Deep Science Publishing
https://doi.org/10.70593/978-93-7185-164-0_7

Chapter 7: Multicomponent synthesis of functionalized 4*H*-pyrans

Swadhin Swaraj Acharya, Bibhuti Bhusan Parida*

Abstract: 4*H*-Pyran nucleus is broadly distributed in many bioactive natural products and synthetic molecules. Therefore, huge attention has been devoted to synthesize functionalized 4*H*-pyrans. Multicomponent reactions (MCRs) are considered as greener alternatives to the traditional synthetic procedures, owing to several advantages such as pot-, and step-economy, high bond forming efficiency and no extra work-up steps. This chapter specifically highlights the multicomponent synthesis of medicinally relevant functional 4*H*-pyrans.

Keywords: 4*H*-pyran, multicomponent reactions (MCRs), one-pot reaction, step economy, green chemistry.

1 Introduction

Heterocycles (Walsh et al. 2015; Acharya et al. 2024; Acharya et al. 2024; Kumari et al. 2024; Acharya et al. 2024; Acharya et al. 2025) is the most important class of molecules broadly distributed in natural products, pharmaceuticals and bioactive molecules. Among the heterocycles, the *O*-heterocycle (Singh et al. 2018) occupies a special position. The pyran nucleus, (Auria-Luna et al. 2020; El-Khateeb et al. 2022) in this context is a celebrated scaffold owing to its natural abundance, and promising bioactivities.

Swadhin Swaraj Acharya

P. G. Department of Chemistry, Berhampur University, Bhanja Bihar, Odisha, India.

Dr. Bibhuti Bhusan Parida

P. G. Department of Chemistry, Berhampur University, Bhanja Bihar, Odisha, India.

Pyran, a six-membered oxygen heterocycle contain five C-atoms (four sp^2 carbon and one sp^3 carbon), and one *O*-atom along with two double bonds. The nomenclature of this ring is assigned by adding H with the position of sp^3 carbon atom. For example, in structures **I** and **II**, the C-2, and C-4 carbons are sp^3 thus, they are named as 2*H*-pyran, and 4*H*-pyran respectively. The reduced pyrans **III**, and **IV** are named as 3,4-dihydro-2*H*-pyran and 3,6-dihydro-2*H*-pyran respectively. When the sp^3 carbon is replaced with carbonyl, the same trend is followed by prioritizing the carbonyl group (Fig. 1). (Goel et al. 2009)

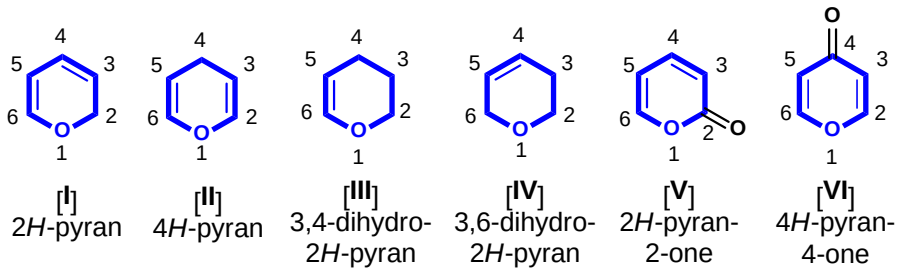


Fig. 1. Isomers of pyran

Among all the derivatives of pyran, the 4*H*-pyrans exhibit numerous bioactivities including antidiabetic, anti-proliferative, anti-HIV, anti-tuberculosis, anti-cancer, anti-microbial, anti-anaphylactic and anti-Alzheimer's activities (Samai et al. 2025). Some representative examples of functionalized 4*H*-pyrans are displayed in the Fig. 2 (Patra et al. 2024; Lukashenko et al. 2019).

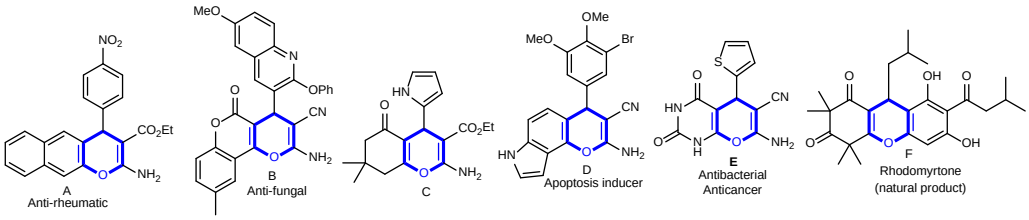


Fig. 2. Bioactive functionalized pyrans.

In the last two decades, organic synthesis witnessed tremendous growth in green chemistry, which advocates for the design of eco-friendly synthetic methods to minimize the waste generated from conventional approaches (Acharya et al. 2024; Patra et al. 2025; Panda et al. 2024). Multicomponent reactions (MCRs) are meeting the criteria of green chemistry to a great extent since, it offers step-, and pot-economic approach for the synthesis of complex molecules by avoiding the extra work-up steps, which attributes for its cost-, time-, and energy saving aspects and increase of its greenness (Acharya et al. 2024; Acharya et al. 2025; Acharya et al. 2025; Kumar et al. 2023). The MCRs may be defined as the reactions where more than two substrates react in one-pot to form the product with maximum contribution of all the reactants. The present chapter deal with the multicomponent synthesis of functionalized 4*H*-pyran derivatives. The outline of the current chapter is shown in the Fig. 3.

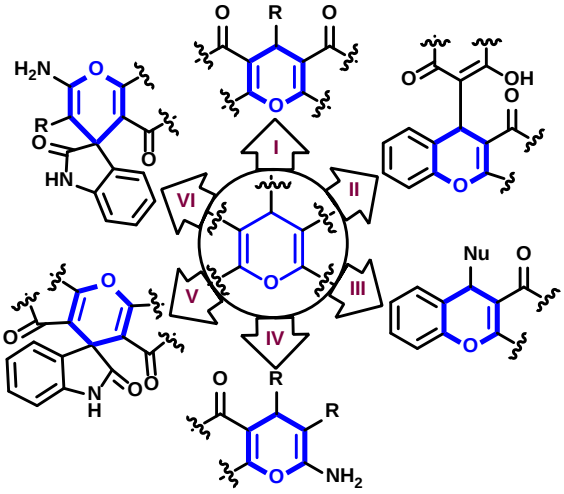


Fig. 3. Various types of pyran derivatives synthesized by MCRs

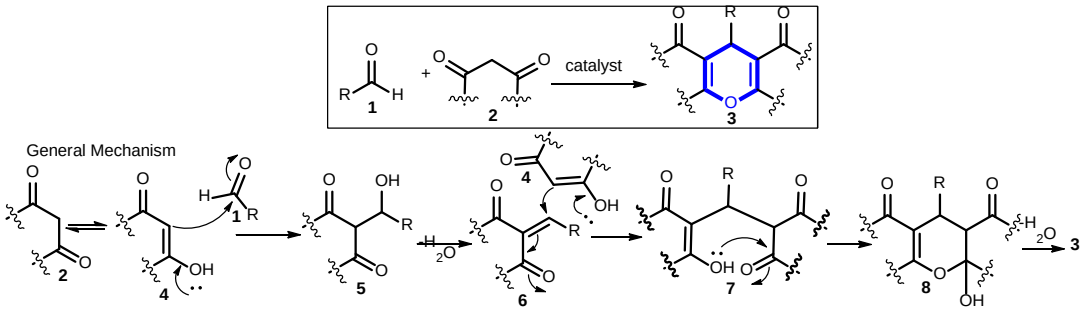
2 Methods and maretials

The chapter includes the multicomponent synthetic approaches of functionalized pyrans and spiropyrans. The chapter discusses in detail various literatures available on pyrans and spiropyran synthesis.

3 Results and discussion

3.1 Multicomponent synthesis of functionalized pyrans

3.1.1 From aldehyde and 1,3-dicarbonyl

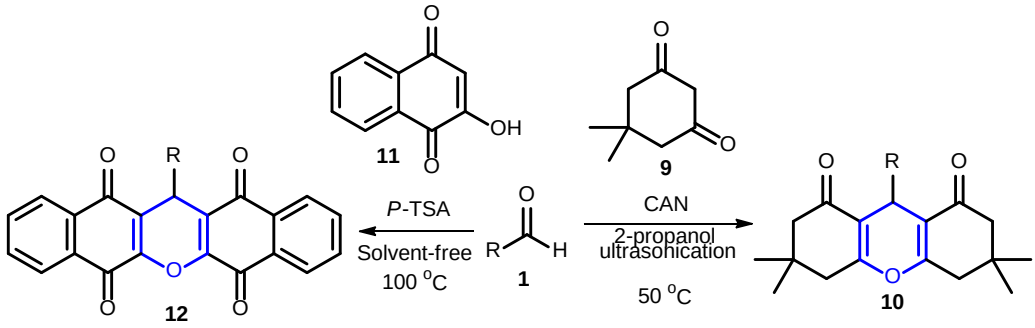


Scheme 1. General reaction scheme and mechanism of fully substituted 4*H*-pyran.

