 6.87 (*m*, 2 CH), 7.54 (br. *d*, $^3J_{HH}$ =3.9, SCH), 7.95- 8.60 (*m*, $CH_{3\text{-}8\ iq}$), 9.89 (*s*, CH_{1iq}) ppm. ^{13}C-NMR: 48.5 (CH), 53.0 (OMe), 54.6 (OMe), 70.7 (CH), 101.1 (C$^-$), 119.6 (*q*, $^1J_{CF}$ = 172.5, CF_3), 123.0 (CH), 123.7 (CH), 125.5 (CH_{iq}), 127.4 (SCH), 127.9 (CH_{iq}), 130.3 (C_{iq}), 131.7 (CH_{iq}), 132.0 (CH_{iq}), 136.0 (C_{iq}), 138.3 (SC), 138.6 (CH_{iq}), 152.1 (CH_{iq}), 167.0 (CH_{iq}), 167.6 (C=O), 172.4 (C=O), 174.3 (*q*, $^2J_{CF}$ = 34.3, CF_3C=O), 184.6 (C=O) ppm. EI-MS: 288 (7, M^+), 123 (34), 105 (56), 91 (100), 32 (13), 28 (30), 19 (27). Anal. calc. for $C_{15}H_{13}FN_2OS$ (288.35): C 62.48, H 6.59, N 9.72; found: C 62.68, H 6.42, N 9.84.

1-(diethylsuccinate-3-isoquionolinium-2-yl)-1-(2-thenoyl)-3,3,3-trifluoro-acetone-1-yl anion (10b)

Yellow powder, m.p 115-116°C; yield: 0.83g (80%). IR(KBr): 1739, 1648, 1610 (C=O) cm^{-1}.^{1}H-NMR: 1.15 (br. *t*, Me), 1.32 (*t*, $^3J_{HH}$ = 7.1, Me), 4.15 (*m*, ABX_3 system, OCH_2), 4.37 (*q*, $^3J_{HH}$ = 7.1, OCH_2), 6.55 (*d*, $^3J_{HH}$ = 4.3, CH), 6.92 (*d*, $^3J_{HH}$ = 4.3, CH), 7.35 (br. *s*, CH), 7.39 (*d*, $^3J_{HH}$ = 5.0, CH), 7.91- 8.15 (*m*, $5CH_{iq}$), 8.30 (br. *d*, CH), 8.50 (br. *d*, CH), 9.54 (*s*, CH) ppm. ^{13}C-NMR: 14.4 (Me), 14.4 (Me), 33.9 (CH), 61.4 (CH), 61.8 (OCH_2), 62.8 (OCH_2), 103.5 (C$^-$), 118.0 (*q*, $^1J_{CF}$ = 284.5, CF_3), 121.8 (CH), 127.0 (CH), 128.4 (CH), 128.5 (CH), 128.7 (CH), 129.9 (C), 132.0 (CH), 134.9 (CH), 135.4 (CH), 136.2 (C), 140.9 (C), 151.6 (CH), 164.4 (CH), 165.5 (C=O), 170.4 (C=O), 174.3 (*q*, $^2J_{CF}$ = 34.3, CF_3C=O), 183.5 (C=O) ppm.

1-(dimethyl succinate-3-N-methylimid- azolium-2-yl)-1-(2-thenoyl)-3,3,3-trifluo -ro-acetone-1-yl anion (12a)

Yellow powder, m.p 104-105°C; yield: 0.77 g (86%). IR(KBr): 1734, 1690, 1594 (C=O) cm^{-1}. ^{1}H-NMR: 3.54 (*s*, NMe), 3.74 (*s*, OMe), 3.76 (*s*, OMe), 4.74 (br. *d*, $^3J_{HH}$ = 9.6, CH), 5.74 (*d*, $^3J_{HH}$ = 9.6, CH), 6.86- 6.98 (*m*, 2CH), 7.49 (br. *s*, SCH), 7.58- 7.63 (2*d*, $^3J_{HH}$ = 5.2, NCH), 9.08 (br. *s*, NNCH) ppm. ^{13}C-NMR: 36.5 (NMe), 48.6 (CH), 52.7 (OMe), 54.0 (OMe), 60.9 (CH), 101.1 (C^-), 123.3 (CH), 123.6 (*q*, $^1J_{CF}$ = 288.0, CF_3), 123.7 (CH), 127.2 (SCH), 129.5 (NCH), 130.4 (NCH), 138.0 (SC), 149.5 (NNCH), 169.3 (C=O), 169.6 (*q*, $^2J_{CF}$ = 33.5, CF_3C=O), 173.4 (C=O) 184.1 (C=O) ppm.

1-(diethyl succinate-3-N-methylimidaz- olium-2-yl)-1-(2-thenoyl)-3,3,3-trifluoro-acetone-1-yl anion (12b)

Yellow powder, m.p 115-116°C; yield: 0.80 g (84%). IR (KBr): 1726, 1692, 1592 (C=O) cm^{-1}. ^{1}H-NMR: 1.06 (*t*, $^3J_{HH}$ = 7.0, Me), 1.19 (*t*, $^3J_{HH}$ = 7.0, Me), 3.74 (*s*, NMe), 4.03 (*m*, ABX_3 system, OCH_2), 4.17 (*m*, ABX_3 system, OCH_2), 4.73 (br. *d*, $^3J_{HH}$ = 9.7, CH), 5.72 (*d*, $^3J_{HH}$ = 9.7, CH), 6.90-7.06 (*m*, 2CH), 7.49 (br. *s*, SCH), 7.57- 7.63 (2*d*, $^3J_{HH}$ = 5.2, NCH), 9.08 (br. *s*, NNCH) ppm.^{13}C-NMR: 14.5 (Me), 14.8 (Me), 36.5 (NMe), 48.7 (CH), 61.1 (OCH_2), 61.2 (CH), 62.9 (OCH_2),. 101.1 (C^-), 119.8 (*q*, $^1J_{CF}$ = 289.2, CF_3), 123.3 (CH), 123.7 (CH), 127.1 (SCH), 129.6 (NCH), 130.4 (NCH), 138.0 (SC), 149.7 (NCHN), 168.8 (C=O), 169.5 (*q*, $^2J_{CF}$ = 29.8, CF_3C=O), 172.8 (C=O) 184.3 (C=O) ppm.

CONCLUSION

This article described a novel and mild method for the synthesis of 1, 4- diionic compounds. The cheapness, easy avail -ability of the reagents, mild reaction conditions, and excellent yield of the products are the advantages that make this protocol a useful addition to the existing methodologies.

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