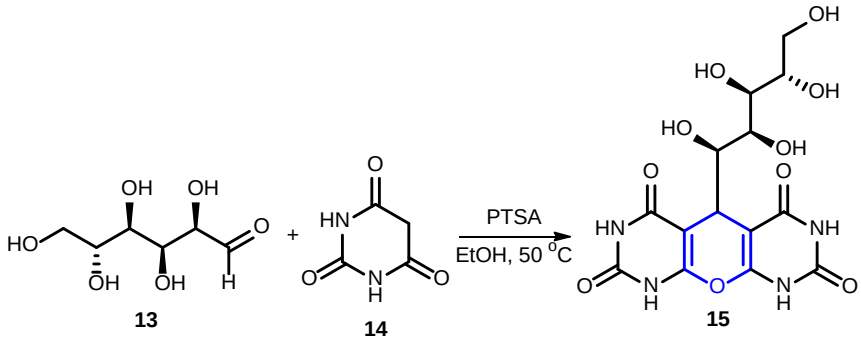
The one-pot reaction of an aldehyde with two 1,3-dicarbonyl compounds (same or different) forms a functionalized 4*H*-pyran **3** (Scheme 1). Typically acid-catalyzed, the reaction begins with condensation of the aldehyde **1** and a 1,3-dicarbonyl **2** to form a Michael acceptor **6**. This is then attacked by another 1,3-dicarbonyl **4**, leading to

intermediate **7**, which undergoes 6-*exo-trig* cyclization and dehydration to yield the pyran **3**.

Dimedone **9**, a 1,3-dicarbonyl compound, reacts with aldehydes in the presence of ceric ammonium nitrate (CAN), which activates the carbonyl group by coordination with Ce^{4+}. Under ultrasonic irradiation at 50 °C, this leads to the formation of pyran derivatives **10** (Mulakayala et al. 2012). Lawsone **11**, a natural compound from henna leaves, also contains a 1,3-dicarbonyl system (in enol form) (Acharya et al. 2025; Acharya et al. 2025). In the presence of *p*-toluenesulfonic acid (P-TSA), which protonates and activates the carbonyl, it undergoes a similar reaction to form pyran **12** (Scheme 2) (Tisseh et al. 2008).



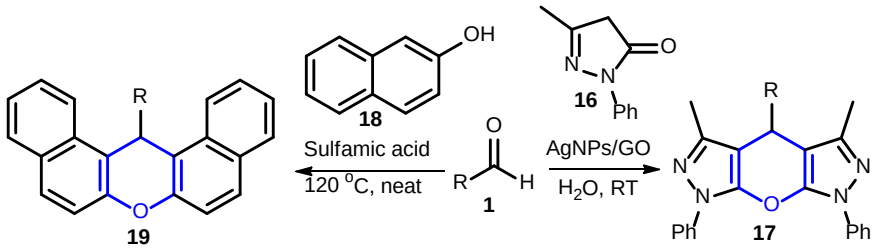
Scheme 2. Acid catalyzed synthesis of fused pyran **10**, and **11**.



Scheme 3. *P*-TSA catalyzed synthesis of pyran **15**.

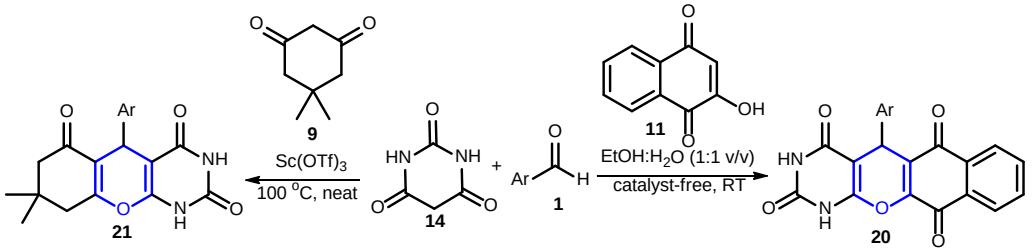
Barbituric acid **14**, a 1,3-dicarbonyl compound present in the core of many bioactive compounds. D-(+)-glucose **13**, also present in nature has an aldehyde group. In the presence of PTSA (Bronsted acid), they react to form the pyran **15** in ethanol at 50 °C (Scheme 3) (Nourisefat et al. 2014).

Apart from 1,3-dicarbonyl compounds there are also examples of compounds having acidic methylene groups, for example pyrazolone **16**, and *β*-naphthol **18**. The acidic methylene group in pyrazolone behaves same way as in 1,3-dicarbonyl compounds. The silver based nanocatalyst (AgNPs/GO), and sulfamic acid have been employed as acid catalysts for the synthesis of pyrans **17** and **19** (Scheme 4) (Dandia et al. 2017, Rajitha et al. 2005).



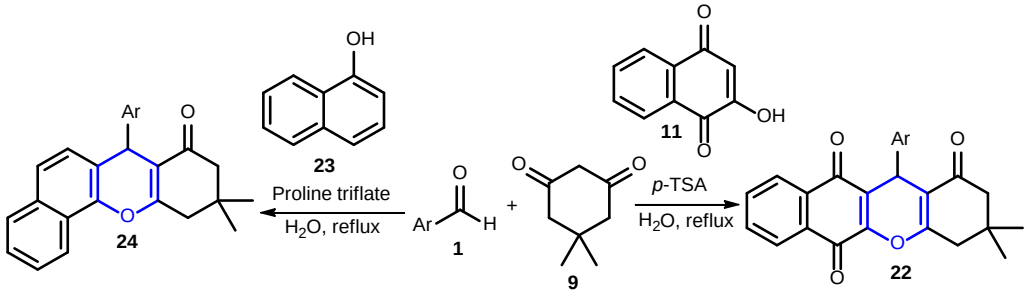
Scheme 4. Multicomponent synthesis of pyran **17**, and **19**.

Till now, the pseudo-multicomponent synthesis of fused pyran derivatives where one active methylene compound reacts twice has been discussed. Let us see the examples of some multicomponent reaction, where there are two different 1,3-dicarbonyl compounds have been utilized for the synthesis of fused pyrans **20** and **21** (Scheme 5) (Brahmachari et al. 2017, Kumari et al. 2019).



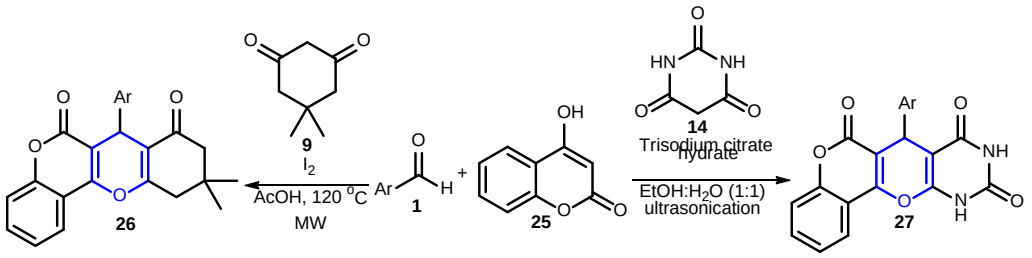
Scheme 5. Catalyst-free synthesis of pyran **20**, and **21**.

There are numerous reactions known where two different 1,3-dicarbonyls reacted to give interesting pyran derivatives in the presence of acid catalysts (Scheme 6) (Dabiri et al. 2010, Li et al. 2010).



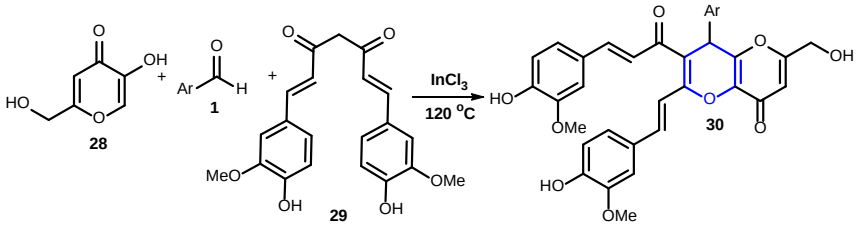
Scheme 6. PTSA catalyzed synthesis of pyran **22**.

4-Hydroxycoumarin **25** is a useful nucleus broadly found in the core of natural products, pharmaceuticals, and bioactive molecules (Borah et al. 2021). It also possesses 1,3-dicarbonyl functionality thus, it has also been explored in the synthesis of pyrans (Scheme 7) (Brahmachari et al. 2019, Sun et al. 2012).



Scheme 7. Iodine catalyzed synthesis of pyran **26**, and **27**.

Kojic acid **28** (Cook et al. 1945; Phasha et al. 2022) and curcumin **29** (Nicoliche et al. 2024; Dai et al. 2022) are bioactive natural products with 1,3-dicarbonyl functionality, making them useful in heterocycle synthesis (Borah et al. 2022; Chaudhary et al. 2020, Nagargoje et al. 2023). Kojic acid is known for skin-whitening properties, while curcumin shows broad biological activity. Using both as starting materials, benzopyran (**30**) was synthesized *via* a multicomponent reaction catalyzed by $InCl_3$ under solvent-free conditions at 120 °C (Scheme 8) (Reddy et al. 2010).

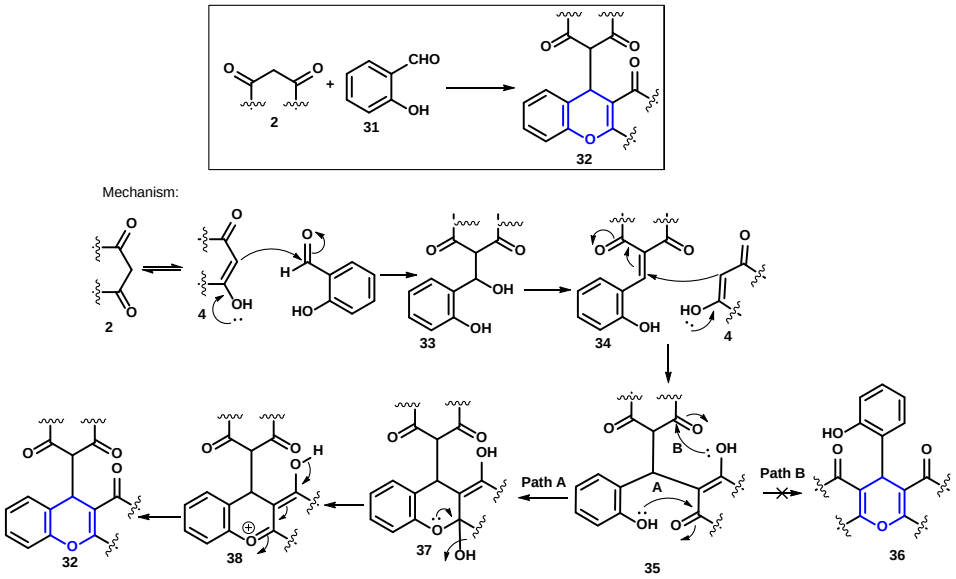


Scheme 8. $InCl_3$ catalyzed synthesis of pyran **30**.

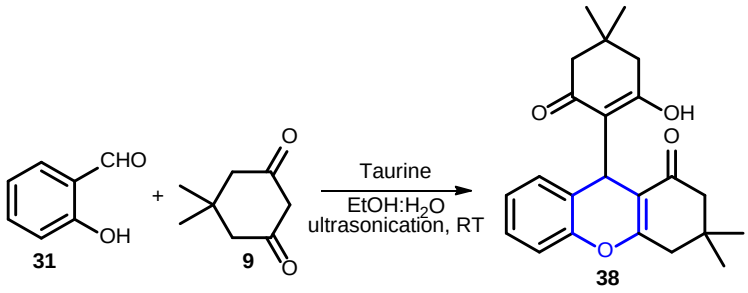
3.1.2. From salicylaldehyde with 1,3-dicarbonyl

In the above section, the aromatic aldehydes react with 1,3-dicarbonyls to provide the pyran where the carbonyls of the two active methylene are condensed. The reaction is different when there is a hydroxyl group at the *ortho*-position of the aromatic aldehyde. In the presence of *ortho*-OH group, the condensation takes place between the *ortho*–OH group and carbonyl group of the dicarbonyl (Scheme 9).

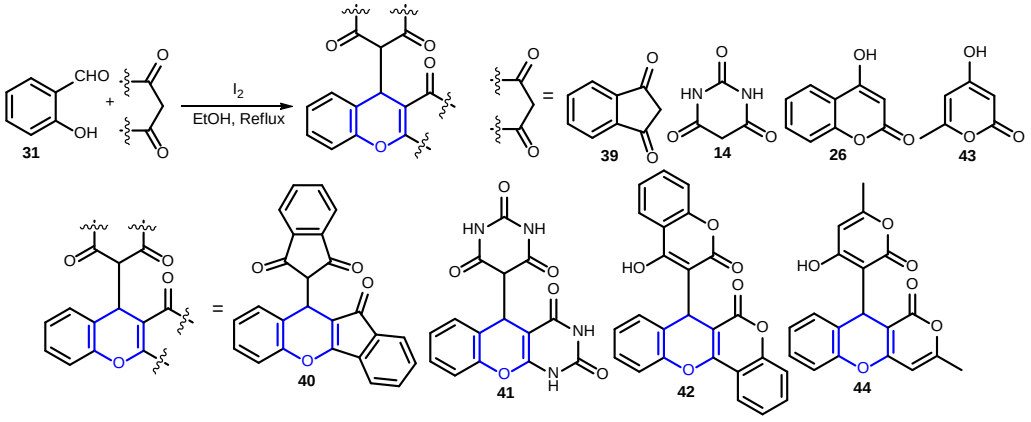
The salicylaldehyde is widely used for pyran synthesis owing to the presence of *ortho*-hydroxy group (Heravi et al. 2018). The reaction of salicylaldehyde and dimedone in the presence of taurine, a *β*-amino sulfonic acid produced the benzopyran **38** in aqueous ethanol under ultrasonication irradiation at room temperature (Scheme 10) (Acharya et al. 2025).



Scheme 9. Reaction of salicylaldehydes with 1,3-dicarbonyls.



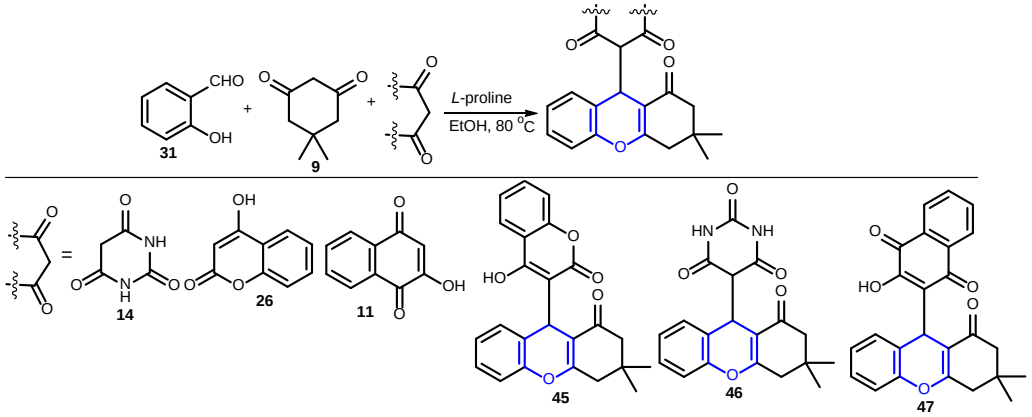
Scheme 10. Taurine catalyzed synthesis of pyran **38**.



Scheme 11. Iodine catalyzed synthesis of pyrans **40**-**44**.

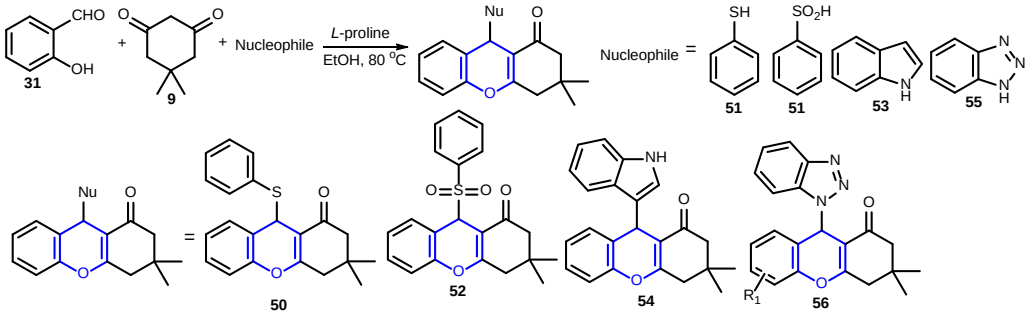
In the series other 1,3-dicarbonyl compounds have been explored and the similar results have been observed in the presence of iodine catalyst in ethanol under reflux conditions (Schemes 11) (Zeng et al. 2012).

Two different 1,3-dicarbonyl compounds can also provide the benzopyrans selectively. When salicylaldehyde reacts with two different 1,3-diketones in the presence of *L*-proline in ethanol at 80 ^{o}C (Scheme 12) (Li et al. 2012).

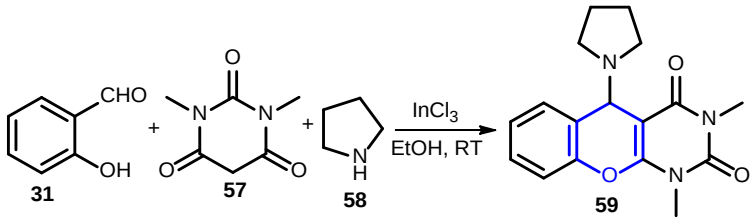


Scheme 12. L-proline catalyzed synthesis of pyrans **45-47**.

Besides 1,3-dicarbonyls, other nucleophiles also provide interesting pyran derivatives. In this case, salicylaldehyde at first react with 1,3-dicarbonyl compound to form the Michael acceptor **34**. Next, other nucleophiles attack in a conjugate manner to form interesting pyran derivatives (Scheme 14). This concept was applied for the synthesis of pyran derivatives **50**, **52**, **54**, **56**, and **59** by reacting thiophenol **49**, benzenesulfinic acid **51**, indole **53**, 1*H*-benzo[*d*][1,2,3]triazole **56**, and pyrrolidine **58** respectively (Scheme 13-14) ((Li et al. 2012; Sharma et al. 2015).



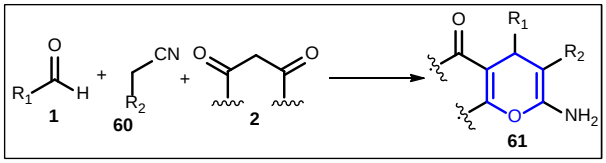
Scheme 13. *L*-proline catalyzed synthesis of pyran **52**.



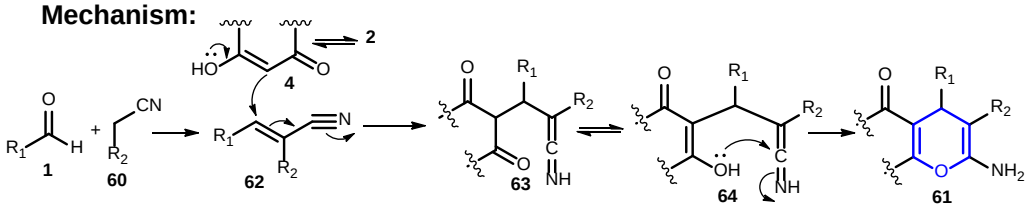
Scheme 14. *L*-proline catalyzed synthesis of pyran **59**.

3.1.3. From aldehyde, 1,3-dicarbonyl and other active methylene compound

The aminopyrans are privileged molecules owing to their promising bioactivities. Apart from 1,3-dicarbonyl compounds there are other active methylene compounds those can perform the task. In this section, the multicomponent reaction of aldehyde, active methylene compound, and 1,3-dicarbonyl compounds for the synthesis of 2-aminopyrans have been discussed. The mechanism for the formation of aminopyran proceeds by the condensation of active methylene compound **60** and aldehyde **1** followed by the Michael attack of 1,3-dicarbonyl. Intramolecular cyclization then furnishes the aminopyran **61** (Scheme 15).

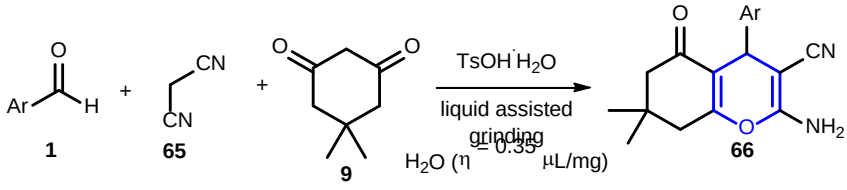


Mechanism:



Scheme 15. General reaction and mechanism for the synthesis of pyran **61**.

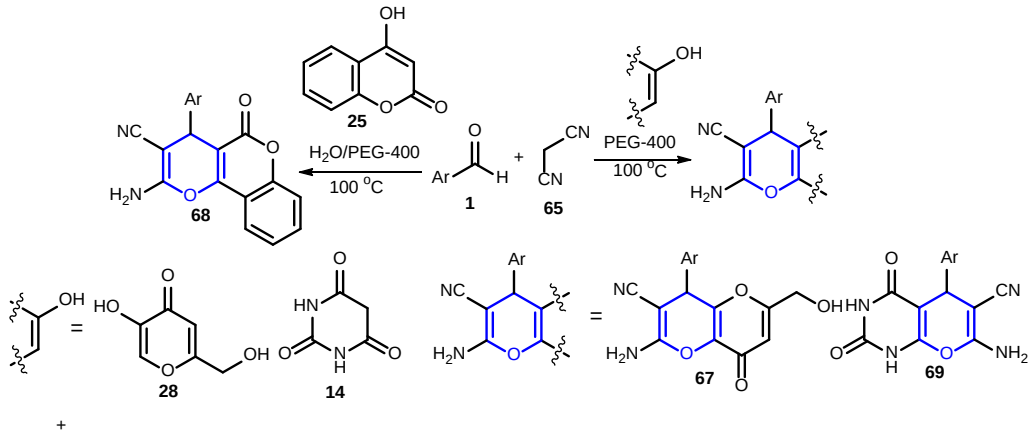
Aldehyde **1**, malononitrile **65**, and dimedone **9** were reacted in the presence of Bronsted acid $TsOH{\cdot}H_2O$ resulted the aminopyran **66** (Scheme 16) (Borah et al. 2023).



Scheme 16. General reaction and mechanism for the synthesis of pyran **66**.

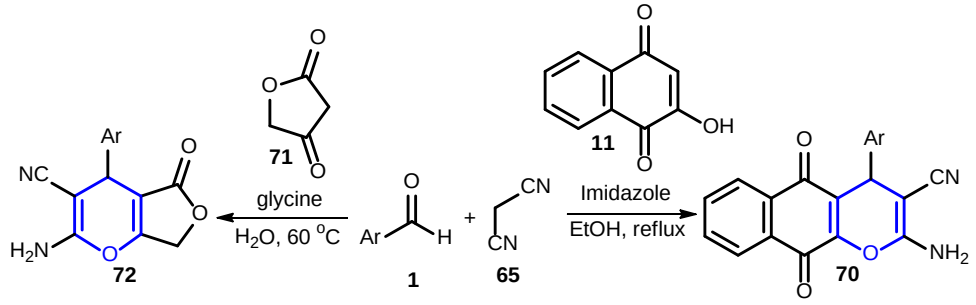
PEG-400 (polyethylene glycol) is considered as a green and sustainable solvent in modern organic synthesis since it is water soluble, biodegradable, non-toxic, inexpensive, readily available and recyclable. It activates the carbonyl group by

coordination thereby avoids the use of metal-based catalysts (Hasaninejad et al. 2018; Servesh et al. 2024; Raghu et al. 2013). In the presence of PEG-400, pyran **67, 68** and **69** have been synthesized (Scheme 17) (Kale et al. 2024; Lü et al. 2018; Mohamadpour et al. 2020).



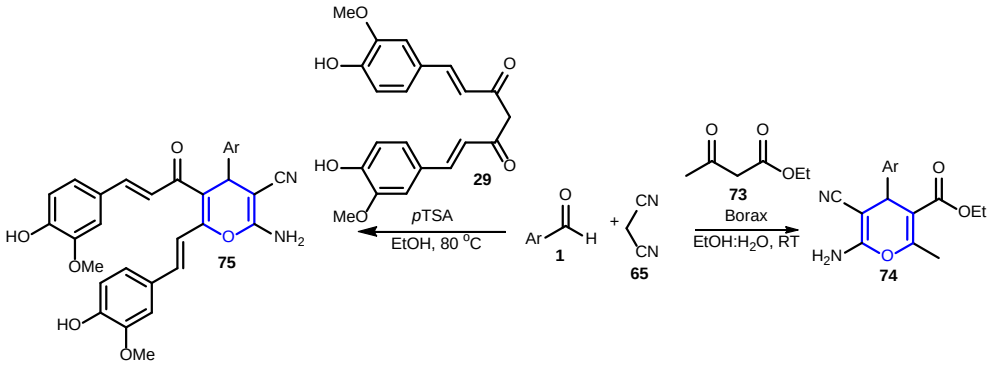
Scheme 17. PEG-400 mediated synthesis of pyran **67**.

The three-component reaction of aldehyde **1**, malononitrile **65**, with lawsone **11** and tetronic acid **71** in the presence of imidazole, and glycine respectively provided the pyran **70**, and **72** respectively (Scheme 18) (Khan et al. 2014, Singh et al. 2018).



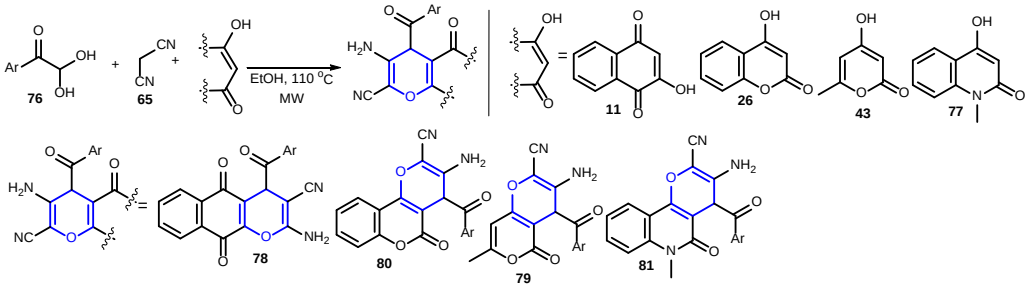
Scheme 18. Multicomponent synthesis of pyran **70**, and **72**.

Acyclic 1,3-dicarbonyl compounds have also been utilized in the synthesis of aminopyran **74** and **75** (Scheme 19) (Molla et al. 2013; Tavaf et al. 2020).



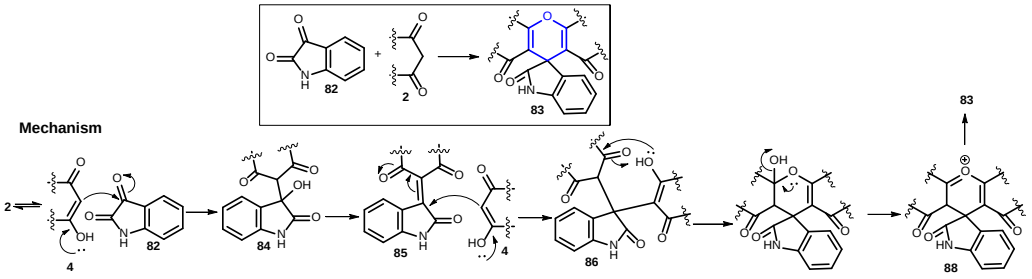
Scheme 19. Borax catalyzed synthesis of pyran **74**.

Till now, we have seen the multicomponent synthesis of 4-aryl pyrans, where the aryl moiety comes from the aldehyde. Other aldehydes have also been explored. The arylglyoxals have been utilized in the synthesis of 4-acylpyrans (Scheme 20) (Mishra et al. 2016).



Scheme 20. Multicomponent synthesis of 4-acylpyrans.

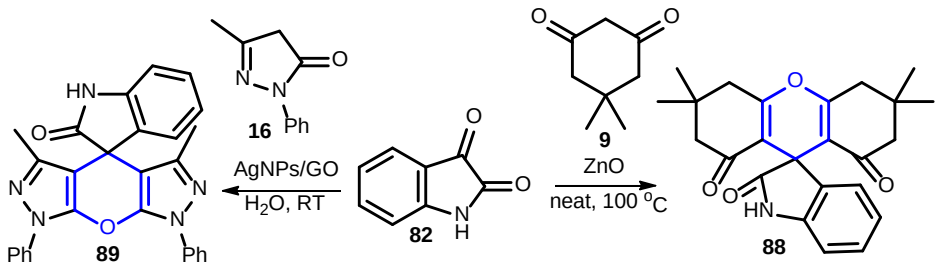
3.2. Synthesis of spiropyran



Scheme 21. Multicomponent synthesis of spiropyrans.

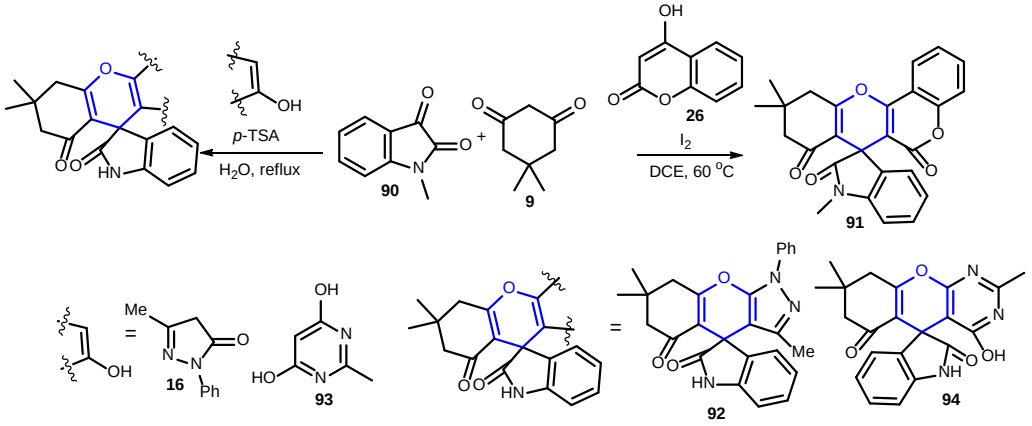
Along with aldehyde, there is another class of electrophile, called isatin, which has been widely utilized for the synthesis of spiro compounds. Isatin has also been utilized in the synthesis of spiropyrans as depicted in the Scheme **21**. The isatin condenses with 1,3-dicarbonyl to form the Michael acceptor **85**, which is then attacked by another 1,3-dicarbonyl compound followed by intramolecular cyclization resulted the spiropyran **83** (Scheme 21).

Lewis acids have been explored for the synthesis of spiropyran **88** and **89**, from the reaction of isatin **82**, with dimedone **9** and pyrazolone **16** respectively (Scheme 22) (Dandia et al. 2017, Kothandapani et al. 2016).



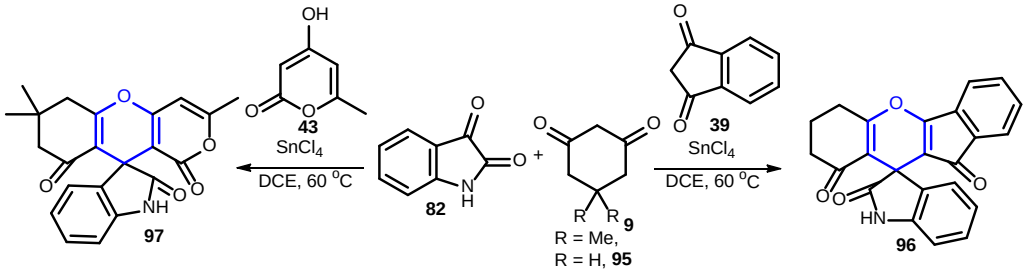
Scheme 22. ZnO catalyzed synthesis of spiropyran **88**.

The reaction of isatin with two different 1,3-dicarbonyls provides the spiropyran **90** in the presence of molecular iodine in DCE at 60 °C (Scheme 23) (Ghahremanzadeh et al. 2010, Zhang et al. 2018).

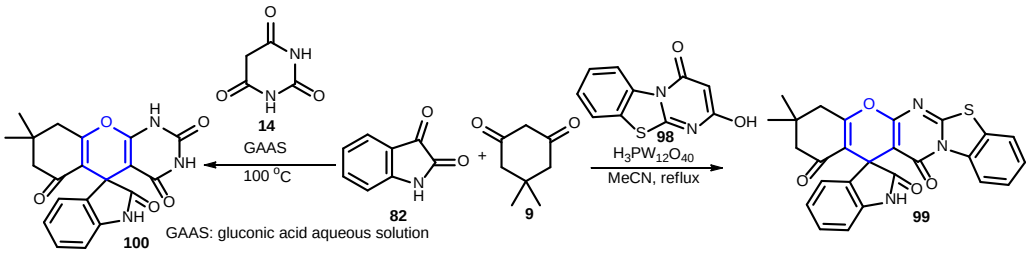


Scheme 23. *p*TSA catalyzed synthesis of spiropyran **91**, **92**, and **94**.

There are some examples of multicomponent spiropyrans employing several acid catalysts displayed in Scheme 24-25 (Liang et al. 2010; Jannati et al. 2018; Guo et al. 2013).

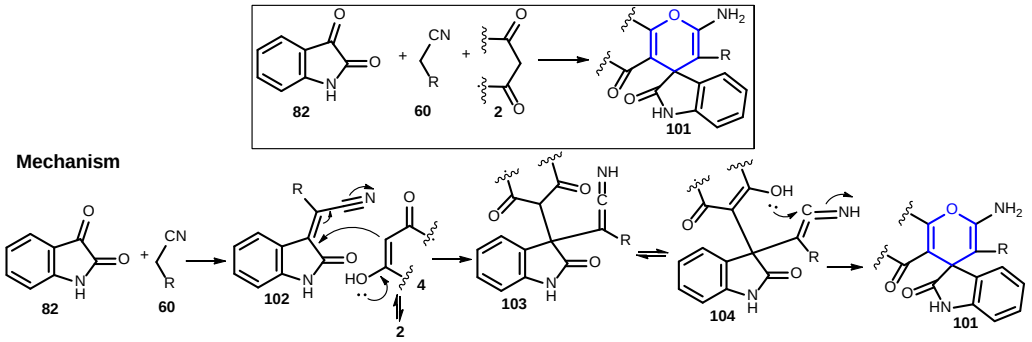


Scheme 24. $SnCl_4$ catalyzed synthesis of spiropyran **96**, and **97**.



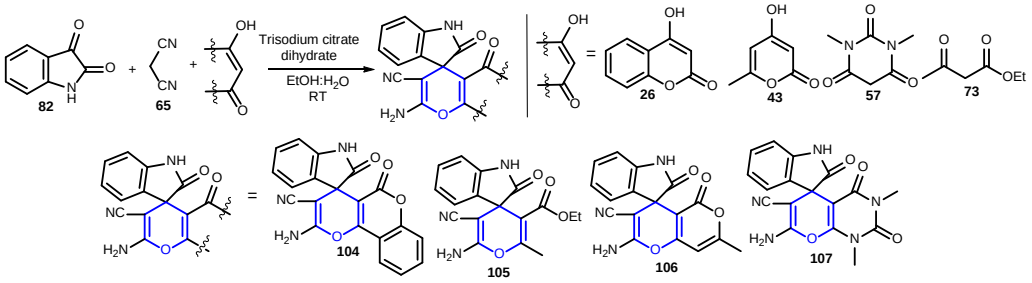
Scheme 25. $H_3PW_{12}O_{40}$ catalyzed synthesis of spiropyran **99**.

The reaction of isatin **82**, 1,3-dicarbonyl compound **2** and malononitrile provides the 2-aminospiropyran **101** proceeds via the initial Michael acceptor formation followed by the conjugate attack of 1,3-dicarbonyl and subsequent intramolecular cyclization (Scheme 26).



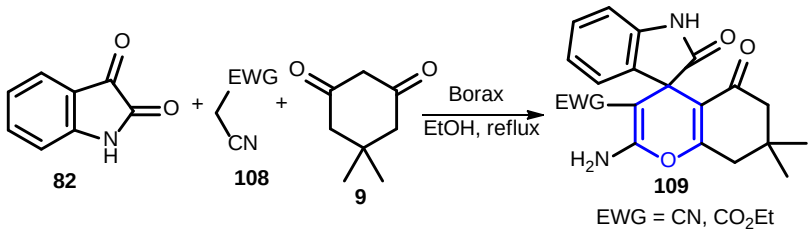
Scheme26. Reaction scheme and mechanism spiropyran **100**.

Isatin and malononitrile reacts to form the Michael acceptor, which then reacts with several cyclic and acyclic 1,3-dicarbonyls to form the spiropyrans **104**, **105**, **106**, and **107** (Scheme 27) (Brahmachari et al. 2016).



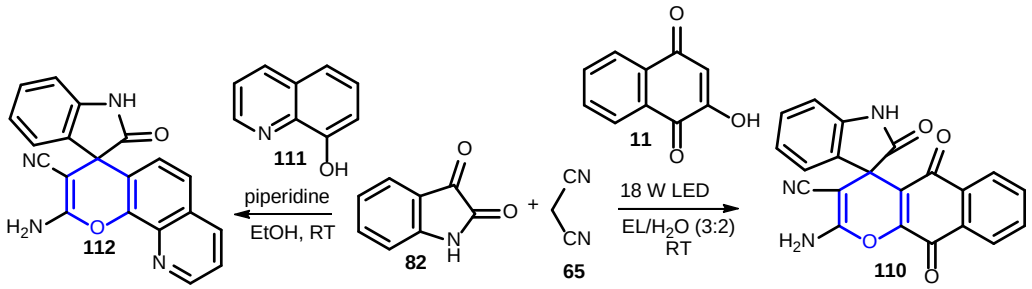
Scheme 27. Trisodium citrate dehydrate catalyzed synthesis of spiropyrans.

Isatin, malononitrile, and dimedone in the presence of borax in ethanol forms spiropyran **109** under reflux conditions (Scheme 28) (Molla et al. 2018).



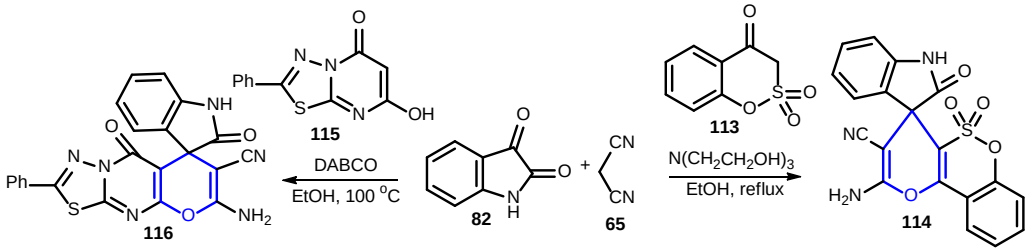
Scheme 28. Borax catalyzed synthesis of spiropyran **109**.

Visible light mediated organic synthesis is one of the greener alternatives to the traditional organic synthesis. The visible-light mediated reaction of isatin, malononitrile, and lawsone forms the spiropyran **110** (Scheme 29) (Zhang et al. 2017). Isatin **82** malononitrile **65**, and quinolin-8-ol **111** provided spiropyran **112** in the presence of piperidine in ethanol at room temperature (Scheme 29) (Shi et al. 2016).



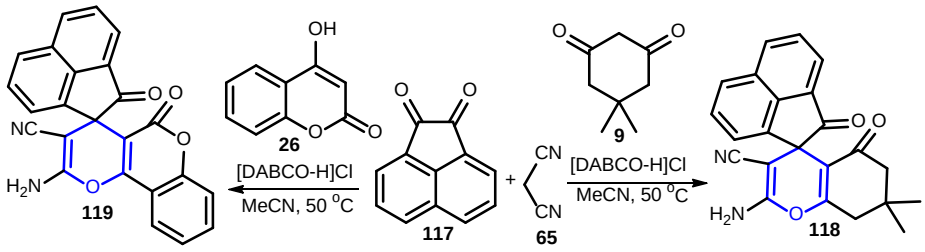
Scheme 29. Visible-light mediated synthesis of spiropyran **110**, and **112**.

1,2-Benzoxathiin-4(3*H*)-one 2,2-dioxide **113**, and 7-hydroxy-2-phenyl-5*H*-[1,3,4]thiadiazolo[3,2-*a*]pyrimidin-5-one **115** are interesting active methylene compounds, have been explored in the synthesis of spiropyrans **114** and **116** (Scheme 30) (Grygoriv et al. 2019).

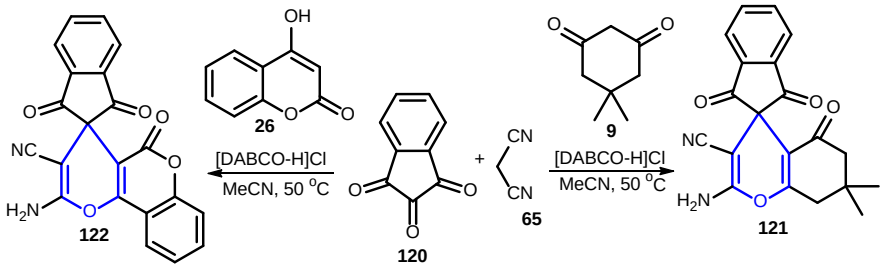


Scheme 30. Multicomponent synthesis of spiropyran **114**, and **116**.

Apart from isatin, other molecules can also form spiropyrans. The acenaphthylene-1,2-dione **117**, and ninhydrin **120** can also provide the spiropyrans (Scheme 31-32) (Li et al. 2018).



Scheme 31. Acenaphthylene-1,2-dione in the synthesis of spiropyran **118** and **119**.



Scheme 32. Ninhydrin in the synthesis of spiropyran **121** and **122**.

Conclusions

The 4*H*-pyran is a privileged nucleus broadly found in natural product, and bioactive molecules. There are several approaches for the synthesis of 4*H*-pyrans. In this chapter, six types of multicomponent reactions have been discussed with various interesting examples, which will provide valuable insights to the readers and researchers.

References

Acharya, S. S., Patra, S., Maharana, R., Dash, M., Barad, L. M., & Parida, B. B. (2024). Recent advances in spirocyclization of maleimides via transition-metal catalyzed C–H activation. *Organic & Biomolecular Chemistry*, *22*(15), 2916-2947.

Acharya, S. S., & Parida, B. B. (2024). Synthetic routes to access dicarbonylated aryls and heteroaryls. *Organic & Biomolecular Chemistry*, *22*(41) 8209-8248.

Acharya, S. S., Patra, S., Barad, L. M., Roul, A., & Parida, B. B. (2024). Recent advances in iodine–DMSO mediated C (sp 3)–H functionalization of methyl-azaarenes via Kornblum oxidation. *New Journal of Chemistry*, *48*(17), 7614-7638.

Acharya, S. S., & Parida, B. B. (2024). Humic acid: A promising and green bioorganic catalyst in organic syntheses. *ChemistrySelect*, *9*(12), e202305233.

Acharya, S. S., Sahoo, R. K., Mohanty, P., Panda, P., & Parida, B. B. (2024). Arylglyoxal-based multicomponent synthesis of C-3 functionalized imidazoheterocycles. *Chemical Papers*, *78*(15), 8107-8126.

Acharya, S. S., Rout, P. R., Sutar, R., Pradhan, C., & Parida, B. B. (2025). Transition Metal-Catalyzed Directing Group-Assisted Site-Selective Di-Ortho C-H Functionalizations via Double C-H Activation. *Advanced Synthesis & Catalysis*, 2500184.

Acharya, S. S., Samantaray, D., Sibakrishna, C., & Parida, B. B. (2025). Pseudo-Multicomponent Reactions of Lawsone: Synthetic Strategies of Bis-Lawsone. *ChemistrySelect*, *10*(1), e202403416.

Acharya, S. S., Guin, B. K., & Parida, B. B. (2025). One-Pot Multicomponent Synthesis of Fully Substituted 1, 3-Thiazoles Appended with Naturally Occurring Lawsone. *The Journal of Organic Chemistry*, *90*(7), 2717-2727.

Acharya, S. S., Barad, L. M., Rout, P. R., Bisoyi, A., & Parida, B. B. (2025). Ultrasonication-assisted Multicomponent Green and Sustainable Synthesis of Benzopyrans Employing Taurine as a Bioorganic catalyst. *New Journal of Chemistry*, *49*(28) 12090-12101.

Auria-Luna, F., Fernández-Moreira, V., Marqués-López, E., Gimeno, M. C., & Herrera, R. P. (2020). Ultrasound-assisted multicomponent synthesis of 4 H-pyrans in water and DNA binding studies. *Scientific Reports*, *10*(1), 11594.

Borah, B., Dhar Dwivedi, K., & Chowhan, L. R. (2021). 4-Hydroxycoumarin: A versatile substrate for transition-metal-free multicomponent synthesis of bioactive heterocycles. *Asian Journal of Organic Chemistry*, *10*(12), 3101-3126.

Borah, B., Dwivedi, K. D., & Chowhan, L. R. (2022). Review on synthesis and medicinal application of dihydropyrano [3, 2-b] pyrans and spiro-pyrano [3, 2-b] pyrans by employing the reactivity of 5-hydroxy-2-(hydroxymethyl)-4 H-pyran-4-one. *Polycyclic Aromatic Compounds*, *42*(9), 5893-5937.

Borah, B., Swain, S., Patat, M., Kumar, B., Prajapat, K. K., Biswas, R., Vasanta, R., & Chowhan, L. R. (2023). Brønsted acid catalyzed mechanochemical domino multicomponent reactions by employing liquid assisted grindstone chemistry. *Scientific Reports*, *13*(1), 1386.

Brahmachari, G., & Banerjee, B. (2016). Facile and chemically sustainable one-pot synthesis of a wide array of fused O-and N-heterocycles catalyzed by trisodium citrate dihydrate under ambient conditions. *Asian Journal of Organic Chemistry*, *5*(2), 271-286.

Brahmachari, G., & Nayek, N. (2017). Catalyst-free one-pot three-component synthesis of diversely substituted 5-aryl-2-oxo-/thioxo-2, 3-dihydro-1 H-benzo [6, 7] chromeno [2, 3-d] pyrimidine-4, 6, 11 (5 H)-triones under ambient conditions. *ACS omega*, *2*(8), 5025-5035.

Brahmachari, G., & Nurjamal, K. (2019). Ultrasound-assisted and trisodium citrate dihydrate-catalyzed green protocol for efficient and one-pot synthesis of substituted chromeno [3′, 4′: 5, 6] pyrano [2, 3-d] pyrimidines at ambient conditions. *Tetrahedron Letters*, *60*(29), 1904-1908.

Chaudhary, A. (2020). Recent advances in the exploitation of kojic acid in multicomponent reactions. *Current Organic Chemistry*, *24*(14), 1643-1662.

Cook, A. H., & Lacey, M. S. (1945). Kojic Acid and the Antibiotic Action of Species of Aspergillus. *Nature*, *155*(3948), 790-791.

Dabiri, M., Tisseh, Z. N., & Bazgir, A. (2010). An efficient three-component synthesis of benzoxanthenes in water. *Journal of Heterocyclic Chemistry*, *47*(5), 1062-1065.

Dai, C., Lin, J., Li, H., Shen, Z., Wang, Y., Velkov, T., & Shen, J. (2022). The natural product curcumin as an antibacterial agent: Current achievements and problems. *Antioxidants*, *11*(3), 459.

Dandia, A., Gupta, S. L., Indora, A., Saini, P., Parewa, V., & Rathore, K. S. (2017). Ag NPs decked GO composite as a competent and reusable catalyst for 'ON WATER'chemoselective synthesis of pyrano [2, 3-c: 6, 5-c′] dipyrazol]-2-ones. *Tetrahedron Letters*, *58*(12), 1170-1175.

Dandia, A., Gupta, S. L., Indora, A., Saini, P., Parewa, V., & Rathore, K. S. (2017). Ag NPs decked GO composite as a competent and reusable catalyst for 'ON WATER'chemoselective synthesis of pyrano [2, 3-c: 6, 5-c′] dipyrazol]-2-ones. *Tetrahedron Letters*, *58*(12), 1170-1175.

El-Khateeb, A. Y., Hamed, S. E., & Elattar, K. M. (2022). Recent advancements in the multicomponent synthesis of heterocycles integrated with a pyrano [2, 3-d] pyrimidine core. *RSC advances*, *12*(19), 11808-11842.

Ghahremanzadeh, R., Fereshtehnejad, F., Yasaei, Z., Amanpour, T., & Bazgir, A. (2010). One-pot and three-component synthesis of spiro [chromeno [2, 3-d] pyrimidine-5, 3′-indoline]-diones and spiro [chromeno [2, 3-c] pyrazole-4, 3′-indoline]-diones. *Journal of Heterocyclic Chemistry*, *47*(4), 967-972.

Goel, A., & Ram, V. J. (2009). Natural and synthetic 2H-pyran-2-ones and their versatility in organic synthesis. *Tetrahedron*, *65*(38), 7865-7913.

Grygoriv, G. V., Lega, D. A., Zaprutko, L., Gzella, A. K., Wieczorek-Dziurla, E., Chernykh, V. P., & Shemchuk, L. A. (2019). Synthesis of novel spiro-condensed 2-amino-4 H-pyrans based on 1, 2-benzoxathiin-4 (3 H)-one 2, 2-dioxide. *Chemistry of Heterocyclic Compounds*, *55*(3), 254-260.

Guo, R. Y., Wang, P., Wang, G. D., Mo, L. P., & Zhang, Z. H. (2013). One-pot three-component synthesis of functionalized spirooxindoles in gluconic acid aqueous solution. *Tetrahedron*, *69*(8), 2056-2061.

Hasaninejad, A., & Beyrati, M. (2018). Eco-friendly polyethylene glycol (PEG-400): a green reaction medium for one-pot, four-component synthesis of novel asymmetrical bis-spirooxindole derivatives at room temperature. *RSC advances*, *8*(4), 1934-1939.

Heravi, M. M., Zadsirjan, V., Mollaiye, M., Heydari, M., & Koshvandi, A. T. K. (2018). Salicylaldehydes as privileged synthons in multicomponent reactions. *Russian Chemical Reviews*, *87*(6), 553.

Hosseini, S., Esmaeili, A. A., Khojastehnezhad, A., & Notash, B. (2021). An efficient synthesis of novel spiro [indole-3, 8′-pyrano [2, 3-d][1, 3, 4] thiadiazolo [3, 2-a] pyrimidine derivatives via organobase-catalyzed three-component reaction of malononitrile, isatin and heterocyclic-1, 3-diones. *Journal of Sulfur Chemistry*, *42*(6), 628-644.

Jannati, S., & Esmaeili, A. A. (2018). Synthesis of novel spiro [benzo [4, 5] thiazolo [3, 2-a] chromeno [2, 3-d] pyrimidine-14, 3′-indoline]-1, 2′, 13 (2H)-triones via three component reaction. *Tetrahedron*, *74*(24), 2967-2972.

Kale, A. D., Pawara, R. H., Patel, H. M., & Dalal, D. S. (2024). A facile and efficient one-pot procedure for the synthesis of 2-amino-4, 8-dihydropyrano [3, 2-b] pyran-3-carbonitriles in PEG-400 and glycerol. *Research on Chemical Intermediates*, *50*(2), 853-880.

Khan, M. N., Pal, S., Karamthulla, S., & Choudhury, L. H. (2014). Imidazole as organocatalyst for multicomponent reactions: diversity oriented synthesis of functionalized hetero-and carbocycles using in situ-generated benzylidenemalononitrile derivatives. *RSC Advances*, *4*(8), 3732-3741.

Kothandapani, J., Ganesan, A., Mani, G. K., Kulandaisamy, A. J., Rayappan, J. B. B., & Ganesan, S. S. (2016). Zinc oxide surface: A versatile nanoplatform for solvent-free synthesis of diverse isatin derivatives. *Tetrahedron Letters*, *57*(31), 3472-3475.

Kumar, R., Acharya, S. S., Bhaumick, P., Parvin, T., & Choudhury, L. H. (2023). HFIP-mediated multicomponent reactions for the synthesis of fluorescent quinoline-fused pyrroles. *Tetrahedron*, *132*, 133250.

Kumari, S., Kumar, D., Gajaganti, S., Srivastava, V., & Singh, S. (2019). Sc $(OTf)_3$ catalysed multicomponent synthesis of chromeno [2, 3-d] pyrimidinetriones under solvent-free condition. *Synthetic Communications*, *49*(3), 431-443.

Kumari, V., Acharya, S. S., Mondal, N., & Choudhury, L. H. (2024). Maleimide-Dependent Rh (III)-Catalyzed Site-Selective Mono and Dual C–H Functionalization of 2-Arylbenzo [d] thiazole and Oxazole Derivatives. *The Journal of Organic Chemistry*, *89*(24), 18003-18018.

Li, J., Lu, L., & Su, W. (2010). A new strategy for the synthesis of benzoxanthenes catalyzed by proline triflate in water. *Tetrahedron letters*, *51*(18), 2434-2437.

Li, M., Zhang, B., & Gu, Y. (2012). Facile construction of densely functionalized 4 H-chromenes via three-component reactions catalyzed by l-proline. *Green Chemistry*, *14*(9), 2421-2428.

Li, M. M., Duan, C. S., Yu, Y. Q., & Xu, D. Z. (2018). A general and efficient one-pot synthesis of spiro [2-amino-4H-pyrans] via tandem multi-component reactions catalyzed by Dabco-based ionic liquids. *Dyes and Pigments*, *150*, 202-206.

Liang, B., Kalidindi, S., Porco Jr, J. A., & Stephenson, C. R. (2010). Multicomponent reaction discovery: three-component synthesis of spirooxindoles. *Organic letters*, *12*(3), 572-575.

Lü, C. W., Wang, J. J., Li, F., Yu, S. J., & An, Y. (2018). Efficient synthesis of 2-amino-3-cyano-4H-pyran derivatives via a non-catalytic one-pot three-component reaction. *Research on Chemical Intermediates*, *44*(2), 1035-1043.

Lukashenko, A. V., Osipov, D. V., Osyanin, V. A., & Klimochkin, Y. N. (2019). The reaction of 1, 2-naphthoquinone 1-methides with syncarpic acid. *Chemistry of Heterocyclic Compounds*, *55*(10), 1004-1006.

Mishra, R., & Choudhury, L. H. (2016). Catalyst-free microwave-assisted arylglyoxal-based multicomponent reactions for the synthesis of fused pyrans. *RSC Advances*, 6(29), 24464-24469.

Mohamadpour, F. (2020). Catalyst-free synthesis of pyrano [2, 3-d] pyrimidine scaffolds via Knoevenagel-Michael cyclocondensation Using PEG-400 as a green promoting medium. *Organic Preparations and Procedures International*, *52*(6), 503-509.

Molla, A., Hossain, E., & Hussain, S. (2013). Multicomponent domino reactions: borax catalyzed synthesis of highly functionalised pyran-annulated heterocycles. *RSC Advances*, *3*(44), 21517-21523.

Molla, A., Ranjan, S., Rao, M. S., Dar, A. H., Shyam, M., Jayaprakash, V., & Hussain, S. (2018). Borax Catalysed Domino Synthesis of Highly Functionalised Spirooxindole and Chromenopyridine Derivatives: X-Ray Structure, Hirshfeld Surface Analysis and Molecular Docking Studies. *ChemistrySelect*, *3*(30), 8669-8677.

Mulakayala, N., Kumar, G. P., Rambabu, D., Aeluri, M., Rao, M. B., & Pal, M. (2012). A greener synthesis of 1, 8-dioxo-octahydroxanthene derivatives under ultrasound. *Tetrahedron Letters*, *53*(51), 6923-6926.

Nagargoje, A. A., Shaikh, M. H., & Shingate, B. B. (2023). Curcumin-based bioactive heterocycles derived via multicomponent reactions. *Archiv der Pharmazie*, *356*(8), 2300171.

Nicoliche, T., Bartolomeo, C. S., Lemes, R. M. R., Pereira, G. C., Nunes, T. A., Oliveira, R. B., Nicastro, A. L. M., Soares, E. N., da Cunha Lima, B. F., Rodrigues, B. M., Maricato, J. T., Okuda, L. H., de Sairre, M. I., Prado, C. M., Ureshino, R. P., & Stilhano, R. S. (2024). Antiviral, anti-inflammatory and antioxidant effects of curcumin and curcuminoids in SH-SY5Y cells infected by SARS-CoV-2. *Scientific Reports*, *14*(1), 10696.

Nourisefat, M., Panahi, F., & Khalafi-Nezhad, A. (2014). Carbohydrates as a reagent in multicomponent reactions: one-pot access to a new library of hydrophilic substituted pyrimidine-fused heterocycles. *Organic & Biomolecular Chemistry*, *12*(46), 9419-9426.

Panda, S., Patra, S., Acharya, S. S., Phaomei, G., & Parida, B. B. (2024). Recyclable LaF_3· Pd nanocatalyst in Suzuki coupling: green synthesis of biaryls from haloarenes and phenylboronic acids. *RSC advances*, *14*(30), 21269-21276.

Patra, S. A., Nandi, M., Maurya, M. R., Sahu, G., Mohapatra, D., Reuter, H., & Dinda, R. (2024). Ni–Unsymmetrical Salen Complex-Catalyzed One-Pot Multicomponent Reactions for Efficient Synthesis of Biologically Active 2-Amino-3-Cyano-4 H-Pyrans. *ACS omega*, *9*(29), 31910-31924.

Patra, S., Panda, S., Acharya, S. S., Phaomei, G., & Parida, B. B. (2025). Green and Sustainable Synthesis of Biaryls Using $LaPO_4$·Pd Recyclable Nanocatalyst by the Suzuki–Miyaura Coupling in Aqueous Medium. *ACS omega*, *10* (23), 24105–24116.

Phasha, V., Senabe, J., Ndzotoyi, P., Okole, B., Fouche, G., & Chuturgoon, A. (2022). Review on the use of kojic acid—A skin-lightening ingredient. *Cosmetics*, *9*(3), 64.

Raghu, M., Rajasekhar, M., Reddy, B. C. O., Reddy, C. S., & Reddy, B. S. (2013). Polyethylene glycol (PEG-400): a mild and efficient reaction medium for one-pot synthesis of 3-hydroxy-3-(pyridin-2-ylmethyl) indolin-2-ones. *Tetrahedron Letters*, *54*(27), 3503-3506.

Rajitha, B., Kumar, B. S., Reddy, Y. T., Reddy, P. N., & Sreenivasulu, N. (2005). Sulfamic acid: a novel and efficient catalyst for the synthesis of aryl-14H-dibenzo [aj] xanthenes under conventional heating and microwave irradiation. *Tetrahedron Letters*, *46*(50), 8691-8693.

Reddy, B. S., Reddy, M. R., Narasimhulu, G., & Yadav, J. S. (2010). $InCl_3$-catalyzed three-component reaction: a novel synthesis of dihydropyrano [3, 2-b] chromenediones under solvent-free conditions. *Tetrahedron letters*, *51*(43), 5677-5679.

Samai, S., Atta, S., & Singh, M. S. (2025). Synthetic Strategies Toward 2H-, 4H-Pyrans, and Pyranones: Recent Advances. *ChemistrySelect*, *10*(21), e01023.

Servesh, A., Lokesh Kumar, S., Govindaraju, S., Tabassum, S., Raj Prasad, J., Kumar, N., & Ramaraj, S. G. (2024). Recent advances in polyethylene glycol as a dual-functional agent in heterocycle synthesis: Solvent and catalyst. *Polymers for Advanced Technologies*, *35*(6), e6433.

Sharma, M., Borah, P., & Bhuyan, P. J. (2015). $InCl_3$-Catalyzed, Three-component reactions for the synthesis of some novel functionalized/annulated barbituric acids. *Synthetic Communications*, *45*(15), 1792-1798.

Shi, R. G., & Yan, C. G. (2016). Three-component reaction for synthesis of functionalized spiro [indoline-3, 4′-pyrano [3, 2-h] quinolines]. *Chinese Chemical Letters*, *27*(4), 575-578.

Singh, P. K., & Silakari, O. (2018). The current status of O-heterocycles: A synthetic and medicinal overview. *ChemMedChem*, *13*(11), 1071-1087.

Singh, S., Tiwari, J., Jaiswal, D., Sharma, A. K., Singh, J., Singh, V., & Singh, J. (2018). Organocatalyst Mediated One Pot Synthesis of 4H-furo [3, 4-b] pyran, 4H-

benzo [g] chromene and 1H-benzo [b] xanthene Derivatives in Aqueous Medium: A Green Approach. *Current Organocatalysis, 5*(1), 51-57.

Sun, X. J., Zhou, J. F., & Zhi, S. J. (2012). Efficient one-pot synthesis of tetrahydrobenzo [c] xanthene-1, 11-dione derivatives under microwave irradiation. *Synthetic Communications, 42*(13), 1987-1994.

Tavaf, Z., Dangolani, S. K., Yousefi, R., Panahi, F., Shahsavani, M. B., & Khalafi-Nezhad, A. (2020). Synthesis of new curcumin derivatives as influential antidiabetic α-glucosidase and α-amylase inhibitors with anti-oxidant activity. *Carbohydrate Research*, *494*, 108069.

Tisseh, Z. N., Azimi, S. C., Mirzaei, P., & Bazgir, A. (2008). The efficient synthesis of aryl-5H-dibenzo [b, i] xanthene-5, 7, 12, 14 (13H)-tetraone leuco-dye derivatives. *Dyes and pigments, 79*(3), 273-275.

Walsh, C. T. (2015). Nature loves nitrogen heterocycles. *Tetrahedron Letters*, *56*(23), 3075-3081.

Zeng, L. Y., Lv, M. F., & Cai, C. (2012). Iodine catalyzed synthesis of the chromene derivatives in one-pot. *Chinese Chemical Letters, 23*(12), 1347-1351.

Zhang, M., Fu, Q. Y., Gao, G., He, H. Y., Zhang, Y., Wu, Y. S., & Zhang, Z. H. (2017). Catalyst-free, visible-light promoted one-pot synthesis of spirooxindole-pyran derivatives in aqueous ethyl lactate. *ACS Sustainable Chemistry & Engineering, 5*(7), 6175-6182.

Zhang, M., Yang, W., Qian, M., Zhao, T., Yang, L., & Zhu, C. (2018). Iodine-promoted three-component reaction for the synthesis of spirooxindoles. *Tetrahedron, 74*(9), 955-961.